

RESEARCH PROJECTS

A Prospective Evaluation of Bispectral Index Monitoring to Prevent Postoperative Cognitive Dysfunction

✍ CHAN Matthew Tak Vai • CHAN Sui Yin Agnes (Psychology) • GIN Tony • POON Wai Sang (Surgery) • NG Ho Keung (Anatomical & Cellular Pathology)

☐ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

It is widely believed, among clinicians that the effect of anesthetics is transient and that postoperative adverse outcomes cannot be attributed to residual drug effects. However, recent animal and human data suggested that this may not be true. There are now compelling reasons to believe that standard doses of anesthetics may produce profound neurochemical changes which last for days or months. These “anesthetic imprints” in the brain may contribute to postoperative cognitive impairment. Such “toxicity” is most apparent in the elderly patients undergoing major surgery. Intraoperative monitoring with the bispectral electroencephalogram (BIS) will allow precise delivery of anesthetics and better drug utilization. We believe this will prevent inadvertent drug overdose and better control of anesthetic depth. We hypothesize that BIS-guided drug delivery will avoid “unnecessary” deep levels of anesthesia and should reduce the incidence of postoperative cognitive impairment.

In this randomized, double-blind, pilot study, 200 elderly (> 60 years) patients undergoing major non-cardiac surgery will be randomly allocated to

receive additional BIS monitoring or routine anesthetic care. Postoperative cognitive function will be assessed at baseline, 1 week and 3 months after surgery, using a battery of established neurocognitive tests.

(MD04496)

Improving Perioperative Outcome in the Elderly Surgical Patients. An Evaluation of Nitrous Oxide in the Gas Mixture for Anesthesia

✍ CHAN Matthew Tak Vai • GIN Tony

☐ 1 January 2005

❖ Health & Health Services Research Fund

Objective: There are compelling reasons to question the routine use of nitrous oxide (N₂O) in geriatric anesthesia. N₂O impairs methionine synthase, resulting in a decrease of DNA production, potential immunosuppression, anemia and hyperhomocystinemia. N₂O may worsen perioperative outcomes (e.g. postoperative vomiting, wound infection, sepsis and cardiac morbidity). This is most likely to be a problem with elderly patients after long surgical exposure. However, outcome data are currently lacking. The present study will determine the effectiveness and safety of N₂O in modern anesthesia.

Design: Randomized control trial in which elderly patients undergoing major surgery will be assigned to receive general anesthesia with or without N₂O.

Setting: Tertiary and district hospitals (PWH, AHNH NDH) in the New Territories East cluster.

Participants: Elderly (age ≥ 65 years) patients undergoing major elective or emergency (> 2 hours) surgery.

Main Outcome Measures: The primary endpoint is time to medical fitness to discharge. This is an overall marker of perioperative morbidity and has

direct healthcare resource implications. Other outcome measures include incidence of sepsis, cardiac and cerebrovascular morbidities, severity of vomiting and health related quality of life measures. (MD04736)

A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Phase II Study to Evaluate the Safety and Efficacy of Oral Dosing with GW69769 (50mg or 150 mg) for Three Consecutive Days When Administered with a Single Intravenous Dose of Ondansetron Hydrochloride for the Prevention of Post-Operative Nausea and Vomiting and Post-Discharge Nausea and Vomiting in Female Subjects with Known Risk Factors for Post-Operative Nausea and Vomiting Who are Undergoing Laparoscopic/ Laparotomic Surgical Procedures Associated with an Increased Emetogenic Risk (Protocol No.: NKT102245)

✍ GIN Tony • CHAN Matthew Tak Vai • CHUI Po Tong

□ 1 May 2005

❖ GlaxoSmithKline Limited

Post-operative nausea and vomiting (PONV) often occurs following anesthesia and is the most frequently reported patient complaint. There is a growing consensus that prophylaxis against PONV, especially in high risk populations, may be better achieved by use of a combination of drugs targeting on different receptors involved in the vomiting pathway. Studies using experimental NK-1 receptor antagonists have demonstrated that NK-1 receptor antagonists have antiemetic activity in the post-operative setting for both prevention and treatment.

These drugs may have utility in improving response rates over those seen with existing PONV therapies. The present study proposes to investigate the safety and efficacy of the NK-1 receptor antagonist, GW69769 (50 mg and 150 mg), administered orally for three consecutive days in combination with a single standard dose of ondansetron hydrochloride (Day 1, 4 mg IV) to prevent post-operative and post-discharge nausea and vomiting in high risk female subjects undergoing surgical procedures. (MD04335)

Teaching Intensive Care to Non-Intensive Care Doctors

✍ GOMERSALL Charles David • JOYNT Gavin Matthew

□ 1 February 2005

❖ Applicant's contribution • Pfizer Corporation Hong Kong Limited • Professional Services Development Assistance Scheme, Commerce, Industry and Technology Bureau, HKSAR Govt

The aim of the project is to produce a self-perpetuating course to teach non-Intensive Care doctors sufficient Intensive Care for them to work effectively in an Intensive Care team in the event of a disaster. This will be achieved by developing course material and training a sufficiently large faculty that will, in turn, run the course themselves (and train more instructors), in a similar fashion to Advanced Trauma Life Support courses. This will result in a high efficiency, low cost training scheme for training a large pool of doctors.

The teaching package will consist of a course manual, a series of lecture slides with notes for the lecturer, a series of scenarios (with teaching notes) for use as skill stations and pre and post course multiple choice question test papers. The purpose of the teaching

package is to facilitate the setting up and running of courses in other institutions with the intention that each major hospital will train their own staff. Tentative topics for lectures are: infection control, burns, trauma, biological weapons, chemical weapons, decontamination, drowning, radiation sickness, mechanical ventilation, weaning from mechanical ventilation, advanced haemodynamic monitoring, metabolic and electrolyte disturbance, X-ray interpretation, nosocomial infections, asthma and ARDS, renal replacement therapy and paediatric considerations. Skill stations will include trauma, infection control and decontamination, mechanical ventilation, electrolyte disturbance, X-ray interpretation and interpretation of haemodynamic measurements.

In addition to the course material potential instructors will receive training on teaching methods, obtain practical experience in presenting the lectures and teaching the skill stations and will be familiarized with the administrative procedures for running a course.

(MD04713)

Survey and Scientific Evaluation of Modified Oxygen Delivery Devices Used for Suspected SARS and High Risk Patients in Hong Kong

✍ KHAW Kim Sun • NGAN KEE Warwick Dean
• TAM Yuk Ho

☐ 16 March 2005

❖ Research Fund for the Control of Infectious Diseases - Health, Welfare and Food Bureau

Background: In order to minimize cross infections, modifications have been made to oxygen delivery devices. Patients wear either a surgical or N95 mask over nasal cannula or oxygen facemask. Such modifications introduce respiratory deadspace,

breathing resistance and also alter the inspiratory percentage of oxygen, which have never been scientifically evaluated. Also, the extent and type of modifications in the various hospitals in Hong Kong is unknown.

Objective:

- (1) To perform a cross sectional survey of the modifications to oxygen delivery devices in hospitals throughout Hong Kong.
- (2) To scientifically evaluate the performances of the modified oxygen delivery devices.

Design:

Phase 1: A postal survey supplemented with telephone follow up and site visits.

Phase 2: Observational study using a patient simulator under different respiratory parameter settings to assess for:

- (1) inspiratory percentage of oxygen
- (2) respiratory deadspace
- (3) work of breathing

Potential applications:

- (1) Modification of oxygen delivery devices throughout hospitals in Hong Kong will be summated and scientifically evaluated.
- (2) The performance characteristics, limitations and safety profile will be known, enabling a physician to decide if the breathing system is the most suitable for a particular patient.

(MD04734)

Vasopressor Drugs in Regional Anaesthesia for Obstetrics: Quantification of Transplacental Transfer and Determination of Metabolic Effects on the Fetus

✍ NGAN KEE Warwick Dean • KHAW Kim Sun

☐ 1 January 2005

❖ Research Grants Council (Earmarked Grants)

Spinal anaesthesia for Caesarean section has been shown to be associated with a high incidence of fetal acidosis. The exact mechanism for this is unknown but may be related to metabolic effects on the fetus of vasopressor drugs given to maintain maternal blood pressure. This study is a randomized, doubled blinded study of 104 parturients who will receive either ephedrine or phenylephrine to maintain blood pressure during elective Caesarean section. Our aims are: 1) comparison of the relative extent of transfer across the placenta of the vasopressors ephedrine and phenylephrine and 2) comparison of the relative effects of these two vasopressors on metabolism in the fetus. Transplacental transfer of ephedrine and phenylephrine will be quantified by measuring their concentration in maternal and umbilical cord blood. We will assess the effects of these drugs on markers of metabolism in the fetus. These markers will include blood gases, oxygen content, and concentrations of glucose, lactate, epinephrine and norepinephrine. The results will be utilized to provide important information on the optimal management of haemodynamic changes during spinal anaesthesia in pregnancy and thus will have important implications for the safe practice of obstetric anaesthesia.
(CU04467)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

Edition Title/Investigators

2001-02 Postoperative Cognitive Function in Children (MD01002)
✍ AUN Sui Tee Cindy • MCBRIDE Catherine Alexandra (Psychology) •

YEUNG Chung Kwong (Surgery) •
LAI Yee Ching Kelly (Psychiatry) •
GIN Tony

2002-03 A Randomized Controlled Trial of Auditory Evoked Potential Monitoring to Improve Recovery from General Anaesthesia (CU02054)
✍ CHAN Matthew Tak Vai • GIN Tony • IRWIN Micheal Garnet*

2002-03 Perioperative Ischemic Evaluation Study (MD02634)
✍ CHAN Matthew Tak Vai • YIP Wai Kwok Gabriel*

2003-04 Evaluation of Nitrous Oxide in the Gas Mixture for Anesthesia (MD03569)
✍ CHAN Matthew Tak Vai • GIN Tony

2002-03 Safety of Traditional Chinese Medicine in Patients Undergoing Anaesthesia (CU02056)
✍ GIN Tony • AUN Sui Tee Cindy • CHUI Po Tong • LEE Anna

2001-02 Does the Enteral Administration of Lactobacillus Species to Critically Ill Patients Reduce the Severity of Multi-Organ Dysfunction and Decrease Mortality? (MD01005)
✍ GOMERSALL Charles David • CALCROFT Ross Michael* • JOYNT Gavin Matthew

2002-03 Thoracic Paravertebral Block for Patients with Refractory Angina Pectoris (MD02938)

	✍ HO Ming Hei Anthony • KARMAKAR Manoj Kumar • WOO Kam Sang (Medicine & Therapeutics) • LAM Wai Man Wynnie (Diagnostic Radiology & Organ Imaging) • ELAREFI Ahmed Abdalla (Surgery) • LEE Anna • GIN Tony		Trial of Anaesthetic Interventions (CU03405) ✍ KHAW Kim Sun • LAU Tze Kin (Obstetrics & Gynaecology) • LEUNG Tak Yeung (Obstetrics & Gynaecology) • NGAN KEE Warwick Dean
1998-99	Ropivacaine as an Intrathecal Agent: Part I – A Dose Response Study (MD98153) ✍ KHAW Kim Sun • NGAN KEE Warwick Dean • CRITCHLEY Lester Augustus Hall	2002-03	A Comparative Traditional Dose-Response Study of Ropivacaine and Bupivacaine for Epidural Analgesia in the First Stage of Labour (MD02786) ✍ NGAN KEE Warwick Dean • KHAW Kim Sun • LEE Bee Beng*
2002-03	The Effects of Maternal Oxygen Therapy during Emergency Caesarean Section (CU02060) ✍ KHAW Kim Sun • NGAN KEE Warwick Dean • ROGERS Michael Scott (Obstetrics & Gynaecology) • TAM Wing Hung (Obstetrics & Gynaecology) • WANG Chi Chiu (Obstetrics & Gynaecology)	2003-04	The Effect of Vasopressor Choice on Fetal Acid-Base Status During Spinal Anaesthesia for Emergency Caesarean Section (CU03406) ✍ NGAN KEE Warwick Dean • KHAW Kim Sun • LAU Tze Kin (Obstetrics & Gynaecology)
2003-04	External Cephalic Version for Breech Presentation : A Randomised Controlled		

RESEARCH PROJECTS

Functional Role of RASSF1A in Nasopharyngeal Carcinoma Tumorigenesis

✍ LO Kwok Wai • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute)# • LAM Ching Wan (Chemical Pathology) • TSAO Sai Wah (Anatomy)# • HUI Bik Yu

☐ 15 September 2004

❖ Research Grants Council (Earmarked Grants)

In our previous studies, we have identified frequent epigenetic inactivation of *RASSF1A*, a tumor suppressor gene at 3p21.3, in the primary tumors of NPC. Ecotopic expression of *RASSF1A* in NPC cells led to retarded cell proliferation *in vitro* and dramatic reduction of tumorigenic potential *in vivo*. In order to uncover the biological pathways to which *RASSF1A* functions in tumor suppression, we have performed a comprehensive investigation of the transcription profiles of stable *RASSF1A* transfected NPC cells using high-density oligonucleotide array. We have identified a significant change in the expression of *Activin beta E (INHE)* in the *RASSF1A*-expressing cells. Based on this preliminary finding, we hypothesize that the tumor suppression function of *RASSF1A* in NPC is associated with activation of the TGF-beta superfamily pathways. In this proposal, we seek for continuous support to study the role of *RASSF1A* in NPC tumorigenesis. First, we aim to elucidate the functional relationship between *RASSF1A* and the TGF-superfamily pathways. We will examine the molecular mechanisms by which *RASSF1A* regulates *Activin beta E* expression and TGF-beta superfamily pathways. To enhance our understanding on the

functions of *RASSF1A* mediated through upregulation of *Activin beta E*, the biological properties and downstream target genes of *Activin beta E* will be determined by transfection study and oligonucleotide array assays. Secondly, we plan to investigate the effects of *RASSF1A* silencing in immortalized nasopharyngeal epithelial cell by RNAi mediated reduction of endogenous *RASSF1A*. The tumorigenic properties of the stable clones will be examined *in vivo* and *in vitro*.

(CU04255)

Functional Characterization of EMS1 Oncogene at 11q13.3 in Nasopharyngeal Carcinoma

✍ LO Kwok Wai

☐ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

Chromosome locus 11q13 is frequently amplified in NPC cell lines and primary tumors. By systematic screening of multiple candidates in this region, we found that amplification and overexpression of the *EMS1 (Cortactin)* oncogene are highly correlated in the NPC cell lines and xenografts. Studies have shown that *EMS1* is frequently overexpressed in breast cancer and squamous cell carcinoma of head and neck. The gene is a src kinase substrate and may be involved in the signaling pathway of mitogenic receptors and adhesion molecules. The aberrant regulation of this gene contributes to tumor cell invasion and metastasis. Based on these findings, we hypothesize that activation of *EMS1* oncogene contributes to the initiation or progression of NPC. The gene will be a candidate target for the development of more effective diagnostic strategies and anticancer therapies for this common malignancy affecting our population. In this study, we will

elucidate the amplification and expression of *EMSI* in primary tumors and its correlation with the clinical parameters (e.g. staging and disease outcome). By overexpressing *EMSI* in an immortalized nasopharyngeal epithelial cell line, the oncogenic properties of *EMS* will be examined *in vitro* and *in vivo*. Antitumor effect of siRNA targeted against *EMSI* will also be investigated in NPC cell lines. The results will shed light on the role of *EMSI* in NPC tumorigenesis.

(MD04633)

Study on Nasopharyngeal Carcinoma Genetics

✍ LO Kwok Wai • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute)# • TO Ka Fai • HUI Bik Yu • TSAO Sai Wah (Anatomy)#

□ 1 January 2005

❖ Michael Kadoorie Cancer Genetics Research Programme

Amongst the cancers prevalent in Hong Kong, nasopharyngeal carcinoma (NPC) poses a special health concern to our community in which more than 95% of population is southern Chinese. This “Cantonese Cancer” shows the highest incidence (~25-30/10000/year) in Hong Kong and affects the younger age groups. Its impact on the work force of our community is considerable. Over the past few years with the support of Kadoorie Charitable Foundation, we have made important progress in the area of NPC research. Our genetic studies of NPC contributed significantly to the groundwork on deciphering its molecular genetic basis. The findings have also opened up new avenues of research in the field. In this proposal, we propose to seek research funding for the continuation of work in NPC genetic studies. The major aims of our studies are: (1) to elucidate the novel tumor suppressor

gene(s) at 14q which are deleted in more than 85% of NPC; (2) to identify and characterize candidate oncogenes at the most common amplicons, 3q and 12q; (3) to uncover the function of EBV and its contribution in NPC tumorigenesis by high-density oligonucleotide array analysis. These proposed studies will improve our understanding on the genetic basis for development of NPC, elucidate the role EBV plays in the cancer, and discover new targets for diagnosis and treatment, findings of which will help us to better control this common malignant disease in our population.

(MD04387)

The Role of Pif1 DNA Helicase Homolog in Telomere Maintenance and Chromosome Stability in Mouse Embryonic Stem Cells

✍ LO Wing Ip Anthony

□ 1 November 2004

❖ CUHK Research Committee Funding (Direct Grants)

Telomere is an important nucleoprotein structure protecting the ends of the chromosomes and maintaining chromosome stability. Dysfunction of the telomere is important in the aging process and cancers. Pif1 DNA helicase was identified in yeast. In the single cell eukaryotes, Pif1 inhibits telomere lengthening and aberrant addition of telomere sequences to double strand breakage sites. It seems to be involved in maintaining chromosome stability at the telomeres. The role of Pif1 in mammalian cells and its contribution to human diseases is unknown. This project aims at studying the function of Pif1 in telomere dynamics in mouse embryonic stem (ES) cells. We have cloned and characterized the mouse homologs of Pif1 gene. We propose to study the change in telomere stability and

maintenance after disruption of Pifl in mouse ES cell culture by sequentially targeting of the gene. Telomere dynamics and chromosome stability will be studied in wild type, heterozygous and homozygous Pifl deleted ES cells. The creation of the tissue culture model of defective Pifl gene will provide further insight into the general telomere dynamics and the understanding of the aging and malignant processes.

(MD04324)

Immunogenetic Study of Nasopharyngeal Carcinoma in Hong Kong Chinese

✍ NG Heung Ling Margaret • LAU Kin Mang • LO Kwok Wai • ZEE Chung Ying Benny (Community and Family Medicine) • WOO Kong Sang John (Surgery) • VAN HASSELT Charles Andrew (Surgery)

□ 1 January 2005

❖ Michael Kadoorie Cancer Genetics Research Programme

Nasopharyngeal carcinoma (NPC) is a highly prevalent Epstein-Barr virus (EBV) associated disease with significant mortalities in Southern China including Hong Kong. It is rare throughout the world otherwise. By contrast to the ubiquity of the EBV infection worldwide, the marked differences in the incidences across racial groups indicate that host genetic factors play a role in the disease pathogenesis.

Polymorphism of Human Leukocyte Antigen (HLA), which governs individual variations in immune-responses to infection, showed strong association with susceptibility to various virus-induced cancers. Moreover, machinery for EBV entry into cells, including polymeric immunoglobulin receptor (PIGR), may vary the

disease susceptibility. We hypothesize that these immunogenetic factors may be associated with NPC and clinical outcomes. Here, we will determine the HLA Class I and II and PIGR genotypes in Cantonese NPC patients and assess their associations with the disease and other clinico-pathological parameters. We aim to identify the NPC associated HLA and PIGR genotypes, protective or susceptible, specific to Cantonese in Hong Kong and their potential correlation with clinico-pathological parameters.

The findings from the proposed study could facilitate the ongoing developments and applications of HLA-restricted cytotoxic T cell immune responses for NPC treatment. The HLA and PIGR polymorphisms associated with clinical outcomes may be utilized as prognostic biomarkers for cancer chemoprediction and prognosis.

(MD04572)

A Family Based Case-Control Study of Immunogenetics in Severe Acute Respiratory Syndrome (SARS)

✍ NG Heung Ling Margaret • LAU Kin Mang* • ZEE Chung Ying Benny (Community and Family Medicine) • SUNG Joseph Jao Yiu (Medicine & Therapeutics)

□ 15 April 2005

❖ Research Fund for the Control of Infectious Diseases - Health, Welfare and Food Bureau

Purpose -

Clinical severities among severe acute respiratory syndrome (SARS) patients vary from febrile condition to severe respiratory distress and even death. In addition, individual susceptibilities to the infection appear to be variable. However, the mechanism for these variations remains unclear.

Human leukocyte antigens (HLA) are polymorphic and the polymorphism contributes to variations in susceptibility to infection and severity of inflammation. Our previous study demonstrated increased frequency of HLA-B*0703 and decreased frequency of HLA-DRB1*0301 in SARS patients. Because environmental factors are also important determinants for the infection, controlling these factors in the current study using subjects with similar environments is critical for the assessment of the genetic contribution such as HLA and for verification of our previous findings.

Objectives/hypothesis -

We hypothesize that the immunogenetic factors such as HLA may be associated with SARS infection. In this application, we propose to conduct a family based Case (SARS family members)-Control (non-SARS family members) study to assess the associations of HLA genotypes with SARS infection

Subjects -

SARS patients managed in the NT East cluster and their family members will be recruited.

Design -

HLA class I and II alleles of the subjects will be genotyped using PCR-SSP assay. The association of HLA alleles with SARS infection will be assessed by comparing the Case (SARS) and Control (non-SARS) groups using statistical analyses. Any combination of HLA alleles associated with the SARS infection will be identified by multivariate statistical analyses.

Expected results -

Specific HLA genotypes associated with SARS will be identified. The HLA information could be included in SARS risk stratification assignment and the SARS associated HLA alleles could provide critical information for vaccine development using reverse immunogenetic approach.

(MD04752)

Development of a Treatment Response Prediction System for Multiple Myeloma (MM) Patients at Diagnosis

✍ NG Heung Ling Margaret • LAU Kin Mang • LAM Ching Wan (Chemical Pathology) • ZEE Chung Ying Benny (Community and Family Medicine) • LEI Ieng Kit Kenny (Clinical Oncology) • HOU Jian* • Chan CW Joyce*

☐ 30 June 2005

❖ CUHK Research Committee Funding (Direct Grants)

Multiple myeloma (MM) is a clonal plasma cell malignancy with no effective treatment for cure. Only 50-60% of patients respond to the common chemotherapy. Yet effective prediction of the chemo-response is currently unavailable prior to deciding on the treatment option. Recently, DNA microarray has been successfully utilized as a tool for predicting chemosensitivity before treatments in various cancers. The beauty of this technology is to detect and monitor expression changes simultaneously in thousands of both known and uncharacterized genes involved in multiple cellular pathways in a comparative manner. Our previous experience in the management of DNA microarray data using multivariate statistical analyses and developments of pattern recognition algorithms will certainly be very useful in our current application, in which we propose to develop a system to predict patient's responsiveness prior to chemotherapy treatment using this technological platform. Once this prediction system is established, non-responder MM patients can be treated alternatively for more effective results. Moreover, the panel of predictors identified will be evaluated as prognostic factors for disease outcomes such as overall survival. Last but

not least, the proposed study can establish our Chinese MM gene expression profile (GEP) database. In comparison with those of Caucasian, our data can help to clarify the ethnic implication in MM. In addition, the database can serve as the training set in the rapid growing system of molecular tumor classification and clinical outcome predictions with GEP for our locality.

(MD04864)

Characterization of Medulloblastoma Related Tumor Suppressor Gene(s) Located on a Novel Homozygous Deletion Region 6q23.1

✍ NG Ho Keung • HUI Bik Yu • LO Kwok Wai

□ 1 November 2004

❖ CUHK Research Committee Funding (Direct Grants)

Our previous whole genome analysis of medulloblastomas using high resolution array comparative genomic hybridisation analysis had identified several chromosomal aberrations. One of the most notable finding is detection of homozygous deletion on chromosome 6q23. Homozygous deletion of this region was found on cell line DAOY whereas loss of heterozygosity was detected on 30% primary medulloblastomas. Further study confined a 0.887Mb minimal region of homozygous deletion at 6q23.1 which was flanked by markers SHGC-14149 (6q22.33) and SHGC-110551 (6q23.1). According to the data from Human Genome Working Draft sequence Browser, BC060845 (L3MBTL3 protein), AK091351 (Hypothetical protein FLJ34032) and KIAA1913 are the three genes located at this region. Hence, the objective of our project is to identify target tumor suppressor genes (TSGs) located at this homozygous deletion region and investigate their roles in the development of medulloblastomas.

Expression levels of the candidate genes in medulloblastoma cell lines will be investigated with real-time quantitative RT-PCR analysis. Tumor suppressor functions of target gene(s) will be investigated by in vitro transfection and re-expression of the gene(s) into cells deficient in that gene(s). This information will lead to a better understanding of medulloblastoma tumorigenesis and identify new targets for therapeutic intervention and drug discovery of this cancer.

(MD04328)

Characterization of Epstein Barr Virus Status in Squamous Cell Carcinoma of Nasopharynx and Other Head and Neck Regions

✍ TO Ka Fai • LO Kwok Wai • HUANG Dolly P (Clinical Oncology)*

□ 1 November 2004

❖ CUHK Research Committee Funding (Direct Grants)

Nasopharyngeal carcinoma (NPC) is prevalent in Southern China, including Hong Kong and poses a severe health problem. Apart from NPC, other Head and Neck cancers are also associated with high mortality and morbidity. Majority of NPC are undifferentiated carcinomas while most of the non-NP head and neck cancers are squamous cell carcinoma (SCC). Undifferentiated carcinomas of NP and other head and neck regions are consistently associated with Epstein Barr virus (EBV). However, the status of EBV in SCC of NP and other head and neck region is unclear. Our previous studies have suggested that molecular genetic alterations of NPC differ from the conventional head and neck SCC. However, a comparative and comprehensive analysis of the genetic alterations and EBV status in NPC and non-NP Head and Neck carcinoma is lacking. We

aim to comprehensively investigate the EBV status, including typing of EBV strains/variants, expression of latent EBV proteins of SCC of NP and other head and neck regions as compare to the undifferentiated carcinoma. Moreover, we have shown that a distinct EBV variant (Zp-V3) in the BZLF1 promoter Zp is associated with NPC. The results support the hypothesis that EBV variants in the BZLF1 promoter Zp might result in different lytic potentials and be differentially expressed among individuals with nonmalignant and malignant diseases. Thus, we would also study the transcriptional regulatory activity of different Zp variants and provide further insights of EBV related carcinogenesis. The findings will enhance our understanding of molecular events that lead to head and neck cancer, and most importantly will enable the identification of potential markers of early detection, prevention or intervention for our local population.

(MD04998)

Identification of Human Cell Line Model of Persistent Coronavirus (SARS-CoV) Infection and Studies in the Cytokines and Chemokines Response

✍ TO Ka Fai • CHAN Kay Sheung Paul
(Microbiology)

📅 3 January 2005

❖ Research Fund for the Control of Infectious Diseases - Health, Welfare and Food Bureau

Purpose:

Severe Acute Respiratory Syndrome (SARS) is caused by a new coronavirus (SARS-CoV). However, the pathogenesis is unclear and current choices of effective or specific treatments are limited. Our previous studies indicated persistent SARS-CoV infection in human lung pneumocytes and intestinal

enterocytes. Our purposes are to identify human cell line models that maintain persistent SARS-CoV infection and investigate the expression profile of cytokines and chemokines. Based on our initial observations, a human intestinal cell line that maintained persistent SARS-CoV infection can be identified. Such models not only provide an alternative for diagnostic use but also greatly facilitate the laboratory investigations of various therapeutic interventions. The results will also enhance our understanding of pathogenesis of SARS and provide information for rational therapeutic approaches.

Objectives:

1. Identification of human lung and intestine epithelial cell lines that can maintain persistent SARS-CoV infection.
2. To study the expression profiles of cytokines and chemokines in cells lines infected with SARS-CoV. Study design & material:

Human lung and intestine cell lines are used. No clinical subjects or human tissue is required. This is an observational study and only involve laboratory investigations.

Methods & Analysis:

Standard viral culture study is used. The presence of virus and viral effect on each cell lines will be documented by observation of viral cytopathic effect, confirmed by PCR, in-situ hybridization study and ultrastructural examination. Upregulation or down-regulation of mRNA levels of various cytokines and chemokines will be documented by quantitative RT-PCR.

(MD04503)

Characterization of the Tumor Suppressive Role of Activating Transcriptional Factor, ATF5, in Hepatocellular Carcinoma

✍ WONG Nathalie • CHAN Yuen Yee

(Paediatrics) • LAI Bo San Paul (Surgery)

□ 1 January 2005

❖ Research Grants Council (Earmarked Grants)

Whilst surgical resection represents the only hope of long-term survival for patients with hepatocellular carcinoma (HCC), the relatively high incidences of recurrence, possibly through micro-metastasis prior to surgical treatment, has rendered the five-year survival rate to be low. In an effort to characterize the genetic abnormalities participating in liver carcinogenesis, we have performed genome-wide explorations on more than 150 HCC tumors by comparative genomic hybridization analysis (RGC project: CUHK4044/01M). Correlation of CGH findings with clinicopathological features suggested a subset of chromosomal changes, in particular diminutions on 19q, in association with disease progression. Transcriptional mapping on chromosome 19q by cDNA array indicated a strikingly consistent down-regulation of the *ATF5* gene (cyclic-AMP-dependent Activating Transcriptional Factor 5) at 19q13.33. The array-derived observation was further substantiated by quantitative RT-PCR, which also pinpointed to the repressed *ATF5* expression in relation to advanced metastatic tumors. A growth inhibitory effect of *ATF5* on cell survival was also demonstrated from our transient transfection study. While several lines of evidence have indicated the *ATF* family to be involved in cell adhesion, cell invasion, apoptosis and signaling pathways, little is known about the function of *ATF5*. The aim of this work is thus to define the role of *ATF5* in HCC oncogenesis (CU04289)

✍ WONG Nathalie • CHAN Lik Yuen (Medicine & Therapeutics) • Smith David I.*

□ 1 January 2005

❖ Michael Kadoorie Cancer Genetics Research Programme

Hepatocellular carcinoma (HCC) is a highly malignant tumor that is prevalent in China, including Hong Kong, and Southeast Asia. Epidemiological studies have shown a clear association between chronic infection with viral hepatitis B (HBV) and the development of HCC. HBV is a hepadna virus that almost invariably integrates into the host genome of HCC tumors. Early reports using low-resolution methods of Southern blotting and conventional cloning strategies have suggested the viral integration sites to occur randomly throughout the genome, leading to the presumption that there are no preferred sites of integration. Recent cloning studies, on the other hand, have begun to show that HBV integrants occur in common chromosome fragile sites and within the vicinity of important cancer-related genes. Since only a limited number of such HBV integrants have been completely analyzed to date, here we propose to clone and analyze a large series of HBV infected HCC tumors and cell lines for their sites of integration and flanking cellular sequences. Detail characterization of integration sites will be carried out by the high-throughput technique of restriction site (RS)-PCR followed by direct DNA sequencing. The effect on juxtaposition gene expression will be assessed by quantitative RT-PCR and the functional importance will be examined in transfection assays. (MD04723)

Characterizing the Viral Hepatitis B Integrants in Human Hepatocellular Carcinoma

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

Edition Title/Investigators

2003-04 Interleukin-10 Gene Polymorphisms in Malignancies Associated with Infectious Agents in Hong Kong (CU03408)

✍ CHAN Bik Wan • CHAN Wing Yee# • LEI Ieng Kit Kenny (Clinical Oncology)

2003-04 Genomic Aberrations of Squamous Cell Carcinoma of Larynx Associated with Tumor Progression (MD03328)

✍ CHAN Bik Wan • LO Wing Ip Anthony • TSANG King Yin Raymond (Surgery)

2002-03 The Investigation of Multiple Mutations in Hepatocellular Carcinoma (CU02066)

✍ LIEW Choong Tsek • LAI Bo San Paul (Surgery) • LAU Wan Yee Joseph (Surgery) • LI Hiu Ming (Pathology Teaching Laboratory) • WONG Nathalie

2002-03 Molecular and Functional Characterization of a Novel Tumor Suppressor Gene, TSLC1, in Nasopharyngeal Carcinoma (CU02067)

✍ LO Kwok Wai • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute)# • TEO Man Lung Peter (Clinical Oncology) • TO Ka Fai • TSUI Kwok Wing (Biochemistry)

2003-04 Comprehensive Characterization of Common Amplicons in Nasopharyngeal Carcinoma (CU03410)

✍ LO Kwok Wai • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute)# • HUI Bik Yu • TEO Man Lung Peter (Clinical Oncology) • TO Ka Fai

2003-04 Antitumor Effects of Histone Deacetylase Inhibitors in Epstein-Barr Virus-positive Nasopharyngeal Carcinoma (MD03393)

✍ LO Kwok Wai • HUI Bik Yu • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute)#

2002-03 Molecular Genetics of Mucopolidosis II (MD02358)

✍ LO Wing Ip Anthony • TANG Leung Sang Nelson (Chemical Pathology)

2003-04 The Role of Pif1 DNA Helicase Homolog in Telomere Maintenance and Chromosome Stability in Mammalian Cells (CU03411)

✍ LO Wing Ip Anthony • MURNANE John P.* • NG Ho Keung • PANG Chung Sean Jesse

2002-03 Study of the Multi-Step Molecular Pathogenesis of Multiple Myeloma (MM) in Chinese: Identification of Early and Sequential Molecular Targets in MM Transformation and Progression and Mapping of MM-Related Tumor Suppressor Loci on Chromosomes 4q and 13q (CU02068)

	✍ NG Heung Ling Margaret • CHAN Chee Wun Joyce (Medicine & Therapeutics)# • HOU Jian* • LEI Ieng Kit Kenny (Clinical Oncology) • LO Kwok Wai • TSANG Kam Sze Kent		✍ PANG Chung Sean Jesse • NG Ho Keung • POON Wai Sang (Surgery)
2002-03	Studies on the Possible Association of ApoE and Receptor Genes with Vascular Dementia in Hong Kong Chinese (CU02069)	2002-03	Molecular Alterations in Normal Looking Nasopharyngeal Epithelia - Implication in the Molecular Carcinogenesis of Nasopharyngeal Cancer (NPC) (CU02071)
	✍ NG Ho Keung • BAUM Lawrence William (Medicine & Therapeutics) • CHAN Yu Leung (Diagnostic Radiology & Organ Imaging)# • CHIU Fung Kum Helen (Psychiatry) • PANG Chi Pui Calvin (Ophthalmology and Visual Sciences) • WONG Ka Sing Lawrence (Medicine & Therapeutics)	2003-04	SOCS-1 Hypermethylation in Gastric Cancer, Intestinal Metaplasia and Tumor Suppressor Effect of SOCS-1 in Gastric Cancer (MD03826)
			✍ TO Ka Fai • LEUNG Wai Keung (Medicine & Therapeutics) • CHAN Ka Leung Francis (Medicine & Therapeutics) • CHAN Wing Yan Michael (Medicine & Therapeutics)#
2002-03	High-Resolution Genomic Profiling of Medulloblastomas Using Array-Based Comparative Genomic Hybridization Analysis (MD02423)	2002-03	Characterizing Drug Resistance Pattern in Doxorubicin Insensitive Hepatocellular Carcinoma (CU02097)
	✍ NG Ho Keung • HUI Bik Yu • LO Kwok Wai		✍ WONG Nathalie • JOHNSON Philip James (Clinical Oncology) • LAI Bo San Paul (Surgery) • ZEE Chung Ying Benny (Community and Family Medicine)
2003-04	Isolation of Oligodendroglioma-Associated Tumor Suppressor Genes on Chromosome 1p36.3 (MD03543)	2002-03	Hepatocellular Carcinoma Research Group: Clinical Applications of Functional Genomics (MD02380)
	✍ NG Ho Keung		✍ WONG Nathalie • LAI Bo San Paul (Surgery) • POON Y C Randy* • MOK Shu Kam Tony (Clinical Oncology) • TO Ka Fai • LIEW Choong Tsek • POON Chuen Wai
2003-04	Identification of Multiple Tumor Suppressor Genes on Chromosome 8p21-23.1 in Medulloblastoma (CU03414)		

(Medicine & Therapeutics) •
JOHNSON Philip J*

(Surgery) • ZEE Chung Ying Benny
(Community and Family Medicine)

2003-04 Characterisation of Genomic Amplicons
in Hepatocellular Carcinoma : Targeting
Candidate Genes by Array-CGH,
Transcriptional Profiling and Functional
Study (CU03467)
✍ WONG Nathalie • CHAN Yuen Yee
(Paediatrics) • LAI Bo San Paul

2003-04 Characterization of Drug Resistance
Phenotype in Hepatocellular Carcinoma
in-vitro Models (MD03589)
✍ WONG Nathalie

RESEARCH PROJECTS

Expression and Functional Study of Estrogen Receptors in Prostate Cancer

✍ CHAN Leung Franky

📅 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

Prostate cancer is a commonly diagnosed cancer in men in western countries. Recently, its rates are increasing rapidly in Asian countries, including China and Hong Kong. This cancer will usually progress from an initial androgen-dependent stage to androgen-independent in later development, of which is a serious clinical problem. Despite much research works have been conducted in this area, the mechanisms underlying the development and progression of prostate cancer are still poorly understood. Androgens have been considered to play a major role in the normal growth and functions of prostate gland, and also in the development of prostate cancer. Besides androgens, estrogens have also been suggested for a long time to play certain roles in these regulatory processes. However, the exact functions of estrogens and the estrogen-signaling pathway in prostate and prostate cancer are still unclear and undefined. Estrogenic effects in prostate are complex and might involve direct and indirect effects. Direct estrogenic effects in prostate are believed to be mediated mainly through estrogen receptors (ER), ER α and ER β , both of which are functionally expressed in human and rodent prostates. However, recent studies from ER-knockout mouse models show that the prostate glands in ER-deficient mice are normal in structure

and functions. These results suggest that other ER-related proteins or estrogen-signaling pathways may be present as well to modulate the prostatic growth and functions. *Estrogen receptor-related receptors* (ERRs) are close relatives of ERs and consist of three closely related isoforms: α , β and γ . Although ERRs are closely related to ERs in their protein structures, ERRs do not bind estrogens or other physiological ligands and thus they are classified as “*orphan nuclear receptors*”. Unlike classical steroid hormone receptors, ERRs are constitutively transactivated without binding to any natural ligands. Similar to ERs, ERRs can bind to consensus estrogen response elements (ERE) and other related DNA response elements, which are also recognized by other nuclear receptors. Therefore, ERRs could interact or cross-talk with ERs or other nuclear receptors via regulation of similar genes and competition for limited co-regulatory proteins in target cells. We have shown in our preliminary studies that ERRs are widely expressed in many human prostatic cell lines and tissues, and over-expression of ERRs can increase cell proliferation and modulate ER expression in prostate cancer cells. These results suggest that ERRs may play a significant role in cell proliferation and regulation of prostate cancer cell behavior. Through this in-depth proposed study, we strongly believed that valuable information on ERRs and their importance in prostatic functions and prostate cancer development will be obtained. This information will be extremely valuable in our understanding on the role of ERRs in prostate carcinogenesis and better management of prostate cancer.

(MD04386)

Differential Responses of Mouse Nasal and Temporal Retinal Neuritis to Chondroitin Sulfates - The Roles of Protein Kinases C

✍ CHAN Sun On

☐ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

In the mouse optic chiasm, axons from one eye segregate into a crossed and an uncrossed pathway that relay visual information to targets on both sides of the brain. This axon divergence pattern forms the foundation of binocular vision in the mammals. The focus of this proposal is to determine mechanisms that control formation of this routing pattern. Previous findings from our laboratory have shown that the axon divergence pattern is partly controlled by a selected inhibition of axons arise from the ventral temporal retina (uncrossed) but not of those from the nasal retina (which are crossed) towards a contact with chondroitin sulfates at the midline of the chiasm. Here using a culture model of mouse retina that demonstrates consistently a differential inhibition of neurite growth to CS, we will investigate the function of a signal transduction molecule, protein kinase C (PKC), in the selective inhibition of ventral temporal retinal neurites during a CS contact. The level of PKC activity within the retinal growth cones in explant culture or in brain slice preparations of the visual pathway will be modulated by specific activators or inhibitors. Furthermore, the expression of various isoforms of PKC in the ventral temporal and dorsal nasal retinal growth cones will be determined. These findings will provide important information on mechanisms that control axon guidance at the midline of the mammalian central nervous system.

(MD04596)

The Role of DOC-2 / Dab2 in the Prenatal Development of the Neocortex

✍ CHAN Wood Yee • YEW Tai Wai David • MOK Chi Ho Samuel*

☐ 1 January 2005

❖ Research Grants Council (Earmarked Grants)

Disturbances that occur in the neocortex of the brain during fetal development have been recognized as the causes of many congenital diseases including lissencephaly, holoprosencephaly, cortical heterotopia, double cortex and developmental delay in children and adults. However, cellular and molecular events even in normal cortical development have not yet been fully characterized. Recently we have identified and characterized DOC-2/Dab2 as a mammalian ortholog of *Drosophila Disabled*, which has been known to be involved in neuronal development. Our studies have shown that DOC-2/Dab2 was expressed in different cortical layers of the developing brain in a specific temporal and spatial manner both in human fetuses and mouse embryos. Disruption of the gene expression during early development of the mouse embryo resulted in the malformation of the neural tube and disorganization of the neuroepithelial cells of the brain. In order to establish the roles of DOC-2/Dab2 during neocortical development, we propose: (1) to characterize the temporal and spatial expression of the gene in human fetal brains; (2) to ascertain in parallel with the human studies the gene expression in mouse embryos; and (3) to alter the gene expression in mouse embryos to determine the pathological sequences, and wherever possible to correlate the expression with the functions of the gene. The results will give us information on both the possible roles of DOC-2/Dab2 in normal neocortical development and the pathological alterations following changes of gene expression.

(CU04262)

Effects of Lens Epithelial Cells on Retinal Ganglion Cell Regeneration

✍ CHO Yu Pang Eric

📅 1 December 2004

❖ CUHK Research Committee Funding (Direct Grants)

Despite recent advance in our understanding of the failure of regeneration in the central nervous system of adult mammals, experimental paradigms which can achieve significant functional recovery are still lacking. Recently, it has been observed that an experimental injury of the optic nerve of one eye in the rat coupled with a concurrent damage to the lens of the same eye will result in significant regeneration of retinal ganglion cells, and more importantly, some degree of recovery of visual activity. Although activation of macrophages and/or release of factors stimulating regeneration as a result of the lens damage have been proposed as putative mediators, the possibility of direct activation of the lens epithelial cells (LECs), the main cell type of the lens, and their role in promoting regeneration, has not been considered previously. Thus, in this study, we aim to further elucidate the potential and mechanisms of this cell type with respect to its ability to induce robust regrowth of ganglion cells. The approach will involve studying the interactions of LECs with the retina in culture, as well as transplanting cultured or freshly isolated LECs to the damaged eye. The results may provide a framework not only for enhancing our understanding of the regeneration of retinal ganglion cells, but also of other neurons in the brain and spinal cord as well.

(MD04917)

A Novel Function of the Male Accessory Sex Gland Secretions on Male Germ Cell Development in the Testis

✍ CHOW Pak Ham Patricia • O Wai Sum*

📅 1 November 2003

❖ HKU small project funding (UGC)

Male accessory sex gland (ASG) secretions contributes to the bulk of seminal fluid and is made up of a variety of constituents including proteins, carbohydrates, lipids, ions that affect the metabolism and function of the spermatozoa. Recently, The reactive oxygen species (ROS) have been recognised as a marker to evaluate sperm fertilizing capacity and to identify men with silent genital tract inflammation (Aitken *et al.*, 2003, *Reprod. BioMed.* Online 7, 65-70). Antioxidant enzymes and free radical scavengers secreted by ASGs offer significant protection on spermatozoa against peroxidative damage on sperm DNA (van Overveld *et al.*, 2000; *Chemo-Biological Interaction*, 127, 151-161).

In our recent studies of sperm DNA protection by antioxidant enzymes secreted by male ASG in the golden hamsters, we have found that hamsters with major ASGs removed have a significantly higher incidence of DNA damaged in caput epididymal sperm than in the control (Chen *et al.*, 2002; *Reproduction* 124, 491-499). The damaged sperm come from the testis that is upstream to the ASGs, and *how ASG removal can affect testicular germ cell development is unknown*. One possible explanation is that removal of ASGs can remove the source of the protective antioxidant enzymes against sperm DNA damage (Chen *et al.*, 2003; *J. Androl.*, In Press). Moreover, removal of the prostate could elevate the plasma Zn⁺⁺ level (Wong *et al.*, 2000; *Tumour Biol.* 21, 328-336). Both the decrease in antioxidant enzymes and increased in Zn⁺⁺ level can affect the

p53, a cell cycle checkpoint regulator, activity in male germ cells in the testis (Hainaut and Hollstein, 2000; Adv Cancer Res. 77, 82-137; Hainaut & Mann 2001; Antioxidants & Redox signalling 3, 611-623).

The objective of this study is to find out (1) how the removal of male accessory sex glands can affect the male germ cell development in terms of p53 conformation from “wild type” to “mutation” form; (2) to measure the plasma Zn^{++} levels in plasma; and (3) to co-localise by immuno-histochemical and histochemical methods the repair enzyme, RAD51 and Zn^{++} in the male germ cells in the testis.

This will throw light on a novel function of male accessory secretions on male germ cell development (MD03796)

Offspring of Males without Accessory Sex Glands, are They Different?

✍ CHOW Pak Ham Patricia

☐ 1 April 2005

❖ CUHK Research Committee Funding (Direct Grants)

Intracytoplasmic sperm injection (ICSI) was introduced in 1991 and has become the method of choice for assisting couples suffering from various male factor problems in producing offspring. So far the emphases have been on improving the rate of success, reducing multiple birth and eliminating gametes/embryos with chromosomal defects. Data on risk assessment largely based on structural malformation has also been initiated. Increasingly sperm at various stages of maturation are used. To dissociate the effects of in vitro manipulation of embryo from sperm origin, we carry out a study in an in vivo model in which male hamsters with ablation of accessory sex gland deliver epididymal sperm not exposed to seminal plasma. In this model, removal

of all the glands considerably reduces fertility even though the rate of successful fertilization in vivo and in vitro are not affected. Significant number of embryos so derived fail to develop to term even though some survive to be born. We shall compare physical and functional development of F1 pups from these sires with the controls. Physical development parameters such as body weight, femur length, muscle strength and relative organ weight will be measured. Behavioral patterns such as olfactory preferences, exploring a new environment (ambulation and rearing) and acoustic startle response (startle amplitude and startle habituation) will be studied. We hope that the outcome of this study will add insight to risk assessment associated with sperm origin in assisted reproduction.

(MD04851)

Can Silencing the Growth Arrest Specific 1 (Gas 1) Gene in Tendon Cells Promote Cell Cycle Progression?

✍ LEE Ka Ho Kenneth • CAI Dong Qing (Orthopaedics & Traumatology)

☐ 1 December 2004

❖ CUHK Research Committee Funding (Direct Grants)

A torn anterior cruciate ligament is the most commonly encountered sport injury. The patellar tendon is now widely used as an autograft in the reconstruction of this ligament. It has been reported that, after the extraction of the autograft, the patellar tendon donor site heals very slowly. In addition, the surgery produces many complications that include: patello-femoral pain, rupture of the patellar tendon and weakness in the quadriceps skeletal muscles. The root cause of these symptoms is because the tenocytes at the patellar wound site proliferate too

slowly. Hence, it is important that understand the cellular and molecular processes involved in tendon healing. In this study, we propose to examine the role of growth arrest specific 1 (*gas1*) gene plays in the regulation of tenocyte growth following experimentally induced injury. We have previously established that over-expression of *gas1* in NIH 3T3 fibroblasts induces growth arrest (Lee et al., 2001). We will first establish the spatio-temporal expression pattern of *gas1* following experimentally induced injury in the patellar tendons of mice. Specifically, we want to establish whether *gas1* tightly regulates the proliferation of tenocytes during tendon healing. We will also use *gas1*-siRNAs to knockdown *gas1* gene expression in growth-arrested tenocytes, *in vitro*. The object is to determine whether by silencing *gas1* expression, we could entice growth-arrested tenocytes to reenter the cell cycle. Clinically, this study is very important because all torn tendons and ligaments generally heal very poorly. Therefore, it is highly desirable to develop methods that would stimulate tenocyte proliferation to speed up the healing process.

(MD04393)

Proteomic Analysis of Differentially Expressed Proteins during the Onset of Programmed Cell Death in Mouse Embryonic Limb Interdigital Tissues

✍ LEE Ka Ho Kenneth • CAI Dong Qing*

📅 1 January 2005

❖ Research Grants Council (Earmarked Grants)

Programmed cell death (PCD) is an important process in both embryo development and homeostasis in adult tissues. The process removes excess, infected, transformed and damaged cells through the activation of the cells' own intrinsic suicide program.

PCD is currently the subject of considerable interest because of the potential for understanding oncogenesis and the possibility of exploiting the cell death program for therapeutic purposes. In our propose study, we will use the classical 'interdigital tissue' (tissues found between digits of the embryonic limb) model to identify novel factors involved in PCD. To achieve our aim, we will use state-of-the-art proteomic technique to identify proteins that are differentially expressed in the interdigits during the onset of PCD. We have already carried out a pilot study using this technique and have identified 2 differentially expressed proteins that we believe are important for interdigital cell death - namely: Peroxiredoxin 1 and Protein disulfide isomerase 3. We propose to analyze the function of these proteins and determine their role in interdigital cell death and survival. In addition, our pilot proteomic study has also established that there are between 150-200 interdigital proteins that are differentially displayed in the 2-dimensional gels which we have not identified. We aim to establish the identity of all of these proteins because it will allow us to understand the vast interconnecting network of proteins involved in the etiology of interdigital cell death and survival.

(CU04265)

Sources, Fates, Environmental and Health Effects of Persistent Toxic Substances from E-waste Recycling in Southeast China

✍ LIU Wing Keung Ken • WONG T.W. (Community and Family Medicine)* • WONG M. H.* • C K C Wong* • YUNG Kin Lam Ken* • WONG Ngok Shun Ricky* • MAK Nai Ki* • K C Cheung* • M S Yang* • A Leung* • C W Cai* • C K M Leung* • P K K Louie* • N S Duzgoren-Aydin* • J Fu* • J Lu*

❑ 1 May 2004

❖ RGC Central Allocation

The disposal, recycling and part salvaging of discarded electronic devices such as computers, printers, televisions and toys every year are now creating a new set of waste (E-waste) problems. It has been estimated that 50-80% of the e-waste from industrial countries such as the US ends up in recycle plants in Asian countries, where primitive and unsafe techniques are used. Stripping of metals in open-pit acid baths, removing electronic components from a circuit board by heating it over a grill, chipping and melting plastics without proper ventilation, and recovering metals by burning cables and parts are common practices. Unsalvageable materials are disposed of either by dumping in the fields and rivers or by burning in open air. The uncontrolled combustion has the potential to produce highly toxic polyhalogenated pollutants, including polychlorinated and polybrominated dibenzo-*p*-dioxins and furans (PXDDs/Fs, X=C1, Br), which may have an adverse effect on both the local and global environment. In addition to contaminating the environment, these processes expose workers to toxic chemicals through oral intake (of contaminated food), inhalation and skin exposure. Most of the people involved in this 'recycling' industry seem to be unaware of the threats to their health or may be ignoring the dangers in order to earn an income. The open burning of E-waste is undoubtedly affecting the health of the workers and the local residents, and perhaps even the populations of nearby cities due to the contamination of the environment including foodstuff. The major objective of the present proposal is to quantify the sources, fates and environmental and human health effects of these persistent toxic substances (PTS), by making a thorough study of an E-waste processing site in Guiyu, Guangdong Province, China.

(BL03916)

Molecular Mechanisms Underlying the Anti-Proliferative Activity of Edible Mushroom Lectin on Colon Cancer Cells

✍ LIU Wing Keung Ken

❑ 1 January 2005

❖ CUHK Research Committee Funding (Direct Grants)

Colorectal cancer is one of the leading killer diseases in the Western world. This malignant disease is hideous because usually it is detected only at an advanced stage. The incidence of colorectal cancer in Asian countries is, however, relatively low, particularly in Japan and China. Epidemiological evidence suggests that a high intake of dietary fat and a low intake of vegetables and fibers increase the risk of this disease, indicating a role of environmental factors, particularly dietary factors, in the etiology of this type of cancer. The rising incidence in China in the past decades owing to changes in dietary habit is alarming. The proposed project is prompted by the report of the inhibitory effect of broad bean lectin, which is resistant to digestion and remains active in the colon, on the growth and differentiation of colon cancer LS174S cells. Bean and mushroom lectins have thus been put forward as health food or even colon cancer-preventive supplements in our daily life. It is anticipated, through a study of the anti-proliferative effects of lectins from several common edible mushrooms on a battery of colon cancer cell lines will provide an insight into the regulatory mechanisms of proliferation and differentiation of malignant colon cells at both cellular and molecular levels.

(MD04656)

Receptor Gene Polymorphisms and Cold-Pressor Test as Predictors for Heroin Dependence and Treatment Outcome - A Case Control Association Study

✍ STADLIN Alfreda • CHEUNG Kin Leung Ben (Psychiatry)#

□ 1 August 2004

❖ CUHK Research Committee Funding (Direct Grants)

Heroin is the most common drug of abuse in Hong Kong. In 2003, 78.5% of reported drug abuse cases in Hong Kong are known to abuse heroin, its abuse has serious repercussions on the government's health and social welfare system. Both genetic and environmental factors play a role in the risk of developing heroin addiction. Possession of gene mutations associated with heroin dependence may predispose individuals to drug-seeking behavior and to the development of heroin addiction. Some of these candidate genes are also involved in pain control. Individuals genetically predisposed to heroin dependence may also exhibit abnormal pain sensitivity and tolerance. If such associations exist, pain sensitivity and gene variants could act as predictors of heroin dependence as well as treatment outcome. The present study aims to examine polymorphisms of the DRD2, DRD3, DRD4, GABAA, COMT, μ - and δ -opioid receptors genes in 300 subjects and 100 controls, with subjects divided into: i) heroin-dependent patients with successful treatment outcome; ii) heroin-dependent patients with poor treatment outcome; iii) subjects who have used heroin at least once in their lifetime and are not and have never been heroin-dependent. In order to elucidate whether gene variants and physiological function like pain sensitivity/tolerance can act as predictors of treatment outcome, we plan to a)

compare pain responses (using cold-pressor test for pain detection and tolerance) within and between these 3 groups of heroin users and controls; b) determine whether there is a genotype difference within and between the 3 groups of cases and the controls; c) to ascertain whether there is a correlation between pain response, genotype and the 3 groups of cases studied. This is based on the hypothesis that heroin-dependent subjects with successful treatment outcome will carry significant differences in allelic frequencies and genotypes and have different levels of pain sensitivity/tolerance to those with a poor treatment outcome. The ability to use gene polymorphisms and physiological functions such as pain sensitivity/tolerance as predictors of treatment outcome has serious implications for the diagnosis and treatment of those who are at risk for addiction and can thus influence the treatment outcome of these subjects.

(MD04594)

The Proteomics of the Brains of Human and Primate in Development

✍ YEY Tai Wai David • KUNG Hsiang Fu (Centre for Emerging Infectious Diseases) • LAI Li Hui* • Maria Lin*

□ 1 December 2004

❖ Shanghai City Scientific Council

The protein changes of the brain in human and monkey at various stages of gestation will be analysed and compared. The patterns will reflect on the functional maturation of the brain.

(MD04603)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>		
2003-04	A Study of Carcinogenicity of Estrogen in Prostatic Cells (MD03875) ✍ CHAN Leung Franky	2003-04	✍ LEE Ka Ho Kenneth • CHAN John* • CHING Kar Keung (Clinical Immunology Unit) • CHUI Yiu Loon (Clinical Immunology Unit)
2003-04	Developmental Controls of Axon Patterning in the Retinofugal Pathway of Mouse Embryos (CU03417) ✍ CHAN Sun On	2003-04	The Mechanism of Increased Susceptibility to Retinoic Acid Teratogenicity in Diabetic Pregnancy (CU03397) ✍ SHUM Sau Wun Alisa • COPP A J* • WANG Chi Chiu (Obstetrics & Gynaecology)
2001-02	Migration of Neural Crest Cells to the Bowel in Normal and Congenitally Aganglionic Mutant Mice (MD01016) ✍ CHAN Wood Yee • COPP A J*	2000-01	Genes and Heroin Addiction in the Chinese Population: Association Studies on Receptor Gene (MD98904) ✍ STADLIN Alfreda • LEE Tak Shing Dominic (Psychiatry) • TANG Leung Sang Nelson (Chemical Pathology) • LOH El-Wui* • CHEN Chih Ken* • CHAN Pui* • CH'IENT James*
2003-04	Is Abnormal Sacral Neural Crest Cell Migration to the Gut Involved in Aganglionosis : An Investigation Using an Animal Model for Hirschsprung's Disease (CU03418) ✍ CHAN Wood Yee • ALAN J. Burns*	2003-04	Personality Traits and Substance Abuse - A Case/Control Association Study on Receptor Gene Polymorphisms in Chinese Psychostimulant Users (MD03520) ✍ STADLIN Alfreda • LEUNG Yiu Kin Freedom (Psychology)
2001-02	A Study on the Use of Sertoli Cells to Promote Retinal Ganglion Cell Regeneration (MD01017) ✍ CHO Yu Pang Eric	2001-02	Cellular Mechanisms of Neuronal Loss During Aging (MD01023) ✍ YEW Tai Wai David • CHAN Wood Yee
2003-04	Does Deletion of Male Accessory Sex Glands Produce Heritable Changes in Spermatozoa? (CU03419) ✍ CHOW Pak Ham Patricia • ANNE Ferguson-Smith* • O Wai Sum*	2003-04	Characterization of the Metabolic Events Associated with Ocular Enlargement in the Black Moor Goldfish (MD03750)

✍ YEW Tai Wai David • TSANG

David Sau Cheuk (Biochemistry)

RESEARCH PROJECTS

Molecular Mechanism of Prolactin Gene Regulation in Fish

✍ CHAN King Ming • CHENG Hon Ki Christopher

□ 15 September 2004

❖ Research Grants Council (Earmarked Grants)

Prolactin (PRL) is a pituitary polypeptide hormone first found in mammals for control of milk production with many other neuro-endocrine-immune functions, but its function in fish is less well understood. Most studies on PRL in fish are conducted in euryhaline species in relation to its role in freshwater adaptation migrated from seawater, however we are interested in studying the primary physiological function of PRL in freshwater teleosts using goldfish as a model. We would like to study the molecular mechanism of goldfish PRL (gfPRL) gene regulation using goldfish as a model to examine the hormone or chemical agents that could affect the expression of gfPRL gene. The regulation of gene transcription of the gfPRL gene promoter will be studied *in vitro* following the administration of hormones. The cloned gfPRL gene promoter will be characterized using deletion mutants and gel-mobility shift assays. The role of Pit-1/GHF-1 and other *cis*-acting elements will be investigated in transfected cells following exposures to various hormonal challenges. Results obtained from this project will shed lights on the understanding of the physiological roles of PRL not only in fish, but also in mammals and humans. (CU04410)

Attenuation of Oxidative Stress and Tissue Injury during Pancreatitis by Xanthine Oxidase Inhibitors, Antioxidants and Natural Products

✍ CHENG Hon Ki Christopher • LEUNG Po Sing (Physiology)

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

Pancreatitis is a common disease of the pancreas involving tissue injury and the subsequent release of digestive enzymes into the circulation. The generation of reactive oxygen species has been implicated in the pathogenesis of the disease. In the present investigation, we plan to use both an acute pancreatitis animal model and a chronic pancreatitis animal model to carefully define the progress of oxidative stress which occurs during the disease process. Moreover, to ascertain the causative role of the reactive oxygen species produced during pancreatitis, we plan to use both xanthine oxidase inhibitors and antioxidants on these animal models to investigate whether these agents could reduce or prevent the tissue injury associated with pancreatitis. Apart from the known xanthine oxidase inhibitor and antioxidants, we would also explore into the effectiveness of natural enzyme inhibitors and antioxidants of phytochemical origin with the view of identifying better and more efficacious alternatives. (MD04783)

Immunomodulatory Activities of Herbal Formulate 'Kwan Du Bu Fei Dang' in Healthy Subjects: A Randomized Double-Blind Placebo-Controlled Study

✍ FUNG Kwok Pui • LEUNG Ping Chung (Orthopaedics & Traumatology) • TSUI Kwok

Wing • WAN Chi Cheong David • WAYE Mary Miu Yee • WONG Chun Kwok (Chemical Pathology) • LAM Wai Kei Christopher (Chemical Pathology) • AU Wing Ngor Shannon (Biochemistry) • LAU Bik San Clara (School of Pharmacy)

□ 3 May 2005

❖ Research Fund for the Control of Infectious Diseases - Health, Welfare and Food Bureau

Severe Acute Respiratory Syndrome (SARS) has become a global health hazard. Since there is no effective preventive and treatment of SARS, agents against the disease is urgently needed. Developing a western drug which can inhibit SARS coronavirus and with established safety data may take many years. On the other hand, herbal medicine [such as traditional Chinese medicine (TCM)] may provide a rapid preventive and treatment since they have already been used for long time. Hence, one possible quick strategy to fight against SARS is to consider the development of herbal formulae. While herbal products may offer good potential candidates, their evidence of beneficial effects against coronavirus need to be established. Thus, we propose to determine the most effective herbal products, in a expeditious but scientific manner for the prevention and treatment of SARS.

Based on in-depth literature search and our preliminary results, the following TCM formulae will be chosen for further investigation in this proposal:

- 1) Investigation on the efficacy of TCM formulae for prevention of SARS: 'Kwan Du Bu Fei Dang (抗毒補肺湯)', Lingzhi and Yunzhi.
- 2) Investigation on the efficacy of TCM formulae/products for treatment of SARS: 'Kwan Du Bu Fei Dang (抗毒補肺湯)', *Houttuynia cordata* and a formula of mixture of 3 herbs (*Sinomenium acutum*, *Paeonia lactiflora*

and *Angelica sinensis*).

We plan to investigate whether these formulae/products exhibit any inhibiting effect on the growth of coronavirus *in vitro*, and modulate the immunological activities *in vitro*, *in vivo* (in mice) and in human subjects. The results obtained from this study will therefore provide scientific evidence for further drug development.

(MD04432)

Expression and Functional Characterization of the Putative SARS Coronavirus (SARS-CoV) Non-Structural Proteins X1-X5

✍ HO Yuanyuan

□ 1 January 2005

❖ Research Fund for the Control of Infectious Diseases

Purpose: Develop research tools and use them to characterize the roles of SARS-CoV non-structural proteins X1-X5 in cell growth and survival. **OBJECTIVES:** 1. Construction of vectors for the expression of SARS-CoV X1-X5 proteins in human cells. 2. Study the localization of the X1-X5 proteins in human cells. 3. Characterize the effects of X1-X5 proteins on human cell proliferation and viability. **DESIGN:** The SARS-CoV X1-X5 cDNA will be subcloned into mammalian expression vectors with or without the green fluorescent protein (GFP) fusion to the viral proteins followed by expression in human cell lines that are representative of the tissues most affected by SARS, i.e. the lung epithelium and lymphocytes. The viral-GFP fusion proteins facilitate the observation of the cellular localization of viral proteins independent of using X1-X5 antibodies that are currently unavailable. The expression of X1-X5 proteins without GFP fusion allows for the direct assessment of the effects of these

proteins on cell proliferation and viability. *SETTING:* Human A549 lung epithelial cells, K562 B lymphocytes, and Jurkat T lymphocytes will be transfected to express the viral X1-5 proteins for cellular localization and proliferation/viability studies. *OUTCOME MEASURES:* Cellular localization of viral proteins will be determined by fluorescence and con-focal microscopy. Cell proliferation and viability will be measured by DNA synthesis, MTT, flow cytometry, or DNA fragmentation assays. *IMPLEMENTATION OF RESULTS:* The effects of the X1-X5 proteins on cell proliferation/viability will be established and thus the roles of the viral non-structural proteins in the biology of SARS-CoV will be further elucidated.
(BS04562)

The Roles of Apolipoprotein E Non-Coding Single Nucleotide Polymorphisms in the Transcriptional Control of the Gene

✍ HO Yuanyuan

☐ 1 January 2005

❖ CUHK Research Committee Funding (Direct Grants)

Background: ApoE coding region polymorphisms $\epsilon 2$, $\epsilon 3$, and $\epsilon 4$ have been associated with allelic-specific risk predictions of Alzheimer's disease (AD) and coronary heart disease (CHD). Recently, several APOE non-coding single nucleotide polymorphisms (ncSNPs), have also been associated with risk modification of AD and CHD as well as altered plasma apoE concentrations. Most previous studies characterized the non-coding regulatory elements of the APOE gene in hepatoma cells. However, the functional significance of the disease-associated ncSNPs in normal and extra-hepatic tissues is poorly understood. The purpose of this proposal is to

characterize the roles and mechanisms of ncSNPs at nucleotides -580, -491, -429, -219, and +113 relative to the transcription start site in the transcriptional control of the APOE gene. *Hypothesis:* ApoE ncSNPs at nucleotides -580, -491, -429, -219, and +113 relative to the transcription start site modulate the transcriptional activity of the APOE gene in a tissue-specific manner. *Specific Aim 1:* Generation of the apoE proximal promoter-intron1-reporter construct and determination of transcriptional activities of the reporter construct in cultured hepatocytes, astrocytes, monocytes, and smooth muscle cells. *Specific Aim 2:* Generation of apoE proximal promoter-intron1-reporter constructs harboring disease-associated APOE ncSNPs and determination of tissue-specific transcriptional activity of the ncSNP-carrying reporter constructs. *Significance:* Understanding the roles of disease-associated ncSNPs in the regulation of APOE gene expression will facilitate the elucidation of the mechanistic link between APOE ncSNPs and disease susceptibility in human.
(MD04349)

Riboregulator Modulation of Drug Resistance in Human Cancer Cells

✍ KWOK Tim Tak • KONG Siu Kai
(Biochemistry)

☐ 1 January 2005

❖ Research Grants Council (Earmarked Grants)

Although it is generally believed that a gene may exert its biological function thru its protein product, a group of genes that is known as riboregulator is believed to function as RNA. H19 is one of the riboregulators and is known to be associated with fetal development and cancer development. Preliminary results from the present study indicated

that the riboregulator H19 may regulate the drug resistance in human cancer cells. Since anticancer drug resistance is one of the major causes for treatment failure in cancer therapy, the identification and characterization of the role of H19 in drug resistance are therefore important and are of potential benefit to cancer patients including those prevalent in Hong Kong. The aim of this study is to investigate the underlying mechanisms for the role of H19 in drug resistance in human cancer cells. In addition to the understanding of drug resistance mechanism, the results from the proposal will also be useful in dissecting the biological function and regulation mechanisms of H19 that are not yet clearly established.

(CU04270)

Effect of Dietary Phytoestrogens on Estrogen Metabolism In Vitro and In Vivo.

✍ LEUNG Lai Kwok • CHAN Leung Franky
(Anatomy)

□ 1 April 2005

❖ CUHK Research Committee Funding (Direct Grants)

Phytoestrogens are polyphenolic compounds widely distributed in plant foods and TCM herbs. Because of their structural resemblance to estrogen, these chemicals can act as agonists/antagonists on estrogen receptor and initiate many physiological or pharmacological effects. These properties could be applicable in preventive medicine. Many studies have shown that estrogen is a crucial player in the etiology of breast cancer. The hormone can stimulate breast cell proliferation and it also undergoes biotransformation into DNA-attacking moiety. Polymorphisms of the genes *cyp1a1*, *cyp1b1* and *cyp19*, which encode enzymes for estrogen

synthesis and hydroxylation, are associated with breast cancer risk. Our preliminary studies indicated that phytoestrogens might have different actions on these enzymes at the activity as well as the gene expression level. Because changes in the enzyme activities could affect the concentrations of estrogen and its metabolites in human body and the subsequent risk of breast carcinogenesis, we have proposed some *in vitro* and *in vivo* studies to document the profiles of estrogen and its metabolites altered by phytoestrogen administration. Cell culture models are employed to address the mechanisms of enzyme inhibition, transcriptional regulations, and the metabolisms of estrogen. The overall aim is to institute a mechanism for phytoestrogens as natural cancer-preventive agents.

(MD04406)

Biological Characterization of Recently Reported New Classes of Ribosome Inactivating Proteins

✍ NG Tzi Bun • WANG Hexiang*

□ 1 October 2004

❖ Research Grants Council (Earmarked Grants)

Ribosome inactivating proteins (RIPs), which arrest protein synthesis by virtue of their N-glycosidase activity, which cleaves the adenine at position 4324 of ribosomal RNA, are classified into different types. Type 1 RIPs are single-chained proteins with a molecular mass of approximately 30 kDa. Type 2 RIPs are composed of an RIP chain and a lectin chain.

Recently, new types of RIPs have been isolated. The seeds of two Cucurbitaceae plants, the bottle gourd and the hairy gourd, produce two 20-kDa RIPs, that are structurally different from plant type 1 RIPs. Other Cucurbitaceae plants produce ribosome inactivating peptides, with a molecular mass of about

10 kDa, and characterized by an abundance of arginine and glutamate/glutamine residues in their N-terminal sequences. The seeds of the garden pea produce a 20-kDa RIP that is different from other plant RIPs but resembles miraculin in N-terminal sequence. The fruiting bodies of several mushroom species produce RIPs distinctly different from angiosperm type I RIPs in N-terminal sequence.

Plant type I RIPs have captured the attention of many investigators because they are endowed with a host of activities including translation-inhibitory, immunomodulatory, antitumor, antiproliferative, and antiviral activities. By contrast, the biological activities of the aforementioned cucurbitaceous 20-kDa RIPs and ribosome inactivating peptides, garden pea RIPs and the mushroom RIPs, other than translation-inhibiting and N-glycosidase activities, have not been extensively investigated. The aim of the proposed project is to investigate the possible inhibitory effects of these RIPs on HIV-1 enzymes, SARS virus proteinase, other proteases such as trypsin and chymotrypsin, proliferation of tumor cell lines and splenocytes, and fungal and bacterial growth. They will also be examined for embryotoxicity and hepatotoxicity. It is hoped that novel and useful compounds for therapeutic applications with minimal untoward side effects can arise from this proposed investigation.

(CU04272)

Characterization of a Glycoprotein with Immunostimulatory and Antiproliferative Activities from Fresh *Smilax Glabra* Rhizomes, the Chinese Medicinal Material Tufuling

✍ NG Tzi Bun

□ 1 December 2004

❖ CUHK Research Committee Funding (Direct Grants)

Smilax glabra Rox B. (Family Liliaceae) is the Chinese medicinal herb called tufuling. It has antipyretic, detoxifying and diuretic actions. It may be beneficial in treatments for brucellosis, syphilis, furunculosis, eczema, dermatitis, nephritis, cystitis, and mercury and silver poisoning.

From *S. glabra* rhizomes a glycoprotein was isolated in a preliminary experiment in the P.I.'s laboratory. In gel filtration and also in SDS-PAGE it exhibited a molecular mass of 30 kDa. It stimulated uptake of [methyl-³H]-thymidine by both murine peritoneal macrophages and murine splenocytes. It also augmented nitric oxide production by murine peritoneal macrophages. In inhibited [methyl-³H]-thymidine uptake by a variety of tumor cells. It exhibited HIV-1 reverse transcriptase inhibitory activity. It displayed an N-terminal sequence that has not been previously reported.

The purpose of the proposed research is to further characterize the isolated *S. glabra* glycoprotein by examining it for other potentially exploitable activities such as antifungal, antibacterial, cytokine inducing HIV-1 protease inhibitory, and HIV-1 integrase inhibitory activities. Possible untoward activities including embryotoxicity and hepatotoxicity will also be investigated.

(MD04838)

Characterization of RhoC in Tumor Cell Invasion

✍ WAYE Mary Miu Yee

□ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

In a previous study with the transforming gene (HBX) of hepatitis virus, we observed that RhoC is up-regulated in cells that over-express HBX gene. RhoC is a member of the small guanosine triphosphatases (GTPases). It is also a member of Rho subfamily. Members of the Rho family are involved in the regulation of cellular processes, such as microfilament network organization, cell cycle control and malignant transformation. We also observed that transient transfection of RhoC into normal mouse hepatocyte AML12 cells induced the formation of stress fibers and trigger the reorganization of actin cytoskeleton. Preliminary experiments of cell invasion assays also supported a direct correlation of RhoC in cellular invasion activities. Thus we believe that RhoC has an important role in tumorigenesis and progression of hepatocellular carcinoma. RhoC mRNA is approximately 580 bp and encodes a protein of 193 amino acids with a molecular weight of approximately 22 kDa. There is a GTP-binding region (insert region, residues 117-139) which is required for interaction with guanine nucleotide dissociation inhibitors (GDIs) and guanine nucleotide exchange factors (GEFs). The insert region forms part of an extra α -helical domain that is not present in Ras. Although the conformation of this insert region is not altered in the GDP- and GTP-bound forms, it is believed that this conformation may play some functions for Rho GTPases. The goal of this project is to find out whether the insert region is important for the function of Rho GTPases by studying the cell invasion activity of RhoC mutants. (MD04620)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
2003-04	Regulation of Prolactin and Prolactin Receptor Gene Expression (MD03342) ✍ CHAN King Ming • CHENG Hon Ki Christopher
1990-91	Comparative Endocrinology of Prolactin, Growth Hormone, and Their Receptors (BP88031) ✍ CHENG Hon Ki Christopher • NG Tzi Bun • WONG Chun Cheung (Physiology)
2001-02	Molecular and Functional Characterization of Ghrelin and Its Receptors in Seabream (BL01149) ✍ CHENG Hon Ki Christopher • WOO Norman Ying Shiu (Biology) • YU K L*
2002-03	Identification and Development of Xanthine Oxidase Inhibitors from Chinese Medicinal Natural Products with Therapeutic Potentials (CU02269) ✍ CHENG Hon Ki Christopher • FUNG Kwok Pui
2001-02	Mechanistic Study of Anti-Tumour Effect of Natural and Synthetic Saponins (MD01668) ✍ FUNG Kwok Pui
2003-04	Bioassay-Guided Isolation, Characterization, and Mechanistic Study of the Bioactive Components from <i>Paeonia Lactiflora</i> , <i>Sophora Flavescens</i> , <i>Oldenlandia Diffusa</i> and <i>Scutellaria</i>

	Barbata for the Anti-Proliferative Effect on Human Hepatoma Cells In Vitro (CU03399)		✍ WAYE Mary Miu Yee • ZIMMERMANN Rene* • CHAN Hei (Biochemistry)
	✍ FUNG Kwok Pui • KONG Siu Kai (Biochemistry) • MAK Thomas Chung Wai (Chemistry) • TSUI Kwok Wing • WAYE Mary Miu Yee	2003-04	Study of the Function of the HBX Gene of Hepatitis B Virus Using the Tetracycline-inducible System (BL03958)
			✍ WAYE Mary Miu Yee
2002-03	Identification and Characterization of Apolipoproteine E Polymorphism-Induced Variation of Cell Function Involved in Atherosclerosis (CU02274)	2003-04	Establishment of a SARS Coronavirus Protein/Peptide Library and an Antibody Library as Common Platforms for Biological and Medical Applications (CU03536)
	✍ HO Yuanyuan • FUNG Kwok Pui • WAYE Mary Miu Yee		✍ WAYE Mary Miu Yee • AU Wing Ngor Shannon (Biochemistry) • CHAN Ho Yin Edwin (Biochemistry) • CHENG Hon Ki Christopher • CHEUNG Wing Tai • CHUI Yiu Loon (Clinical Immunology Unit) • FUNG Kwok Pui • HO Walter K. K. (Biochemistry) • HO Yuanyuan • KONG Siu Kai (Biochemistry) • KWOK Tim Tak • LEUNG Kwok Nam (Biochemistry) • NG Tzi Bun • NGAI Sai Ming (Biology) • TAM Siu Lun John (Microbiology)# • TSUI Kwok Wing • WAN Chi Cheong David • WONG Kam Bo (Biochemistry)
2003-04	Functional Characterization of a Novel SNF2/SW12-like Gene and Its Role in Drug Resistance (MD03421)		
	✍ KWOK Tim Tak		
2003-04	Effect of Flavonoids on the Initiation and Promotion of Breast Carcinogenesis (MD03933)		
	✍ LEUNG Lai Kwok • CHAN Leung Franky (Anatomy)		
2003-04	Promoter Analysis of Chicken Acetylcholinesterase Gene (CU03311)		
	✍ WAN Chi Cheong David • TSIM Wah-keung Karl (Biochemistry)#		
2002-03	Characterization of a RING-H2 Finger Protein, ANAPC11, the Human Homologue of Yeast Apc11p (BL02860)		

RESEARCH PROJECTS

Quantitative Aberrations in Circulating RNA in Maternal Plasma: Clinical and Biological Implications in Preeclampsia

✍ CHIU Wai Kwun Rossa • LO Yuk Ming Dennis
• LAU Tze Kin (Obstetrics & Gynaecology) •
LEUNG Tse Ngong (Obstetrics & Gynaecology)

□ 20 December 2004

❖ Research Grants Council (Earmarked Grants)

Preeclampsia is a disorder that develops during pregnancy and affects up to 8% of all pregnancies. Despite the advancement of modern medical care, preeclampsia still accounts for up to 20% of all maternal deaths globally, including Hong Kong. Improvements in the diagnosis and management of preeclampsia have been hindered by our poor understanding of the underlying pathophysiology, albeit intense research devoted to this area. In recent years, genetic materials (DNA and RNA) have been shown to be released by the unborn child into its mother's circulation. The detection of circulating fetal DNA in maternal plasma has been shown to be a promising marker for pregnancy monitoring. Abnormalities in fetal DNA concentrations in maternal plasma have been found to be associated with preeclampsia. However, a limitation of the study of fetal DNA relates to the fact that it can only be conveniently applied to pregnancies with male fetuses. This limitation can now be overcome by the study of fetal RNA in maternal plasma, which is gender-independent. In this project, we propose to evaluate the value of circulating RNA for the prediction and prognostication of preeclampsia. Furthermore, we propose to investigate the effects of

preeclampsia on the clearance kinetics and the physical characteristics of circulating RNA molecules in maternal plasma. These investigations may reveal clues to the pathological processes associated with preeclampsia and the biological processes that affect the levels of circulating nucleic acids in maternal plasma.

(CU04277)

Global Gene-Expression Analysis and Functional Clustering in Sporadic Basal-Cell Carcinoma of the Skin in Chinese Using High-Density Oligonucleotide Arrays

✍ LAM Ching Wan

□ 1 September 2004

❖ Research Grants Council (Earmarked Grants)

The incidence of sporadic basal-cell carcinomas (BCCs) of the skin in Hong Kong has increased three-fold from 1990 to 1999. The process of oncogenesis involves dysregulation of multiple cellular processes and pathways including cell cycle, cell proliferation, and apoptosis, and insight into these multiple cellular processes and pathways can now easily be gained by the use of microarray analysis. We now propose to use whole-genome microarrays to perform a genome-wide study to identify genome networks dysregulated in sporadic BCCs. We will be able to achieve a biological interpretation of the microarray data through functional clustering of the differentially expressed genes and provide insights into the mechanism of tumorigenesis of BCCs using functional clustering techniques. Because the oncogenic pathway in BCCs, the sonic hedgehog pathway, is activated irrespective of ethnicity and genetic alterations in BCCs, the finding of novel expression alterations in sporadic BCCs promises to further our understanding of the

role of this signaling pathway in human carcinogenesis.

(CU04278)

Adhesion between Mast Cells and Epithelial Cells: Its Regulatory Mechanism for the Release of Chemokines in Allergic Inflammation

✉ LAM Wai Kei Christopher • WONG Chun Kwok

□ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

Allergic diseases such as asthma and allergic rhinitis are prevalent and have been increasing in Hong Kong. Mast cells are central effector cells in type 1 hypersensitivity. Activated airway epithelial cells are potent sources of cytokines and chemokines. The interaction of human mast cells and lung fibroblast can induce inflammatory cytokine release in co-culture. This project will study the following: (1) Effects of mast cell activators including stem cell factor and tumor necrosis factor- α on (i) adhesion of human mast cells HMC-1 onto human bronchial epithelial BEAS-2B cells, (ii) expression of chemokines including regulated upon activation normal T cell expressed and secreted, monokine induced by interferon- γ monocyte chemoattractant protein-1, interleukin-8, interferon-inducible protein-10, and thymus and activation-regulated chemokine in co-culture of HMC-1 cells and BEAS-2B cells and (iii) expression of intercellular adhesion molecule-1 (ICAM-1) on mast cells and BEAS-2B cells upon the cell-cell interaction of mast cells and BEAS-2B cells. (2) Relationship between the activation of nuclear factor (NF)- κ B, Janus kinase (JAK), phosphoinositide 3-kinase (PI3-kinase)-AKT, c-Jun amino-terminal kinases (JNK) and p38

mitogen-activated protein kinase (MAPK), and the adhesion, expression of adhesion molecule ICAM-1 and release of chemokines in co-culture of mast cells and BEAS-2B cells. (3) Specific inhibitors of JNK, p38 MAPK, JAK, PI3-kinase and NF- κ B on ICAM-1 expression on epithelial cells and the release of chemokines in co-culture. This study will widen our knowledge of the immunopathogenesis of mast cell mediated allergic inflammation and provide a biochemical basis for the development of novel treatment of allergic inflammation.

(MD04464)

Evaluation of Mass Spectrometry for the Detection of Fetal Nucleic Acids in Maternal Plasma

✉ LO Yuk Ming Dennis • CHIU Wai Kwun Rossa

□ 3 August 2004

❖ Sequenom, Inc.

This project aims to evaluate the performance of a state-of-the-art mass spectrometry system for the analysis of fetal DNA and RNA in maternal plasma. The results will be expected to have a major impact on the development of non-invasive prenatal diagnosis on a variety of diseases, for example, beta-thalassaemia.

(MD04545)

Development of Maspin as an Epigenetic Fetal DNA Marker in Maternal Plasma for All Pregnancies

✉ LO Yuk Ming Dennis • CHIU Wai Kwun Rossa

- LAU Tze Kin (Obstetrics & Gynaecology) •
- LEUNG Tse Ngong (Obstetrics & Gynaecology)
- CHIM Siu Chung Stephen (Obstetrics & Gynaecology)

❑ 6 August 2004

❖ Research Grants Council (Earmarked Grants)

This project focuses on the investigation of the DNA methylation status of the maspin gene in the placenta. The biology of this phenomenon will be studied and its potential implication as a fetal DNA marker will be investigated in preeclampsia.

(CU04279)

Investigation on the Origin, Molecular Characteristics and Clearance of Plasma Nucleic Acids in Nasopharyngeal Carcinoma Patients

✍ LO Yuk Ming Dennis • CHAN Kwan Chee •
CHAN Anthony Tak Cheung (Clinical Oncology)
• LEUNG Sing Fai (Clinical Oncology) • LO
Kwok Wai (Anatomical & Cellular Pathology)

❑ 1 January 2005

❖ Michael Kadoorie Cancer Genetics Research
Programme

Nasopharyngeal carcinoma (NPC) is closely related to Epstein-Barr virus (EBV) infection. Over the past 5 years, our group has shown that plasma EBV DNA analysis is useful for the detection, monitoring and prognostication of NPC. We have also demonstrated that these DNA molecules are short DNA fragments instead of intact viral genomes. However, several important questions concerning the mechanism of release and elimination of EBV DNA remain unanswered. Furthermore, despite the fact that EBV RNA has been demonstrated in the plasma of NPC patients, information on the clinical applications of quantitative analysis on plasma EBV RNA and the molecular characteristics of these RNA molecules is lacking.

In this study, we plan to:

1. investigate if EBV DNA is present in the urine of

NPC patients;

2. investigate the clinical significance of plasma EBV RNA measurement;
3. investigate the molecular characteristics of plasma RNA molecules in NPC patients, including their partiality, integrity and the relative abundance of 5' and 3' ends; and
4. establish xenografts in nude mice for the investigation of tumour-derived nucleic acids from different cellular compartments (nuclear DNA, mitochondrial DNA, viral DNA, cellular and viral RNA) and their relationship with tumour mass.

The findings of this study are important for the understanding the biology of plasma nucleic acids in NPC patients and the further development of non-invasive techniques for NPC detection.

(MD04617)

Adhesion between Eosinophils and Epithelial Cells: Its Regulatory Mechanism for Eosinophil Degranulation and the Expression of Cytokines and Leukotrienes in Allergic Inflammation

✍ WONG Chun Kwok • LAM Wai Kei
Christopher

❑ 1 September 2004

❖ Research Grants Council (Earmarked Grants)

Allergic diseases such as asthma are prevalent and reaching epidemic proportions in Hong Kong and worldwide. Eosinophils are principal effector cells of allergic inflammation, characterized by the accumulation and infiltration of eosinophils in tissues mediated by chemokine eotaxin, and adhesion molecules on epithelial cells. The interaction of eosinophils and epithelial cells can induce the release of inflammatory mediators and enhance eosinophil degranulation. The objective of this project is to

study the intracellular signal transduction mechanisms mediating the activations of human eosinophils and epithelial cells in the coculture of these two cells. We plan to study: (1) Effects of various eosinophil activators including IL-3, -5, -13, and granulocyte-macrophage colony-stimulating factor on (i) adhesion of human eosinophils onto human bronchial epithelial BEAS-2B cells, (ii) expression of inflammatory cytokines including IL-6, tumor necrosis factor (TNF)- α , IL-12, IL-18, chemokines including RANTES, MIG, MCP-1, IL-8, IP-10 and TARC, and cysteinyl leukotrienes in co-culture, (iii) eosinophil cationic protein release from eosinophil degranulation, and (iv) expression of adhesion molecule intercellular adhesion molecule-1, vascular cell adhesion molecule-1 and CD 18 on eosinophils and BEAS-2B cells in co-culture of eosinophils and BEAS-2B cells; (2) Relationship between the activation of NF- κ B, signal transducer and activator of transcription factor (STAT)6, c-Jun amino-terminal kinases (JNK) and p38 mitogen-activated protein kinase (MAPK), and the adhesion, expression of adhesion molecules, leukotrienes, cytokines, and eosinophil degranulation in co-culture of eosinophils and BEAS-2B cells. Results of this basic study may provide a biochemical basis for the development of new therapeutic intervention for the treatment of allergic inflammation.

(CU04281)

Intracellular Signal Transduction Mechanisms Regulating the IL-25 Induced Expression of Adhesion Molecules and Cytokines of Human Eosinophils

✍ WONG Chun Kwok • LAM Wai Kei
Christopher

□ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

Allergic diseases such as asthma and allergic rhinitis are prevalent and have been increasing in Hong Kong. Allergic asthma is characterized by the activation, accumulation and degranulation of eosinophils in inflammatory sites. Cytokines and chemokines produced by T helper (Th)-2 cells orchestrate most pathophysiological processes of an allergic reaction. Interleukin (IL)-25 is a novel Th2 cytokine which plays an important role in late phase allergic reactions. We plan to study the following. (1) Effects of IL-25 on (i) expression of intercellular adhesion molecule (ICAM)-1 and ICAM-3 on human eosinophils and (ii) expression and release of inflammatory cytokines including IL-1, IL-6, IL-12, IL-18 and transforming growth factor- β , and chemokine including regulated upon activation normal T cell expressed and secreted (RANTES), monokine induced by interferon (IFN)- γ (MIG), monocyte chemoattractant protein-1 (MCP-1), IL-8, IFN-inducible protein-10 (IP-10) and macrophage inflammatory protein (MIP). (2) Relationship between the activation of intracellular signal transduction molecules including nuclear factor (NF)- κ B, c-Jun amino-terminal kinases (JNK), p38 mitogen-activated protein kinase (MAPK) and Janus kinase (JAK) and phosphoinositide 3-kinase (PI3-kinase)-AKT with the expression of adhesion molecules, and the release of inflammatory cytokines and chemokines of eosinophils. (3) Specific inhibitors of JNK (SP600125), p38 MAPK (SB 203580), JAK (AG-490), PI3-kinase (LY294002) and NF- κ B (BAY117082) on ICAM-1,3 expression and the release of inflammatory cytokines and chemokines of eosinophils. This study will widen our knowledge of the immunopathogenesis of IL-25 mediated allergic inflammation and provide a

biochemical basis for the development of a target for therapeutic intervention in the treatment of allergic inflammation.
(MD04629)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

Edition Title/Investigators

2003-04 Investigation of the Differences in the Concentrations and Molecular Characteristics of DNA in the Plasma and Serum of Healthy Subjects (MD03988)
✍ CHAN Kwan Chee • LO Yuk Ming Dennis

2003-04 Origins of Circulating mRNA in Maternal Plasma (MD03839)
✍ CHIU Wai Kwun Rossa • LO Yuk Ming Dennis • LAU Tze Kin (Obstetrics & Gynaecology) • LEUNG Tse Ngong (Obstetrics & Gynaecology) • CHAN Ho Ming • NGAN KEE Warwick Dean (Anaesthesia & Intensive Care)

2003-04 Non-Invasive Prenatal Diagnosis of b-thalassaemia through Maternal Plasma Analysis: A Multi-Centre Collaborative Study (CU03395)
✍ CHIU Wai Kwun Rossa • CHAN Li Chong* • CHUI David H.K.* • LAU Tze Kin (Obstetrics & Gynaecology) • LEUNG Tse Ngong (Obstetrics & Gynaecology) • LO Yuk Ming Dennis

2002-03 A Comprehensive Survey of Mutations in the Wilson Disease Gene (ATP7B) in Hong Kong Chinese: Frequencies, Haplotypes and Genotype-Phenotype Correlations (CU02084)
✍ LAM Ching Wan

2003-04 Genome-Wide Detection of Allelic Imbalance in Sporadic Basal Cell Carcinoma of the Skin in Chinese: Probing Etiologically Different Genetic Alterations Using High-Density Single-Nucleotide Polymorphism Arrays (CU03472)
✍ LAM Ching Wan

2002-03 Study of Immunomodulatory and Anti-Tumor Activities of HERBSnSENSESTM Cordyceps (Dong Chong Xia Cao) (MD02709)
✍ LAM Wai Kei Christopher • WONG Chun Kwok • LEUNG Kwok Nam (Biochemistry) • KONG Siu Kai (Biochemistry)

2003-04 Roles of Mitogen Activated Protein Kinases and Transcription Factor NF-κB Controlling the Recruitment, Inflammatory Mediator Release and Apoptosis of Human Mast Cells in Allergy (CU03473)
✍ LAM Wai Kei Christopher • WONG Chun Kwok

2003-04 Intracellular Signal Transduction Mechanisms Mediating the Induction of Adhesion Molecule and Cytokine Expression in the Co-Culture of Human

	Eosinophils and Epithelial Cells (MD03552)		LEUNG Tse Ngong (Obstetrics & Gynaecology)
	✍ LAM Wai Kei Christopher • WONG Chun Kwok	2003-04	Development of Maspin as An Epigenetic Fetal DNA Marker in Maternal Plasma for All Pregnancies (MD03364)
2001-02	Development of Genomic Strategies for the Non-Invasive Detection of Down Syndrome (MD01862)		✍ LO Yuk Ming Dennis • CHIM Siu Chung Stephen (Obstetrics & Gynaecology) • LEUNG Tse Ngong (Obstetrics & Gynaecology) • CHIU Wai Kwun Rossa • LAU Tze Kin (Obstetrics & Gynaecology)
2002-03	Molecular Characterization of Circulating Epstein-Barr Virus DNA in Nasopharyngeal Carcinoma Patients (CU02086)	2003-04	A Centre for the Study of Fetal Nucleic Acids in Maternal Plasma (MD03672)
	✍ LO Yuk Ming Dennis • CHAN Anthony Tak Cheung (Clinical Oncology) • TO Wai Hei Edward*		✍ LO Yuk Ming Dennis • LAU Tze Kin (Obstetrics & Gynaecology) • LEUNG Tse Ngong (Obstetrics & Gynaecology) • WONG Hing Nam (Obstetrics & Gynaecology) • CANTOR Charles* • HUANG H M Tim*
2002-03	Treatment and Diagnosis of Severe Acute Respiratory Syndrome (MD02397)		
	✍ LO Yuk Ming Dennis		
2003-04	Quantitative Analysis of Plasma Viral and Host RNA in Severe Acute Respiratory Syndrome (CU03508)	2001-02	Is Thyrotoxic Periodic Paralysis Resulted from a Calcium Ion Channelopathy? (MD01035)
	✍ LO Yuk Ming Dennis • CHIU Wai Kwun Rossa • LEE Nelson (Medicine & Therapeutics)* • NG Pak Cheung (Paediatrics) • POON Lei Lit Man* • TAM Siu Lun John (Microbiology)#		✍ TANG Leung Sang Nelson • CHOW Chun Chung Francis (Medicine & Therapeutics) • COCKRAM Clive Stewart (Medicine & Therapeutics) • YAO Xiaoqiang (Physiology)
		2002-03	Establish a Diagnostic Laboratory for Inherited Metabolic Diseases in Hong Kong (MD02558)
2003-04	Molecular Analysis of Placental RNA in Maternal Plasma (CU03474)		✍ TANG Leung Sang Nelson • FOK Tai Fai (Paediatrics) • LAM Wai Kei Christopher • CHEUNG Kam
	✍ LO Yuk Ming Dennis • CHIU Wai Kwun Rossa • LAU Tze Kin (Obstetrics & Gynaecology) •		

- Lau (Paediatrics) • HUI Joannie (Paediatrics)
- 2003-04 To Develop a Clinical Prognostic Profile for Severe Disease Course in SARS with Serum Cytokines Measurements and Genomic Markers - A Retrospective Case Control Study (CU03507)
✍ TANG Leung Sang Nelson • CHAN Kay Sheung Paul (Microbiology) • HUI Shu Cheong David (Medicine & Therapeutics) • LAM Wai Kei Christopher • TO Ka Fai (Anatomical & Cellular Pathology) • WONG Chun Kwok
- 2003-04 Elucidation of Nitric Oxide Mediated Mechanisms Controlling the Recruitment and Apoptosis of Human Eosinophils in Allergic Inflammation (MD03943)
✍ WONG Chun Kwok • LAM Wai Kei Christopher • FISCUS Ronald Ray (Physiology)
- 2003-04 Study of Predisposition Genes Underlying IgA Nephropathy and Their Genetic Interactions (MD03407)
✍ TANG Leung Sang Nelson • SZETO Cheuk Chun (Medicine & Therapeutics) • TO Ka Fai (Anatomical & Cellular Pathology) • LI Kam Tao Philip (Medicine & Therapeutics)

RESEARCH PROJECTS

Identification of Plasma Prognostic Proteomic Patterns in Nasopharyngeal Carcinoma - Development of Clinical Assay Prototype with the Combined Use of SELDI-TOF Mass Spectrometry and Bioinformatic Analyses

✍ CHAN Anthony Tak Cheung • MA Buig Yue Brigitte • WONG Sze Chuen Cesar • HUI Edwin P* • POON Chuen Wai (Medicine & Therapeutics)

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

Nasopharyngeal carcinoma (NPC) is a serious public health problem in Hong Kong and Southern China. Over 60% of NPC patients present with advanced stage (UICC stages III and IV) disease. Despite a high initial local control rate, the subsequent rates of local recurrences and distant metastasis in patients with locoregionally advanced disease are high (30% - 40%) after radiotherapy. Once the patients have developed local recurrences or distant metastases, the treatment outcome is poor with a median survival of around 12 months. Our collaborative group has performed considerable amount of research work in diagnostic and prognostic markers of NPC. Our group is the first Asian group successfully identifying the serum diagnostic proteomic patterns of liver cancer with the combined use of SELDI-TOF mass spectrometry (MS) and bioinformatic analysis. The merit of SELDI-TOF MS-based assay is of a protein chip format, which is high-throughput and readily adoptable by clinical practice. We propose to combine our clinical oncology and proteomics

expertise to identify prognostic proteomic patterns in the plasma of NPC patients, and develop a prototype proteomic pattern assay that is clinically practical.

The proposed project is aimed to:

1. To identify the plasma proteomic signatures of NPC patients at presentation with the use of the SELDI-TOF protein chip platform and bioinformatic analyses;
 2. To identify the plasma proteomic pattern associated with different prognoses (no recurrence, local recurrence, distant recurrence, progression-free survival and overall survival);
- (MD04525)

MVA-EBNA1/LMP2 Vaccine: Phase I Trial in Patients with EBV-Positive Nasopharyngeal Carcinoma (MTA)

✍ CHAN Anthony Tak Cheung • HUI Pun* • CHAN Lam* • MA Buig Yue Brigitte • TAO Qian

□ 1 October 2004

❖ Cancer Research UK

This joint project with Cancer Research UK aims at testing a novel form of vaccine therapy for NPC. The methodology is to induce de novo responses and/or boost pre-existing T cell responses to the relevant EBV target proteins in NPC patients by vaccination with a recombinant Modified Vaccinia Ankara (MVA)-based vaccine encoding EBV target antigens.

It is an open label Phase I dose escalation trial aiming to determine the safety and characterize the toxicity profile and immunogenicity of the vaccine. An identical study design is being initiated in the UK for other EBV-related cancers including non-Hodgkin's lymphoma

(MD04307)

Biweekly Gemcitabine and Oxaliplatin (GEMOX) in First-Line Metastatic or Recurrent Nasopharyngeal Carcinoma (NPC)

✍ CHAN Anthony Tak Cheung • MA Buig Yue
Brigette • MOK Shu Kam Tony • LEUNG Sing
Fai • HUI Pun* • KAM K Michael* • Kwan
Wing Hong* • Chiu Kwok Wing*

□ 1 November 2004

❖ Sanofi Sunthelabo

This is a phase II single-arm open-labeled study that evaluates the efficacy and safety of Gemcitabine in combination with Oxaliplatin (third generation platinum compound with better toxicity profile compared with cisplatin and a dose-limiting peripheral neuropathy) in the first line treatment of metastatic or recurrent Nasopharyngeal Carcinoma with primary endpoint as response rate. Target number of patients is 35.

(MD04697)

EMR 62 202-013, Open, Randomized, Controlled, Multicenter Phase III Study Comparing 5FU/FA plus Cetuximab vs 5FU/FA plus Irinotecan as First-Line Treatment for Epidermal Growth Factor Receptor-Expressing Metastatic Colorectal Cancer

✍ CHAN Anthony Tak Cheung • MA Buig Yue
Brigette • HO Wing Ming • CHAN Lam

□ 1 December 2004

❖ Merck & Co., Inc.

This is a multicenter, multinational, randomized, comparative efficacy and safety 3-arm study. The treatment phase consists of two parts of 24 weeks for a total 48 weeks in order to find the different

combination of drugs with its effect on disease free survival. Target patient of this study is 10.

The main endpoints are:

- (1) To demonstrate that the combination of bevacizumab and FOLFOX-4 is superior to FOLFOX-4 alone in terms of disease-free survival in chemotherapy-naïve patients who underwent surgery with curative intent for colon carcinoma.
- (2) To demonstrate that the combination of bevacizumab and XELOX is superior to FOLFOX-4 alone in terms of disease-free survival in chemotherapy-naïve patients who underwent surgery with curative intent for colon carcinoma

(MD04747)

A Randomized, Three Arm Multinational Phase III Study to Investigate Bevacizumab (q3w or q2w) in Combination with Either Intermittent Capecitabine plus Oxapliplatin (XELOX)(q3w) or Fluouracil/Leucovorin with Oxaliplatin (FOLFOX-4) versus FOLFOX-f Regimen Alone as Adjuvant Chemotherapy in Colon Carcinoma

✍ CHAN Anthony Tak Cheung • MA Buig Yue
Brigette • HO Wing Ming • CHAN Lam

□ 25 April 2005

❖ Roche Hong Kong Limited

This is a randomized, three arm multinational Phase III study with the objective to demonstrate that the combination of bevacizumab and FOLFOX-4 is superior to FOLFOX-4 alone in terms of disease-free survival in chemotherapy-naïve patients who underwent surgery with curative intent for colon carcinoma, and to demonstrate that the combination of bevacizumab and XELOX is superior to FOLFOX-4 alone in terms of disease-free survival in

chemotherapy-naïve patients who underwent surgery with curative intent for colon carcinoma.

(MD04635)

A Randomized Phase II Study to Investigate the Effects of Recombinant Intestinal Trefoil Factor (ITF) on Oral Mucositis in Patients Receiving Radiation Therapy for Nasopharyngeal Cancer

✍ LEUNG Sing Fai • CHAN Anthony Tak Cheung

□ 1 July 2004

❖ The GI Company, Inc

Mucositis of the oral cavity and oropharynx is the most common acute toxicity of radiation therapy of nasopharynx cancer. Intestinal Trefoil Factor (ITF) is an endogenous peptide factor with reported wound healing properties in the gastrointestinal tract. In the present placebo-controlled randomized Phase II study, the efficacy of oral ITF spray on healing radiation-induced mucositis would be assessed. 40 patients with nasopharynx cancer who had developed significant radiation mucositis would be recruited.

(MD04516)

Development of a System of Virtual Extrapolation of Treatment Target Image for Intensity-Modulated Radiation Therapy for Nasopharyngeal Carcinoma

✍ LEUNG Sing Fai • KAM Koon Ming Michael • CHEUNG Kin Yin • Chau Ming Chun Ricky*

□ 15 December 2004

❖ CUHK Research Committee Funding (Direct Grants)

The standard treatment for nasopharynx cancer (NPC), a very common cancer in Hong Kong, is radiation therapy. Intensity-modulated radiation

therapy (EVIRT) is a new form of radiation therapy that can modify the radiation dose distribution to match the extent and shape of the tumor three-dimensionally. This can reduce the radiation side-effects (such as mouth dryness) on organs next to the cancer, (such as the salivary glands), and improve the coverage of the cancer by radiation. However, EVIRT is very time resource-intensive because of the need to map out the cancer target on a large number (about 90) of computed tomography (CT) images for each patient. This bottlenecks the application of EVIRT to the large number of NPC patients currently requiring radiation therapy. The aim of this study is to develop and assess the accuracy of an innovative method of semi-automated cancer target definition, by virtual extrapolation of the cancer target from a smaller number of CT images (two alternative models of using 45 images and 30 images only), to the other CT images in-between. The radiation dose distribution resulting from the virtual extrapolated plans would be assessed according to a set of constraint criteria (percentage of target receiving a prescribed dose, percentage of normal organ exceeding a reference dose). A successful model is defined as the fulfillment of constraint criteria not inferior to the reference model for all patients (sample size = 15) in the study. Further details can be found in the study protocol.

(MD04506)

Effect of Celecoxib on Apoptosis and Proliferation in Nasopharyngeal Carcinoma Cell Lines and Evaluation of Its Underlying Mechanisms

✍ MA Buig Yue Brigitte • CHAN Ming Lok • CHAN Anthony Tak Cheung

□ 15 November 2004

- ❖ CUHK Research Committee Funding (Direct Grants)

Nasopharyngeal carcinoma (NPC) is common in Hong Kong and patients with locally advanced disease often develop disease recurrence despite treatment. Yet, no effective secondary chemopreventive agent is available for NPC. Celecoxib is a selective inhibitor of the cyclooxygenase-2 enzyme (COX-2) that has been used as a chemopreventive agent in patients with colonic adenomas. This may be partly attributed to the ability of celecoxib in inhibiting growth and promoting apoptosis in preclinical models of some cancers, possibly through COX-2 (and prostaglandin E₂, PGE₂) dependent and independent mechanisms (e.g. inhibition of Akt phosphorylation). Our preliminary work demonstrates that COX-2 is expressed in 81% of primary NPC and is associated with advanced nodal stage. Furthermore, celecoxib can induce dose-dependent growth inhibition in NPC *in vitro*. Therefore, our objectives are to: (1) characterize the prognostic significance of COX-2 expression in NPC; (2) determine if celecoxib can induce apoptosis in NPC *in vitro*; (3) determine if celecoxib-induced apoptosis is mediated via prostaglandin-dependent pathways, or COX-2 independent pathways, or via inhibition of Akt signaling pathway. This study will lay the foundation of future studies on celecoxib as a chemopreventive or therapeutic agent in xenograft models of NPC.

(MD04352)

Antitumor Activities of Histone Deacetylase Inhibitor PDX101 in Hepatocellular Carcinoma Cell Lines

✍ MA Buig Yue Brigitte • TAO Qian • CHAN Anthony Tak Cheung • YEO Winnie • MOK Shu Kam Tony

□ 31 January 2005

- ❖ National Cancer Institute, Cancer Therapeutics Evaluation Program

In Asia, over 80% of hepatocellular carcinoma (HCC) cases are etiologically associated with hepatitis B virus (HBV) infection. Studies have shown that epigenetic silencing of gene expression via CpG island hypermethylation is common in HCC. These genes include tumor suppressor genes or genes that regulate key cellular processes. Histone deacetylases (HDAC) are enzymes involved in the epigenetic regulation of gene expression, and HDAC inhibitors have been shown to reactivate expression of certain genes. PDX101 is a zinc-chelating hydroxamic acid inhibitor of class I and II HDAC, which has potent anti-tumor activity in a variety of epithelial cancer cell lines. This pilot study evaluates the effect of PDX101 on cellular proliferation, cell colony formation, apoptosis (TUNEL labeling), changes of nuclear histone acetylation levels, expression of apoptosis-associated proteins (bax, bcl-2, bid, and caspase 3), and expression of cell cycle-associated proteins (p27, p21^{cip/waf}, cyclin A, cyclin D) in HBV-related HCC cell lines. Results of this study will lay the foundation of future studies on elucidating the effect of PDX101 on transcriptional activation of certain cellular genes in HCC.

(MD04636)

Radiosensitization of Hepatocellular Carcinoma by Epidermal Growth Factor Receptor Inhibition

✍ MOK Shu Kam Tony

□ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

Hepatocellular carcinoma (HCC) is a fatal illness with limited therapeutic option. Our group has developed selective internal radiation for treatment of local advanced HCC and reported moderate improvement in tumor response and palliation. However, radiation tolerance remained to be the limiting factor. The new molecular targeted agents may enhance tumor response by augmentation of radiation effect. Inhibition of epidermal growth factor receptor (EGFR) function can modulate radiation response in lung, colon, and head and neck cancer. There is no existing data on HCC. Part 1 of the project is an *in vitro* study on enhancement of radiation by ZD 1839 (an EGFR tyrosine kinase inhibitor) in 10 HCC cell lines (status of EGFR expression to be defined). We shall use clonogenic survival assay to determine the survival fraction of exponentially growing cell and compare the effect of radiation to radiation plus ZD 1839. Part 2 is an *in vivo* experiment of four HCC xenografts in nude mice. HCC cell lines will be cultured in medium as suggested. When reached 80% confluence, cells will be removed from the culture flasks with 0.05% trypsin and 0.05% EDTA in a balanced salt solution (Life Technologies, Inc.). Approximately $1-5 \times 10^6$ cells re-suspended in growth medium will be injected into the backs of the mice and allowed to grow for 18 days before randomization into one the four treatment groups. Groups of 5 mice with tumor xenograft will be treated by control, radiation, ZD1839 or combination of both. Comparison is made on the optimal growth inhibition. Results from these pre-clinical studies will serve as foundation for development of a phase I clinical trial on combination

of selective internal radiation and EGFR inhibitor in treatment of local advanced HCC.
(MD04694)

A Randomized, Double-Blind Multicentre 2-Stage Phase III Study of Bevacizumab in Combination with Cisplatin and Gemcitabine versus Placebo, Cisplatin and Gemcitabine in Patients with Advanced Recurrent Non-Squamous Non-Small Cell Lung Cancer, Who Have Not Received Prior Chemotherapy

✉ MOK Shu Kam Tony • LAM Kwok Chi • CHAN Lam

□ 1 February 2005

❖ Roche Hong Kong Limited

This study is a randomized, multicenter Phase III study targeting locally, advanced, metastatic or recurrent non-squamous non-small cell lung cancer patients with the aim to select the optimal dose of bevacizumab by assessing toxicity, overall survival and response rate. This multicenter study will last for over two and a half years with target recruitment of 1150 patients.
(MD04411)

Identification of Novel Tumor Suppressor Genes at 16q in Nasopharyngeal Carcinoma through a Combination of Genetic and Epigenetic Approaches

✉ TAO Qian

□ 1 January 2005

❖ Michael Kadoorie Cancer Genetics Research Programme

Nasopharyngeal carcinoma (NPC) is a prevalent tumor in southern China and Southeast Asia, including Hong Kong. Genetic analyses such as

loss of heterozygosity (LOH) and comparative genomic hybridization (CGH), have identified frequent chromosomal alterations at 16q in NPC. LOH of 16q has also been frequently reported in other solid tumors, including hepatocellular (which is also prevalent in Hong Kong), breast, prostate, lung, and gastric cancer. The critical deletion region has been mapped to 16q22.1-16q24.3. These studies suggest the presence of functional TSG(s) in the locus. So far, several candidate TSGs have been identified, with only *WWOX* and *MTG16* being verified as functional TSGs. However in NPC, no candidate TSG has been identified in this region yet.

It is well established that, in addition to numerous genetic abnormalities, multiple epigenetic alterations are also involved in tumor pathogenesis, including the aberrant silencing of a series of tumor suppressor genes (TSGs) promoters through CpG hypermethylation. The epigenetic alteration also provides us with a novel epigenetic way of identifying candidate TSGs.

We intend to identify novel functional TSGs at 16q in NPC, by using a combination of genetic and epigenetic approaches, human genome database mining and bioinformatics analyses. We will refine the critical tumor suppressor region by array-CGH analysis; map the differential expression profiles of all EST/genes at the identified regions in normal tissue and NPC tumor cell lines; and study the epigenetic and genetic alterations of the identified candidate genes. We also plan to develop molecular diagnostic and therapeutic strategies to NPC using the identified genes.

(MD04376)

Plasma β -Catenin mRNA as a Potential Marker in Colorectal Cancer

✍ WONG Sze Chuen Cesar • LO Yuk Ming Dennis (Chemical Pathology) • CHAN Anthony Tak Cheung • LAI Bo San Paul (Surgery)

□ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

Colorectal cancer (CRC) is a prevalent cancer, and tremendous efforts have been made for its early detection so as to improve the outcome. Our previous findings indicated that β -catenin protein in tumour nuclei could act as a potential diagnostic and prognostic marker in CRC patients. We recently devised a new and consistent protocol to extract mRNA from human plasma. Our pilot study with plasma β -catenin mRNA assay using this novel extraction protocol and quantitative PCR shows that this blood test can aid in diagnosis of colorectal carcinomas and adenomas. Among 58 CRC patients, 49 colorectal adenoma patients and 43 apparently normal subjects, β -catenin mRNA was detected with median concentrations of 8737, 1218 and 291 copies per ml plasma, respectively. Therefore, plasma β -catenin mRNA appears a promising marker for diagnosis and monitoring in CRC. This study continues to evaluate the clinical relevance of plasma β -catenin mRNA intensively in three cohorts and the quantity of blood taken is 6 ml only. The 1st cohort includes 60 CRC patients (pre-OT & on first follow-up before home leave) and 60 colorectal adenoma patients (pre-endoscopy and on first follow-up). The 2nd cohort consists of other benign colorectal diseases including 40 patients each for colitis, piles, colorectal ulcers and hyperplastic polyps. The 3rd cohort includes other non-colorectal cancers, with 40 patients each of breast cancer, prostate cancer, liver cancer, pancreaticobiliary cancer and lung cancer. The blood samples should reach the laboratory once taken. mRNA is extracted,

reverse transcribed to cDNA, and assayed for plasma β -catenin level using quantitative PCR.

(MD04566)

A Phase III, Randomized, Open-Label, Multicenter Study Comparing GW572016 and Capecitabine (Xeloda®) versus Capecitabine in Women with Refractory Advanced or Metastatic Breast Cancer

✍ YEO Winnie • HO Wing Ming • POON Annette
Ngar Ying

□ 19 July 2004

❖ GlaxoSmithKline Research and Development
Limited

This is a Phase III, Randomized, Open-Label, Multicenter Study Comparing GW572016 and Capecitabine (Xeloda®) versus Capecitabine in Women with Refractory Advanced or Metastatic Breast Cancer. Patients must have received prior anthracycline and/or taxane therapy with Her2 positive tumours.

(MD04942)

The Role of Drug Resistance Genes in Chemotherapy Resistance in Patients with Inoperable Hepatocellular Carcinoma - Analysis of Cytogenetic, Genetic and Clinical Factors

✍ YEO Winnie • WONG Nathalie (Anatomical & Cellular Pathology)

□ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

Hepatocellular carcinoma (HCC) is one of the commonest causes of cancer morbidity and mortality in this geographical region. For the majority of

patients, one of the main modalities of palliative treatment is chemotherapy. Unfortunately, the response to chemotherapy has been poor due to marked drug resistance. The drug resistance phenotype is most likely a result of several inter-related molecular pathways. Correlations of the drug resistance genes with treatment response and clinical outcomes in patients with solid tumours have been limited and to date, there has been no data reported on patients with HCC.

Using pre-treatment biopsy tissues from patients who have undergone chemotherapy, of whom the treatment response and clinical outcome are available, we propose to identify potential multi-drug resistance genes.

(MD04910)

A Phase II Multicenter, Randomized, Double-Blind, Placebo and Active-Controlled, Dose-Ranging, Parallel Group Study of the Safety and Efficacy of the Oral Neurokinin-1 Receptor Antagonist, GW679769 when Administered at Daily Doses of 50 mg, 100 mg, and 150 mg Oral Tablets in Combination with Ondansetron Hydrochloride and Dexamethasone for the Prevention of Chemotherapy-Induced Nausea and Vomiting in Cancer Subjects Receiving Highly Emetogenic Cisplatin-Based Chemotherapy

✍ YEO Winnie • CHAN Lam • POON Annette
Ngar Ying

□ 11 March 2005

❖ GlaxoSmithKline

Treatment with a serotonin receptor antagonist such as the five hydroxytryptamine, subtype 3 (5-HT₃) receptor antagonist ondansetron, given in combination with corticosteroids such as dexamethasone, is the current standard of care that

significantly reduces acute emesis resulting from highly emetogenic chemotherapy. However, the success achieved in the prevention of acute emesis with 5-HT₃ receptor antagonists and corticosteroids has not been extended to the control of delayed emesis induced by high-dose cisplatin. Recent studies have suggested that antiemetic therapy with a triple combination of a neurokinin, subtype 1 (NK-1) receptor antagonist, a 5-HT₃ receptor antagonist, and dexamethasone provide enhanced control of cisplatin-induced acute and delayed emesis compared with standard dual therapy regimens of a 5-HT₃ receptor antagonist and dexamethasone. Recently, this antiemetic triple therapy approach has been endorsed by the Antiemetic Subcommittee of the Multinational Association of Supportive Care in Cancer (MASCC) at their consensus conference in March 2004.

GW69769 is a potent and selective NK1 receptor antagonist being developed for the treatment of chemotherapy-induced nausea and vomiting. (MD04547)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

Edition Title/Investigators

2002-03 Studies on Markers of Tumor Hypoxia in Nasopharyngeal Carcinoma (CU02093)
 ✍ CHAN Anthony Tak Cheung • HARRIS Adrian L* • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute)# • HUI Pun • POON Chuen Wai (Medicine & Therapeutics) • TO Ka Fai (Anatomical & Cellular Pathology)

2003-04 An Open Label Randomized Phase III Study of Intermittent Oral Capecitabine in Combination with Intravenous Oxaliplatin (Q3W) ("XELOX") versus Bolus and Continuous Infusion Fluorouracil/Intravenous Leucovorin with Intravenous Oxaliplatin (Q2W) ("FOLFOX-4") as First-Line Treatment for Patients with Metastatic Colorectal Cancer (MD03467)

✍ CHAN Anthony Tak Cheung • MA Buig Yue Brigitte • MOK Shu Kam Tony • YEO Winnie • HO Wing Ming

2003-04 EMR 62 202-025, A Phase III Randomized, Open-Label, Multicenter Study of Irinotecan and Cetuximab vs. Irinotecan as Second-Line Treatment in Patients with Metastatic, EGFR-Positive Colorectal Carcinoma (MD03817)

✍ CHAN Anthony Tak Cheung • MA Buig Yue Brigitte • HO Wing Ming • WONG Tze Ming

2000-01 Phase III Randomized Multicenter Comparatives Study of Peginterferon alpha2a vs. Roferon-A for the Treatment of Patients with Recently Diagnosed Chronic Phase Chronic Myelogenous Leukemia (CML) not Previously Treated with Interferon (MD20042)

✍ LEI Ieng Kit Kenny • LEUNG Wai Tong Thomas# • HUI Pun

2003-04 A Phase 1/2 Open-Label Study to Assess the Safety, Tolerability, and Pharmacokinetics of Intravenous Infusion

	of MB07133 in Subjects with Unresectable Hepatocellular Carcinoma and Child-Pugh Class a Liver Function (MD03679)			✍ MOK Shu Kam Tony • JOHNSON Philip James • ZEE Chung Ying Benny (Community and Family Medicine)
	✍ MA Buig Yue Brigitte • CHAN Anthony Tak Cheung • MOK Shu Kam Tony • YEO Winnie	2002-03	A Phase II/III, Multicenter, Randomized, Controlled, Open Label Study of Intravenous T138067-sodium versus Intravenous Doxorubicin in Subjects with Chemotherapy-Naïve, Unresectable Hepatocellular Carcinoma (MD02843)	✍ MOK Shu Kam Tony • MA Buig Yue Brigitte • ZEE Chung Ying Benny (Community and Family Medicine)
2003-04	Enhancing the Anti-Tumor Activity of Chemotherapy with the Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor ZD1839 in Nasopharyngeal Carcinoma Cell Lines - Comparison between Different Schedules of Administration (MD03347)			
	✍ MA Buig Yue Brigitte • CHAN Anthony Tak Cheung • MOK Shu Kam Tony • SUNG Lan (Hong Kong Cancer Institute) • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute)#	2003-04	To Evaluate the Safety and Efficacy of Certain Products Developed by CKLS in the Treatment of Hepatocellular Carcinoma (MD03834)	✍ MOK Shu Kam Tony • YAU S H*
2003-04	A Randomized, Double-Blind, Placebo-Controlled, Phase III Study of Oxaliptin/5-fluorouracil/leucovorin with PTK787/ZK 22584 or Placebo in Patients with Previously Treated Metastatic Adenocarcinoma of the Colon or Rectum (MD03899)	2003-04	A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study of Temozolomide or Placebo Added to Whole Brain Radiation Therapy for the Treatment of Brain Metastases from Non-Small Cell Lung Cancer (MD03309)	✍ MOK Shu Kam Tony
	✍ MA Buig Yue Brigitte • CHAN Anthony Tak Cheung • HO Wing Ming	2003-04	Open-Label Single-Arm Phase 2 Study of ALIMTA in Patients with Advanced Non-Small Cell Lung Cancer Who Have Had Prior Chemotherapy (MD03542)	✍ MOK Shu Kam Tony • LAM Kwok Chi
2001-02	A Double-Blind Placebo Controlled Randomized Study on the Use of Chinese Herbal Medicine in Treatment of Advanced Non-Small Cell Lung Cancer (MD01043)	2003-04	A Randomized Phase II Study to Evaluate the Effect of CKBM-T01 vs.	

	Tamoxifen on Quality of Life (QOL) of Patients with Inoperable Hepatocellular Carcinoma (HCC) (MD03455)		✍ YEO Winnie • JOHNSON Philip James • LEUNG Wai Tong Thomas#
	✍ MOK Shu Kam Tony • ZEE Chung Ying Benny (Community and Family Medicine) • YAU Sau Han • POON Annette Ngar Ying • KOH Chun • WONG Tze Ming	2002-03	A Randomised Three-Arm Multi-Centre Comparison of 1 Year and 2 Years of Herceptin® versus no Herceptin® in Women with HER2-positive Primary Breast Cancer Who Have Completed Adjuvant Chemotherapy (MD02457)
2003-04	A Randomized, Open-Label, Parallel Group, International, Multicenter, Phase III Study of Oral ZD1839 (IRESSA®) Versus Intravenous Docetaxel (TAXOTERE®) in Patients with Locally Advanced or Metastatic Recurrent Non-Small Cell Lung Cancer Who Have Previously Received Platinum-Based Chemotherapy (MD03803)	2002-03	✍ YEO Winnie
	✍ MOK Shu Kam Tony • LAM Kwok Chi • HO Wing Ming • CHAN Chung Sau# • CHAK Yin Mui Karen	2002-03	Genetic and Epigenetic Study of RASSF1A Gene in Hepatocellular Carcinoma (CU02098)
			✍ YEO Winnie • JOHNSON Philip James • ZHONG Sheng#
		2002-03	Phase II Study of Gemcitabine/Carboplatin Combination Chemotherapy as First Line Therapy for Recurrent or Metastatic Breast Cancer (MD02630)
1997-98	High Dose Adjuvant Chemotherapy and Peripheral Stem Cell Transplant for High Risk Breast Cancer Patients (MD95266)		✍ YEO Winnie • MOK Shu Kam Tony • LAM Kwok Chi • HO Wing Ming • ZEE Chung Ying Benny (Community and Family Medicine) • CHAN Anthony Tak Cheung • LEUNG Wai Tong Thomas# • JOHNSON Philip James
	✍ YEO Winnie • KWAN Wing Hong • TEO Man Lung Peter • LEUNG Wai Tong Thomas# • SUEN Wang Ming Michael (Anatomical & Cellular Pathology) • KING Wing Keung Walter (Surgery)	2003-04	An Open-Label Phase IIa Trial Evaluating the Safety and Efficacy of EPO906 as Therapy in Patients with Advanced Local or Metastatic Gastric Cancer (MD03307)
1997-98	Randomized Trial of Tamoxifen versus Placebo for the Treatment of Inoperable Hepatocellular Carcinoma (MD97169)		✍ YEO Winnie • LAM Kwok C* • POON Annette*

2003-04 Predictors of Lymphedema and Quality
of Life in Breast Cancer Patients
Undergoing auxiliary Lymph Node
Dissection (MD03999)

✍ YEO Winnie • ZEE Chung Ying
Benny (Community and Family
Medicine) • MAK Suzanne* • LEE
Idy* • HO Fung Ping* • TSE Suet
Mun*

RESEARCH PROJECTS

Review of Mass Transit Railway Corporation Policy on Public Health and Hygiene and Its Implementation

✍ LEE Albert • CHENG YAM Fung Khing Frances (Centre for Health Ed. & Health Promotion)

☐ 1 November 2004

❖ Mass Transit Railway Corporation

This project has been commissioned by the MTR Corporation to review the corporation's policy on Public Health and its implementation.

The project investigator will review the documents provided and recommendations will be made based on the review, interview and observation made.

(MD04960)

Health Promoting School Programme

✍ LEE Albert • CHENG YAM Fung Khing Frances (Centre for Health Ed. & Health Promotion) • YUEN Suk Kwan (Centre for Health Ed. & Health Promotion)

☐ 1 December 2004

❖ Various Schools

The Health Promoting School Programme is a Project that is a sequel to the project "New Initiatives for School Based Management to Promote Healthy Educational Environments: The Hong Kong Healthy Schools Award Scheme (2000/2128)", which was sponsored by QEF and has now completed. On completion of this scheme the schools however felt the need of our services to provide continuing advice

and support so this programme will be set up to cater for any schools wishing to receive these services. As we do not have any further funding from QEF, these services will have to be fee-paying services. The services that the Centre aim to provide any health related programmes that the schools require to become a health promoting school. The scope of service includes but not limited to school audits, student surveys, conduct health educational or health-promoting events for school, act as advisor or consultant for school health curriculum.

As there is a wide variety of service to be provided, a budget cannot be provided. Moreover the services provide are rather ad hoc based on schools' invitation.

(MD04696)

Tung Chung Community Diagnosis Project

✍ LEE Albert • CHENG YAM Fung Khing Frances (Centre for Health Ed. & Health Promotion) • SIU Chi Hong, Damian (Centre for Health Ed. & Health Promotion) • FUNG Wing Yan (Centre for Health Ed. & Health Promotion) • WONG Wing Suen (Centre for Health Ed. & Health Promotion)

☐ 1 January 2005

❖ Occupational Safety and Health Council Research Grant

Objective:

To explore community safety and health problems and recommend any feasible solution via data collection, data analysis and survey study.

Study Design:

A cross-sectional study.

Methods:

Residents living in Tung Chung will be randomly sampled. Household survey will be conducted in order to understand Residents' quality of life.

Result:

The data collected in the study will provide a baseline data prior to develop relevant health promotion policies and campaign in the community. In addition, it will also serve as a programme evaluation tool for the Safe and Healthy Project.

(MD04390)

General Practice Management of Osteoarthritis

✍ LEE Albert • WONG Chi Wai • WONG Yeung Shan Samuel • TSANG Kwong Ka

□ 1 May 2005

❖ GlaxoSmithKline

The Family Medicine Unit of Department of Community and Family Medicine, Chinese University of Hong Kong has developed clinical guideline for primary management of 'lower limb osteoarthritis'. This project aims to:

- ◆ To study the knowledge of and attitudes to OA management amongst the primary care practitioners in Hong Kong
- ◆ To determine how the primary care practitioners manage and treat the patients with OA
- ◆ To study how the Hong Kong OA clinical guidelines' recommendations are implemented by primary care practitioners

(MD04469)

Community Development Approach to Create Better Health of our Young Generation within the Settings of Their Daily Life

✍ LEE Albert • CHENG YAM Fung Khing Frances (Centre for Health Ed. & Health

Promotion) • HO Man (Centre for Health Ed. & Health Promotion) • YUEN Wing Ki (Centre for Health Ed. & Health Promotion) • YUEN Suk Kwan (Centre for Health Ed. & Health Promotion)

□ 1 June 2005

❖ Health Care & Promotion Fund

It is a 2-year project aims to promote a healthy lifestyle in adolescents by community development approach and through providing a supportive school and home environment. It is proposed to establish a mentoring system in which 8 experienced Health Promoting Schools (HPS) in NT West (NTW) region will paired up with 8 apprentice schools to develop HPS which has been proven to be effective in reducing health problems and increasing the efficiency of education system. They will be trained, guided and supported by the applicant organization to become HPS. Parents training will be provided to reinforce health lifestyle of adolescents at home and in the community. Through the joint effort of schools, families and community, students will be empowered to adopt healthy lifestyles. A HPS network will be formed in the NTW and the model could be adopted in other regions so that more adolescents and also a wider community could be benefited.

(MD04356)

The Health Consequences and Economic Costs of Physical Abuse on Adolescents in China

✍ WONG Chi Wai • LEE Albert • TANG So Kum Catherine (Psychology) • Chen Wei-qing* • Ling Darvia*

□ 19 May 2005

❖ CUHK Departmental Funding

Interpersonal violence, such as the violence between family members, has significant negative social and economic impacts on developed and developing nations. Particularly for low- and middle-income countries, not only is interpersonal violence more prevalent, it also has more severe economic consequences. Unfortunately there are few studies on the economic effects of interpersonal violence in low- and middle-income countries. For China, due to cultural reasons, domestic violence and child abuse have been taboo subjects for a very long time. In this study, we aim to examine the long-term health, economic, and social impact of child abuse and to increase awareness and provide a multi-disciplinary analyses on this issue in China. We also aim to collaborate with schools in China in educating and training their staff to identify potential signs of family violence and to promote ways to intervene in culturally sensitive ways.

In this study, the economic costs we measure will include direct costs as well as indirect costs such as indirect productivity losses (from long-term mental health effects of child abuse) or “intergenerational productivity impacts” (e.g., grade repetition and lower educational attainment), psychological costs and costs of health problems in adulthood due to child abuse, as well as future criminality and subsequent incarceration as adults or adolescents. We hope that our study will shed light on this widespread issue not only in low- and middle-income countries, but may inform analyses in developed nations.

Before conducting the study, informed consent forms are distributed in schools for students to bring the forms back to obtain signatures from their parents in order for them to participate in the study.

(MD04860)

The Andropause in Chinese Men - A First Epidemiological Study

✍ WONG Yeung Shan Samuel • WOO Jean (Medicine & Therapeutics) • LYNN Sui Heng Henry (School of Public Health) • LEUNG Ping Chung (Orthopaedics & Traumatology)

☐ 1 November 2004

❖ CUHK Research Committee Funding (Direct Grants)

The andropause is a critical phase in life, when men undergo striking biological changes, so that many health problems will emerge. Nothing is known about the epidemiology of the andropause in Asian men. The objectives of this case-control study are to describe the prevalence of low testosterone levels, and its effects on the health of Chinese men aged 45-64. Predisposing factors to low testosterone levels and poor health during the andropause will also be explored.

Five hundred community dwelling middle aged to elderly men aged 45-64 have been recruited from a men's health survey project. Information on their andropause symptoms and lifestyle i.e. erectile dysfunction, depression, prostatism, cigarette smoking, alcohol consumption, medical history and physical activity has been collected as part of the project.

In this proposed study, two hundred and fifty men stratified by age and type of household (private versus public) will be invited to the clinics at the School of Public Health and their testosterone levels will be measured. Men with low testosterone levels (defined from cut off of reference range from the laboratory) will be defined as cases, with the rest as controls.

Symptoms obtained from the standardized questionnaires will be compared between “cases” and

“controls”. Moreover, risk factors for ‘low testosterone level’ will also be compared. The original proposal for the RGC grant calculated a sample size of 500 with a power of 0.99. With a sample size of 250, the power of the study will reduce to 0.96.

The results of this study are applicable to improving men’s health by dealing with testosterone deficiency and changes in lifestyle.

(MD04520)

Genitourinary Problems and Mood Disorders in Elderly Chinese Men - A First Epidemiological Cohort Study in Hong Kong

✍ WONG Yeung Shan Samuel • WOO Jean (Medicine & Therapeutics) • LYNN Sui Heng Henry (School of Public Health)

□ 4 February 2005

❖ Health & Health Services Research Fund

Purpose and Objectives

To investigate the prevalence, incidence and risk factors for Lower Urinary Tract Symptoms (LUTS), Erectile Dysfunction (ED) and depression, their relationship and impact on health status and quality of life in Hong Kong elderly men.

Design and Subjects

A large prospective cohort study entitled “Mr Os, Hong Kong” is being conducted by the investigators. Mr Os, Hong Kong is designed to study osteoporosis and its risk factors in Hong Kong Chinese men. For a cost-effective way to study men’s health, we propose to use this unique opportunity to study lower urinary tract symptoms, erectile dysfunction and depression in elderly Chinese men.

Study instruments

Urologic symptoms will be measured by the International Prostate Symptom Score (IPSS).

Erectile dysfunction will be measured by the validated Cantonese version of the International Scale of Erectile Function (IEFF-5). Depression will be measured by Geriatric Depression Scale (GDS). The Chinese version of the SF-12 will be used to measure quality of life.

Lifestyle risk factors to be studied are: cigarette smoking, alcohol consumption, coffee consumption, medical disorders (diabetes, hypertension and coronary artery diseases), physical activity, obesity and calorie and protein intake. These will be measured by a standardized questionnaire developed for this study.

Interventions

There will be no interventions.

Main outcomes and analysis

The incidence and prevalence of the three conditions and their association will be documented. In addition, multiple regression will be used to study the relationship between various risk factors and these disorders.

(MD04760)

Pearl-Postmenopausal Evaluation and Risk-Reduction with Lasofoxifene

✍ WONG Yeung Shan Samuel • WOO Jean (Medicine & Therapeutics) • LEUNG Ping Chung (Orthopaedics & Traumatology) • GRIFFITH James Francis (Diagnostic Radiology & Organ Imaging)

□ 1 June 2005

❖ Pfizer Corporation Hong Kong Limited

This is a multi-center prospective, phase-III, randomized, double-blind study of a new selection estrogen receptor modulator for treatment of osteoporosis. 168 patients have been recruited locally in Hong Kong. They have all completed the

first two years of visits. The compliance rate so far is very good with retention of 96%. The study duration was originally planned for 3 years but now has been extended to five years in total. We are now at the end of second year.

(MD04831)

Data Management Services for "Randomized Phase II Study to Investigate the Effects of Recombinant Intestinal Trefoil Factor (ITF) on Oral Mucositis in Patients Receiving Radiation Therapy for Nasopharyngeal Cancer with Protocol Number 2004-ITF-004"

✍ ZEE Chung Ying Benny

□ 1 July 2004

❖ The GI Company, Inc

Provide data management and analysis services for the Study.

(MD04927)

An Open Labeled, Randomized, Multicenter, Phase II Study to Determine Hemoglobin Dose Response, Safety and Pharmacokinetic Profile of Ro 50-3821 Given Subcutaneously Once Weekly or Once Every 3 Weeks to Anemic Patients with Stage IIIB or IV Non-Small Cell Lung Carcinoma Receiving Antineoplastic Therapy

✍ ZEE Chung Ying Benny

□ 2 October 2004

❖ Roche Pharmaceuticals & Chemicals Ltd

An open labeled, randomized, multicenter, phase II study to determine hemoglobin dose response, safety and pharmacokinetic profile of Ro 50-3821 given subcutaneously once weekly or once every 3 weeks

to anemic patients with stage IIIB or IV non-small cell lung carcinoma receiving antineoplastic therapy. (MD04877)

Quality of Life Analysis with Non-Ignorable Missing Data Using Pattern-Mixture Models with Generalized Estimating Equation (GEE) and Multiple Imputation (MI)

✍ ZEE Chung Ying Benny • MOK Shu Kam Tony
(Clinical Oncology)

□ 1 January 2005

❖ Research Grants Council (Earmarked Grants)

Quality of life (QOL) has now been incorporated in many cancer clinical trials as one of the important endpoints in addition to overall survival. Since QOL data is usually obtained through patients' self-administered questionnaire, missing items are common. In cancer trials, QOL is also likely to be affected by various critical clinical events such as treatment toxicity and progression. The whole questionnaire may be omitted when patients were hospitalized due to serious adverse event (SAE) or when disease progressed. This type of missing data is called "non-ignorable" in the statistical literature. The assumption that the missing data occurred at random is therefore no longer valid, and the conventional analysis could be seriously biased. In this study, we propose to use a pattern-mixture model approach to deal with the non-ignorable missing data problem, and develop a generalized estimating equation (GEE) model under this setting. We would also study the multiple imputation (MI) techniques under the pattern-mixture model using both analytic imputation based on GEE and a hot-deck imputation to select a close candidate to impute. The results of these methods will be validated and compared using simulated data with non-ignorable but known missing

data mechanism. A real clinical trial data set in non-small cell lung cancer will also be used to evaluate the performance of the proposed methods. (CU04291)

Data Management Service for the Study "Gemcitabine and Oxaliplatin (GEMOX) in First-Line Metastatic or Recurrent Nasopharyngeal Carcinoma (NPC)"

✍ ZEE Chung Ying Benny

☐ 15 March 2005

❖ Sanofi-Synthelabo Hong Kong Limited

To provide data management services (include planning and documentations, design of tables and listings, data management and preparation of statistical report) of a Single-arm, open labeled phase II clinical study entitled "GEMICITABINE AND OXALIPLATIN (GEMOX) IN FIRST-LINE METASTATIC OR RECURRENT NASOPHARYNGEAL CARCINOMA (NPC)" (MD04407)

Phase I Study on the Safety and Pharmacokinetics of IMD-1041 in Healthy Male Volunteers

✍ ZEE Chung Ying Benny

☐ 15 April 2005

❖ Institute of Medicinal Molecular Design Inc.

The purpose of this phase I clinical study is to study whether an experimental drug, IMD-1041, is safe for use in human beings and the length of time that IMD-1041 will stay in human body. IMD-1041 is developed by Institute of Medicinal Molecular Design Inc. (IMMD), Japan, for the treatment of heart failure following myocardial infarction. It has

been shown to be safe in animals, but not yet in humans.

In this study, 32 healthy male volunteers will be assigned to receive 4 different doses (50, 150, 300, 600mg) of IMD-1041. The study will proceed to a higher dose level only after the safety of the previous group receiving lower dose is confirmed by the investigator. The safety of each dose will be learned by performing routine clinical examinations and the length of time each dose will stay in the body will be learned by measuring plasma and urine IMD-1041 concentration after dosing.

(MD04402)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
2000-01	Effects of Phytoestrogens on Calcium Metabolism in Chinese Postmenopausal Women (CU00162) ✍ HO CHAN Suzanne • John J Anderson* • LEE Simon K. M.* • WOO Jean (Medicine & Therapeutics) • YU Jimmy C. (Chemistry)
2002-03	A Study of the Prevalence of Subclinical Atherosclerosis and the Associated Risk Factors in Early Postmenopausal Chinese Women in Hong Kong (MD02374) ✍ HO CHAN Suzanne • WOO Kam Sang (Medicine & Therapeutics) • WOO Jean (Medicine & Therapeutics) • CHAN Sieu Gaen# • HO Sin Yee Stella (Diagnostic

	Radiology & Organ Imaging) • LAM Wai Kei Christopher (Chemical Pathology) • AHUJA Anil Tejbhan (Diagnostic Radiology & Organ Imaging)	2003-04	Provision of Population Health Survey - Second Module on Cardiovascular Disease and Risk Factor (MD03481) ✍ HO CHAN Suzanne • WOO Jean (Medicine & Therapeutics)
2002-03	A Study of Informal Caregivers and Association of Caregiving Status with Health and Quality of Life (MD02923) ✍ HO CHAN Suzanne • WOO Jean (Medicine & Therapeutics) • LAU Tak Fai Joseph (Centre for Epidemiology & Biostatistics) • CHAN C M Alfred*	1998-99	“Healthy Schools” and “Healthy Society”: Quality Education for Children and Teachers (MD98068) ✍ LEE Albert • LEE Shiu Hung • TO Cho Yee (Psychology)
2003-04	Effects of Soy Isoflavones Supplementation on Cognitive Function in Chinese Postmenopausal Women : A Double-Blind Randomized Controlled Trial (CU03471) ✍ HO CHAN Suzanne • CHAN Sui Yin Agnes (Psychology) • HO Yee Ping (School of Pharmacy) • WOO Jean (Medicine & Therapeutics) • ZEE Chung Ying Benny	2000-01	New Initiatives for School Based Management to Promote Healthy Educational Environments: The Hong Kong Healthy Schools Award Scheme (MD00896) ✍ LEE Albert • LEE Shiu Hung • TO Cho Yee (Psychology)
2003-04	Adolescent and Adult Soy Intake and Breast Cancer Risk in Chinese Pre-Menopausal Women (MD03666) ✍ HO CHAN Suzanne • WOO Jean (Medicine & Therapeutics) • CHU Chiu Wing Winnie (Diagnostic Radiology & Organ Imaging) • YEO Winnie (Clinical Oncology) • TANG Leung Sang Nelson (Chemical Pathology) • LAU Tak Fai Joseph (Centre for Epidemiology & Biostatistics)	2003-04	21st Century Hong Kong, a Health Promoting Society: A Territory Wide Community Participation in Promoting Health (MD03863) ✍ LEE Albert • CHENG YAM Fung Khing Frances (Centre for Health Ed. & Health Promotion)
		2003-04	Professional Development Program for Primary Care Practitioners (MD03795) ✍ LEE Albert • CHENG YAM Fung Khing Frances (Centre for Health Ed. & Health Promotion) • YUEN Suk Kwan (Centre for Health Ed. & Health Promotion) • HO Man (Centre for Health Ed. & Health Promotion) • SIU Chi Hong, Damian (Centre for Health Ed. & Health Promotion) • YUEN Wing Ki

	(Centre for Health Ed. & Health Promotion)		✍ WONG Tze Wai • LAU Kai Hon Alexis* • LOH Kung Wai Christine*
2003-04	Study on Quality of Life on Carers of Childhood Asthma (MD03692) ✍ LEE Albert	2003-04	A Review of Air Pollutants and Health Effects in Hong Kong and the Asia Pacific Region (MD03881) ✍ WONG Tze Wai
2003-04	Evidence Based Primary Care: Management Guidelines for Osteoarthritis in Primary Care Setting (MD03823) ✍ LEE Albert • WONG Chi Wai • WONG Yeung Shan Samuel • TSANG Kwong Ka	2001-02	Postmenopausal Evaluation And Risk Reduction with Lasofoxifene (PEARL) (MD01823) ✍ WONG Yeung Shan Samuel • WOO Jean (Medicine & Therapeutics) • LEUNG Ping Chung (Orthopaedics & Traumatology) • CHAN Wan Kin
2003-04	Programme for Extended Courses on "Health Promoting School" to School Heads and Teachers (ED03838) ✍ LEE Albert • CHENG YAM Fung Khing Frances (Centre for Health Ed. & Health Promotion)	2003-04	Improving General Practitioners' Interviewing Skills in Managing Patients with Common Psychiatric Problems in Primary Care: A Randomized Clinical Trial (MD03945) ✍ WONG Yeung Shan Samuel • LEE Albert • WONG Chi Wai
2003-04	A Randomized Controlled Trial to Evaluate the Credibility of a Sham Placebo Acupuncture Design (MD03557) ✍ TANG Jinling	2002-03	Female Lung Cancer and Cooking Practice - A Case-Control Study in Hong Kong (CU02103) ✍ YU Tak Sun Ignatius • CHIU Yuk Lan • TANG Jinling • WONG Tze Wai
2002-03	TROHI Project on Statutory Medical Examination in Occupational Health (MD01678) ✍ WONG Tze Wai • YU Tak Sun Ignatius • LAM Tai Hing* • LEUNG Lai Man Raymond* • LO Wai Kee*	2003-04	Male Lung Cancer, Occupational Exposures and Smoking - A Case-Control Study in Hong Kong (CU03460) ✍ YU Tak Sun Ignatius • TSE Lap Ah (School of Public Health) • WONG Tze Wai
2003-04	Assessment of Toxic Air Pollutant Measurements in Hong Kong - An Extended Study (MD03450)		

2003-04	Multivariate Dependencies Approach in the Prognostic Modelling of Microarray Data Based on CGH Information in Hepatocellular Carcinoma (HCC) (CU03469) ✍ ZEE Chung Ying Benny • WONG Nathalie (Anatomical & Cellular Pathology) • LEUNG Wai Tong Thomas (Clinical Oncology)#	Receptor Positive Breast Cancer (MD03379) ✍ ZEE Chung Ying Benny
2003-04	Protocol Development for a Randomized Clinical Trial to Evaluate the Safety and Efficacy of Letrozole in the Treatment of Premenopausal Women with Hormone	Data Management Services for the Study "A Multicentre Double-Blind Double-Dummy Randomized Controlled Trial Comparing the Efficacy and Safety of the Vira-38 versus Oseltamivir in Patients with Acute Influenza" (MD03637) ✍ ZEE Chung Ying Benny

RESEARCH PROJECTS

Magnetic Resonance Ventilation Scan for Obstructive Airways Disease

✍ ANTONIO Gregory • HUI Shu Cheong David
(Medicine & Therapeutics) • WONG Ka Tak
Jeffrey

☐ 1 July 2004

❖ Research Grants Council (Earmarked Grants)

Chronic obstructive airways disease (COAD) which is linked to smoking affects a significant proportion of the population and is a major contributor to the general morbidity and mortality. Various tests for lung function are available.

Lung ventilation is the measure of air moving to of various parts of the lungs. This is abnormal in patients with COAD.

Radiological imaging tests are used to show the distribution of inspired air to different parts of the lungs. This presently requires inhaling radioactive material (nuclear medicine ventilation scan) and is considered the gold standard.

Recently, there have been breakthroughs in Magnetic Resonance Imaging (MRI). It is now possible to image the amount of gas (in this case, Non-radioactive oxygen) inhaled by a person with a fast MRI scan. The benefit of a faster, “no radiation” scan for lung ventilation to the huge population of lung disease patients is obvious.

The magnetic resonance scanner in our institute will be upgraded in November 2003 to become the most advanced scanner of its kind in Asia and will be able to perform this test. The present proposal concerns a clinical trial on the accuracy of this MRI test on patients with COAD.

(CU04296)

Kinematics of the Osteoporotic Spine

✍ GRIFFITH James Francis • Raymond Lee* •
Malcolm Pope*

☐ 1 November 2004

❖ Research Grants Council (Earmarked Grants)

Osteoporosis is a worldwide public health problem, but there is currently a lack of understanding of how it may affect the kinematics of the spine which will lead to serious functional impairment. The purpose of the study is to examine the kinematic characteristics of lumbar spines with different degree of osteoporosis and to develop a simple and non-invasive method of determining such characteristics using skin-mounted electromagnetic sensors. Motions of the trunk of 90 elderly subjects will be measured using radiographic images and skin-mounted sensors. The lumbar spine will be represented by a kinematic model (a five-link open kinematic chain) using geometrical data obtained from the radiographic images. The motions of each link of the chain will be computed. The total motions of the chain (the motions of the end effector) will be derived from the radiographic images and the sensor data. These values will be compared so as to determine the feasibility of the skin sensor method. The differences in the kinematic characteristics among spines of different degree of osteoporosis will be determined. The relationship between the kinematic variables and the morphological features of the spine will be established.

(EE04301)

Functional Magnetic Resonance Imaging of Osteoporosis

✍ GRIFFITH James Francis • ANTONIO Gregory
• YEUNG Ka Wai David* • WONG Yeung Shan Samuel (Community and Family Medicine)
• LEUNG Ping Chung (Orthopaedics & Traumatology)

□ 1 November 2004

❖ CUHK Research Committee Funding (Direct Grants)

Recent advances in MR imaging have enabled physiological or functional information to be obtained in addition to morphological data. MR diffusion, perfusion and spectroscopy are functional techniques now routinely used in assessment of neurological, cardiac and liver disorders. However, these functional techniques have not been developed for use in the evaluation of osteoporosis.

Bone demineralization is a complex process involving changes in microcirculatory blood flow, metabolism of bone cells and structure of bone matrix. It is likely that diffusion, perfusion and metabolic changes associated with osteoporosis can be evaluated with functional MRI. Current techniques such as CT and bone densitometry used in the evaluation of osteoporosis assess only the end-result of osteoporosis (i.e. reduced bone density), do not pre-empt osteoporosis and provide little or no information regarding underlying pathophysiology.

The aim of this study is to apply functional MR imaging techniques to evaluate physiological changes associated with osteoporosis. Measurements will be performed at the L1 vertebrae in four groups of 25 men (with normal bone density, reduced bone density, osteoporosis and severe osteoporosis respectively). Bone density status will be determined on DEXA imaging within one month of MRI examination.

Perfusion MR imaging shall provide a measure of microcirculatory blood flow in the vertebral body. MR diffusion data shall provide a measure of molecular diffusion while proton MR spectroscopy shall provide a measure of percentage fat within the vertebral body. Functional MRI data shall be directly related to the degree of bone loss (as determined by DEXA examination).
(MD04693)

Prospective Randomised Study of Endovenous Radiofrequency Obliteration (Closure Procedure) Versus Ligation and Stripping in the Treatment of Varicose Veins in a Hong Kong Chinese Population

✍ HO Sze Ming Simon • LAU Yun Wong James (Surgery) • HO Sin Yee Stella • LEUNG Yee Fong

□ 2 January 2005

❖ CUHK Research Committee Funding (Direct Grants)

Varicose veins are common and problematic, and are frequently related to incompetence of saphenofemoral junction and saphenous vein reflux. Ligation and stripping has been the standard for treatment. It is generally believed that symptomatic varicose veins are best treated with removal of the greater saphenous vein from the saphenofemoral junction to the level of the knee or below, along with individual ligation of the saphenous branches. Until recently, ligation and stripping has had the highest initial success and lowest recurrence rate.

A new technique has been developed for the management of saphenous vein reflux which uses a radiofrequency (RF) generated heating probe placed through a percutaneous saphenous vein puncture under ultrasound guidance to obliterate the saphenous

vein. This is known as the Closure procedure and the initial results from two randomised studies comparing its use with ligation and stripping are encouraging. There were no serious complications from the Closure procedure, and patients from the RF obliteration group returned to work earlier.

We plan to bring the Closure procedure to Hong Kong, and the current study is designed to compare the safety and efficacy of this new technique with ligation and stripping in the Hong Kong Chinese population.

(MD04317)

Squamous Cell Carcinoma of the Head and Neck: Can In Vivo Proton Magnetic Resonance Spectroscopy (¹H-MRS) Predict and Monitor Therapeutic Response?

✍ KING Ann Dorothy • AHUJA Anil Tejbhan • YEUNG Ka Wai David • YUEN Hok Yuen# • YU Kwok Hung (Clinical Oncology) • TSE Man Kit Gary (Anatomical & Cellular Pathology)

□ 1 January 2005

❖ Research Grants Council (Earmarked Grants)

Head and neck cancer caused by squamous cell carcinoma accounts for approximately 3% of cancers annually in Hong Kong. There have been important advances in the management of head and neck cancer as a result of better imaging techniques to localize and stage cancer prior to surgery. More recently there has been a trend to treat patients with advanced cancer with organ preserving radiotherapy or radiochemotherapy. However, in order to improve the outcome of treatment for these patients, a diagnostic tool is required to predict and monitor the therapeutic response. A test to predict therapeutic response would lead ultimately to a reduction in the amount of treatment for sensitive cancers, while more

resistant cancers could be treated at the outset by more aggressive therapies. A test applied early during a course of treatment to monitor the response to treatment potentially could identify non-responders earlier thereby enabling a prompt change in the treatment regime. These issues are important because radiotherapy and chemotherapy have not only beneficial effects on cancer but also harmful effects on the normal tissues. Proton magnetic resonance spectroscopy (¹H-MRS) is a non-invasive technique that provides information on the cellular metabolism of cancers. It is a technique that can be performed in conjunction with the conventional MR scan that is used to routinely to image and stage the cancer. We propose to evaluate ¹H-MRS in order to determine if it is a useful clinical test for predicting and monitoring the therapeutic response of head and neck squamous cell carcinoma.

(CU04300)

Remodeling and Plaque Composition of Middle Cerebral Artery: Its Significance in Development of Thrombotic and Embolic Stroke in Patients with Middle Cerebral Artery Stenosis

✍ LAM Wai Man Wynn • WONG Ka Sing Lawrence (Medicine & Therapeutics) • CHU Chiu Wing Winnie

□ 1 May 2005

❖ CUHK Research Committee Funding (Direct Grants)

In Hong Kong, stroke is the commonest cause of death after cancer and ischaemic heart disease. It also causes disability in thousands of people every year. Stroke in Chinese is unique, in which intracerebral artery stenosis, rather than extracranial carotid stenosis, accounts for the pathophysiology. Our previous RGC funded researches have

documented a 50% incidence of middle cerebral artery disease in acute stroke Chinese patients. We have also detected a correlation of microembolic signal (MES) diagnosed by transcranial doppler and the number of acute infarcts diagnosed by diffusion weighted images of MRI. In our RGC funded projects, we have also found an association of MES and an increased risk of recurrent stroke. Our previous research findings therefore indicate two major mechanisms in stroke in Chinese: progress in stenosis in middle cerebral artery causing atherosclerotic thrombotic infarcts and continuous embolization from middle cerebral artery plaques causing embolic infarcts. We propose to assess the middle cerebral artery by high resolution MRI. The aim of the study is to: 1. To investigate the remodeling in stenosed middle cerebral artery so as to further our understanding in thrombotic infarcts and 2. To delineate and characterise the middle cerebral artery plaque which are associated with embolic infarcts. The results of this study may allow choice of the optimal treatment for two different mechanisms of acute ischaemic stroke in Chinese. (MD04753)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

Edition Title/Investigators

2003-04 The Effect of Rigid Underarm Brace on the Correction of Spinal Curve in Idiopathic Adolescent Scoliosis during Sleeping (MD03341)

✍ CHU Chiu Wing Winnie • LAM Wai Man Wynn • CHENG Chun Yiu Jack (Orthopaedics & Traumatology) • NG B K W* • LAM T. P.* • WONG M S*

2002-03 Proton Magnetic Resonance Spectroscopy (¹H-MRS) for the Investigation of Extracranial Head and Neck Cancers (MD02539)

✍ KING Ann Dorothy • LAM Sik Lok (Chemistry) • AHUJA Anil Tejbhan • VAN HASSELT Charles Andrew (Surgery) • CHAN Bik Wan (Anatomical & Cellular Pathology) • TSE M K Gary* • YEUNG Ka Wai David*

2003-04 Radio-Frequency Ablation for Better Quality of Life (MD03435)

✍ LEE Sing Fun Paul • HO Sze Ming Simon • LEUNG Sing Fai (Clinical Oncology) • CHAN Lung Wai (Surgery)

2003-04 Prevention and Treatment of Ischaemic Stroke by Endovascular Stenting of Intracranial Vascular Stenosis (MD03571)

✍ YU Chun Ho • WONG Ka Sing Lawrence (Medicine & Therapeutics) • LAM Wai Man Wynn • POON Wai Sang (Surgery)

RESEARCH PROJECTS

Mechanisms of Action of Potential Alzheimer's Disease Drug Curcumin, an Extract of *Geung Wong*

✍ BAUM Lawrence William • NG Ho Keung (Anatomical & Cellular Pathology) • CHUI Yiu Loon (Clinical Immunology Unit)

☐ 1 November 2004

❖ Research Grants Council (Earmarked Grants)

Alzheimer's disease (AD) is a common cause of disability and death, affecting 2-16% of people over 65. Inflammation, oxidation, and A β amyloid peptide toxicity are possible paths by which AD destroys the brain. Curcumin, a food coloring from *geung wong*, reduces amyloid deposition, brain pathology, and memory impairment in AD animal models, but the mechanism is unknown. We will test several likely mechanisms by which curcumin may act. Curcumin inhibits JNK, a kinase that transduces amyloid neurotoxicity. Similar kinases, GSK3 and CDK5, also transduce amyloid toxicity, thus we will investigate whether curcumin inhibits them in SH-SY5Y neuronal cells and AD model transgenic mice. Zinc, copper, and iron accumulate in AD brain and can aggregate amyloid. Chelators can prevent aggregation in animals. Curcumin binds metals, therefore we will determine curcumin's affinity for metals and ability to prevent amyloid aggregation. ApoE can induce amyloid formation. ApoE secretion requires prenylation, which curcumin inhibits. Thus, we will test whether curcumin decreases ApoE in SH-SY5Y cells and transgenic mice. PPAR γ reduces A β neurotoxicity. Curcumin activates PPAR γ in hepatic cells, thus we

will test whether curcumin activates PPAR γ in SH-SY5Y cells, monocytes, and transgenic mice. LRP expression may reduce A β levels. PPAR γ increases LRP expression in adipocytes, thus we will measure the effect of curcumin on LRP level in SH-SY5Y cells and transgenic mice. Determining which of these mechanisms are relevant to inhibition of AD by curcumin would shed light on AD etiology, help in design of clinical trials of curcumin, and suggest new, specific AD drugs.
(CU04302)

A 24-Week Randomized, Double-Blind, Double-Dummy, Multicentre Study to Compare the Efficacy or Extended Release AVANDIA® (8mg OD) and Immediate Release AVANDIA® (8mg OD) in Subjects with Type 2 Diabetes Mellitus

✍ CHAN Chung Ngor Juliana • CHAN W. B.* • Chan Norman*

☐ 1 August 2004

❖ Glaxo Smith Kline Ltd.

The purpose of this study is to demonstrate the statistical superiority of AVANDIA XR 8mg OD when compared to AVANDIA IR 8mg OD with respect to mean change from baseline in HbA_{1c} after 24 weeks of double-blinded treatment in type 2 diabetes mellitus subjects. This study is designed with a 1-week pre-screening period and a 2-week screening/washout period followed by a 4-week single-blind run-in period. The 24-week double-blind treatment will include subjects receiving AVANDIA IR 8mg once daily or XR 8mg once daily. Subjects with type 2 diabetes must have been treated with either diet and exercise (drug naive) (HbA_{1c} of ≥ 7.5 to $\leq 11\%$), prior monotherapy (HbA_{1c} of ≥ 7 to \leq

10%), or combination therapy ((HbA_{1c} of ≥ 6.5 to $\leq 10\%$) to be eligible for the study.

(MD04331)

A 52-Week Randomized, Double-Blind, Parallel-Group, Multi-Centre, Active-Controlled (Glibenclamide) Study to Evaluate the Efficacy, Safety and Tolerability of Tesaglitazar Therapy when Administered to Patients with Type 2 Diabetes

✉ CHAN Chung Ngor Juliana • TONG Peter Chun Yip • CHAN Wing Bun • OSAKI Risa*

□ 1 September 2004

❖ AstraZeneca Hong Kong Limited

This is a 52 week phase 3 multicentre randomized clinical study to compare the effects of tesaglitazar monotherapy versus glibenclamide monotherapy in modifying lipids and lipoproteins in patients with type 2 diabetes. Tesaglitazar is a new class of antidiabetic drug called PPAR α /dual agonist which has both lipid and glucose lowering effects. Given the important role of glucotoxicity and lipotoxicity in the progression of β cell function and vascular complications, this new class of agents, if proven safe and effective, will provide additional benefits to these high risk patients in term of metabolic control and eventually vascular protection. Men or women who are ≥ 18 years of age diagnosed with type 2 diabetes and treated with diet alone or on treatment with a single oral anti-diabetic agent or low doses of two agents receive advice on lifestyle modification and randomised in a double blind manner to receive either tesaglitazar, 0.5 mg increasing to 1 mg once daily or glibenclamide 2.5 increasing to 5, 10 and 15 mg with matching placebo tablets and followed up for a total of 52 weeks. The primary endpoint is reduction in

HbA_{1c} and the secondary endpoints are other parameters of the metabolic syndrome.

(MD04482)

A Multicenter, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of MK-0431 Monotherapy in Patients with Type 2 Diabetes Mellitus Who Have Inadequate Glycemic Control

✉ CHAN Chung Ngor Juliana • CHAN Wing Bun • SO Wing Yee • LAU Wing Yan • CHENG Yuen Shan Angela

□ 1 October 2004

❖ Merck Research Laboratory

Following a meal, incretins, gut-derived hormones, are released into the circulation, leading to enhanced insulin secretion in a glucose-dependent fashion. Two such factors, Glucagon-like peptide-1 (GLP-1) and Gastric Inhibitory Peptide (GIP), are believed to account for the majority of the incretin response. In some studies, the incretin response is modestly impaired in patients with T2DM; however, the response to GLP-1 appears to be intact. Other mechanisms which mediate the glucose-lowering effect of GLP-1 include inhibition of glucagon release, reduction in the rate of gastric emptying, reduction in food intake, and increased insulin sensitivity. Two strategies have been applied to utilize the incretin axis to treat patients with T2DM: first, treating with GLP-1, either with chronic infusions or with analogues with diminished clearance, and, second, inhibiting DP-IV, the enzyme that inactivates and clears both GLP-1 and GIP. By inhibiting DP-IV, the half-life and, consequently, the plasma concentrations of active GLP-1 and GIP are increased. MK-0431 is an orally active, potent, and selective DP-IV inhibitor which has demonstrated potent and selective DP-IV inhibition, augmentation

of active GLP-1 concentrations, and glucose-lowering effects in diabetic animal models. The present study will examine the safety and efficacy of monotherapy MK-0431 in patients with T2DM who have inadequate glycemic control on diet and exercise after treatment with 24 weeks with the primary endpoint as reduction in HbA_{1C}.

(MD04662)

Development of a Statistical Model to Predict Risk and Assess Effects of Targeted Treatment on Diabetic Complications Using A Diabetes Registry

✍ CHAN Chung Ngor Juliana • TONG Peter Chun Yip • KONG Pik Shan • SO Wing Yi *

□ 12 December 2004

❖ Merck Sharp & Dohme (Asia) Ltd

Diabetes is now the leading cause of cardiovascular and kidney diseases, which account for more than 50% of premature mortality and morbidity in developed countries. The majority of diabetic patients have multiple risk factors, which give rise to widespread vascular damage. Since 1995, as part of a continuous quality improvement program, the Prince of Wales Hospital (PWH) has established a Diabetes Registry documenting all complications, risk factors and utilisation of health care resources in newly referred patients using structured protocols. On average, 30-50 patients are enrolled weekly and to date, more than 15,000 records from 7000 patients are available on this database.

In this study, we aim to develop a user-friendly statistical model to compute the risk of all-cause and cardiovascular mortality as well as end stage renal disease (ESRD) based on patients' baseline demographics and risk factors. The effects of attaining treatment goals and appropriate drug use on

clinical outcomes will also be examined. In light of the rising diabetic population in China estimated to be 40 million, these clinical data will greatly improve our understanding of the natural history of diabetes in Chinese. Since many of these patients remain undiagnosed, unmanaged or suboptimally managed, this predictive model with particular emphasis on risk profiling and cost-effective use of medications should also allow patients, health care providers and payers to formulate the most appropriate and cost-effective treatment strategy to preserve health and quality of life in these high risk subjects.

(MD04680)

A Multicenter, Randomized, Double-Blind Study to Evaluate the Safety of MK-0431 Monotherapy in Patients with Type 2 Diabetes Mellitus and Chronic Renal Insufficiency Who Have Inadequate Glycemic Control

✍ CHAN Chung Ngor Juliana • KONG Pik Shan • CHAN W. B.*

□ 1 February 2005

❖ Merck Sharp & Dohme (Asia) Ltd

This is a multinational, randomized, double-blind, parallel-group study. The duration of the study will be up to 69 weeks (with 14 visits) for each patient. Chronic renal insufficiency patients who are ≥ 18 years of age with type 2 diabetes mellitus (T2DM) who are either: (1) not on antihyperglycemic medication (off for ≥ 8 weeks); or (2) on a single antihyperglycemic agent; or (3) on a low dose dual oral combination agent therapy (i.e., at $< 50\%$ of maximal dose of both components) may participate if they meet enrollment criteria. At Visit 4/Day 1, patients who meet the study enrollment criteria will enter Phase A of the double-blind treatment period. They will be randomized to receive once-daily

administration of MK-0431 or placebo in a 2:1 ratio. At Visit 7/Week 12, patients will enter Phase B of the double-blind treatment period. Patients in the placebo treatment group in Phase A will receive glipizide 5 mg (or a lower dose, at the option of the investigator). MK-0431 is an orally active, potent, and selective DP-IV inhibitor being developed for the treatment of patients with T2DM. MK-0431 is an agent that both enhances insulin secretion and lowers hepatic glucose production by suppressing glucagon with elevated active glucagons like peptide (GLP-1) levels which may promote beta cell neogenesis. Thus, MK-0431 has the potential to improve glycemic control through this new mechanism of enhancement of the incretin-axis and beta cell protection. Through this phase 2 multicentre clinical trial, both patients and investigators will have first hand experience with this new class of agent while allowing patients to receive the best of care during a clinical trial setting.

(MD04795)

A Phase III, 18 Month, Multicenter, Randomized, Double-Blind, Active-Controlled Clinical Trial to Compare Rosiglitazone versus Glipizide on the Progression of Atherosclerosis in Subjects with Type 2 Diabetes Mellitus and Cardiovascular Disease

✍ CHAN Chung Ngor Juliana • CHAN W. B.* • KONG Pik Shan • SANDERSON John Elsby# • CHAN Wai Man Wilson • Chan Norman*

☐ 1 March 2005

❖ Glaxo Smith Kline

This a an 18-month, multicenter, randomised, double-blind, active-controlled clinical trial to evaluate the effect of rosiglitazone vs. glipizide on the progression of atherosclerosis in subjects with

type 2 DM and cardiovascular disease. More than 600 patients from 100 cities all over the world will be randomised. Type 2 diabetic patients who undergo coronary angiography or percutaneous coronary angiogram will undergo intravenous ultrasound (IVUS) in one of the non-intervened coronary blood vessels before being randomized to receive either rosiglitazone or glipizide. The primary endpoint is the volume of atheroma in the non-intervened vessel after 18 months of therapy. At least 10 patients or more will be recruited from the PWH and managed jointly by the Endocrine and Cardiology Teams at the CUHK-PWH and Qualigenics Diabetes Centre. This study will provide major insights into the possible independent effects of PPAR_γ agonist on progression of atherosclerosis in a high risk population for coronary heart disease.

(MD04363)

A Multidisciplinary Project to Identify Major Genes for Diabetes and Metabolic Syndrome in Chinese and to Assess Its Functional Significance

✍ CHAN Chung Ngor Juliana • TONG Peter Chun Yip • ZEE Benny (Clinical Oncology)* • LEUNG Po Sing (Physiology) • WAYE Mary Miu Yee (Biochemistry) • Maggie CY Ng* • SO Wing Yee

☐ 1 June 2005

❖ RGC-Central Allocation Scheme - Group Research • Supplementary Funding for RGC Central Allocation

There is now a burgeoning epidemic of diabetes and obesity which account for 30-50% of heart disease, stroke and kidney failure. Genetic factors and aging interact with rapid changes in lifestyle to give rise to this complex syndrome, now often referred as the metabolic syndrome. Since 1995, the CUHK

Diabetes Care and Research Group, supported by a series of competitive grants, and in collaboration with the University of Chicago, led by Professor G Bell and N Cox, has initiated the Hong Kong Chinese Diabetes Family Study to use the genome scan approach to search for diabetes genes using family-based cohorts and large unrelated case-control cohorts with deep phenotyping. We have recently identified several chromosomal regions including chromosome 1, 2 and 16 with strong signals linked to diabetes and all traits related to metabolic syndrome. In this proposal, we aim to combine the 2 Chinese genome scans performed in Hong Kong and Shanghai to fine map these chromosomal regions for identification of positional and candidate genes. In collaboration with HKU Genome Centre, we shall use *state of the art* high throughput genotyping techniques as well as capitalize on the publicly available bioinformatics including the haplotype map (HAPMAP) and high density SNP map (dbSNP) databases to validate disease-related SNPs and their haplotypes. This genetic information, which is of particular relevance to Chinese population, will open up novel physiological pathways to improve our understanding of these complex diseases to improve diagnosis and treatment

(MD04484)

Endoscopic Evaluation of the Incidence and Etiology of Lower Gastrointestinal Bleeding in Patients with Melena

✍ CHAN Ka Leung Francis • LEUNG Wai Keung
• SUNG Joseph Jao Yiu

☐ 1 October 2004

❖ Pfizer Inc.

Although tarry stool is a common feature of peptic ulcer bleeding, it can also be a manifestation of lower

gastrointestinal (GI) bleeding. Examples include colonic cancer, small bowel tumors, and small or large bowel ulcers induced by aspirin or painkillers (NSAIDs). However, clinicians are often misled by the finding of peptic ulcers as the source of GI bleeding. It is not uncommon to detect peptic ulcers incidentally but the source of bleeding is actually in the lower GI tract. Delay in diagnosis of lower GI bleeding often leads to serious consequences. The preferred investigations for lower GI bleeding are colonoscopy plus video capsule endoscopy. Colonoscopy has been the gold standard for the diagnosis of colonic bleeding. Video capsule endoscopy is a noninvasive, safe and accurate technology that has been approved by the FDA for investigation of small bowel diseases. The video capsule is an 11 x 26mm capsule that encases a digital camera, light-emitting diodes, batteries, and a transmitter. The patient needs to swallow the video capsule after an overnight fast and wear a recording device for eight hours. Images are taken twice-per-second and transmitted to the recording device. Oral feeding can be resumed after four hours. The swallowed capsule will be expelled naturally after 5 to 12 hours virtually in all patients. The risk of capsule retention is very low and only occurs in patients with severe small bowel stricture. This study aims to assess the incidence and etiology of lower GI bleeding in patients presenting with tarry stool. The result will provide important information about the magnitude of the problem of lower GI bleeding that will improve our patient care.

(MD04705)

Cytokine Gene Polymorphism and Liver Fibrosis in Chronic Hepatitis B

✍ CHAN Lik Yuen • SUNG Joseph Jao Yiu • LIEW Choong Tsek (Anatomical & Cellular Pathology)

□ 1 September 2004

❖ Research Grants Council (Earmarked Grants)

Recent studies suggest that human genetic makeup regulating cytokine production affects the severity of liver injury in several liver diseases including chronic hepatitis C, primary biliary cirrhosis and alcoholic liver disease. Liver fibrosis is the wound healing response and its severity reflects the degree of liver damage. Chronic hepatitis B is the commonest cause of liver disease in this locality with a wide range of presentations from inactive liver disease to liver cirrhosis. Our extensive research work in the past have found that viral factors alone cannot explain the divergence of disease presentations in chronic hepatitis B, but the impact of human genetic makeup has never been studied. We plan to study the association of the genotypes of several pro-inflammatory and fibrogenic genes and the severity of liver fibrosis in chronic hepatitis B. The results of this study will improve the understanding of host influence on the natural history of chronic hepatitis B and will be useful for risk stratification and patient monitoring in the management of this condition.

(CU04304)

A Randomized, Open Label Trial of Telbivudine (LdT) versus Adefovir Dipivoxil in Adults with Compensated Chronic Hepatitis B

✍ CHAN Lik Yuen • HUI Yui • WONG Wai Sun • SUNG Joseph Jao Yiu

□ 1 November 2004

❖ Idenix Pharmaceuticals, Inc

This is a multi-center, open labeled study comparing the anti-viral efficacy of 1-year treatment of telbivudine versus adefovir dipivoxil in the treatment of HBeAg-positive chronic hepatitis B. Patients are randomized into one of the following 3 treatment arms: telbivudine x 52 weeks, adefovir x 24 weeks followed by telbivudine x 28 weeks and adefovir x 26 weeks. The primary endpoint will be HBV DNA suppression at week 24. Treatment will be stopped at the end of one year for sustained response.

(MD04746)

Serum Genomic Markers of Hepatitis B Virus for Hepatocellular Carcinoma

✍ CHAN Lik Yuen • TSUI Kwok Wing (Biochemistry) • MOK Shu Kam Tony (Clinical Oncology) • SUNG Joseph Jao Yiu

□ 1 January 2005

❖ Michael Kadoorie Cancer Genetics Research Programme

Chronic hepatitis B is the commonest cause of hepatocellular carcinoma (HCC) in Hong Kong. In a previous case-control study, we have performed complete genome sequencing of hepatitis B virus (HBV) for 100 HCC patients and 100 non-HCC chronic hepatitis B controls. Several genomic markers that can predict HCC development have been identified. An algorithm based on the genetic markers with an over 75% accuracy of predicting HCC has been developed. In this study, we aim to validate the genomic algorithm with a prospective longitudinal cohort of 1000 patients who have participated in a HCC surveillance program since 1999. All patients have complete database and serial serum samples stored. We plan to investigate the HCC genomic markers in the serial serum samples to validate the accuracy of HCC prediction

as well as the timing of emergence of these mutations. The validation of this potentially useful molecular tool may revolutionize the clinical strategy of HCC surveillance. The results of this study can also improve the understanding of the carcinogenic mechanisms of HBV.

(MD04701)

A Randomized, Blinded, Phase IIB Trial of Telbivudine (LdT) versus the Combination of Telbivudine and Valtorcitabine (val-LdC) in Patients with Chronic Hepatitis B

✍ CHAN Lik Yuen • HUI Yui • WONG Wai Sun
• SUNG Joseph Jao Yiu

□ 1 June 2005

❖ Idenix Pharmaceuticals, Inc

This is a phase IIB, blinded, multicenter study comparing the anti-viral efficacy of telbivudine (LdT) versus combination of LdT and valticitabine (val-LdC) in the treatment of chronic hepatitis B patients with active disease. Patients will be divided into 2 groups receiving (1) 52 week LdT and val-LdT combination, (2) 52 week LdT and placebo val-LdC. Sixty-five patients will be recruited into each treatment arm in 1:1 randomization. The primary endpoint is the proportion of patients with non-detectable HBV DNA at week 24 by COBAS Amplicor PCR assay for patients receiving combination regime versus those receiving LdT monotherapy.

(MD04646)

European EnPulse Registry

✍ CHAN Yat Sun Joseph • SANDERSON John
Elsby#

□ 23 August 2004

❖ Medtronic International Limited

The patients included into the registry are those with standard clinical indication for a pacemaker implant (under American College of Cardiology and American Heart Association Practice Guideline). The purpose of the European EnPulse Registry is to collect demographical, clinical and technical data on the patients receiving this therapy and to assess the benefit of each functionality of the implanted device. The registry will be conducted in about 100 hospitals all over Europe and Hong Kong; baseline and one year follow-up information will be collected from approximately 1000 patients. This information includes medical and health data. These data will be used and processed manually and by computer by Medtronic or any other designated party that is involved in the study. These data are collected for medical research purpose to gather information on products and their performance during and after the current clinical study.

(MD04861)

Microwave Ablation for the Treatment of Atrial Fibrillation and Atrial Flutter

✍ CHAN Yat Sun Joseph • FUNG Wing Hong •
YU Cheuk Man

□ 9 June 2005

❖ MedWaves, Inc.

Atrial fibrillation (AF) is a very common arrhythmia in the general population. Atrial fibrillation may cause serious symptom and complications. At present atrial fibrillation is mainly controlled with medications however the efficacy of preventing the occurrence of AF is only 50% in two years. In recent years the technique of catheter ablation has

gradually refined to be a mature technique for atrial fibrillation management. Catheter ablation for AF mainly involves using radiofrequency energy to form a heat source to create barrier in the left atrium to prevent initiation and perpetuation of AF. This technique has a success rate of around 70%. However radiofrequency ablation of AF is associated serious complication including stenosis of pulmonary vein. Another important trigger for atrial fibrillation is atrial flutter that originates in the right atrium. Atrial flutter like AF can be cure by radiofrequency ablation, but usually required multiple energy application and long procedure time.

The aim of this study is to investigate the usefulness of new microwave delivery by pre-shaped catheter developed by MedWaves in catheter ablation of AF and atrial flutter. There is potential advantages of microwave energy over radiofrequency catheter ablation in that it does not appear to disrupt or damage the endocardial surface to the extent caused by radiofrequency ablation and therefore less chance of thrombus formation. Microwave ablation also require significant less time for application of energy when compare to radiofrequency ablation.

(MD04589)

Deep Vein Thrombosis Surveillance in Medical Ward

✍ CHENG Gregory • WONG Siu Ming Raymond

□ 1 September 2004

❖ Aventis Pharma Ltd.

Deep venous thrombosis (DVT) and pulmonary embolism (PE) are common and serious complications occurring in hospitalized patients. The frequency of DVT is well documented in surgical, gynecologic and intensive care unit patients, and prophylaxis has been shown to significantly

reduced the risk of venous thromboembolism. Many medical condition such as malignancy, neurological disease with paresis, cardiac failure and acute myocardial infarction are associated with increased risk of thromboembolism, and prophylaxis had also been recommended. There was little data about the incidence of DVT among Chinese patients admitted to a medical ward. In the past, it was widely believed that the incidence of DVT was much lower among Chinese, and prophylaxis was generally not given. In a retrospective analysis we found that the overall incidence rate of proximal DVT among hospitalized medical patients is at least 0.3% (110/36051). This is likely an under-estimate because Doppler ultrasonography was ordered only for patients with clinically suspected DVT and we did not perform routine Doppler screening. We therefore suspected that the overall risk of DVT among hospitalized Chinese patients is probably higher and could be similar to that in Caucasian populations.

The aim of this prospective study is to find out the incidence of DVT among hospitalized medical patients in Hong Kong using d-dimer as the initial screening test and carrying out ultrasound study on those with a rising d-dimer.

(MD04699)

A Prospective, Randomised, Double-Blind, Placebo Controlled, Dose Ranging, Multi-Centre Study of the Safety and Efficacy of Three Days Continuous Intravenous Infusion of GR270773 in the Treatment of Suspected or Confirmed Gram-Negative Severe Sepsis in Adults (EMD20001)

✍ CHENG Gregory • WONG Raymond*

□ 1 October 2004

❖ Glaxo-Smith-Kline

Sepsis is an often lethal disease with mortality rate of 20-50% in severe cases. The current standard of care of sepsis includes antimicrobial therapy, surgical drainage of abscess and supportive care. Endotoxin is an important early initiator of inflammatory response in sepsis, and its level remains elevated for several days. Serum lipoproteins have been shown to have strong bindings to endotoxin and neutralize its pro-inflammatory effects. There is also an association of low lipids level with poor outcome in critically ill septic patients. Reducing serum endotoxin levels have been associated with improved outcomes in septic patients. GR270773 is a lipid emulsion developed by GSK. It has been shown to be effective in reducing multi-organ damage and mortality in a Porcine model of Gram negative sepsis. A prospective, randomised, double-blind, placebo controlled study of the safety and efficacy of three days continuous infusion of GR270773 in patients with suspected or confirmed Gram-negative Severe Sepsis will be conducted.

(MD04466)

A Double-Blind, Randomized, Placebo-Controlled, Parallel Group Study to Investigate the Efficacy, Safety Tolerability, Pharmacokinetics and Pharmacodynamics of SB 497115-GR, A Thrombopoietin Receptor Agonist in Adult Male and Female Subjects with Refractory, Chronic Immune Thrombocytopenia

✍ CHENG Gregory • WONG Raymond*

□ 1 February 2005

❖ Glaxo Smith Kline

Immune thrombocytopenia is a very common hematological condition. Patients have increased

bleeding tendency and sometimes fatal hemorrhage. High dose steroid is usually the first line of treatment with response rate of 30-60%. For patients not responding to steroid therapy, splenectomy, anabolic steroids, cytotoxic drugs, intravenous immunoglobulin, are alternative treatment options. However, 10-15% of patients are refractory despite the above treatment modalities. These patients have frequent admission to hospitals with uncontrolled bleeding. SB 497115-GR, a thrombopoietin receptor agonist had been shown to increase platelet counts in patients with refractory immune thrombocytopenia in preliminary studies. A double-blind, randomized, placebo-controlled, parallel group study to will be carried out to investigate the efficacy, safety tolerability, pharmacokinetics of SB 497115-GR, in adult male and female subjects with refractory, chronic immune thrombocytopenia.”

(MD04780)

A 6-Month Extension of a Double-Blind, Double-Dummy, Multi-Centre, Parallel Group Trial Evaluating Long-Term Efficacy and Safety of NNC 61-0029 in Combination with Glibenclamide versus Glibenclamide Monotherapy and versus Combination Therapy of Glibenclamide and Metformin in the Treatment of Type 2 Diabetic Subjects (Phase III A)

✍ CHOW Chun Chung Francis • COCKRAM Clive Stewart • OZAKI Risa • CHAN W. B.* • SO Wing Yi *

□ 10 November 2004

❖ Novo Nordisk Asia Pacific Pte Ltd

This is an addendum 2 of a 6-month extension of a, double-blind, double dummy, multi-centre, asymmetrically randomised (2:2:1:2), 4

armed-parallel group trial of two doses of NNC 61-0029 in combination with glibenclamide versus glibenclamide monotherapy and versus combination therapy of glibenclamide and metformin in patients with type 2 diabetes.

The primary objectives are:

- a) To compare the efficacy of two doses of NNC 61-0029 in combination with glibenclamide versus glibenclamide monotherapy and versus glibenclamide and metformin combination therapy on glycaemic control in the treatment of type 2 diabetes as assessed by HbA_{1c}
- b) To compare the triglyceride lowering effects of two doses of NNC 61-0029 in combination with glibenclamide versus glibenclamide monotherapy and versus glibenclamide and metformin combination therapy as assessed by triglyceride.

(MD04561)

A Multicenter, Randomized, Double-Blind, Active Controlled Study to Compare the Long-Term Effect (up to 5 Years) of Treatment with LAF237 50 mg bid to Glimepiride up to 6 mg Daily as Add-On Therapy in Patients with Type 2 Diabetes Inadequately Controlled with Metformin Monotherapy

✍ CHOW Chun Chung Francis • SO Wing Yee • KONG Pik Shan • OZAKI Risa • CHAN Wing Bun • LAU Wing Yan • LUK On Yan Andrea# • YU Wai Ling Linda • CHENG Yuen Shan Angela

☐ 1 March 2005

❖ Novartis Pharmaceuticals Corporation

This research study is to assess the safety and effectiveness for treating diabetes of adding LAF237 compared to glimepiride to the metformin treatment

in patients with Type 2 Diabetes inadequately controlled with Metformin alone.

Each patient will attend one screening visit (Week -4) where the inclusion/exclusion criteria will be assessed. Eligible patients will then be randomly assigned at baseline (Day 1) and complete up to 25 additional visits over a period of up to 5 years of treatment with LAF237 or glimepiride added to metformin.

Patients will have physical examinations, electrocardiograms (ECG- a tracing of the electrical activity of the heart); vital signs, blood drawn for laboratory tests, and monitoring of adverse events during the study. Patients may be asked to participate in an optional standard meal challenge at up to 8 visits during the study. A meal will be provided by the clinic and have blood taken through a needle in your vein twice prior to starting the meal, and up to 7 times over the 4 hours following the meal.

In all, up to

about 300 mL per year will be removed during the study.

Patient participation in the study, including treatment with LAF237, glimepiride and rescue medication (pioglitazone), will continue until a common closing date. The study is currently projected to last for a maximum duration of 5 years.

(MD04418)

A 24-Week Randomised, Double-Blind, Parallel-Group, Multi-Centre, Active-Controlled (Metformin or Metformin Combined with Fenofibrate) Study to Evaluate the Lipid Metabolic Effects, Safety and Tolerability of Tesaglitazar Therapy in Patients with Type 2 Diabetes and Low HDL-Cholesterol on a Fixed Background Therapy with a Statin Gallant 14

✍ KONG Pik Shan • CHAN Chung Ngor Juliana •
LUK On Yan Andrea# • SO Wing Yee •
CHENG Yuen Shan Angela • TONG Peter Chun
Yip • OZAKI Risa • YU Wai Ling Linda •
LAU Wing Yan

□ 15 February 2005

❖ AstraZeneca Hong Kong Limited

This is a 24-week study to determine the lipid metabolic effects, safety, and tolerability of tesaglitazar compared to metformin and metformin in combination with fenofibrate in patients with type 2 diabetes and low HDL-C with the following primary objectives

1. Tesaglitazar is superior to metformin in increasing HDL-C
2. Tesaglitazar is non-inferior to metformin combined with fenofibrate in increasing HDL-C

The study comprises a 2-week enrolment period, 6-week run-in and a 24-week randomized, double-blind, parallel-group, multicentre, active-controlled (metformin with or without fenofibrate) treatment period and a 3-week follow-up. From visit 2 (run-in) all patients will receive a standardized dose of statin (rosuvastatin). After a 2-week enrolment period and a 6-week placebo single-blind run-in period the patients will be given the investigational product for 24 weeks in a double-blind fashion. During the run-in period and throughout the study all patients will also receive as additional drug 10 mg rosuvastatin daily (open label). From randomization, tesaglitazar and metformin will be titrated to optimal effect on glucose level or highest tolerable dose during the first 12 weeks. After the titration period, the dose of tesaglitazar and metformin will remain constant. Patients will be counselled on dietary and life-style modifications according to normal clinical routine, with reinforcement throughout the treatment period.

(MD04492)

Can Oral Vitamin B12 and Folate Supplementation Preserve Cognitive Function of Patients with Early Dementia?

✍ KWOK Chi Yui Timothy • LAM Chiu Wa
(Psychiatry) • WOO Kam Sang • ZEE Chung
Ying Benny (Community and Family Medicine)

□ 1 September 2004

❖ Research Grants Council (Earmarked Grants)

Background: Vitamin B₁₂ and folate are essential to brain health. Sub optimal status of vitamin B₁₂ and folate leads to elevation of plasma homocysteine concentration, which is associated with Dementia. Vitamin B₁₂ and folate supplementation improved the cognitive function of demented subjects with hyperhomocysteinaemia in a pilot study.

Objective: To determine the effectiveness of vitamin B₁₂ and folate supplementation in preserving cognitive function of subjects with early dementia.

Design: a randomized, double blind, placebo controlled trial

Subject: 180 subjects, aged > 60 years, with early clinical dementia in psychogeriatric outpatient and memory clinics.

Method: After stratified randomization by mini mental state examination scores, supplement group subjects take 1 mg of methylcobalamin (a metabolically active derivative of vitamin B₁₂) and 5 mg of folic acid daily, while placebo group subjects take placebo capsules. The primary outcome is Mattis dementia rating scale. The secondary outcomes are mini mental state examination, neuropsychiatric inventory, and Cornell scale for depression in dementia. These measurements will be performed at baseline and every six months for 18

months. Fasting plasma homocysteine concentrations are measured at baseline.

Data analysis: Intention to treat analyses will be used for outcome variables. Repeated-measures analysis of variance will be used to determine the effects of supplementation.

(CU04307)

A Multinational, Multi-Centre, Randomised, Double-Blind, Double-Dummy, Stratified, Active Controlled Parallel Group Study Comparing the Efficacy and Safety of Intravenous Zoledronic Acid, 5 mg Once Yearly, and Oral Risedronate, 5 mg Daily, in the Prevention and Treatment of Corticosteroid Induced Osteoporosis

✍ LI Kwok Ming Edmund • TAM Lai Shan

□ 1 July 2004

❖ Novartis Pharmaceuticals Corporation

Study purpose:

Evaluate the efficacy and safety of zoledronic acid compared to risedronate to support regulatory submissions for zoledronic acid in the prevention and treatment of patients with corticosteroid induced osteoporosis.

Objectives:

Co-Primary objectives:

- The primary efficacy objective for the prevention and treatment sub-population is to demonstrate that the percent change in lumbar spine bone mineral density (BMD) at Month 12 relative to baseline in male and female patients treated with on iv zoledronic acid 5 mg dose at randomization is not inferior to the percent change in lumbar spine BMD at Month 12 compared to baseline in those patients who are treated with oral risedronate 5 mg daily.

Secondary objectives:

- To assess the percent change in BMD at the total hip, femoral neck, trochanter, and distal radius at Month 6 and Month 12 relative to baseline in patients treated with zoledronic acid compared to patients treated with risedronate.
- To assess changes in biochemical markers of the bone turnover in patients treated with zoledronic acid compared to patients treated with risedronate.
- To evaluate the overall safety of zoledronic acid compared to risedronate in patients receiving corticosteroid therapy.

Population:

The trial population will consist of male and female patients aged from 18 to 85 years old, corresponding either to the definition of the treatment of the prevention sub-population for corticosteroid induced osteoporosis, as defined in the inclusion criteria. All patients are expected to continue on corticosteroid therapy over a 12 month period. Approximately 760 patients (504 in the treatment group and 256 in the prevention group) will be randomized from approximately 74 centers in North and South America, Asia, Oceania and Europe.

(MD04790)

The Effect of Lingzhi (Ganoderma Lucidum) and Sen Miao San Supplementation in Rheumatoid Arthritis (RA): Biomarkers of Antioxidant, Inflammatory Status and Clinical Efficacy

✍ LI Kwok Ming Edmund • TOMLINSON Brian
• TAM Lai Shan* • Iris FF Benzie*

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

Rheumatoid arthritis (RA) is an inflammatory joint disorder occurring world-wide with a prevalence of

0.35% in Hong Kong. It affects female nearly 4 times more than in male, with age ranges from 16 to 65 years old. RA has the potential to cause severe disability with devastating social and economic consequences for the individual concerned. Most of the current drugs available in the treatment in RA have numerous side effects and do not alleviate the symptoms that are associated with this disease. In the past several years, complementary and alternative practices has taken a much more important role in the treatment of the rheumatic disease.

Ganoderma lucidum or Lingzhi, a medicinal mushroom, is widely used and highly regarded in the Chinese culture for augmentation of health and general well-being. Sen miao San (SMS) 三妙散 (黄柏、苍术、牛膝) Powder of Three Wonderful Drugs is a most commonly used herbal formula to treat *Bi Zheng* in ancient China.

This is a 52 - weeks prospective, double-blind, randomized, placebo-controlled study involving 90 patients with RA. Those with the presence of 2 or more swollen or tender joints, morning stiffness lasting for 30 minutes, and an erythrocyte sedimentation rate (ESR) of 28 mm/hour, despite treatment with disease modifying agent including MTX, sulphasalazine, hydroxychloroquine, auranofin or azathioprine were recruited, and they will be randomized to receive active treatment or placebo in addition to their current drugs.

They will be evaluated clinically and blood tests for inflammatory mediators and oxidative stress.

(MD04956)

A Randomized, Double-Blind, Parallel Group Study of the Safety and Reduction of Signs and Symptoms during Treatment with MRA versus Placebo, in Placebo, in Combination with Methotrexate, in Patients with Moderate to Severe Active Rheumatoid Arthritis

✍ LI Kwok Ming Edmund • TAM Lai Shan*

☐ 1 January 2005

❖ Roche Products Pty. Limited

The purpose of the study is to investigate MRA, an experimental new drug being studied by F Hoffmann-La Roche AG for treating patients with rheumatoid arthritis. MRA has been studied in over 500 patients with rheumatoid arthritis in Europe and Japan, with encouraging results.

MRA (myeloma receptor antibody) is an antibody (a protein produced by specific cells in the immune system) that has been designed to block the action of IL-6, a protein involved in many inflammatory pathways linked to rheumatoid arthritis.

This study is being carried out to see if MRA given together with methotrexate can reduce the symptoms of rheumatoid arthritis. Approximately 630 patients will take part in this study which is being conducted throughout North and South America, Europe, Asia, and Australia and is expected to last for at least 6 months

During this study, the patient will be randomly assigned to one of three different treatment arms. All of the treatment arms contain methotrexate; in addition, two of the treatment arms contain MRA in different doses while one of the arms contains a placebo (a substance with no effect which allows us to determine the true effect of MRA). Because MRA is an antibody it cannot be taken as a tablet but has to be given intravenously. This is done by inserting a needle into patient's arm and allowing the drug to slowly enter patient's body over a period of time (approximately 1 hour). The patient will receive an infusion of MRA/placebo every four weeks for a total of six infusions, with interim visits scheduled 2 weeks after the first two infusions and 2 weeks after the fourth infusion. After completion of

24 weeks of randomized treatment, patients may roll-over into an open-label extension study.

(MD04763)

Characterization of Serum Proteomic Signatures of Hepatocellular Carcinomas

✉ POON Chuen Wai • PANG Ting Kai Ronald (Centre for Emerging Infectious Diseases) • MOK Shu Kam Tony (Clinical Oncology) • CHAN Anthony Tak Cheung (Clinical Oncology)

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

Currently alpha-fetoprotein (AFP) is the only available serum marker in assisting the diagnosis of hepatocellular carcinoma (HCC). However, its usage is limited by its low specificity in the identification of early cases arising in patients with chronic liver diseases (CLD). Recently, we have developed a high-throughput multidimensional strategy employing the cutting-edge SELDI TOF MS technology for comprehensive profiling of serum proteomes in terms of mass value and physico-chemical properties, and successfully identified 250 proteomic features levels of which are significantly different between the HCC and CLD patients. Most of HCC cases and chronic liver disease (CLD) cases were correctly classified on the basis of these 250 serum proteomic features at both sensitivity and specificity of over 90%. This study indicates that complex HCC-specific proteomic signatures are present in serum. Although they could be reliably identified and quantified by the SELDI TOF MS technology, the exact protein identities of them remain unknown. As a continuation of our recent study, we propose to

isolate and examine the protein identities of the proteomic features forming the proteomic signatures of HCC. Knowing the protein identifies will allow us to develop new diagnostic assays to quantify the HCC-specific proteomic signatures more efficiently and cost-effectively with the use of other assay platform, such as multiplex immunoassay.

(MD04724)

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of the Addition of MK-0431 to Patients with Type 2 Diabetes Mellitus Who Have Inadequate Glycemic Control on Glimepiride Alone or in Combination with Metformin

✉ SO Wing Yee • CHAN Chung Ngor Juliana • KONG Pik Shan • OZAKI Risa • LUK On Yan Andrea#

□ 1 May 2005

❖ Merck & Co., Inc.

This is a 24-week study to determine the effect as well as the safety and tolerability of the addition of treatment with MK-0431 compared to placebo on HbA1c in patients with type 2 diabetes mellitus having inadequate glycaemic control on glimepiride at dose of $\geq 4\text{mg/day}$, alone or in combination with metformin at dose of $\geq 1500\text{mg/day}$.

Patients enrolled into the study will go through a 1-week screening period and then dose titration period of their original regime up to 10 weeks. Then they would undergo 2-week single-blind placebo run-in period and a 54-week double-blind treatment period. The 54-week double blinded treatment period will include 24-week placebo-controlled period (phase A) and a 30-week active-controlled period (phase B) when patients in the placebo group will start treatment with

pioglitazone as control. Patients will be counselled on dietary and life-style modifications according to normal clinical routine, with reinforcement throughout the treatment period.

(MD04403)

Chinese Herbal Medicine for Irritable Bowel Syndrome: From Basic Mechanism to Clinical Cure

✍ SUNG Joseph Jao Yiu • WU Che Yuen Justin • LEUNG Wai Keung • CHAN Ka Leung Francis • BIAN Zhaoxiang* • LIU Liang* • ZHAO Zhongzhen* • JIANG Zhi-hong*

□ 1 August 2004

❖ Hong Kong Jockey Club Institute of Chinese Medicine Limited

Irritable bowel syndrome (IBS) is a diagnosis in Western Medicine characterized by recurrent abdominal pain associated with disturbance in bowel habit such as diarrhea or constipation. Treatment for IBS has so far been unsatisfactory. With the unsatisfactory treatment response of western medicine, many turned to alternative treatment modalities for IBS. Traditional Chinese medicine is particularly attractive as their effectiveness in treating functional disorders and retaining balance of body functions has been known for centuries. There is a long history using Chinese herbal medicine to treat abdominal pain and change in bowel motions mimicking the symptoms of IBS. However, there is a lack of convincing clinical data demonstrating the effectiveness of Chinese medicine in this condition.

The study objectives are:

- (1) To investigate a proper form of prepared Chinese medicinal herbs for the clinical and basic research for IBS.

- (2) To evaluate the herbal medicine on sensory and motor response and expression of neurotransmitter in rat model of IBS and test the change in visceral sensitivity in patients with IBS after receiving herbal medicine.

- (3) Clinical study to test the efficacy of herbal medicine in relieving symptoms and change of quality of life of patients with IBS.

The ultimate goal is to develop a TCM formula for the treatment of IBS. Moreover, the animal model and validated questionnaire developed in this project will be useful machinery for future studies in IBS.

(MD04788)

Functional Bowel Disorders in Chinese Medicine

✍ SUNG Joseph Jao Yiu • CHE Chun Tao (School of Chinese Medicine) • LEUNG Wai Keung • LIU Wing Keung Ken (Anatomy) • WU Che Yuen Justin • YEW Tai Wai David (Anatomy)

□ 1 October 2004

❖ Planning Grant for International Centres for Research on Complementary and Alternative medicine (PICRC)

We have established a consortium between the University of Maryland, The Chinese University of Hong Kong and the University of Chicago at Illinois with a PICRC Grant awarded in 2003.

The consortium supported a multi-disciplinary team of researchers and developed institutional collaborations to conduct basic science and clinical research initially investigating the use of complementary and alternative medicine in the treatment of irritable bowel syndrome. There were three specific areas of study the consortium will target:

1. Validation of an animal model of IBS and the application of the animal model for acupuncture

- and herbal medicine study,
2. Conduct feasibility study of the use of rectal barostat and functional MRI for evaluation of efficacy of acupuncture and herbal medicine,
 3. Standardization of herbs and investigation of their pharmacological action

The results of these studies provide foundation for more in-depth research on the use of traditional Chinese medicine for treatment of irritable bowel syndrome.

(MD03458)

Genomic Study of Viral Hepatitis B to Predict Development of Liver Cancer in Asian Patients

✍ SUNG Joseph Jao Yiu

□ 30 June 2005

❖ RGC-Central Allocation Scheme - Group Research

We aim to validate the temporal sequence of hepatitis B virus (HBV) mutations related to hepatoma development identified in a previous project using a longitudinal cohort and to study the functional genomics of these cancer-associated mutations. We plan to study a cohort of HB V-infected patients with longitudinal follow-up. Serial blood samples will be studied to monitor the viral mutations among patients who had developed hepatoma. Based on the identifiable mutations, wild type and mutant plasmid will be generated and transfected into a replicative HBV cell line system. Microarray will be performed to compare the upregulation and downregulation of gene by the wild type and mutant system. The clinical study will confirm these mutations are the cause rather than results of hepatoma development. The genomic study provides information on the functional aspect of the

HBV mutations, and serves as the starting point for future functional assays.

(MD04467)

Molecular Mechanism of Epithelial-to-Mesenchymal Transdifferentiation of Mesothelial Cells in Peritoneal Dialysis - A Study of Transforming Growth Factor Beta and Its Downstream Mediators by a Cell Culture Model

✍ SZETO Cheuk Chun

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

Introduction. Peritoneal dialysis (PD) is the first-line treatment of kidney failure in Hong Kong. Peritoneal fibrosis is the major cause of treatment failure in PD patients. Transforming growth factor beta (TGF) plays an important but conflicting role in the pathogenesis of peritoneal fibrosis. Recent studies find that TGF induces transdifferentiation of peritoneal mesothelial cell (PMC) from epithelial to fibroblast-like cells, resulting in peritoneal fibrosis. However, the underlying mechanism is unknown. *Hypothesis.* TGF induces transdifferentiation of PMC via the downstream mediator connective tissue growth factor (CTGF), and the effect is modified by another downstream mediator, vascular endothelial growth factor (VEGF). The relative expression of CTGF versus VEGF, and as a result the effect of TGF on PMC transdifferentiation, is modulated by exogenous stimuli. *Method.* Primary culture of rat PMC is used. Up-regulation of CTGF and VEGF in TGF-stimulated PMC has been documented previously. In this project, we plan to study the effects of CTGF and VEGF on PMC by culturing PMC with recombinant CTGF and VEGF. Transdifferentiation of PMC will be assessed by the

change in morphology, surface markers and pattern of gene expression of PMC. *Significance.* We propose to study the mechanism of PMC transdifferentiation after prolonged exposure (3 to 21 days) to TGF, which will likely advance our understanding on the mechanism of peritoneal failure after prolonged dialysis. Identifying the key determinants of peritoneal fibrosis will establish a firm scientific foundation for further development of therapeutic strategies.

(MD04989)

An Open-Label 7-Day Study to Determine the Influence of CYP2C19 Genotype on the Pharmacokinetics of RO2052349 in Patients with Type 2 Diabetes Mellitus in the Asia-Pacific Region

✍ TOMLINSON Brian • CHOW Sing Sum Moses (School of Pharmacy) • FOK Siu Pong (School of Pharmacy)

□ 1 January 2005

❖ Quintiles Hong Kong Limited

This is a pharmacokinetic study to examine the effect of different genetic forms of the drug metabolising enzyme CYP2C19 (a liver enzyme) on the metabolism of RO2052349, a new drug for diabetes, which is a thiazolidinedione or insulin sensitizer. In the first part of the study, Type 2 diabetic patients who agree to take part will have a blood sample (3 ml) taken to check which genetic form of CYP2C19 they have. Poor metabolisers and extensive metabolisers will be identified by their CYP2C19 alleles and from these results, 45 poor metabolisers and 45 extensive metabolisers from the Asia-Pacific region will be recruited for a study on the metabolism of RO2052349. Patients with Type 2 diabetes who are otherwise well will be recruited in pairs, one poor and

one extensive metaboliser. Two days after a screening visit, patients will be asked to start taking the drug and 16 ml of blood will be taken for baseline measurements. Patients will take RO2052349 12 mg once daily for 7 days and on the last day stay at the study facility for 24 hours. On the last day, blood will be taken from the subjects before they take the drug, and also at 1, 2, 4, 6, 9, 12, and 24 hours after drug administration. These samples from 0 to 12 hours will be taken from a cannula inserted into a forearm vein to avoid multiple venepunctures. The total amount of blood taken on the last day will be 55 ml. A follow-up visit will be scheduled 4 to 10 days after last drug administration to check for any abnormalities (requires 11 ml of blood). Patients will be reimbursed for each visit. Spot urine samples will be obtained at each visit in the second part of the study to test for abnormalities (dipstick at study site). All blood samples will be delivered through pre-arranged transport to a specified central laboratory for testing.

(MD04720)

Phase I Study on the Safety and Pharmacokinetics of IMD-1041 in Healthy Male Volunteers

✍ TOMLINSON Brian

□ 15 April 2005

❖ Institute of Medicinal Molecular Design Inc.

The purpose of this phase I clinical study is to study whether an experimental drug, IMD-1041, is safe for use in human beings and the length of time that IMD-1041 will stay in human body. IMD-1041 is developed by Institute of Medicinal Molecular Design Inc. (IMMD), Japan, for the treatment of heart failure following myocardial infarction. It has been shown to be safe in animals, but not yet in humans.

In this study, 32 healthy male volunteers will be assigned to receive 4 different doses (50, 150, 300, 600 mg) of IMD-1041. The study will proceed to a higher dose level only after the safety of the previous group receiving a lower dose is confirmed by the investigator. The safety of each dose will be learned by performing routine clinical and laboratory examinations and the length of time each dose will stay in the body will be learned by measuring plasma and urine IMD-1041 concentrations after dosing.

(MD04849)

Biological Activities of Recombinant Insulin-Like Growth Factor 1 and Insulin-Like Growth Factor Binding Protein 3 from Transgenic Tobacco Plant

✍ TONG Peter Chun Yip • SUN Sai Ming Samuel (Biology) • CHAN Chung Ngor Juliana

□ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

Abnormal growth hormone / insulin-like growth factor-I regulation contributes to the deterioration in glycaemic control in diabetic patients with insulin deficiency. Treatment with recombinant human insulin-like growth factor 1 (rhIGF-1) and recombinant IGF Binding Protein 3 (rhIGFBP-3) have been shown to reduce plasma glucose and insulin doses in both type 1 and type 2 diabetic patients. The lack of sufficient quantity of recombinant proteins has hindered further research on the potential use of rhIGF-1 and rhIGFBP-3 in diabetes. In a proof-of-concept study, protein expression of rhIGF-1 and rhIGFBP-3 in the transgenic tobacco plant was demonstrated.

In the present proposal, we aim to extract recombinant proteins from seeds of transgenic tobacco plant. Biological activities of rhIGF-1 will

be tested on a rat skeletal muscle cell line. The anti-proliferative effects of rhIGFBP-3 on human breast cancer cell line (MCF-7) will be examined. The results will advance our understanding on the synthesis of human proteins in transgenic plant and provide a firm foundation to explore the use of rice in the production of high-value proteins.

(MD04395)

A Phase-3 Randomized, Three Arm, Double-Blind, Active Controlled, Parallel Group, Multicenter Trial to Evaluate the Safety and Efficacy of Muraglitazar in Combination with Metformin Compared to Glimepiride in Combination with Metformin in Subjects with Type 2 Diabetes Who Have Inadequate Glycemic Control on Metformin Therapy Alone

✍ TONG Peter Chun Yip • CHAN Chung Ngor Juliana • SO Wing Yee • Winnie Lau*

□ 28 October 2004

❖ Bristol Myers Squibb (HK) Ltd

Muraglitazar is a PPAR α/γ agonist developed as a treatment of type 2 diabetes. It has significant dose-dependent HbA1c and glucose lowering effects as well as positive effects on most lipid parameters. This study is part of the multicenter trial involving a total of 1752 subjects globally. The objective is to determine the effect on glycaemic control and to assess the safety and tolerability of muraglitazar added in combination with metformin as compared to glimepiride in combination with metformin. This is a phase 3 randomised, double-blind, three-arm, active controlled, parallel group, multicenter trial with both short and long term extensions resulting in a study duration of 2 years. Primary efficacy outcome measure is change in HbA1c from baseline to week 32. Percent changes in fasting lipid levels

(HDL-cholesterol, triglycerides, non-HDL-cholesterol and apoB will be measured for secondary efficacy outcome. The incidence of adverse events and of marked abnormalities in clinical laboratory tests will be monitored.

(MD04461)

PRoFESS - Prevention Regimen For Effectively Avoiding Second Strokes: A Double-Blind, Active and Placebo Controlled Study of Aggrenox® vs. Clopidogrel Aspirin, with and without Micardis®

✍ WONG Ka Sing Lawrence • MOK Chung Tong Vincent • KWAN Kwok Leung Patrick • LEUNG Wai Hong Thomas • LIANG Ka Shing Eric • WONG H C Edward* • LEUNG Howan*

□ 1 July 2004

❖ Boehringer Ingelheim (Hong Kong) Limited

Multi-national, double-dummy, active and placebo controlled, parallel, group, 2X2 factorial design. The randomization is stratified by baseline usage of an ACE-inhibitor. Enrollment period is projected to be 2 years; total study duration is projected to be 4 years, based on the estimated time until 2280 strokes occur among randomized patients.

This study objective is to compare the efficacy and safety of Aggrenox to Clopidogrel, and to compare Micardis to placebo in the prevention of recurrent stroke. The first primary analysis will sequentially test if Aggrenox is non-inferior, and then superior to Clopidogrel in reducing the risk of recurrent stroke. The second primary analysis will test if Micardis is superior to placebo, separately in the absence and presence of an ACE-inhibitor, in reducing the risk of recurrent stroke.

Male or female patients at least 55 years of age with an ischemic stroke who are neurologically and

clinically stable. The qualifying stroke must be within 90 days of entry into the study.

(MD04510)

Effect of Multivitamins Supplementation on the Progression of Cerebral White Matter Changes and Cognitive Impairment in Chinese Stroke Patients with Moderate to Severe Leukoaraiosis

✍ WONG Ka Sing Lawrence • MOK Chung Tong Vincent • CHAN Yu Leung (Diagnostic Radiology & Organ Imaging)# • LAM Wai Man Wynn (Diagnostic Radiology & Organ Imaging) • WOO Kam Sang • TANG Wai Kwong (Psychiatry)

□ 1 September 2004

❖ Research Grants Council (Earmarked Grants)

Stroke damages the brain, and this brain damage can produce cognitive impairment and dementia. Cerebral small vessel disease including cerebral white matter changes and small subcortical infarct are common in the Chinese population. These lesions may produce significant cognitive impairment or dementia. Plasma levels of homocysteine are proportionally related to cerebrovascular disease and are inversely related to cognitive performance. Furthermore, plasma homocysteine levels can be reduced by oral vitamin (especially folate) therapy. Our group is currently participating in an international randomised, placebo controlled, clinical trial of vitamin therapy to prevent recurrent stroke (VITATOPS study). We propose to perform a neuroimaging and cognitive substudy for patients recruited in our site to document to progression of cerebral white matter changes and cognitive decline over a two years' period.

We have accurately measured stroke related cognitive impairment and executive dysfunction using a battery

of locally validated neuropsychological instruments including minimal state examination (MMSE), Frontal Assessment Battery (FAB). We have also quantified the amount of brain damage using magnetic resonance imaging coupled with computer-assisted image analysis (qMRI). We have experience in longitudinally following patients with qMRI to determine the progression of cerebral white matter changes and the course of cognitive decline.

In this project, we will identify and describe the relationships between cognitive impairment as measured by the MMSE and FAB, cerebral ischemic lesions as measured by qMRI, and plasma homocysteine levels in a cohort of stroke survivors. We hypothesize that elevated levels of plasma homocysteine will be associated with greater burden of cerebral ischemic lesions, and with greater cognitive impairment. In addition, we will test the hypothesis that oral vitamin therapy (as compared to placebo) significantly attenuates the progression of cerebral ischemic lesions over a two-year period.

(CU04317)

CHANT (Cerebral Hemorrhage - NXY Treatment)
A Double-Blind, Randomized, Placebo-Controlled, Parallel-Group, Multicenter, Phase IIB Study to Assess the Safety and Tolerability of 72 Hours Intravenous Infusion of NXY-059 in Adult Patients with Acute Intracerebral Hemorrhage

✍ WONG Ka Sing Lawrence • GRAHAM C A (Accident and Emergency Medicine Academic Unit) • MOK Chung Tong Vincent • HUI Andrew Che Fai • LIANG Ka Shing Eric • WONG Ho Chung Edward • SOO Oi Yan • LEUNG Howan*

☐ 30 November 2004

❖ AstraZeneca R & D Sodertalje S-151 85
Sodertalje

The study is double-blind, randomised, placebo-controlled with parallel-group carried out on a multicenter basis to assess the safety and tolerability of iv NXY-059 given within 6 hours of onset of symptoms in acute ICH. The planned total number of patients is 600. The investigational product will be given as a 1-hour loading infusion (2270 mg/h NXY-059 or placebo) followed by a maintenance infusion for 71 hours (up to 960 mg/h NXY-059 according to the subject's renal function, or placebo). Subjects will be assessed, at regular intervals during the treatment period and will be followed up at the 72-hour assessment or End Of Infusion, Discharge Assessment, Day 7 and at each of the scheduled follow-up assessments at 30, 60 and 90 days after onset of stroke. The primary objective of this study is to assess the safety and tolerability of NXY-059 compared to placebo in patients with acute ICH by assessment of mortality (overall and by cause), the incidence of serious adverse events, the incidence of adverse events, change from baseline in the laboratory parameters, change from baseline in vital signs, incidence of abnormalities and change from baseline in ECG parameters, and change from baseline in neuroimaging scans.

The secondary objectives of the study are: 1. To explore the efficacy of NXY-059 compared to placebo in patients with acute ICH by evaluating the recovery with respect to global disability, neurological recovery, functional recovery and patient reported disability. 2. To investigate the pharmacokinetics of NXY-059 in patients with acute ICH.

(MD04741)

PRoFESS - COG Sub-Study Effects of BP Lowering with Micardis®, and Anti-Platelet Therapy with either Aggrenox® or Clopidogrel, on Cognitive Function and Dementia Following Acute Ischaemic Stroke

✍ WONG Ka Sing Lawrence • MOK Chung Tong Vincent • HUI Andrew Che Fai • KWAN Kwok Leung Patrick • LEUNG Wai Hong Thomas • SOO Oi Yan • WONG Ho Chung Edward • LIANG Ka Shing Eric • LEUNG Howan*

□ 12 May 2005

❖ Boehringer Ingelheim

Twenty five percent of stroke survivors have dementia as a direct result of the stroke event, related to the location and extent of cerebral damage. The prevalence rates are even higher in older stroke patients, with an odds ratio in excess of seven for dementia in stroke patients over the age of 75 years. In addition, the delayed development of incident dementia remains up to nine times greater than the incidence in an age matched community population for 5 years or longer post-stroke, with annual incidence rates of dementia of almost 10% per annum in older stroke patients or amongst those with mild vascular cognitive impairment. The prevention of incident dementia in stroke patients is hence a key treatment target with the potential for huge clinical and economic benefit. Many additional stroke patients have early cognitive dysfunction with a marked impact upon daily functioning and related care needs. To determine whether the rate of cognitive decline can be reduced over a 3 year period following ischemic stroke, with: Micardis® treatment versus placebo and/or Aggrenox® versus Clopidogrel, in a subset of 750 PRoFESS patients from centres in several countries. **PRIMARY ENDPOINT:** Rate of cognitive decline as determined by the slope of

decline in cognitive processing speed, over the time period defined as 3 months following stroke, to study close in the overall sample and in those patients with first stroke only (i.e. excluding recurrent strokes). **SECONDARY ENDPOINTS:** i) Rate of cognitive decline as determined by the average slope of decline in each of four other cognitive domains (executive function, episodic memory, working memory, and attention), over the time period defined as 3 months following stroke, to study close in the overall sample and in those patients with first stroke only (i.e. excluding recurrent strokes); ii) Development of dementia (DSM-IV criteria) at study close in close sample and in patients > 75 years at study entry. (MD04379)

Randomised, Double-Blind, Placebo Controlled, Multi-Center, Parallel Groups Confirmatory Efficacy and Safety Trial of Activated Recombinant Factor VII (NovoSeven ® /Niasase®) in Acute Intracerebral Haemorrhage (Trial Phase: 3A) F7ICH-1641

✍ WONG Ka Sing Lawrence • GRAHAM C A (Accident and Emergency Medicine Academic Unit) • SOO Oi Yan • LEUNG Howan* • WONG H C Edward* • FUNG Kwai Yau (Orthopaedics & Traumatology) • LAW Sheung Wai (Orthopaedics & Traumatology)

□ 1 June 2005

❖ Novo Nordisk Hong Kong Ltd

Trial rationale: This study was designed to confirm the efficacy and safety of the trial drug, rFVIIa (recombinant activated Factor VII) in acute intracerebral haemorrhage (ICH). At present, no specific therapy exists for ICH. Treatment has been symptomatic. A previous trial called F7ICH-1371 was done during 2002 -2004 to evaluate the efficacy

and safety of rFVIIa in the treatment of ICH and the results demonstrated that rFVIIa given within 4 hours of ICH onset significantly reduced subsequent haemorrhage growth and improved clinical outcome. Hence, this new trial, F7ICH-1641, is to further confirm the efficacy and safety results from the F7ICH-1371 and to evaluate a lower dose (20mcg/kg rFVIIa as opposed to 80mcg/kg rFVIIa and placebo) effect.

Trial design: Randomised, double-blind, multi-centre, multi-national, placebo-controlled with 3 treatment arms: 20 mcg/kg rFVIIa / 80 mcg/kg rFVIIa / Placebo

Trial population: Patients with spontaneous ICH

Trial visit procedures: The trial comprises 5 phases - 1. Admission and screening 2. Trial drug administration and the first 24-hour follow-up (i.e. 1-hour and 24-hour post-dose) 3. Day 2 & 3 follow-up 4. Day 15 follow-up or discharge, whichever comes first 5. Day 90 follow-up (end of trial assessments)

(MD04346)

A Multi-Centre, Multinational, Long-Term Extension Study to Assess the Safety and Tolerant of Subject Optimised Treatment Regimens of Oral Sildenafil for Pulmonary Arterial Hypertension in Subjects Who Have Completed Study A1481140

✍ YU Cheuk Man • YIP Wai Kwok Gabriel • TAM Lai Shan • KUM Chi Chiu Leo • LEE Pui Wai • LAM Yat Yin

☐ 1 February 2003

❖ Pfizer Corporation Hong Kong Limited

Pulmonary hypertension can affect all age groups. Many pathologies can cause pulmonary hypertension. Primary pulmonary hypertension is a rare aggressive

disease leading to right heart failure and death. The historical survival rate is 29% at 4 years. Transplantation of the lungs or heart and lungs is the treatment of last resort and 40% of patients receiving heart/lung transplant will survive at 5 years post transplant. Orally administered vasodilating drugs are used, however, the response rate (functional capacity) to individual drugs is usually only around 25% and they are not selective for the pulmonary circulation. Prostacyclin has been shown to be efficacious in patients with pulmonary arterial hypertension, but has to be given by continuous infusion through a central line for life. Recently, the endothelin antagonist, bosentan has provided patients with the first oral treatment available for this life threatening disease. However, there are some concerns around the safety profile of this class of compounds, in particular the hepatotoxicity and teratogenicity.

There is a clear need for a more effective oral therapy to increase functional capacity in these subjects. Pre-clinical and early clinical studies indicate that sildenafil is a selective dilator of the pulmonary vessels. This extension to the 12 week placebo controlled study (A1481140) will investigate the long term safety of oral formulation of sildenafil in treating pulmonary hypertension where chronic therapy is needed.

Sildenafil is marketed for male erectile dysfunction (MED). Adverse events experienced with use of sildenafil in MED (with incidence>1%) are:

Cardiovascular: Headache (12.8%), Flushing (10.4%), Dizziness (1.2%)

Digestive: Dyspepsia (4.6%)

Respiratory: Nasal congestion (1.1%)

Special senses: Altered vision (1.9%; mild and transient, predominantly colour tinge to vision, but also increased perception of light or blurred vision)

In fixed dose studies, dyspepsia (12%), and altered vision (11%) were more common at 100mg than at lower doses. In addition, there were reports of muscle aches when sildenafil was administered more frequently than the recommended dosing regimen. In postmarketing surveillance priapism has been reported. Adverse reactions were mild to moderate in nature and the incidence and severity increased with dose.

(MD02736)

Assessment of Left Ventricular Remodeling with Tissue Doppler Echocardiography and Strain Rate Imaging in Patients after Acute Myocardial Infarction Compared with Contrast-Enhanced Magnetic Resonance Imaging

✍ YU Cheuk Man • YIP Wai Kwok Gabriel • LAM Wai Man Wynn (Diagnostic Radiology & Organ Imaging) • ZHANG Yan

□ 1 September 2004

❖ Research Grants Council (Earmarked Grants)

Remodeling of the heart after a heart attack is the process that leads to gradual enlargement of the ventricles with a change in shape. In this project we will study the effect of loss of synchrony of the contraction of the heart due to damage to the muscle and the conduction system on this process using a new non-invasive ultrasound technique known as strain rate imaging which is based on tissue Doppler echocardiography. The degree of the initial damage to the heart and the degree of remodeling will be accurately measured by contrast-enhanced magnetic resonance imaging which is now considered to be the “gold standard”. However, ce-MRI is expensive and not readily repeatable in contrast to echocardiography. In addition we will assess if strain rate imaging can distinguish between areas of

viable from dead or non-viable heart muscle again using ce-MRI as the reference. This research should yield significant new knowledge with regard to understanding LV remodeling post MI, the impact of asynchrony, the value of TDI and SRI for assessing myocardial function and viability and may help with the development of treatment strategies based on these novel-imaging modalities.

(CU04312)

The Application of Baicalein and Wogonin (Traditional Chinese Medicine) for the Treatment of Pathological Myocardial Fibrosis in an Animal Model of Hypertension

✍ YU Cheuk Man • SANDERSON John Elsby# • HUANG Yu (Physiology) • LUNG Wai Ming Raymond (Anatomical & Cellular Pathology)

□ 1 September 2004

❖ Research Grants Council (Earmarked Grants)

Hypertension is one of the commonest cardiovascular diseases. It is a condition with high blood pressure that causes a number of structural damage to the heart resulting in complications. Hypertension results in left ventricular hypertrophy and increased chamber stiffness. In this disease, the major determinant of increased stiffness of the left ventricular chamber is the development of fibrosis of the heart, which is called interstitial fibrosis (fibrosis between muscle cells) as well as perivascular fibrosis (fibrosis surrounding coronary arteries). The fibrosis is caused by the deposition of collagen fibrils and other matrix protein. As a result, abnormal function of the heart especially during relaxation (called diastolic dysfunction) will lead to the development of diastolic heart failure and its associated morbidity and mortality. Conventional medicine for treatment of hypertension has limited antifibrotic properties. On

the other hand, some traditional Chinese medicine with antifibrotic properties have been used to prevent organ fibrosis with some success (such as liver fibrosis), although they have never been tested in the heart. In the present proposal, two active ingredients extracted from *Scutellaria baicalensis* will be tested, namely Baicalein and Wogonin. The antifibrotic effect of these two active ingredients in the cardiac fibroblasts (the main cell type causing fibrosis) and in genetic hypertension model in rats will be examined. They agents may reduce collagen production and therefore prevent myocardial fibrosis in hypertension. As a result, the stiffness of left ventricle will be improved and diastolic dysfunction of the heart is alleviated.

(CU04318)

The Effects of α - and β - Adrenoreceptor Stimulation on Fibrogenic Cytokines Production and Apoptosis in Cultured Cardiac Fibroblasts

✍ YU Cheuk Man • LAI Ka Bik

📅 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

In a previous study our group found that carvedilol, a non-selective β_1 , β_2 and α blocker significantly reduced myocardial collagen in a non-infarcted myocardium and also reduced cardiac hypertrophy in the right ventricle of rat acute myocardial infarction model, whereas metoprolol had no effect on myocardial collagen deposition. The mechanism for the marked discrepancy between the two beta-blockers are unknown and likely to be complex. In the myocardium there are a number of mechanisms that may promote collagen production including angiotensin II and the sympathetic nervous system. The role of the sympathetic nervous system in

collagen production has been largely ignored but may be important. During a recent study, our group has established cardiac fibroblast culture using 1 week-old rat. We found that both noradrenaline and adrenaline increase collagen production in the fibroblast. However noradrenaline at higher doses cause decrease in collagen production while increasing the dosage of adrenaline cause a plateau in the collagen production response. The results also showed that blockers which acts on different receptor subtypes has different inhibitory effect on the adrenergic stimulated collagen production. Also the expression of TGF- β_1 gene after adrenaline and noradrenaline stimulation has different time course expression pattern.

We wish therefore to further study the effect of α , β_1 and β_2 stimulation and antagonist on isolated cultured cardiac fibroblasts through finding out 1) the signaling pathway of the α - and β - stimulated collagen production response, 2) whether high dosage and long-term stimulation of noradrenaline will cause apoptosis on the fibroblast, 3) to investigate whether the protein and gene expression of cytokine other than TGF such as IL-1 α , β and IFN- β may involved in the adrenergic stimulated response

(MD04759)

CONTAK™ RENEWAL ® 4 AVY System Field Following

✍ YU Cheuk Man • FUNG Wing Hong • SANDERSON John Elsby# • CHAN Yat Sun Joseph • CHAN Chi Kin Hamish • CHEUNG Siu Ping Alice# • KONG Shun Ling#

📅 1 November 2004

❖ Guidant Europe NV/SA

The purpose of this study is to document appropriate system performance of the CONTAK

RENEWAL™ 4 AVT , Implantable Cardioverter Defibrillator system, which provides therapy for Heart Failure patients with risks of death because of Fast Ventricular rate and burden because of fast Atrial rate. This Field Following will supplement these data by confirming that the RENEWAL 4 AVT system functions as designed/intended under field conditions by physicians at multiple centres under varying environmental parameters.

The following is also evaluated,

- Clinical improvement and appropriateness of different timing and configuration to stimulate the left & right Ventricle for heart failure patients
 - The performance of the system on atrial arrhythmia detection algorithm and the therapy suite for induced and spontaneous Atrial Arrhythmias
- (MD04679)

Consultant Agree with Guidant Inc.

✍ YU Cheuk Man

☐ 10 December 2004

❖ Guidant Inc

This is not a research project, but a consultant agreement with Guidant Inc that Professor CM Yu will be a consultant for Guidant Inc on behalf of CUHK. The aim is to enhance academic and knowledge exchange between CUHK and Guidant, and will enhance future collaborative relationship.

(MD04303)

A 26 Week, Double-Blind, Randomized, Multicenter, Parallel Group, Active-Controlled Study Comparing Aliskiren to Ramipril with Optional Addition of Hydrochlorothiazide, Followed by a 4 Week Double-Blind, Randomized, Placebo-Controlled Withdrawal in Patients with Essential Hypertension

✍ YU Cheuk Man • LEE Pui Wai

☐ 15 March 2005

❖ Novartis Pharmaceuticals (HK) Ltd

This research study is demonstrate the efficacy, safety and tolerability of an aliskiren based antihypertensive regimen when compared to a ramipril based antihypertensive regimen over a period of 6 months in patients with essential hypertension. Data from this study will be used to support regulatory submissions seeking approval to market aliskiren worldwide for the treatment of hypertension.

Patients who fulfill the inclusion, exclusion and randomization criteria will be randomized in a double-blind fashion, in the assignment ratio of 1:1, to one of the 2 antihypertensive regimens: aliskiren or ramipril. Double-blind active-controlled treatment will be for a duration of 26 weeks. The double-blind active-controlled treatment will be initiated with either aliskiren 150 mg or ramipril 5 mg and will continue at this dosing regimen for 6 weeks. Following 6 weeks of treatment on the low-dose monotherapy regimen, optional up-titration to high-dose monotherapy, optional addition of low-dose HCTZ (12.5 mg) and optional up-titration of HCTZ to 25 mg will occur in 3 sequential steps at 6 week intervals, based on blood pressure response [i.e. achieving of target blood pressure of < 140/90 mmHg (MSSBP/MSDBP)]. Following 26 weeks of double-blind treatment, patients will be re-randomized to either continue on their existing dosing regimen at the end of the double-blind active-controlled treatment period or to placebo, in the assignment ratio of 1:1 for a 4 week double-blind withdrawal.

It is planned that at least 846 patients with essential hypertension (MSDBP = 95 mmHg and < 110 mmHg)

will be randomized in the study at approximately 80 centers worldwide.

(MD04743)

Cardiac Contractility Modulation for the Treatment of Heart Failure - Impact of Haemodynamic Optimization of Lead Position

✍ YU Cheuk Man • FUNG W. H.* • CHAN Yat Sun Joseph • CHAN Chi Kin Hamish

☐ 25 May 2005

❖ Impulse Dynamics N.V.

Congestive heart failure (CHF) is characterised by ventricular dysfunction which is one of the major causes of cardiac morbidity and mortality. Patients suffering from this condition have major symptoms of exercise intolerance and shortness of breath, which limit their daily activity and hence the quality of life. This condition also carries a high mortality despite advances in treatment. The 5-year mortality is usually over 50%. In addition, heart failure is one of the commonest causes of emergency hospital admission into the medical ward, which has great financial implication to medical care expenses. Currently therapy is primarily relies on medications. Despite the established treatment of heart failure, such as angiotensin converting enzyme inhibitor, beta-blockers, diuretics and other anti-heart failure medications, the mortality and morbidity can only be modestly altered. Recently, the use of device-based therapy opened a new era of heart failure therapy where patients will receive adjunctive implantation of pacemaker for further treatment. Our institute also showed that biventricular pacing causes left ventricular reverse remodeling and improvement of systolic synchronicity of the left ventricular, as illustrated by tissue Doppler imaging (TDI) studies. However, there are limitation of biventricular pacing

therapy in which the device is only indicated for patients with wide QRS complex duration.

Very recently, cardiac contractility modulation (CCM) has become the hope for clinical treatment in nearly all heart failure patients. The system is similar to pacemaker system though it works by a totally different mechanism. CCM improves the contractility of the heart by delivering non-excitatory impulses to the myocardium during the absolute refractory period. Pilot data has shown that CCM improves the contractility of the heart in animal models and in human. The system is implanted by pacing 2 right ventricular leads in the anterior and posterior septum respectively. Improvement of symptoms has been documented in early studies. Currently, acute hemodynamic study is conducted during CCM implantation to guide the placement of right ventricular leads. However, it remains unknown whether this maneuver will ensure further improvement of clinical and echocardiographic end-points. Furthermore, in patients who received biventricular pacing, acute hemodynamic study has never been shown useful to predict the intermediate and long-term clinical improvement or LV reverse remodeling response. Therefore, it is important to examine if hemodynamic study is really necessary during implantation of CCM. In addition, it will also be helpful to identify potentially useful predictors of response to CCM so as to guide the planning of an optimal therapeutic regimen to each patient.

(MD04842)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
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		in Chinese Type 2 Diabetes Patients (MD03790)
2002-03	Use of Software for Design of DNazymes (MD02506) ✍ BAUM Lawrence William	✍ CHAN Chung Ngor Juliana • CHAN Nor Norman (Community and Family Medicine)# • TONG Peter Chun Yip
2003-04	Mechanisms of Action of Potential Alzheimer's Disease Drug Curcumin, and Extract of Geung Wong (MD03921) ✍ BAUM Lawrence William • NG Ho Keung (Anatomical & Cellular Pathology)	2003-04 Olmesartan Reduces Incidence of Endstage Renal Disease in Patients with Type 2 Diabetic Nephropathy Trial (ORIENT) (MD03356) ✍ CHAN Chung Ngor Juliana • TONG Peter Chun Yip • SZETO Cheuk Chun • TOMLINSON Brian • COCKRAM Clive Stewart • OZAKI R* • SO Wing Yee* • CHOW Chun Chung Francis
2002-03	Better Health for Better Hong Kong (MD02424) ✍ CHAN Chung Ngor Juliana • KO T C Gary* • WONG Patrick* • CHAN Amy* • CHAN Cecilia*	
2002-03	Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance (CHARISMA) (MD02861) ✍ CHAN Chung Ngor Juliana • SO Wing Yee* • OSAKI R* • LAI Christopher* • MA Ronald*	2003-04 Prevalence of Diabetes and Metabolic Syndrome in Hong Kong Adolescents (MD03932) ✍ CHAN Chung Ngor Juliana • TONG Peter Chun Yip • OZAKI Risa • QING Qiao* • TUOMILEHTO Jaakko*
2002-03	A Multicentre, Randomised Study to Examine the Effects of Disease Management on Clinical Outcomes in Type 2 Diabetic Patients with Nephropathy (MD02610) ✍ CHAN Chung Ngor Juliana • TONG Peter Chun Yip • COCKRAM Clive Stewart • ZHANG Xuejie (Community and Family Medicine)# • LEUNG Y S Wilson*	2001-02 Cyclooxygenase-2 in Human Gastric Ulcers: Biological and Clinical Perspectives (MD01056) ✍ CHAN Ka Leung Francis • LEUNG Wai Keung • SUNG Joseph Jao Yiu • SZETO Cheuk Chun • TO Ka Fai (Anatomical & Cellular Pathology)
2003-04	The Relationship Between Erectile Dysfunction and Endothelial Dysfunction	2001-02 Cyclooxygenase and Trefoil Peptides in Stomach - Biology & Clinical Diseases (MD01711) ✍ CHAN Ka Leung Francis • LEUNG Wai Keung • YU Jun • SUNG

- Joseph Jao Yiu • NG Enders Kwok-wai (Surgery) • CHUNG Sheung Chee Sydney (Surgery) • TO Ka Fai (Anatomical & Cellular Pathology) • CHEN M H* • HU P J*
- 2001-02 Clinical Protocol for a Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of Celecoxib (SC-58635) in the Prevention of Colorectal Sporadic Adenomatous Polyps (PRESAP) (MD01879)
- ✍ CHAN Ka Leung Francis • SUNG Joseph Jao Yiu • LEUNG Wai Keung • LEE Yuk Tong • CHAN Lik Yuen • WU Che Yuen Justin • HUI Yui • HUNG Cheung Tsui# • HUI Aric Josun
- 2003-04 A Population-Based Study on the Prevalence of SARS-Associated Coronavirus Infection in Hong Kong (CU03532)
- ✍ CHAN Ka Leung Francis • CHAN Kay Sheung Paul (Microbiology) • Douglas G ALTMAN* • LAU Tak Fai Joseph (Centre for Epidemiology & Biostatistics) • McCARTHY Noel* • NG Pak Cheung (Paediatrics) • SUNG Joseph Jao Yiu • WONG Wing-sze* • WU Ka Lun Alan# • YU Ly-mee* • LO Su Vui*
- 2003-04 Preventing NSAID-Associated Ulcer Bleeding for High-Risk Patients: From Cyclooxygenase-2 to Therapeutics (CU03455)
- ✍ CHAN Ka Leung Francis • LEUNG Wai Keung • SUNG Joseph Jao Yiu
- 2003-04 A Randomized Double-Blind Placebo Controlled Study to Assess the Prevention of Low-Dose Acetylsalicylic Acid (ASA) Associated Gastroduodenal Lesions and Upper Gastrointestinal Symptoms in Patients Taking Esomeprazole 20 mg Once Daily (od) for 26 Weeks (MD03325)
- ✍ CHAN Ka Leung Francis • LEE Yuk Tong • LEUNG Wai Keung • WU Che Yuen Justin • HUNG Cheung Tsui# • HUI Aric Josun • WONG Wai Sun
- 2002-03 A Study on the Viral Kinetics of Different Regimes of Pegylated Interferon and Lamivudine Combination Therapy in HBeAg Positive Chronic Hepatitis B (MD02499)
- ✍ CHAN Lik Yuen • SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • LEUNG Wai Yee Nancy* • HUI Y*
- 2002-03 A Multicentre Phase III Study of Interferon-Beta-1a for the Treatment of Chronic Hepatitis C in Asian Patients (MD02926)
- ✍ CHAN Lik Yuen • CHAN Ka Leung Francis • LEUNG Wai Yee Nancy* • HUI Y* • SUNG Joseph Jao Yiu
- 2003-04 A Study on the Serum and Hepatic Viral Dynamics in Chronic Hepatitis B Patients Treated by Pegylated Interferon and

	Lamivudine Combination Therapy (MD03584)		Wing Bun • SO Wing Yee • CHAN N* • MA R*
	✍ CHAN Lik Yuen		
2003-04	A Study of Virodynamics in the Treatment of Chronic Hepatitis B by Pegylated Interferon and Lamivudine Combination (MD03949)	2002-03	A Multicenter, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Safety and Efficacy of MK-0767 Added to Metformin in Patients with Inadequately Controlled Type 2 Diabetes Mellitus (MD02446)
	✍ CHAN Lik Yuen • SUNG Joseph Jao Yiu • ZEUZEM Stefan* • MIHM Ulrike*		✍ CHOW Chun Chung Francis • CHAN Wing Bun* • OZAKI R*
2003-04	A Randomized, Double-Blind Trial of Telbivudine (LdT) versus Lamivudine in Adults with Decompensated Chronic Hepatitis B and Evidence of Cirrhosis (MD03850)	2002-03	A Multicenter, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Safety and Efficacy of MK-0767 Added to Sulfonylurea in Patients with Inadequately Controlled Type 2 Diabetes Mellitus (MD02540)
	✍ CHAN Lik Yuen • HUI Yui • WONG Wai Sun		✍ CHOW Chun Chung Francis • CHAN Wing Bun* • OZAKI R*
2003-04	Catheter Based Interventions for Patients with Symptomatic Peripheral Vascular Disease (MD03998)	2003-04	A 24 Weeks, Multi-Centre, Randomised, 2-Arm Parallel, Open-Labelled Study to Investigate the Efficacy and Safety of Initiating Biphasic Insulin Aspart 30 (BIAsp 30) in Type 2 Diabetes Patients Currently Not Achieving Treatment Targets with Oral Anti-Diabetic Drugs Alone (MD03744)
	✍ CHAN Yat Sun Joseph • YU Cheuk Man • CHAN Wai Man Wilson		✍ CHOW Chun Chung Francis • OZAKI Risa • MA Ching Wan Ronald
2002-03	A Multinational, Randomized, Double-Blind, Placebo-Controlled, Forced-Titration, 2 x 2 Factorial Design Study of the Efficacy and Safety of Long Term Administration of Nateglinide and Valsartan in the Prevention of Diabetes and Cardiovascular Outcomes in Subjects with Impaired Glucose Tolerance (IGT) (MD02454)	2003-04	An International, Randomised, Open-Labelled Parallel Group Four Months Comparison of Basal Bolus Treatment with Insulin Aspart Including NPH and Biphasic Insulin Aspart
	✍ CHOW Chun Chung Francis • COCKRAM Clive Stewart • FUNG Wing Hong • CHAN W* • CHAN		

- Formulations in Subjects with Types 2 Diabetes (MD03708)
 ✍ CHOW Chun Chung Francis • OZAKI R* • MA C W Ronald* • CHAN W B*
- 2003-04 Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events (ACTIVE) - A Parallel, Randomized, Controlled Evaluation of Copidogrel plus Aspirin, with Factorial Evaluation of Irbesartan, for the Prevention of Vascular Events in Patients with Atrial Fibrillation (MD03400)
 ✍ FUNG Wing Hong • SANDERSON John Elsby# • CHAN Yat Sun Joseph • KUM Chi Chiu Leo • WONG Tai Hung John • LAM Yat Yin*
- 2001-02 Evaluation of Subjective Sleepiness and Prevalence of Obstructive Sleep Apnoea and Sleep Disordered Breathing in a Population of Commercial Drivers (MD01948)
 ✍ HUI Shu Cheong David
- 2002-03 A Randomized, Placebo-Controlled Study of the Effect of Nasal CPAP on 24 Hour Blood Pressure and the Sympathetic Nervous System in Obstructive Sleep Apnoea Syndrome (MD02413)
 ✍ HUI Shu Cheong David • KO Wai San Fanny* • FOK Pui Chu Joan* • CHAN Chio Ho Michael*
- 2002-03 A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Trial Assessing the Rate of Decline of Lung Function with Tiotropium 18 mcg Inhalation Capsule Once Daily in Patients with Chronic Obstructive Pulmonary Disease (COPD) (MD02758)
 ✍ HUI Shu Cheong David • KO Wai San Fanny* • FOK Pui Chu Joan* • TONG Mabel* • CHAN Chio Ho Michael* • CHAN Pui Shan • HO Wai Mun
- 2003-04 A Study on Nonalcoholic Steatohepatitis (NASH) in Hong Kong (MD03702)
 ✍ HUI Yui • CHAN Lik Yuen • CHAN Ka Leung Francis • CHOW Chun Chung Francis • WONG W S Vincent* • SO Wing Yee*
- 2003-04 Prevalence of Respiratory Symptoms, Common Respiratory Disease, Atopy and Bronchial Hyperresponsiveness in Elderly Chinese Living In Hong Kong (MD03741)
 ✍ KO Wai San Fanny • HUI Shu Cheong David • WOO Jean
- 2002-03 Mr Os (Hong Kong) - The First Cohort Study on Osteoporosis in Chinese Men (CU02101)
 ✍ KWOK Chi Yui Timothy • LAM Wai Kei Christopher (Chemical Pathology) • LEUNG Ping Chung (Orthopaedics & Traumatology) • LYNN Sui Heng Henry (School of Public Health) • WOO Jean
- 2002-03 The Role of Methylcobalamin in Early Dementia Patients with Vitamin B12

	Deficiency and Hyperhomocysteinaemia? (MD02478) ✍ KWOK Chi Yui Timothy • LAM Chiu Wa (Psychiatry)		Leung Francis • HUNG Cheung Tsui#
2003-04	Can Oral Vitamin B ₁₂ and Folate Supplementation Preserve Cognitive Function of Patients with Dementia? (MD03611) ✍ KWOK Chi Yui Timothy • LAM Chiu Wa (Psychiatry) • WOO Kam Sang • ZEE Chung Ying Benny (Community and Family Medicine)	2002-03	Detection of Aberrantly Methylated DNA in Blood and Feces: A Novel Non-Invasive Screening Method for Gastrointestinal Cancer (MD02474) ✍ LEUNG Wai Keung • TO Ka Fai (Anatomical & Cellular Pathology) • CHAN Ka Leung Francis • SUNG Joseph Jao Yiu
2001-02	Histologic and Cell Kinetic Changes of Premalignant Gastric Lesions with Helicobacter Pylori Eradication and Cyclooxygenase-2 Inhibition (MD01061) ✍ LEUNG Wai Keung • CHAN Ka Leung Francis • CHAN Wing Yee (Anatomical & Cellular Pathology)# • CHUNG Sheung Chee Sydney (Surgery) • NG Enders Kwok-wai (Surgery) • SUNG Joseph Jao Yiu • YU Jun	2002-03	A Randomized, Placebo Controlled Trial of Traditional Chinese Medicine in the Treatment of Irritable Bowel Syndrome (CU02116) ✍ LEUNG Wai Keung • CHAN Ka Leung Francis • CHE Chun Tao (School of Chinese Medicine) • LIANG Songming (School of Chinese Medicine) • SUNG Joseph Jao Yiu
2001-02	A Multicentre, Randomised, Double-Blind, Placebo-Controlled Dose-Finding Phase II Study of Subcutaneously Administered Onercept in the Treatment of Patients with Active Crohn's Disease (Protocol: 22523) and Long-Term Follow-Up of Crohn's Disease Patients Having Completed Serono protocol 22523, Allowing for Re-Treatment with Open-Label Onercept (Protocol: 23054) (MD01458) ✍ LEUNG Wai Keung • LEONG Rupert Wing Loong# • CHAN Ka	2003-04	Chemoprevention and Treatment of Gastric Cancer by Peroxisome Proliferator-Activated Receptor γ Ligands: An <i>in vivo</i> Study (MD03832) ✍ LEUNG Wai Keung • CHAN Wing Yan Michael# • TO Ka Fai (Anatomical & Cellular Pathology) • CHAN Ka Leung Francis • SUNG Joseph Jao Yiu
		2003-04	A Phase III Multi-National, Multi-Centre, Open Label, 52-Week Safety Study to Assess the Safety of Chronic Therapy with the Humanised Anti-TNF PEG Conjugate CDP870 400 mg sc, (Dosed 4-Weekly to Week 48), in the Treatment

- of Patients with Active Crohn's Disease Who Have Previously Completed Studies CDP870-031 or CDP870-032 (MD03369)
✍ LEUNG Wai Keung • CHAN Ka Leung Francis • HUNG Cheung Tsui# • WONG Wai Sun
- 2003-04 A Phase III Multi-National, Multi-Centre, Open Label, 52-Week Safety Study to Assess the Safety of Re-Exposure after a Variable Interval and Subsequents Chronic Therapy with the Humanised Anti-TNF PEG Conjugate CDP870 400 mg sc, (dosed at Weeks 0, 2 and 4 then 4-weekly to Week 48), in the Treatment of Patients with Active Crohn's Disease Who Have Previously Been Withdrawn from Studies CDP870-031 or CDP870-032 Due to an Exacerbation of Crohn's Disease (MD03548)
✍ LEUNG Wai Keung • CHAN Ka Leung Francis • HUNG Cheung Tsui# • WONG Wai Sun
- 2003-04 A Phase III Multi-National, Multi-Centre, Double-Blind Placebo-Controlled Parallel Group, 26-Week Safety Study to Assess the Safety and Efficacy of the Humanised Anti-TNF PEG Conjugate CDP870 400 mg sc, (Dosed at Weeks 0, 2, 4 then 4-Weekly to Week 24), in the Treatment of Patients with Active Crohn's Disease (MD03937)
✍ LEUNG Wai Keung • CHAN Ka Leung Francis • HUNG Cheung Tsui# • WONG Wai Sun
- 2001-02 A Randomized, Double-Blind Study of Treatment with LdT, Lamivudine, or the Combination of Both Agents in Adult Patients with HbeAg-positive Chronic Hepatitis B (MD01585)
✍ LEUNG Wai Yee Nancy
- 2002-03 A Phase IIB Extension Study of LdT (Telbivudine), Lamivudine, or LdT plus Lamivudine in Patients with Chronic Hepatitis B Who Have Completed NV-02B-003 (MD02492)
✍ LEUNG Wai Yee Nancy
- 2003-04 The Effect of Lingzhi (*Ganoderma Lucidum*) and Sen Miao San Supplementation in Rheumatoid Arthritis (RA): Biomarkers of Antioxidant, Inflammatory Status and Clinical Efficacy (MD03646)
✍ LI Kwok Ming Edmund • TAM Lai Shan • TOMLINSON Brian • BENZIE Iris F F*
- 2001-02 Salvage of Infarcted Myocardium by an Extract of Dagencao with Dual Effects on Angiogenesis and Cardiomyogenesis and Investigation of the Molecular Mechanism Involved in Dagencao Induced Angiogenesis & Cardiomyogenesis (MD01972)
✍ LI Ming • SANDERSON John Elsby# • LEE Ka Ho Kenneth (Anatomy) • LEUNG Ping Chung (Orthopaedics & Traumatology)
- 2003-04 The Expression of Human Bone Morphogenetic Protein-4 in *Pichia Pastoris* and the Effects of Site-Directed

- Mutagenesis on Its Expression and Function (MD03888)
✍ LI Ming
- 2003-04 Purification and Cloning of the Novel Muscle Healing Protein(s) that Enhances Muscle Repair and Regeneration (CU03450)
✍ LI Ming • SANDERSON John Elsby# • LEE Ka Ho Kenneth (Anatomy)
- 2003-04 Salvage of Ischemic/Infarcted Myocardium by Dagencao Induced Rapid Angiogenesis and Myogenesis and Its Development (MD03801)
✍ LI Ming • SANDERSON John Elsby# • YU Cheuk Man • LEE Ka Ho Kenneth (Anatomy) • CHEUNG N M Edmund*
- 2003-04 Identification of Tumor-Specific Glycoforms of Serum Proteins from Patients with Early Hepatocellular Carcinoma by Differential Lectin Affinity Chromatography and Quantitative Proteomic Profiling (CU03466)
✍ POON Chuen Wai • CHAN Anthony Tak Cheung (Clinical Oncology) • LAI Bo San Paul (Surgery) • LEE Chi Yan Conrad (Clinical Oncology)# • MOK Shu Kam Tony (Clinical Oncology) • JOHNSON Philip James (Clinical Oncology)
- 2003-04 Identification of Serum Proteomic Patterns for the Prediction of Tumor
- Recurrence in Patients with Hepatocellular after Curative Resection (MD03631)
✍ POON Chuen Wai • LAI Bo San Paul (Surgery) • CHAN Anthony Tak Cheung (Clinical Oncology)
- 1999-00 A Double-Blind Placebo Controlled Clinical End-Points of Lamivudine in Patients with Hepatitis B Related Cirrhosis (MD98164)
✍ SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • TSANG W C Steven* • CHAN Lik Yuen • HUI Y*
- 2001-02 Genomic Study of Viral Hepatitis B to Predict Development of Cancer and Response to Therapy (MD01639)
✍ SUNG Joseph Jao Yiu • CHAN Lik Yuen • LEUNG Wai Yee Nancy • MOK Shu Kam Tony (Clinical Oncology) • JOHNSON Philip James (Clinical Oncology) • TSUI Kwok Wing (Biochemistry) • WAYE Mary Miu Yee (Biochemistry) • LEUNG Kwong Sak (Computer Science and Engineering) • HENG Pheng Ann (Computer Science and Engineering) • LEE Kin Hong (Computer Science and Engineering)
- 2002-03 Acid Suppression by Proton Pump Inhibitor in Peptic Ulcer Bleeding (MD02996)
✍ SUNG Joseph Jao Yiu • LEUNG Wai Keung • CHAN Ka Leung Francis • WU Che Yuen Justin •

- LAU Yun Wong James (Surgery) • CHUNG Sheung Chee Sydney (Surgery)
- 2002-03 Intravenous Pantoprazole in Aspirin-Induced Ulcer Bleeding (MD02933)
 ✍ SUNG Joseph Jao Yiu • WU Che Yuen Justin • CHAN Ka Leung Francis • LEUNG Wai Keung • LEE Yuk Tong • HUNG Cheung Tsui# • HUI Aric Josun
- 2002-03 Efficacy and Tolerability of a Maintenance Treatment over 6 Months with Pantoprazole 20mg o.d. vs. Esomeprazole 20mg o.d. in Patients with Healed GERD (MD02874)
 ✍ SUNG Joseph Jao Yiu • WU Che Yuen Justin • LEUNG Wai Keung • CHAN Ka Leung Francis • LEE Yuk Tong • HUNG Cheung Tsui# • HUI Aric Josun
- 2003-04 Screening of Colorectal Neoplasm in Chinese (MD03767)
 ✍ SUNG Joseph Jao Yiu • LEUNG Wai Keung • TO Ka Fai (Anatomical & Cellular Pathology) • LAM Wai Man Wynn (Diagnostic Radiology & Organ Imaging) • CHAN Ka Leung Francis • YEUNG Deacons*
- 2003-04 Genotypes of Pro-Inflammatory Cytokines (IL-1b, TNF-a and IL-10) Associated with Pre-Malignant Gastric Lesions (CU03436)
- ✍ SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • CHUNG Sheung Chee Sydney (Surgery) • LEUNG Wai Keung • NG Enders Kwok-wai (Surgery) • TO Ka Fai (Anatomical & Cellular Pathology)
- 2003-04 The Role of Cyclooxygenase (COX)-2 Overexpression in Gastric Carcinogenesis: A Transgenic Mouse Model (MD03968)
 ✍ SUNG Joseph Jao Yiu • LEUNG Wai Keung • CHENG Sze Lok# • FU Yuangen# • CHUN Wu Kai* • XU Li* • WANG Xin*
- 2003-04 The Role of Cyclooxygenase-2 in Liver Fibrosis and the Potential of Misoprostol as an Anti-Fibrotic Agent (CU03446)
 ✍ SUNG Joseph Jao Yiu • CHAN Lik Yuen • CHENG Sze Lok# • LEUNG Wai Keung
- 2003-04 Clinical Studies on the Treatment of Severe Acute Respiratory (MD03837)
 ✍ SUNG Joseph Jao Yiu
- 2003-04 Commissioned Projects-Research on the Control of Infectious Diseases (MD03896)
 ✍ SUNG Joseph Jao Yiu • LO Yuk Ming Dennis (Chemical Pathology) • HUI Shu Cheong David • TSUI Stephen Kwok Wing (Biochemistry) • TANG Leung Sang Nelson (Chemical Pathology) • IP Margaret (Microbiology) • POON Chuen Wai • CHEUNG Fanny Mui Ching (Psychology)

2003-04	A Multi-Centre, Randomised, Double-Blind, Parallel Group, Placebo-Controlled Trial on Safety and Efficacy of Activated Recombinant Factor VII (rFVIIa/ NovoSeven®) in the Treatment of Active Variceal Bleeding in Patients with Advanced Cirrhosis (MD03518)	BENZIE Iris F F* • LAM Wai Man Wynnie (Diagnostic Radiology & Organ Imaging) • GRIFFITH James Francis (Diagnostic Radiology & Organ Imaging) • HAINES Christopher John (Obstetrics & Gynaecology) • LAM Wai Kei Christopher (Chemical Pathology) • CHAN Chung Ngor Juliana
	✍ SUNG Joseph Jao Yiu • LAU Yun Wong James (Surgery)	
2002-03	Molecular Biology of Peritoneal Fibrosis and Peritoneal Dialysis Failure - A Study of Transforming Growth Factor Beta and Its Downstream Mediators by a Cell Culture Model (CU02122)	2003-04 A Sibling-Based Study of the Molecular Genetics of Hypertension-Application of Microarray-Based DNA Chip Technology (CU03438)
	✍ SZETO Cheuk Chun • WONG Teresa Y. H.*	✍ TOMLINSON Brian • THOMAS Neil G (School of Pharmacy)# • YANG Michael*
2003-04	Messenger RNA Expression of Glomerular Podocyte Components in the Urinary Sediment of Patients with Acquired Proteinuric Diseases (MD03748)	2003-04 An Open-Label, Randomized, Multi-Centre, Phase IIb/IV, Parallel Group Study to Compare the Efficacy and Safety of Rosuvastatin and Atrovastatin in Subjects with Type IIa and IIb Hypercholesterolaemia (MD03656)
	✍ SZETO Cheuk Chun	✍ TOMLINSON Brian • YU Cheuk Man • KO T C Gary*
2003-04	Treatment of Early Immunoglobulin a Nephropathy by Angiotensin Converting Enzyme Inhibitor - A Randomized Controlled Trial (MD04749)	2002-03 The Participation of the Cytoskeleton in Insulin Action in Human Skeletal Muscle (CU02124)
	✍ SZETO Cheuk Chun • LI Kam Tao Philip* • YU Wai Yin Alex*	✍ TONG Peter Chun Yip • COCKRAM Clive Stewart
2002-03	Oxidative Stress in Patients with Type 2 Diabetes: Are There Benefits from Antioxidant Supplements? (MD02339)	2003-04 Oxidative Stress and Insulin Resistance in Hong Kong Chinese with Thalassaemia Minor (CU03439)
	✍ TOMLINSON Brian • THOMAS Neil G (School of Pharmacy)# •	✍ TONG Peter Chun Yip • CHAN Chung Ngor Juliana • CHAN Yu

	Leung (Diagnostic Radiology & Organ Imaging)# • HO Chung Shun (Chemical Pathology) • LAM Wai Kei Christopher (Chemical Pathology) • NG Heung Ling Margaret (Anatomical & Cellular Pathology)		Pharmacy)# • TOMLINSON Brian • KAY Li Chi Richard
2001-02	Management of Atherothrombosis with Clopidogrel in High-Risk Patients with Recent Transient Ischemic Attack or Ischemic Stroke: A Randomised, Double-Blind Study, with 18 Months of Follow-Up (MD01361) ✍ WONG Ka Sing Lawrence	2002-03	Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance (CHARISMA) (MD02626) ✍ WONG Ka Sing Lawrence • HUI Andrew Che Fai • MOK Chung Tong Vincent • LEUNG Wai Hong Thomas • LIANG K S Eric* • LI Sin Hung*
2002-03	An Open-Label Extension Trial to Assess the Safety of Galantamine HBr in the Treatment of Vascular Dementia (MD02510) ✍ WONG Ka Sing Lawrence • KWOK Chi Yui Timothy • MOK Chung Tong Vincent • HUI Andrew Che Fai • HO W S Wency*	2003-04	A Double-Blind, Randomized, Placebo Controlled, Parallel Group, Multicentre, Phase IIb/III Study to Assess the Efficacy and Safety of Intravenous NXY-059 in Acute Ischemic Stroke (MD03486) ✍ WONG Ka Sing Lawrence • LEUNG Wai Hong Thomas • HUI Andrew Che Fai • MOK Chung Tong Vincent • LIANG K S Eric*
2002-03	An Open-Label, Long-Term, Flexible-Dose Study of Safety, Tolerability, and Therapeutic Response of PNU-95666E in Patients with Parkinson's Disease (MD02481) ✍ WONG Ka Sing Lawrence • MOK Chung Tong Vincent • YEUNG Hon Ming Jonas	2003-04	The Significance of Microembolic Signals and New Cerebral Infarcts on the Progression of Neurological Deficit in Acute Stroke Patients with Middle Cerebral Artery Stenosis (CU03440) ✍ WONG Ka Sing Lawrence • CHAN Yu Leung (Diagnostic Radiology & Organ Imaging)# • LAM Wai Man Wynn (Diagnostic Radiology & Organ Imaging)
2002-03	Genetic Factors in the Etiology of Middle Cerebral Artery Stenosis in Chinese with Diabetes and Hypertension (MD02317) ✍ WONG Ka Sing Lawrence • THOMAS Neil G (School of	2003-04	A Phase II, Double-Blind, Dose-Finding, Placebo Controlled, Study to Assess the Efficacy and Safety of SCH 420814 as Monotherapy in Subjects with Early Parkinson's Disease (MD03427)

- ✍ WONG Ka Sing Lawrence • MOK Chung Tong Vincent • YEUNG Hon Ming Jonas
- 2003-04 An Open-Label Extension Study to Assess the Safety and Tolerability of a 25 mg Dose of SCH 420814 as Monotherapy in Subjects with Early Parkinson's Disease (MD03583)
- ✍ WONG Ka Sing Lawrence • MOK Chung Tong Vincent • YEUNG Hon Ming Jonas
- 2003-04 Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events (ACTIVE): A Parallel Randomized Controlled Evaluation of Clopidogrel Plus Aspirin, with Factorial Evaluation of Irbesartan, for the Prevention of Vascular Events, in the Patients with Atrial Fibrillation (MD03774)
- ✍ WONG Ka Sing Lawrence • LEUNG Thomas WH* • HUI Andrew CF* • MOK Chung Tong Vincent* • LIANG K S Eric*
- 2003-04 A Randomized, Multicenter, Double-Blind, Placebo-Controlled, 18-Month Study of the Efficacy of Xaliproden in Patients with Mild-to-Moderate Dementia of the Alzheimer's Type (MD03610)
- ✍ WONG Ka Sing Lawrence • MOK Chung Tong Vincent • DAI Lok Kwan David
- 2001-02 A Randomized, Controlled Trial of the Effect of Milk Supplementation on Bone Density in Women Aged 20-35 Years in Asia (MD01501)
- ✍ WOO Jean • LEUNG Ping Chung (Orthopaedics & Traumatology)
- 2002-03 Consultancy on Health Care Services in Home and Community Based Model (MD02827)
- ✍ WOO Jean • HUI Elsie
- 2003-04 A Quality Website for Healthy Ageing in Hong Kong (MD03815)
- ✍ WOO Jean • KWOK Chi Yui Timothy
- 2003-04 A Multicentre, Double-Blind, Double-Dummy, Randomized, Controlled Trial Comparing the Efficacy and Safety of the Vira-38 ° versus Oseltamivir in Patients with Acute Influenza (MD03974)
- ✍ WOO Jean • ZEE Chung Ying Benny (Community and Family Medicine)
- 1999-00 A Multicenter, Randomized, Controlled, Double-Blind Trial to Investigate the Clinical Efficacy and Tolerability of Early Treatment with Simvastatin 40mg Daily for 30 Days, Followed by Simvastatin 80mg Daily thereafter in Tirofiban-Treated Acute Coronary Syndrome Patients Who Have Been Randomized to Receive Enoxaparin or Unfractionated Heparin in Conjunction with Aspirin. (A to Z study) (MD99072)
- ✍ WOO Kam Sang • SANDERSON John Elsby# • FUNG Wing Hong* • CHAN W M Wilson*

- 2001-02 A Novel Strategy to Prevent Atherosclerosis in Predialysis Renal Failure: A Clinical Model of Accelerated Atherosclerosis (MD01070)
✍ WOO Kam Sang • CELERMAJER David S* • LAU Tak Fai Joseph (Centre for Epidemiology & Biostatistics) • LUI Siu Fai • METREWELI Constantine (Diagnostic Radiology & Organ Imaging)# • SANDERSON John Elsby# • SZETO Cheuk Chun • YU Wai Yin Alex
- 2002-03 Epidemiological Study of the Correlation Between the Intima-Media Thickness of the Common Carotid Artery and Absolute Cardiovascular Risk (MD02798)
✍ WOO Kam Sang • CHOOK Ping • KUM Chi Chiu Leo
- 2002-03 Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance (CHARISMA) (MD02828)
✍ WOO Kam Sang • SANDERSON John Elsby# • YU Cheuk Man • WONG Ka Sing Lawrence • CHAN Chung Ngor Juliana • CHAN W M Wilson* • TSE Kin Kei Lawrence* • CHAN Anna* • YIP Wai Kwok Gabriel* • WU Eugene Brian* • WONG John* • KUM C.C. Leo* • FUNG W H* • CHAN C K* • KWONG Shu Keung* • CHAN Yau Sung Joseph* • YU Tak Hung* • KWOK Hing Yiu* • YIP W C*
- 2003-04 An International, Randomized, Double-Blind Study Evaluating the Efficacy and Safety of Fondaparinux versus Enoxaparin in the Acute Treatment of Unstable Angina / Non St-Segment Elevation MI Acute Coronary Syndrome (MD03332)
✍ WOO Kam Sang • YIP Wai Kwok Gabriel • CHAN Wai Man Wilson • CHAN Yat Sun Joseph • YU Cheuk Man • WONG Tai Hung John • CHAN Chi Kin Hamish • KWONG Shu Keung • FUNG Wing Hong • YIP Wai Cheong • KUM Chi Chiu* • CHAN Lip Kiong* • CHAN Wai Ling* • YIU Kwok Hing* • CHAN Kin Wing*
- 2003-04 An International Randomised Study Evaluating the Efficacy and Safety of Fondaparinux Sodium versus Control Therapy and Glucose-Insulin-Potassium Infusion versus Control in a Broad Range of Patients with ST Segment Elevation Acute Myocardial Infarction (MD03460)
✍ WOO Kam Sang • YU Cheuk Man • CHAN Wai Man Wilson • CHAN Yat Sun Joseph • WU E B*
- 2002-03 Is Visceral Hyperalgesia the Culprit of Noncardiac Chest Pain in Chinese? (CU02127)
✍ WU Che Yuen Justin • CHAN Ka Leung Francis • FUNG Wing Hong • LEUNG Wai Keung • MOK Chung Tong Vincent • SUNG Joseph Jao Yiu • WONG Ka Sing Lawrence

2003-04	A Randomized, Double-Blind, Placebo-Controlled, Multicenter Evaluation of the Efficacy and Safety of Tegaserod (6 mg b.i.d.), Administered Orally for 12 Weeks, to Male Patients with Chronic Constipation (MD03414)	Arteries by High Dose Atorvastatin Therapy (ANIMATE) (MD02551)
	✍ WU Che Yuen Justin • SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • LEUNG Wai Keung • LEE Yuk Tong • HUNG Cheung Tsui# • HUI Aric Josun • WONG Wai Sun • YIU Chi Him Desmond*	✍ YU Cheuk Man • CHAN Wai Man Wilson • SANDERSON John Elsby#
2002-03	Treatment of Diastolic Heart Failure: The Role of Blockade of the Renin-Angiotensin System. A Comparison of Diuretics with an Angiotensin Converting Enzyme Inhibitor, Angiotensin Receptor Blockade or Diuretics Alone (MD98666)	2002-03 MIDHeft Study (Extension II) (MD02802)
	✍ YU Cheuk Man • SANDERSON John Elsby#	✍ YU Cheuk Man • SANDERSON John Elsby# • FUNG Wing Hong*
2002-03	The Effect of Angiotensin Receptor Blockade Alone or in Combination with Spironolactone on the Process of Ventricular Remodeling in Chronic Heart Failure (MD01512)	2002-03 A Multi-Centre, Multinational, Long-Term, Extension Study to Assess the Safety and Tolerant of Subject Optimised Treatment Regimens of Oral Sildenafil for Pulmonary Arterial Hypertension in Subjects Who Have Completed Study A1481140 (MD02489)
	✍ YU Cheuk Man • SANDERSON John Elsby# • CHAN Kin Yin • YEUNG Leata Y.C.* • WONG John* • WU Eugene Brian* • LAM Wai Man Wynnie (Diagnostic Radiology & Organ Imaging)	✍ YU Cheuk Man • KONG Shun Ling# • MA Wing Yan# • YIP Wai Kwok Gabriel • WANG Zheng (Ophthalmology and Visual Sciences)# • WONG Wing Cheong (Ophthalmology and Visual Sciences) • WONG Tai Hung John • KUM Chi Chiu Leo • LAI Hong Yee Connie*
2002-03	Atherosclerotic Plaque Burden Reduction in Native and Intervened Coronary Arteries as Well as in Other Major	2002-03 A Multinational, Multi-Centre, Randomised, Double-Blind, Double-Dummy, Placebo-Controlled Study to Assess the Efficacy and Safety of 20, 40 and 80 mg TID Sildenafil in the Treatment of Pulmonary Arterial Hypertension in Subjects Aged 18 Years and Over (MD02780)
		✍ YU Cheuk Man • KONG Shun Ling# • MA Wing Yan# • NG Siu King Joan (Ophthalmology and

- Visual Sciences) • YIP Wai Kwok Gabriel* • TAM Lai Shan* • LAI Hong Yee Connie* • WONG Wing Cheung*
- 2003-04 A Randomized, Double-Blind, Double-Dummy, Parallel Group, Multinational, Clinical Study to Evaluate the Efficacy and Safety of Enoxaparin versus Unfractionated Heparin in Patients with Acuted ST-segment Elevation Myocardial Infarction Receiving Fibrinolytic Therapy (MD03404)
✍ YU Cheuk Man • CHAN Wai Man Wilson • CHAN Yat Sun Joseph • YIP Wai Kwok Gabriel • WONG Tai Hung John • CHAN Chi Kin Hamish • KWONG Shu Keung • FUNG Wing Hong • CHAN Lip Kiong* • KUM Chi Chiu* • YIU Kwok Hing* • CHAN Wai Ling* • CHAN Kin Wing*
- 2003-04 A Multi-Center, Double-Blind, Randomized, Parallel Group Study to Evaluate the Effects of Two Different Doses of Losartan on Morbidity and Mortality in Patients with Symptomatic Heart Failure Intolerant of ACE Inhibitor Treatment (MD03316)
✍ YU Cheuk Man • KONG Shun Ling# • YIP Wai Kwok Gabriel • LAM Y Y* • YU Eugene*
- 2003-04 The Benefit of Biventricular Pacing Therapy in Heart Failure Patients with Narrow QRS Complexes Who Had Systolic Mechanical Asynchrony by Echocardiography (MD03394)
✍ YU Cheuk Man • SANDERSON John Elsby# • FUNG Wing Hong
- 2003-04 Predictors of Response To Cardiac Resynchronization Therapy (PROSPECT) (MD03718)
✍ YU Cheuk Man • FUNG Wing Hong • ZHANG Qing*

RESEARCH PROJECTS

A Randomized, Double-Blind Trial to Assess the Safety and Relative Efficacy of CAIV-T against Inactivated Influenza Vaccine in Children 6-59 Months of Age, MI-CP111

✍ CHAN Kay Sheung Paul

📅 1 November 2004

❖ MedImmune Inc.

Influenza remains a major global health impact. The existing vaccines have a number of drawbacks including narrow spectrum of protection, short duration of protection, and requiring painful injection.

This study is to evaluate the efficacy of a new form of influenza vaccine in children. This is a multi-country study with the Department of Microbiology of the Chinese University of Hong Kong serving as a central laboratory for Asian study sites.

(MD04472)

Formulation of a Multiplex-RT-PCR-Based Screening Protocol to Facilitate Rapid Clinical Diagnosis of Respiratory Tract Infections

✍ CHAN Kay Sheung Paul • CHAN Wai Chi • FOK Tai Fai (Paediatrics) • NG Pak Cheung (Paediatrics) • LEUNG Ting Fan (Paediatrics)

📅 15 February 2005

❖ Research Fund for the Control of Infectious Diseases - Health, Welfare and Food Bureau

Objective: To devise, optimize and evaluate a rapid diagnostic scheme for simultaneous screening of

common causative agents for human respiratory tract infections, including the SARS-associated coronavirus (SARS-CoV), so as to facilitate better treatment and control of infectious diseases.

Design: The scheme adopts a two-staged multiplex-RT-PCR approach which will be applied to cultured samples and over 300 clinical specimens in order to evaluate its potential to identify agents responsible for known respiratory tract infections including SARS. To optimize the clinical applicability of the method, the effects of various combinations of primers targetting specific genomic regions of the test agents will be analyzed, along with various parameters known to affect multiplex PCR efficiency, such as primer concentrations and reaction conditions. The primary test initially screens for the presence of influenza A and B viruses, respiratory syncytial viruses (RSV), parainfluenza viruses, human metapneumovirus and the SARS-CoV. A positive result will be followed by a confirmatory test with the corresponding agent-specific primer pair(s), whereas a negative specimen will be subjected to a secondary detection assay for other viral and bacterial agents including, but not limited to adenoviruses, enteroviruses, *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*. Finally, a genome-wide multiplex-nested RT-PCR test will complement the diagnosis by confirming the presence/absence of the SARS-CoV in a specimen.

Results: The optimized detection parameters and degree of correlation between results of the screening tests and that obtained by cultures will be presented and formulated as guidelines for application of this molecular detection scheme for prompt clinical diagnosis of respiratory infections.

(MD04517)

Mechanisms of Lymphocyte Loss in SARS-CoV Infection

✍ CHAN Kay Sheung Paul • CHEN Gong George
(Surgery)

□ 15 February 2005

❖ Research Fund for the Control of Infectious
Diseases - Health, Welfare and Food Bureau

The reason for a high morbidity and mortality of severe acute respiratory syndrome (SARS) is still an enigma. The first clinical phase of the illness is similar to viral infections in general with fever, chill, rigor, myalgia and respiratory symptoms. The progression to a second phase with pneumonic involvement and deterioration is the most characteristic feature of the disease. At present, the mechanisms leading to patient deterioration are not known. One striking finding is the dropping of circulating lymphocyte count, particularly the CD4+ and CD8+ lymphocytes that are the key players in host immune defense. Understanding on the mechanisms leading to the loss of lymphocytes in patients with SARS would be instrumental for developing new prognostic markers as well as novel treatment strategies. In this study, we aim at revealing the mechanisms that lead to lymphocyte loss after infection with SARS-associated coronavirus (SARS-CoV). The uniqueness of our approaches are: (1) conduct experiments using representative strains from each major phylogenetic branch of SARS-CoV; (2) to examine both established lymphocyte cell lines as well as lymphocytes collected from patients during the acute and convalescent phase of the illness; (3) to cover a wide range of possible mechanisms of lymphocyte loss result from SARS-CoV infection.

(MD04850)

Hospital Surveillance of Childhood Respiratory Infections in Hong Kong

✍ IP Margaret • NELSON Edmund Anthony
Severn (Paediatrics) • SUNG Yn Tz Rita
(Paediatrics) • CHAN Kay Sheung Paul

□ 1 March 2005

❖ Wyeth (HK) Ltd

The study will combine active sentinel surveillance data of viral and bacterial causes of respiratory infections with passive surveillance denominator data. Previous studies combining passive and active surveillance methods have provided good baseline data for rotavirus and other causes of diarrhoea in hospitalised children. The present study aims to link these two surveillance mechanisms to provide more reliable estimates of incidence and disease burden of respiratory infections in Hong Kong with a focus on *S pneumoniae*.

The primary objectives are to:

1. To describe the clinical and laboratory features of hospitalised ARI cases who have NPA cultures yielding *S pneumoniae* alone and those with both *S pneumoniae* and another pathogen (bacteria or respiratory virus), those with other pathogens alone, and those with negative NPA cultures.
2. To describe the serotypes of *S pneumoniae* in NPA cultures yielding *S pneumoniae* alone and those dually positive for *S pneumoniae* and a respiratory virus.
3. To describe the proportion of hospitalised ARI cases due to the following *S pneumoniae* serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F.
4. To describe the antibiotic resistance pattern of *S pneumoniae* isolated from patients hospitalised with acute ARI.
5. To extrapolate the number and incidence of acute hospitalised ARI associated with *S pneumoniae*

and other bacterial and viral respiratory pathogens to the population of Hong Kong children.

(MD04526)

Molecular Epidemiology and Characterization of ESBL-Producing Ertapenem Sensitive Community - Acquired Gram - Negative Bacilli from the People's Republic of China

✍ LING Kin Wah Thomas

□ 1 January 2005

❖ Merck Sharp & Dohme (Asia) Ltd

This study will result in the identification and molecular characterisation of ESBL-and plasmidic AmpC-producing Gram-negative bacteria derived from the previous MK 0826 multicenter susceptibility surveillance results (ICAAC04-A-1113-ASM). Our study showed the presence of high levels of presumptive ESBL producing bacteria (14.4%) in *E. coli* and *Klebsiellae* causing community acquired infection in China. Ertapenem may be the first choice drug for such infections. Through molecular characterisation of potential ESBL- and plasmidic AmpC- producers from the MK 0826 study, an accurate picture of the current ESBL rate and the potential resistance mechanisms will allow the prediction of future trends in ESBL and plasmidic AmpC rates. In the proposed study, 1,241 isolates of Enterobacteriaceae with MICs of 1mg/1 or greater to either/or cefotaxime, ceftazidime will be examined in detail for ESBL- and AmpC-production. A full range of phenotypic and genotypic methods such as disc synergy test, IEF, PCR amplification, PCR-RFLP, RSI-PCR and PCR-dHPLC analysis will be used to characterise the production and types of ESBLs and plasmidic AmpC genes in these isolates. A selection of the representative ESBL- and

AmpC-producing isolates will be also looked at in detail for genetic transferability to investigate the possible ESBL and plasmidic AmpC dissemination routes so as to predict future trends in the spread of resistance. The data will be important for the support of the use of ertapenem in the empirical treatment of moderate to severe Gram-negative community acquired sepsis both in China and, potentially, elsewhere in the world.

(MD04840)

Rapid Detection of Food-Borne Pathogens in Clinical Specimens, Foods and Environmental Samples

✍ LING Mei Lun Julia

□ 1 December 2004

❖ Research Fund for the Control of Infectious Diseases - Health, Welfare and Food Bureau

Objective -To develop rapid methods for the detection of food-borne pathogens in clinical specimens, foods and environmental samples and apply these methods to the investigation of food-borne outbreaks.

Design - PCR-based methods will be developed and tested on pure cultures of *Salmonella* sp and *Vibrio cholerae*, on stool specimens, food and environmental samples known to be negative for these organisms and when spiked with different numbers of individual organisms. They will then be tested blindly on these samples.

Samples - Stool samples from diarrhoeal patients sent to the Microbiology laboratory of the Prince of Wales Hospital for routine investigation of bacterial pathogens will be used. Various food items and environmental water samples will also be used.

Main outcome measure(s) and analysis - The sensitivity and specificity of the methods will be

established. Their suitability in terms of labour, cost and ease of performance in a diagnostic Microbiology laboratory and a public health laboratory will be evaluated.
(MD04353)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

Edition Title/Investigators

2003-04 Development of Oligonucleotide Probe Microarrays for Molecular Detection of Drug Resistance in Mycobacterium Tuberculosis (CU03430)
✍ CHAN Chiu Yeung Raphael • CHENG Fun Bun Augustine# • HUI Mamie

2003-04 Study of the Virulence of Mycobacterium Avium Complex (MAC) in Relations to Its Isogenic Morphological Variations (MD03705)
✍ CHAN Chiu Yeung Raphael • HO Lok Ieng Yolanda*

2003-04 Elimination of Dengue Virus in the Chromatographic Fraction of Plasma Proteins (collaboration project with Advantek Serum Laboratories Ltd.) (BL02915)
✍ CHAN Kay Sheung Paul

2003-04 Genetic Variation of the SARS Coronavirus: Molecular Epidemiology and Antigenic Variation (MD03894)

✍ CHAN Kay Sheung Paul • PEIRIS J S M*

2003-04 Development of Monoclonal Antibody Against SARS-Associated Coronavirus (MD03842)

✍ CHAN Kay Sheung Paul • TAM Siu Lun John#

2003-04 Oncogenic Risk Implications of Sequence Variation, Genomic Physical Status and Viral Load of Human Papillomavirus Infection on the Development of Cervical Cancer (CU03429)

✍ CHAN Kay Sheung Paul • CHENG Fun Bun Augustine# • CHEUNG Tak Hong (Obstetrics & Gynaecology) • LAM Ching Wan (Chemical Pathology) • XU Liying (School of Public Health)# • YU Mei Yung (Anatomical & Cellular Pathology)

2001-02 Household Transmission of Methicillin-Resistant Staphylococcus Aureus (MRSA) in Hong Kong - Incidence and Risk Factors (MD01743)

✍ FUNG Sau Chun Kitty • HOUANG Ting Sou Elizabeth • LEE Albert (Community and Family Medicine) • LYON Donald James#

2003-04 The Acquisition of Fluoroquinolone Resistance in Relation to the Competence for Genetic Transformation in Prevalent Clones of Streptococcus Pneumoniae in Hong Kong (CU03432)

✍ IP Margaret • CHENG Fun Bun
Augustine# • LYON Donald James#

RESEARCH PROJECTS

Compare Outcomes of Different Approach for Cardiac Catheterization

✍ CHAIR Sek Ying

📅 1 November 2003

❖ Student Campus Work Scheme - Chiap Hua
Chen's Foundation Fund

Cardiac catheterization is a widely used cardiac diagnostic procedure. Patients are required to remain on bed rest for up to 24 hours after the procedure in Hong Kong. Early ambulation after the procedure and introduction of a transradial approach to the procedure were interventions examined in this study to improve patient outcomes after cardiac catheterization.

After cardiac catheterization, the transradial patient was restricted to bed rest for 4 hours then they were allowed to ambulate. These patients were discharged on the evening of the procedure day unless complications developed. Patients undergoing cardiac catheterization using the transfemoral approach were randomly assigned to the early ambulation group or the control group. Patients in the early ambulation group were ambulated at 4 hours after returning from the cardiac catheterization laboratory, whereas patients in the control group were ambulated the morning after the procedure (routine care).

A total of 129 subjects (43/ group) completed the study. The three groups differed significantly on back pain, urinary discomfort, and puncture site pain after the procedure. Patients in the transradial and early ambulation groups experienced significant less back pain and less urinary discomfort. The transradial

group, however, experienced the highest puncture site pain at discharge. There was no significant difference among the three groups on vascular complications. The three groups were not significantly different in general well-being and patient satisfaction level after the procedure. However, the transradial group had the highest general well-being level and the control group had the lowest.

(MD03508)

Early Ambulation after Coronary Angiography

✍ CHAIR Sek Ying

📅 1 November 2004

❖ Student Campus Work Scheme, CUHK

Aim: The aims of this study were to examine factors associated with vascular complications and back pain on Hong Kong Chinese patients after femoral access for cardiac catheterization.

Methods and Results: Potential factors possibly contributing to patients' back pain after cardiac catheterization were identified through literature review and a panel of 6 experienced cardiac nurses. Back pain was evaluated by the Numeric Pain Intensity Scale (NPIS) (0=none, 10= most severe pain) at 6 hours and the next morning after cardiac catheterization. Vascular complications together with therapy employed were recorded for analysis. 419 Hong Kong Chinese patients were recruited in the study. 5 patients developed puncture site bleeding. Turning privilege and bed rest duration were not associated with puncture site bleeding. Only turning privilege, age, and body weight were simultaneously significant to back pain level at 6 hours and the next morning after cardiac catheterization.

Conclusion:

Other than turning privilege during bed rest, age, and body weight, none of other factors identified by nurses that would contribute to back pain at 6 hours and the next morning after cardiac catheterization. With the results of this study, nurses will have a better understanding about patients' physical needs and appropriate nursing interventions can be planned to enhance patient comfort after cardiac catheterization.

(MD04890)

Quality of Life of Obese Cardiac Patients (Tool Validation)

✍ CHAIR Sek Ying

□ 3 May 2005

❖ Shaw Student Training & Campus Service Award (Shaw College, CUHK)

Obesity is a major public health problem and obesity is defined as an excess accumulation of body fat (Savage et al., 2002).

Obesity increases risk of stroke, hypertension, dyslipidaemia, type 2 diabetes mellitus, osteoarthritis, and sleep apnea (Poirier & Eckel, 2000; Poirier & Eckel, 2002). According to the American Heart Association, obesity is now considered an independent risk factor for CHD, and obesity is a major modifiable risk factor for heart disease (Poirier, & Despres, 2003; Savage et al, 2003). Studies proved that modification of cardiac risk factors, such as lowering lipid levels and weight loss, could significantly contribute to the primary and secondary prevention of coronary events (Katzel et al., 1995; Wager et al., 1995).

Appropriate tools to measure the quality of life of obese patients will be searched and translated into Chinese. The translated Chinese versions of the study measurements will then be validated on obese

cardiac patients. As the fund supports the preliminary work, the results of this search will be used for any grant application to support the validation of translated tools.

(MD04345)

The Provision and Evaluation of a Suicide Prevention and Management Programme by Frontline Nurses in Hong Kong

✍ CHAN Wai Chi Sally • CHIEN Wai Tong • TSO Steve*

□ 1 December 2004

❖ Health & Health Services Research Fund

Purpose: To implement an education programme of prevention and management of suicide for frontline nurses and evaluate the effectiveness of the programme. The objectives are:

To evaluate the effect of an education programme on nurses' knowledge, attitude and competence on suicide prevention and management for patients with suicide attempt or ideation and their family members;
To examine the strengths and weaknesses of the programme from the participants' perspectives;
To enhance nurses' knowledge and competence on suicide prevention and management in their working place.

Design and subjects: An evaluative research design with single-group pre- and post-test approach. It incorporates technique of a quantitative design while utilising qualitative methods to provide additional data of the process. This study consists of two stages: 1) implementing an education programme, and 2) evaluating the effectiveness of the programme. 64 registered nurses will be randomly selected from the medical, surgical and A & E units of two regional hospitals.

Interventions: A 24 hours education programme on suicide prevention and management. *Main outcome measures:* Subjects' attitude, knowledge and competency on suicide prevention and management.

Study instruments: Pre and post test using the 'Suicide Opinion Questionnaire' and Test on knowledge of suicide management' to measure changes in attitude and knowledge. Nursing audit and questionnaire on stress and coping as well as focus group interviews will be conducted to investigate subjects' competence.

Process evaluation: Focus group interviews will be conducted to assess the strengths and limitations of the programme.

Analysis: Descriptive statistics to establish means, standard deviations. One-way ANOVA for changes between pre-test and post-tests in study group. Two-way ANOVA for testing the differences of subgroups. Repeated measures analysis of variance for differences between study and control groups. Content analysis with the help of programme 'Ethnograph' for qualitative data.

(MD04733)

Effects of Psycho-Educational Interventions in Managing Chemotherapy-Associated Nausea and Vomiting (CANV) in Pediatric Oncology Patients: A Pilot Project

✍ CHAN YIP Carmen Wing Han • CHENG Kin Fong • LAM Lai Wah • LI Chi Kong (Paediatrics) • CHIK Ki Wai (Paediatrics) • CHEUNG Sui Sam*

□ 1 January 2005

❖ Health & Health Services Research Fund

Purpose: The proposed study aims at assessing the feasibility of the two major components: relaxation and patient education, of a comprehensive program in

reducing chemotherapy-associated nausea and vomiting (CANV) in pediatric oncology patients.

Design and subjects: A longitudinal exploratory trial consists of two intervention groups. A sample of 20 (10/group) children aged 4-11 will be recruited from a pediatric oncology unit of a public-funded hospital in Hong Kong. Historical data will be used for comparison with the intervention groups.

Study instruments: The Morrow Assessment of Nausea and Emesis (MANE), A-State scale of the State-Trait Anxiety Inventory (STAI), Children STAI A-state scale, Play performance scale for children, Physiological indices, Satisfaction of care, Self-rating of the usefulness of intervention, Intervention activity log, PMR & GI diary, demographic data,

Interventions:

Group 1. Six training sessions (30 minutes/session) of progressive muscle relaxation and guided imagery and daily practice of the skills. A PMR and GI audiotape will be provided.

Group 2. Two educational sessions (30 minutes/session) focusing on risk assessment, advice on the use of antiemetics, and meal planning.

Main outcome measure and analysis: duration and intensity of CANV. Data will be analysed using descriptive statistics, t-test, chi-square, analysis of variance.

(MD04997)

An Evaluation of the SARS and Droplet Infection Control Practices in Acute and Rehabilitation Hospitals in One Region in Hong Kong

✍ CHAU Pak Chun Janita • LOPEZ Violeta (School of Public Health) • THOMPSON David Robert • TWINN Sheila Frances • LEE Tze Fan Diana • SIN Yee Lorna*

□ 23 November 2004

❖ Research Fund for the Control of Infectious Diseases - Health, Welfare and Food Bureau

Background: The recent outbreak of SARS has had a major impact on the health and healthcare services in Hong Kong. In spite of instituting infection control measures, healthcare workers and patients continue to contract the disease. Other health-care associated infections (hospital acquired infections) are today the most common complications affecting patients resulting in increased morbidity, mortality, length of stay, health care cost and loss of productivity. Minimising transmission require sustained attention to infection control interventions within hospitals. Recent report by the SARS Expert Committee identified that there were weaknesses in hospital infection control structures and practices that need to be addressed.

Aims: To investigate the infection surveillance and control practices in acute and rehabilitation hospitals in Hong Kong, and examine the appropriateness of the infection control practices among health care providers and support staff.

Method: A multi-method research design will be used: (1) review of current hospital surveillance activities and infection control guidelines; (2) survey of health care providers and support staffs knowledge of infection control measures; (3) observations of infection control practices; and (4) interviews of participants' perception of the appropriateness of infection control measures, barriers to implementation and training needs.

Sample and setting: Participants will include purposive sample of health care providers and support staff from the seven hospitals within the New Territories East Cluster.

Data analysis: Descriptive, correlational and inferential statistics will be used to analyse the quantitative data using SPSS. Content analysis will

be used to analyse the qualitative data from the observations and semi-structured interviews.

Potential application: The results will enable policy-makers, managers and clinicians to ensure appropriate and timely infection control measures in the advent of any infectious disease outbreak. The study will identify effective strategies for disseminating and implementing infection control measures in hospitals as well as provide criteria for continuous quality improvement activities.

(MD04896)

Privacy and Dignity in Residential Care Homes: A Culturally Relevant Framework for Chinese Elders

✍ LEE Tze Fan Diana • LOW Lisa Pau Le

📅 1 September 2004

❖ Research Grants Council (Earmarked Grants)

The growing number of elderly people moving into residential care homes has led to an increasing concern about the care provided in these homes. However, various local studies have consistently identified the poor quality of psychosocial care provided in these homes. Most strikingly, evidence of infringement of elderly residents' privacy and dignity is abundant. While respecting privacy and dignity is frequently identified as an important goal of residential care, little is known of how these concepts are applied to the care of elders in residential homes. Still less is known of how Chinese elders perceive what supports/undermines their privacy and dignity in residential care homes.

This study is to develop a culturally relevant framework of privacy and dignity in residential care homes for Chinese elders. Approximately 100 elderly residents from 20 residential care homes of Hong Kong will be invited to participate in an

in-depth interview to identify what privacy and dignity mean to them, and what activities, practices or experiences support or undermine their personal sense of privacy and dignity in the care homes. Specific cultural beliefs that contribute to the understanding of these concepts will also be explored. Results of this study will i) produce a sound theoretical basis for residential care professionals to identify and evaluate appropriate interventions to support elders' privacy and dignity and ii) provide a Chinese cultural perspective to understanding privacy and dignity as they are applied to the care of residential home elders.

(CU04161)

Translation and Validation of Two Chinese Health-Related Quality of Life Instruments in Patients with Coronary Heart Disease

✍ THOMPSON David Robert • YU Sau Fung •
OLDRIDGE Neil* • YU Cheuk Man (Medicine
& Therapeutics) • FUNG Nyuk Yin Tracy*

❏ 27 December 2004

❖ Health & Health Services Research Fund

Background:

The prevalence of coronary heart disease (CHD) in Hong Kong and mainland China is increasing and is a major cause of death and disability in Hong Kong. The outcomes of modern treatments of CHD focus increasingly on symptoms, function and health-related quality of life (HRQL). Translation and validation are critical steps when considering the use of HRQL life instruments in a linguistically different population as errors in translation could distort the original intent of the instrument and compromise its reliability and validity.

Aim:

Translate into Chinese and validate the Myocardial Infarction Dimensional Assessment Scale and the MacNew Heart Disease HRQL questionnaire.

Method:

Consecutive patients, diagnosed with myocardial infarction, heart failure, or unstable angina, will be recruited from the New Territories East cluster hospitals until data are available for 130 patients with each diagnosis. A methodological study design is proposed. Tests of reliability, validity and responsiveness of the Chinese versions of the two HRQL instruments will be con.

Significance:

The validated HRQL instruments will be available to health care researchers and professionals to assess the HRQL of Chinese Hong Kong patients with CHD to the HRQL of patients. These disease-specific HRQL outcome measures will add to the pool of reliable and valid instruments that could be accessed and used by researchers and clinicians in Hong Kong and will enable health care professionals to plan more appropriate and culturally-sensitive interventions.

(MD04847)

An Evaluation of the Effectiveness of Different Models of Health Care Delivery in the Primary Care Setting of General Outpatient Clinics in Hong Kong

✍ TWINN Sheila Frances • LOPEZ Violeta
(School of Public Health) • LEE Albert
(Community and Family Medicine) • LAM
Augustine (Community and Family Medicine)*
• THOMPSON David Robert • CHENG YAM
Fung Khing Frances (Centre for Health Ed. &
Health Promotion)

❏ 1 December 2004

❖ Health & Health Services Research Fund

International research demonstrates the effectiveness of a model of primary care in which nurse practitioners working at an advanced level provide patient care. Evidence from a systematic review demonstrates no difference in the health status of patients seen by either the physician or the nurse practitioner. Other research demonstrates the cost effectiveness of such an approach. Little research is available in Hong Kong about the effectiveness of such models of health care delivery. The aims of this study are to evaluate the effectiveness of different health care delivery models of primary care in the GOPC setting and assess the effectiveness of the care provide by the advanced nurse practitioner for patients with chronic health needs. An evaluation research design using a methodology of multiple case study has been selected. Multiple methods of data collection will be used to assess patients' health status, compliance with medication, satisfaction, specific physiological measures and health care utilization. Interviews will be carried out with health care professionals to assess their perceptions of this approach to care. Sampling will include an opportunistic sample of 390 patients in each case study and a purposive sample of health care professionals. Data analysis will include descriptive statistics, Pearson's correlation coefficients and repeated measures ANOVA to assess health outcomes and health care utilization in each model of care. Content analysis of the qualitative data will be undertaken. It is anticipated a model of advanced nurse practice will reduce the demands on physician time thereby allowing physicians more time to devote to the increasingly complex health problems being managed in the community.

(MD04712)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
2001-02	Effectiveness of Interventions for Reducing Breathlessness, Fatigue & Anxiety in Chinese Patients Undergoing Lung Cancer Radiotherapy in Hong Kong (MD01833) ✍ CHAN YIP Carmen Wing Han • CHANG Anne Marie# • LEUNG Sing Fai (Clinical Oncology) • MAK So Shan*
2002-03	Psychosocial and Physical Factors Predicting Handicap (MD02482) ✍ CHAU Pak Chun Janita • WOO Jean (Medicine & Therapeutics) • CHANG Anne Marie* • MACKENZIE Ann E*
2001-02	Effectiveness of Mutual Support and Psychoeducational Group Interventions for Family Caregivers of Patients with Schizophrenia (MD01337) ✍ CHIEN Wai Tong • CHAN Wai Chi Sally • MORRISSEY Jean Mary#
2003-04	Testing the Reliability and Validity of a Chinese Version of the Level of Expressed Emotion Scale (MD03667) ✍ CHIEN Wai Tong • CHAN Wai Chi Sally

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| <p>2002-03 Developing a Culturally Relevant Theoretical Framework of Successful Aging for Chinese Elders (CU02228)</p> <p>✍ LEE Tze Fan Diana</p> | <p>2003-04 Promotion of Evidence Based Nursing Practice (MD03828)</p> <p>✍ THOMPSON David Robert • CHAU Pak Chun Janita</p> |
| <p>2003-04 The Effect of Pre-Operative Therapeutic Play on Post-Operative Outcomes of Hong Kong Chinese Children Having Surgery in a Day Surgery Unit (MD03604)</p> <p>✍ LI Ho Cheung William • LOPEZ Violeta (School of Public Health) • YEUNG Chung Kwong (Surgery)</p> | <p>2003-04 A Longitudinal Cohort Study of Burnout and Attrition in Nursing Students (MD03934)</p> <p>✍ THOMPSON David Robert • Watson Roger* • Deary Ian*</p> |
| <p>2002-03 Establishing Reliability and Validity of the Chinese Version of the Caregiver Strain Index and the Center for Depression (MD02761)</p> <p>✍ LUI How Lin • LEE Tze Fan Diana</p> | <p>2002-03 Beliefs of Older Hong Kong Chinese Women and Medical Practitioners about Mammography Screening: An Explanatory Model Approach (CU02229)</p> <p>✍ TWINN Sheila Frances • HOLROYD Eleanor Anne • SHIU Tak Ying Ann</p> |
| <p>2002-03 Preparation for Surgery in Patients Awaiting Coronary Artery Bypass Surgery (MD02865)</p> | |

RESEARCH PROJECTS

The Impact of Nocturia on Sleep and Quality of Life

✍ KONG Wing Shan • LEUNG Pui Ling • HUI Shu Cheong David (Medicine & Therapeutics) • YIP Shing Kai Alexander

☐ 16 June 2005

❖ The Hong Kong College of Obstetricians and Gynaecologists

Nocturia is one of the several lower urinary tract symptoms reported to be troublesome by middle-aged and older people. An epidemiologic cross-sectional study in a Dutch non-institutionalized elderly population revealed that 58% of the women aged 50-59 and 72% of those aged over 80 suffered from nocturia. A Hong Kong territory-wide telephone survey conducted by us in 1996 also found that 20% of the women aged between 10 and 90 had nocturia.

It is evident that nocturia has a deleterious effect on sleep. For obvious reasons, nocturia is associated with increased awakenings. Also, it is often difficult to regain sleep after nocturnal awakenings, resulting in a feeling of not being well rested in the morning. It has been suggested that nocturia is associated with poor quality of sleep. A questionnaire study on pensioners had shown that nocturnal micturition was often associated with increased sleep disorders, a poorer quality of sleep, increased thirst, particularly at night, and increased fatigue in the daytime and all the relationships were clearer in women than in men.

Interrupted sleep can result in excessive daytime sleepiness and dysphoric mood. A questionnaire study involving over 3000 Swedish women had

shown that nocturnal micturition impaired sleep, and in turn with subsequent decrease in daytime performance and general well-being. A voluntary health screening project found that more than 60% of those women with nocturia reported it having a negative impact on their quality of life.

From the literature, the association between nocturia and its effect on quality of sleep and life was proven. However, how the sleep and quality of life are actually affected in patients with nocturia has not been fully elucidated. Sleep disturbance and quality of life can be objectively assessed by nocturnal polysomnography (PSG) and questionnaires. The aim of our study is to assess the impact of nocturia on sleep and quality of life using PSG and questionnaires.

(MD04663)

An Ethnoepidemiology Study of Psychiatric Morbidity Among Infertile Chinese Women in Hong Kong

✍ LOK Hung Ingrid • LEE Tak Shing Dominic (Psychiatry) • CHEUNG Lai Ping • HAINES Christopher John • Alex Cohen* • Mary-Jo Good*

☐ 1 March 2005

❖ Fogarty International Center, NIH funded by ICOHRTA

About 10% - 15% of couples suffer infertility. While not all couples want children, for those who do, the inability to reproduce may bring about a major life crisis. Previous studies have highlighted the possible significant psychological stress associated with infertility, however, the extent of associated psychiatric morbidity in terms of prevalence of psychiatric disorders among infertile patients has not been well established. In addition, nearly all of the

published literatures have been conducted in the western societies, leaving their Asian counterparts much less studied.

This is a cross-sectional study using both quantitative methods in terms of psychometric questionnaires and qualitative methods in terms of individual in-depth interviews. Data will be compared between infertile Hong Kong Chinese women and normal controls.

The study aims at to:

- 1) study the extent of psychological morbidity that infertile Chinese women experience by studying the prevalence of psychiatric disorders in this population; to assess the performance of the standardized psychometric scales as screening tools in this context;
- 2) study the underlying correlates of psychiatric morbidity, in particular, the possible socio-cultural factors including perceived social stigma, social support and in-law relationship;
- 3) study the perceived need and treatment seeking behavior for psychological support service by infertile Chinese women and how it may correlate with the psychiatric morbidity.

(MD04554)

To Provide Technical Assistance to the Vietnam Ministry of Health in the Development of an Emergency Obstetric Care Training Package and Training Program for Service Providers

✍ ROGERS Michael Scott

□ 20 June 2005

❖ The United Nations Population Fund (UNFPA)

1. Review current training materials on Emergency Obstetric Care in Vietnam and other international organizations
2. Give comments to an outline and format for reference manual, trainees' hand book and trainers'

notebook and training program prepared by national consultants

3. Give comments to drafts of reference manual, trainees' handbook and trainers' note book and training program prepared by national consultants

4. Conduct workshops for finalizing training package and training program on Emergency Obstetric Care for service providers

5. Act as leader of the consultant team, organize the work of the consultant team and present the results of the work to UNFPA and government counterparts as well as provide the mission report not later than two weeks after the mission completed.

(MD04767)

Direct Effects of 8-Iso Prostaglandin F_{2α} on Neural Stem Cell Differentiation in vitro

✍ WANG Chi Chiu

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

Oxygen free radicals and derived lipid peroxidation products are implicated in perinatal asphyxia leading to neuronal damage and subsequent neurodevelopmental handicap, including spastic motor and cognitive/behavioural deficits. We found that free radical derived 8-iso prostaglandin F_{2α} provides a more specific lipid peroxide measurement and accurate indicator of cumulative hypoxic cellular injury in asphyxiated fetus with severe hypoxic ischemic encephalopathy and subsequent neuropsychological morbidity. 8-iso prostaglandin F_{2α} has been investigated as a measure of the vulnerability of precursor cells to free radical attack, as a key mediator in inhibiting cell proliferation, and as an activator of cellular death. However, no study has been performed to date to examine the direct

effects of 8-iso prostaglandin F2 α in neural stem cell damage. By using an *in vitro* neuronal differentiation model, we demonstrated a sustained accumulation of 8-iso prostaglandin F2 α in the differentiating neural stem cells under hypoxic conditions preceding with delay neuronal differentiation and significant apoptotic responses. In this proposal we will use the model to study the direct cellular responses to 8-iso prostaglandin F2 α in the differentiating neural stem cells, the effects of oxygen free radicals and other reactive oxygen species will be compared.

(MD04725)

Epigenetic Profiling of Cervical Cancer in Hong Kong Women Using CpG Island Microarray: A Pilot Study

✍ WONG Yick Fu • CHUNG Kwok Hung Tony •
LO Yuk Ming Dennis (Chemical Pathology) •
CHEUNG Tak Hong* • YU Mei Yung May* •
Huang Hui Ming Tim*

☐ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

Cervical cancer is the most common gynecologic malignancy in Hong Kong. Approximately 95% or more of these cancers are squamous cell in origin. Cervical squamous cell carcinoma is commonly preceded by a well-defined pre-malignant stage, cervical intraepithelial neoplasia (CIN). This offers us an opportunity to study the process of cervical carcinogenesis. A primary risk factor for cervical cancer is infection with oncogenic subtypes of HPV. However, other somatic genetic and epigenetic events are almost certainly required for tumorigenesis. Methylation of gene promoter CpG islands is an epigenetic event that is not accompanied by changes

in DNA sequence. It is associated with transcriptional silencing in many types of human cancer. Previously we have detected the methylation of p16 tumor suppressor gene promoter in a sub-group of cervical cancer and found it might be associated with poor outcome in cervical carcinomas. With development of microarray technique, high throughput global profiling has become the preferred method for studying differential gene methylation in tumor compared to normal tissues.

We propose to perform a pilot study on global analysis of DNA methylation using a novel microarray approach called differential methylation hybridization in a small set of cervical cancer and matched controls in Hong Kong women. This preliminary investigation of the epigenetic profiles in malignant neoplasms of the cervix may advance understanding of the role of gene methylation in cervical tumorigenesis. Based on this pilot study, if a set of genes with differential methylation in tumors compared to normal are further validated in a large number of cervical cancer in different stage as well as in CIN, it may potentially uncover epigenetic targets which can become useful as molecular makers of diagnosis and prognosis of cervical cancer and ultimately inform intervention.

(MD04817)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
2002-03	Identification of Metastasis Related Genes in Ovarian Carcinoma by cDNA Arrays (CU02133)

- ✍ CHUNG Kwok Hung Tony • CHEUNG Tak Hong • CHIN Khew Voon* • WONG Yick Fu • YU Mei Yung (Anatomical & Cellular Pathology)
- 2003-04 Hepatitis B Carriers are More Susceptible to the Development of Cervical Intra-Epithelial Neoplasia and Cervical Carcinoma after Human Papilloma Virus Infection (MD03701)
- ✍ CHUNG Kwok Hung Tony • CHEUNG Tak Hong • SIU Shing Shun Nelson • CHAN Kay Sheung Paul (Microbiology) • LIN Chi Kit* • YIM So Fan
- 2003-04 The Effects of Dong Quai Buxue Tong on Key Regulators of Early Events of Atherogenesis (MD03723)
- ✍ HAINES Christopher John • CHEUNG Che Kwok • PO Lai See • BRITON-JONES Christine May# • FISCUS Ronald Ray (Physiology)
- 2003-04 Expression of Vascular Endothelial Growth Factor and Its Corresponding Receptors in the Human Oviduct: Modulation During the Menstrual Cycle (MD03975)
- ✍ LAM Po Mui • BRITON-JONES Christine May# • HAINES Christopher John • LOK Hung Ingrid • YUEN Pong Mo
- 2003-04 Vaginal Birth after Caesarean Section - Effect on Maternal Psychosocial Function (CU03423)
- ✍ LAU Tze Kin • CHUNG Kwok Hung Tony • LEE Tak Shing Dominic (Psychiatry) • LEUNG Tse Ngong
- 2003-04 Evaluation of Human Chorionic Gonadotropin mRNA in Maternal Plasma as a Potential Marker for Early Diagnosis of Ectopic Pregnancy (MD03779)
- ✍ LAU Tze Kin • LO Yuk Ming Dennis (Chemical Pathology) • CHIU Wai Kwun Rossa (Chemical Pathology) • LEUNG Tse Ngong
- 2003-04 A Study of Transabdominal Pressure Effect on the Feto-Maternal Haemorrhage during External Cephalic Version (MD03354)
- ✍ LEUNG Tak Yeung • SAHOTA Daljit Singh • FOK Wing Yee • CHAN Lin Wai Daniel • LAU Tze Kin
- 2003-04 Women's Demand for Elective Caesarean Section - A Prospective Psychosocial Epidemiological Cohort Study of Parturients (MD03593)
- ✍ LEUNG Tse Ngong • LAU Tze Kin • LEE Tak Shing Dominic (Psychiatry) • LEUNG Kwok Ling Ares*
- 2003-04 Hyperglycemia and Adverse Pregnancy Outcome Study (MD03946)
- ✍ LI Chi Yin • ROGERS Michael Scott • NG Pak Cheung (Paediatrics)
- 2001-02 Evaluation of Green Tea Polyphenols in Pregnancy (MD01077)

	✍ ROGERS Michael Scott • CHU Kai On • HAINES Christopher John • LAU Tze Kin • PANG Chi Pui Calvin (Ophthalmology and Visual Sciences) • WANG Chi Chiu		✍ TSUI Hang Yuet Michelle • LO Yuk Ming Dennis (Chemical Pathology) • LEUNG Tse Ngong
2001-02	To Compare the Levels of Oxidative Stress in Pregnant Women with Varying Degrees of Carbohydrate Intolerance (MD01081)		
	✍ ROGERS Michael Scott • LI Chi Yin • NG Pak Cheung (Paediatrics) • PANG Chi Pui Calvin (Ophthalmology and Visual Sciences) • TAM Wing Hung • WANG Chi Chiu		
2003-04	Measurement of Trocar Insertion Force and Tape Tensile Force during Application of Tension-Free Vaginal Tape for the Treatment of Female Stress Urinary Incontinence (MD03703)		
	✍ SAHOTA Daljit Singh • YIP Shing Kai Alexander • PANG Man Wah Selina		
2003-04	A Pilot Study of Thrombophilia among Chinese Women with Thromboembolism in Pregnancy (MD03544)		
	✍ TAM Wing Hung • WONG Yick Fu • CHENG Gregory (Medicine & Therapeutics) • NG Heung Ling Margaret (Anatomical & Cellular Pathology)		
2003-04	Maternal Plasma Human Placental Lactogen mRNA Level in Pregnancies Complicated by Intrauterine Growth Retardation (MD03927)		
		2003-04	Clinical and Metabolic Effects of Rosiglitazone on Women with Polycystic Ovarian Syndrome (MD03985)
			✍ TSUI Hang Yuet Michelle • TAM Wing Hung • LAM Po Mui • MA Ching Wan Ronald (Medicine & Therapeutics) • CHEUNG Lai Ping • HAINES Christopher John • TONG Peter Chun Yip (Medicine & Therapeutics) • CHAN Chung Ngor Juliana (Medicine & Therapeutics) • LAM Wai Kei Christopher (Chemical Pathology)
		2002-03	High Density Allelotypes on Chromosome 1 in a Large Set of Microdissected Cervical Neoplasms and Their Clinicopathological Significance (CU02138)
			✍ WONG Yick Fu • CHEUNG Tak Hong • CHUNG Kwok Hung Tony
		2003-04	Inhibition of Human Papillomavirus Type 18 Essential Genes by Small Interfering RNAs in Cervical Cancer Cells (MD03754)
			✍ WONG Yick Fu • CHUNG Kwok Hung Tony • CHEUNG Tak Hong • SOHAIL Muhammad* • SOHAIL Muhammad* • KAHN Thomas*
		2003-04	Gene Expression Profiling of Endometrioid Endometrial Carcinoma in Hong Kong Women and Correlation with Clinico-pathological Features (CU03427)

- ✍ WONG Yick Fu • BIRRER, Michael J.* • CHEUNG Tak Hong • CHUNG Kwok Hung Tony • GARDNER, Ginger J.* • YU Mei Yung (Anatomical & Cellular Pathology)
- 2003-04 Microsatellite Instability Profiles and Their Correlation with Clinico-Pathological Features in Endometrial Cancer (MD03434)
✍ WONG Yick Fu • CHUNG Kwok Hung Tony • CHEUNG Tak Hong • HAMELIN Richard* • DUVAL Alex* • BUHARD Oliver*
- 2002-03 A Randomised, Controlled Trial Comparing Different Protocols of Postnatal Pelvic Floor Exercised Program
- and Their Effectiveness in Prevention of Pelvic Floor Dysfunction after Delivery (MD02698)
✍ YIP Shing Kai Alexander • PANG Man Wah Selina* • CHAN Lin Wai Daniel* • YIU Raymond*
- 2003-04 Gene Expression Profiling of Cardinal Ligament in Hong Kong Chinese Women with Pelvic Prolapse (MD03845)
✍ YIP Shing Kai Alexander • WONG Yick Fu • PANG Man Wah Selina

RESEARCH PROJECTS

To Evaluate the Clinical Performance of Bausch & Lomb Purevision® Lenses Compared to Acuvue Advance® Lenses as Measured by the Zywave II Wavefront Aberrometer

✍ CHENG Chak Kwan Arthur • LAM Shun Chiu Dennis • RAO Srinivas Kamalakara • TANG Wai Ho Emily • FAN Hoi • CHEUNG Yan Yan

□ 24 February 2005

❖ Bausch & Lomb (S) Pte Ltd

Myopia is a prevalent problem in Hong Kong. Contact lens is one of the common devices to correct myopia. The objective of the clinical study is to evaluate the performance of 2 types of contact lenses using a wavefront aberrometer and standard diagnostic tools. Subjects enrolled into the study will be fitted and dispensed with one type of contact lenses in which they will wear for 2 weeks and switch to the second pair for a second two-weeks of wear.

(MD04928)

A Prospective Randomized Study to Determine the Minimum Effective Concentration of Trypan Blue to Assist in the Staining and Removal of the Internal Limiting Membrane in Idiopathic Macular Hole Surgery

✍ LAI Wai Kwan Wico • LAM Shun Chiu Dennis • CHAN Wai Man

□ 1 January 2005

❖ Research Grants Council (Earmarked Grants)

Idiopathic macular hole is a common eye condition in Hong Kong and worldwide which may lead to

permanent visual loss if left untreated. Pars plana vitrectomy with intraocular gas or tamponade has achieved closure of the hole 61% to 81% of cases. To improve the closure rate, removal of the internal limiting membrane (ILM) has been employed. Because the ILM is transparent, indocyanine green (ICG) has been used to stain the membrane to facilitate its removal. Various reports, however, have documented toxicity to the retina following the use of ICG. Because of this, we propose to use trypan blue to assist in the visualization and removal of the ILM.

Trypan blue has been used in cataract surgery to facilitate removal of the anterior capsule of the lens. No ocular complication has been reported thus far. In this study, we will use various concentration of trypan blue to stain the ILM. We seek to identify the lowest effective concentration that will allow adequate staining of the ILM and its subsequent peeling and to minimize any potential toxicity that may develop in the long term.

(CU04332)

A Multi-Centered Randomized Controlled Interventional Trial to Compare Cataract Extraction Alone by Phacoemulsification versus Combined Phaco-Trabeculectomy in the Treatment of Chronic Angle-Closure Glaucoma (CACG) with Coexisting Cataract

✍ THAM Chee Yung Clement • CHAN Jonathan Cheuk Hung • CHIU Yee Hang Thomas • LAI Shiu Ming Jimmy • LAM Shun Chiu Dennis • LAM Sze Wing • LEUNG Yu Lung • POON Shuet Yan • SHEN Yu Sunny • YICK Wai Fong

□ 1 January 2005

❖ CUHK Research Committee Funding (Direct Grants)

Glaucoma is the leading cause of irreversible blindness in Hong Kong, accounting for 23.1% of all permanent blindness. Chronic angle-closure glaucoma (CACG) accounts for over 70% of all glaucoma types in Chinese. The management of CACG has not been well studied by Western research establishments because of its low prevalence in Caucasians (0.2%) (cf. 1.74%, i.e. nine times more prevalent, in Chinese).

The incidence of CACG increases with age, and the majority of CACG patients have co-existing cataract. Traditionally, uncontrolled CACG with co-existing cataract has been managed by combined trabeculectomy (glaucoma-controlling surgery) with cataract extraction. Trabeculectomy is associated with risk of serious, blinding complications, such as suprachoroidal hemorrhage and endophthalmitis.

There is emerging evidence showing that cataract extraction alone results in significant control of CACG. The investigators hypothesize that cataract extraction alone may have equivalent efficacy as combined cataract extraction and trabeculectomy in treating CACG with co-existing cataract, but without the risks of combined surgery. This multi-centered randomized controlled trial will test this hypothesis. Similar data is currently not available in the published literature, and this study will have major impact on future clinical practice, well being of patients, and optimal use of limited resources, especially in Chinese communities.

(MD04706)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

Edition Title/Investigators

- | | |
|---------|--|
| 2002-03 | <p>A Randomized, Controlled Trial of Photodynamic Therapy with Verteporfin for Choroidal Neovascularization in Pathologic Myopia in Chinese (CU02140)</p> <p>✍ CHAN Wai Man • FAN Shu Ping Dorothy • KWOK Kwan Ho • LAM Shun Chiu Dennis</p> |
| 2002-03 | <p>Effects of Preoperative Keratometry on Postoperative Refractive Outcomes and Corneal Curvature in Patient with Myopic LASIK (MD02372)</p> <p>✍ CHENG Chak Kwan Arthur • LAW Wai Kee • LAM Shun Chiu Dennis</p> |
| 2003-04 | <p>Control of Myopic Progression in Moderate to High Myopic Chinese Children by Topical Atropine (MD03729)</p> <p>✍ FAN Shu Ping Dorothy • LAM Shun Chiu Dennis • YU Bing On Christopher • WONG Chun Yu • YIP Wai Kuen</p> |
| 2000-01 | <p>Use of Conjunctival-Limbal Autografts Versus Intraoperative Application of Mitomycin-C in Treatment of Recurrent Pterygium in Hong Kong (CU00052)</p> <p>✍ LAM Shun Chiu Dennis • RAO Srinivas Kamalakara • YU Yau Woon Edward# • LAW Wai Kee</p> |
| 2001-02 | <p>A Prospective Randomized Comparative Study on the Safety and Efficacy of Argon Laser Peripheal Iridoplasty (ALPI) versus Systemic Intraocular Pressure Lowering Medications for the Immediate Management of Acute Attack of Primary</p> |

	Angle Closure Glaucoma (PACG) (MD01090)		MOHAMED Shaheeda • TANG Wai Ho Emily
	✍ LAM Shun Chiu Dennis • CHUA Kien Han John • LAI Shiu Ming Jimmy • POON Shuet Yan • THAM Chee Yung Clement	2002-03	A Randomized, Controlled Pilot Study to Evaluate the Safety and Efficacy of an Intravitreal Fluocinolone Acetonide (0.5 or 2 mg) Implants in Patients with Clinically Significant Diabetic Macular Edema (MD02973)
2002-03	A Multi-Center, Randomized, Double-Masked, Controlled Study to evaluate the Safety and Efficacy of an Intravitreal Fluocinolone Acetonide (0.5 or 2 mg) Implant in Patients with Non Infectious Uveities Affecting the Posterior Segment of the Eye (MD02525)		✍ LAM Shun Chiu Dennis • CHAN Wai Man • CHAN Kar Mun Carmen • WONG Tak Hung • LI Kai Wang Kenneth • TSANG Chi Wai • FAN Shu Ping Dorothy • LI Siu Hung • CHONG Kam Lung • MOHAMED Shaheeda • TANG Wai Ho Emily
	✍ LAM Shun Chiu Dennis • CHAN Wai Man • WONG Tak Hung • FAN Shu Ping Dorothy • CHAN Kar Mun Carmen • CHONG Kam Lung • MOHAMED Shaheeda • TANG Wai Ho Emily	2003-04	A Prospective Study to Evaluate the Clinical Performance of the Bausch & Lomb Akreos FIT® Intraocular Lens in Patients Undergoing Routine Cataract Surgery (MD03380)
2002-03	Intraocular Pressure Profile, Endothelial and Nerve Fibre Analysis in Patients on Systemic Steroid (MD02783)		✍ LAM Shun Chiu Dennis • YOUNG Alvin Lerrmann
	✍ LAM Shun Chiu Dennis • FOK Tai Fai (Paediatrics) • CHIK Ki Wai (Paediatrics) • LI Tsz Ha Randa	2003-04	A Prospective Randomized Comparative Study on the Efficacy and Safety of Early Cataract Removal in Preventing Development of Chronic Angle-Closure Glaucoma (CACG) after Aborting Acute Attack of Primary Angle-Closure Glaucoma (PACG) (CU03350)
2002-03	A Second Year of Treatment in a One Year, Multi-Center, Double-Masked, Placebo-Controlled, Safety and Efficacy Study of 2% Pirenzepine Ophthalmic Gel in Children with Myopia -Amendment 2 (13 February 2002) Open Label Safety Study (MD01805)		✍ LAM Shun Chiu Dennis • CHIU Yee Hang Thomas • LAI Shiu Ming Jimmy • LEUNG Yu Lung • THAM Chee Yung Clement • YEUNG Yat Ming Barry • YICK Wai Fong
	✍ LAM Shun Chiu Dennis • FAN Shu Ping Dorothy • LAM Robert Fung • CHENG Chak Kwan Arthur • CHAN Kar Mun Carmen •		

- 2002-03 A Prospective Randomized Comparative Study on the Role of Anterior Capsular Polishing (ACP) Technique in the Subsequent Formation of Post-Operative Posterior Capsule Opacification (PCO) in Senile Cataract Surgery (MD02906)
✍ LAW Wai Kee • LAM Shun Chiu Dennis • CHENG Chak Kwan Arthur
- 2002-03 Gene Expression Profiling of Glaucoma (MD02455)
✍ PANG Chi Pui Calvin • LEUNG Yuk Fai# • LAM Shun Chiu Dennis • FAN Shu Ping Dorothy
- 2001-02 Identification of DNA Methylation Sites in Cancer-Related Genes in Retinoblastoma Genome (MD01091)
✍ PANG Chi Pui Calvin • CHOY Kwong Wai (Obstetrics & Gynaecology) • FAN Shu Ping Dorothy • LAM Shun Chiu Dennis • LO Kwok Wai (Anatomical & Cellular Pathology) • TO Ka Fai (Anatomical & Cellular Pathology) • YU Bing On Christopher
- 2003-04 A Study on Glaucoma Patient's Understanding of Their Own Disease, and Changes in Quality of Life after Glaucoma Surgery (MD03388)
✍ THAM Chee Yung Clement • CHAN Wai Nang Clement • CHAN C K Vesta* • LAM Shun Chiu Dennis • LAM Sze Wing • POON Shuet Yan

RESEARCH PROJECTS

A Study on Pathogenesis of Tendinosis in a Non-Invasive Injury Rat Model - the Influences of Repeated Mechanical Stimulation and Anti-Inflammatory Drug Treatment

✍ CHAN Kai Ming • HUNG Leung Kim • FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)

☐ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

Tendinosis is a common pathological condition in tendons manifested as longstanding pain. Characterized as a non-healing status, tendinosis involves an accumulation of tenoblasts that actively cause matrix disturbances in the affected tendons. When tenoblasts failed to go through the normal healing process under the influences of various risk factors, tendinosis is developed. Potential risk factors like overuse and the use of anti-inflammatory drugs have been suggested, however, there is a lack of experimental model to evaluate the relationship of risk factors and the development of tendinosis. In this project, the contribution of repeated mechanical stimulation and anti-inflammatory drug treatment to pathological changes of tendinosis will be studied in a rat model. Micro injuries in patellar tendons will be generated non-invasively by extra corporeal shockwave treatment. The animals will then be exposed to anti-inflammatory drugs. The development of the non-healing histopathological characteristics of tendinosis will be detected, and an endpoint measurement on the aberrant cellular

responses characteristic to tendinosis will be examined by preparing tendon fibroblast cultures. The proposed study will help to elucidate the pathogenesis of tendinosis with respect to the influences of repeated mechanical stimulation and anti-inflammatory drugs, which will have impacts on the clinical practice for the management of tendon injuries. In the future, the animal model of tendinosis can be used for intervention study, which will help to devise proper strategies for treatment and prevention of tendinosis.

(MD04351)

Effect of Low Intensity Pulsed Ultrasound on RhBMP-4 Induced Osteogenesis in an Spinal Fusion (Collabration with Poly U)

✍ CHENG Chun Yiu Jack • GUO Xia* • MI Yong Li*

☐ 1 January 2003

❖ Research Grants Council (Earmarked Grants)

The advances in biological interventions such as molecular therapy and gene therapy may result in novel approaches for treating some musculoskeletal disorders in which surgeons, who have traditionally used the tools of excision and reconstruction to treat patients, may in the near future serve as surgical gardeners who create microenvironments that are conducive for tissue regeneration. Physical intervention plays important role in postoperative rehabilitation. Whilst gene therapy and other new treatments give optimism for the future to the patients with particular musculoskeletal disorders it is important for physiotherapy to keep in step with the new treatments and to understand the interaction between physical intervention and biological intervention. This is the overall objective of this research project. An important area of research is on

the biological induction, such as application of recombinant human BMPs, to achieve or enhance spinal fusion, since spinal deformities and degenerative diseases are very common, and surgical spinal fusion is complicated and with high risk of non-union. Our previous RGC supported study has successfully shown that site specific application of recombinant human BMP-4 (rhBMP-4) can induce solid spinal fusion via extraskelatal endochondral osteogenesis in rabbit model. However, the success rate was related to relatively high dose of rhBMP-4 that is not practical for clinical application. Incorporation of physical intervention is a possible way to maximize the clinical efficacy of these factors, thus decrease its effective dose for achieving solid bony fusion. Low intensity pulsed ultrasound (LIPUS) has shown to be able to accelerate healing of fresh fractures by enhancing endochondral osteogenesis. In this study we will investigate the feasibility of LIPUS enhancing BMP induced endochondral osteogenesis, thus form sufficient amount of bone for achieving bony fusion with relative low dose of rhBMP-4. A well established rabbit spinal fusion model and evaluation methods in our previous studies will be adopted for this study.

(MD02790)

Identification of Prognostic Disease Modifier Genes in Adolescent Idiopathic Scoliosis - A Six-Year Longitudinal Follow-Up Study

✍ CHENG Chun Yiu Jack • TANG Leung Sang Nelson (Chemical Pathology) • GUO Xia* • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)

☐ 1 December 2004

❖ Research Grants Council (Earmarked Grants)

Adolescent idiopathic scoliosis (AIS) is a complex three-dimensional spinal deformity that commonly occurs in the girls at the peripubertal period between 10-16 years of age. The prevalence of AIS in Hong Kong is nearly 4%. Results of our previous studies have revealed the presence of generalized osteopenia, delayed onset of puberty, taller, longer arm-span and abnormal bone turnover in AIS subjects. These characteristics are related to the prognostic indicators for curve progression such as growth, menarche, and Risser sign. Additional indicators are required to better predict the curve progression. Based on our previous result showing abnormality in growth and sexual maturation, we hypothesize that polymorphism of the major genes of the growth hormone (GH)/insulin-like growth factor I (IGF-I) axis may be associated with the manifestation of abnormality in AIS subjects. GH/IGF-I hormonal control of growth and development has long been shown to play an important role in the pubertal skeletal growth and sexual maturation.

To identify the genetic markers for the disease severity and progression, we propose to continue to follow up our 500 cases of AIS girls between age 10 to 15 years and 300 age-and sex-matched normal control from previous studies for 3 more years to complete the 6-year longitudinal study whereby most subjects would have reached skeletal maturity. The study will include the determination of 1) the curve progression, 2) anthropometric measurement, 3) bone mineral status, and 4) bone turnover markers. The genotypes related to the GH/IGF-I hormone axis will be characterized and its association with the above monitored changes will be analyzed.

The clinical significance of the present study is to provide more comprehensive information to the clinician on early diagnosis of AIS and identify high-risk individual of curve progression who may benefit from appropriate early treatment. Moreover,

the study can enhance our understanding on the pathogenesis of AIS.

(CU04337)

Bioengineering a New Composite with Bone Marrow Derived Stem Cells and Bioceramics for Spinal Fusion

✍ CHENG Chun Yiu Jack • QIN Ling • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • YEUNG Hiu Yan

□ 1 March 2005

❖ CUHK Research Committee Funding (Direct Grants)

Spinal deformities and degenerative diseases are common diseases in orthopaedics, many of which would require surgical stabilization and posterior spinal fusion (PSF). Although autograft and decortication in PSF is “gold standard”, the nonunion rate in PSF has been reported to range 5-35%. An important area of research is on the bone substitute for autograft and the biological enhancement of the bony fusion, in both the quality and the rapidity. The source of osteoprogenitor cells is very important for the success of the PSF because the fusion bed lacks of mesenchymal stem cells (MSCs) to form bone properly.

The development of bone marrow derived mesenchymal stem cell research opens up the possibility of bone tissue engineering. Researches can now isolate and expand the bone marrow MSCs in number and differentiate them directly to osteogenic cells. Application of expanded osteogenic cells from bone marrow seeded on calcium phosphate bioceramic for spinal fusion has not been extensively studied. The objectives of the project are 1) to characterize the differentiated MSCs grown on bioceramic; 2) to use a well established

rabbit PSF model to study the osteogenic effect of bioengineered osteogenic cell-bioceramic composite in fusion process; 3) to explore the possibility of undecorticated PSF surgery when the bioengineered composite is applied to the fusion site.

The outcome of this study will shed light on our understanding of bioengineered autologous MSCs in enhancing bone fusion of PSF without decortication. This new approach would provide unlimited supply of bone substitute and reduce the associated complications at the donor site and during the standard surgical procedures.

(MD04541)

An Experimental Study on the Use of Low Intensity Pulsed Ultrasound to Optimize Patellar Tendon Donor Site Healing in a Rat Model

✍ HUNG Leung Kim • QIN Ling • CHAN Kai Ming • WONG Wan Nar Margaret

□ 1 September 2004

❖ Research Grants Council (Earmarked Grants)

We will study the potential use of Low Intensity Pulsed Ultrasound (LIPUS) to promote patellar tendon donor site healing in a rat model. In stage 1, we will investigate the biological effects of LIPUS treatment on patellar donor site healing at inflammatory, reparative and remodeling stages. In stage 2 we will apply LIPUS at different time points in the healing process in order to determine the optimized time and duration of treatment for the gap healing and restoration of both structural and mechanical properties.

This study will reveal the biological effects of LIPUS on healing tendons at different stages, with respect to cytokine expression, matrix deposition, cell proliferation and apoptosis. This basic information will help to understand the mechanism of the

therapeutic effects of LIPUS on healing tendon and hence enable further modification for better outcome. The stage 2 of this study will investigate the effects of LIPUS treatment to optimize patellar tendon donor site healing, with respect to determine optimized time and duration of LIPUS for better outcome, measured as restoration of structural and mechanical properties. The results of this research project will fill up the voids in the mechanistic studies of the therapeutic effects of LIPUS, and it will provide recommendation for practical treatment with LIPUS with appropriate doses and timing. This study can extend the use of LIPUS for treatment of other types of tendon injuries in future.

(CU04338)

Wholesome Development for Physically Disabled Children - Therapy through Music and Arts

✍ HUNG Leung Kim • NG Kin Wah Bobby • HO Pak Cheong

□ 1 October 2004

❖ S.K. Yee Medical Foundation

The project provides services directly for physically handicapped children in particular those with congenital anomalies of the hands and children who suffer from burn scars. Music classes and Drawing classes are provided to them. Although these activities are common in the development of every Hong Kong child, children with physical disabilities or disfigurements find it difficult to access to such facilities. These activities will enhance the development of self confidence, improve self image and improve social skills. Parents groups will be organized alongside and will enhance the acceptance of parents to their children's disabilities. The course will be held in secondary schools. Ordinary students will be encouraged to participate and will

enhance the understanding and acceptance of disabled children.

(MD04417)

Program of Training Fall and Fracture Prevention Professionals

✍ LEUNG Kwok Sui • CHAN Tan Jessica • SZE Pan Ching • LAM Pui Sze • NG Wai Kin • CHEUNG Wing Hoi

□ 1 December 2004

❖ Asian Association for Dynamic Osteosynthesis • CUHK Matching Contribution (PSDAS) • Professional Services Development Assistance Scheme, Commerce, Industry and Technology Bureau, HKSAR Govt

Fall-related fracture is very common in the world. The cost of hip fracture in Hong Kong is estimated at \$300,000 per patient. Reducing falls will surely help to reduce the healthcare burden. O&T, CUHK is the unique institute to organize large scale comprehensive fall prevention program in Asian regions. Organizing international conference of fall prevention helps to promote the image of high quality professional medical care service in Hong Kong. Fall prevention activities are popular in western countries, which will be a trend to become the most effective way to reduce fall-related fractures. As we have accumulated much experience in this topic, it is a good time to share with other expertise and hence promote the concept to mainland China and other Asia Pacific places. The leading post of Hong Kong in high medical standard can be further consolidated. Aims of this project are: (1) to introduce the concept and importance of fall prevention program in avoiding fall-related fractures for Asia Pacific and overseas medical professional participants through an international conference; (2) To update the latest

knowledge of fall prevention for related professionals by inviting famous speakers in this field in order to enhance participants' medical standard, thus promoting our high quality healthcare service in Hong Kong. By acquiring the knowledge, participants are able to adopt the fall prevention strategies and implement in the local districts; (3) To share the early experience in fall prevention program in Hong Kong with overseas experts and explore the future development.

(MD04556)

Optimization of the Porosity of an Injectable Hydroxyapatite and the Study of Its Effect on Bone Ingrowth with Orthopaedic Implants in Osteoporotic Bone

✍ LEUNG Kwok Sui • QIN Ling • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • CHEUNG Wing Hoi • Leng Yang*

□ 1 January 2005

❖ CUHK Research Committee Funding (Direct Grants)

With fast growing aging population, operative treatments of osteoporotic fractures are the commonest operation done every day. Implant loosening or backout are not infrequently seen due to the poor holding power of osteoporotic bone. Revision surgery and delayed rehabilitation cause more stress to these very fragile patients and may increase the medical cost. Bone cement is commonly used to enhance the holding power of the osteoporotic bone by increasing the contact area between the implants and osteoporotic osseous tissues.

Our previous animal and clinical studies on injectable hydroxyapatite (HA) demonstrated good outcome

without complications by increasing the contact area between the screw and the trabeculae. Microarchitectural analysis, however, found that the injectable HA was of low porosity, which decreases the osteoconductivity for bone ingrowth and hence the holding power. In the present study, we propose to use inexpensive carboxymethylcellulose (CMC) to optimize the porosity of HA without significantly affecting the mechanical strength. The strength properties of the optimized HA will be studied *in vitro*. Microarchitectural and histomorphometrical analysis will also be performed to investigate the effect of different amount of CMC on the porosity of HA.

Our expected outcome is that HA with optimal porosity can increase the bone ingrowth and hence the holding power of osteoporotic bones. This study will help to establish a standard protocol to prepare injectable HA for clinical use. Patients suffering from osteoporotic fractures will be benefited.

(MD04597)

Establishment of Mobile Fall Risk Assessment Center

✍ LEUNG Kwok Sui • CHAN Tan Jessica • SZE Pan Ching • LAM Pui Sze • CHEUNG Wing Hoi

□ 2 March 2005

❖ S.K. Yee Medical Foundation

According to recent researches, there are 21% of elderly falls annually, and among the fallers, 24% of them sustained fractures, which are the leading cause of disability and dependence among elderly (Leung et al, HKAM. 2003, 100; Ho et al, Public health & epidemiology bulletin. 2003; 12:13-17). With the aging population, the problems of elderly falls and fractures would be in increasing severity.

For the implementation of fall prevention program, it is essential to identify the elderly who are at risk of falling to provide intervention for them so as to prevent them from falling. Thus, the purpose of this project is to set up a mobile fall risk assessment center to provide fall risk assessments to elderly living in various districts in Hong Kong, especially for those in remote regions, so that the elderly at risk of fall and their risk factors of fall and fracture can be identified, and intervention programs can be provided to them accordingly.

In summary, with the establishment of a mobile fall risk assessment center, the following objectives will be achieved:

- To provide fall risk assessment to elderly living in all districts of Hong Kong
- To identify elderly who are at risk of falling and their factors associated with falling
- To help elderly to be more aware of their fall risks and reinforce them to take preventive measures in daily living
- To refer elderly at risk of falling to join community fall prevention programs
- And hence, to reduce fall and fracture incidence in the community

(MD04727)

Effect and Mechanisms of LIPUS on Cartilage Regeneration in an Osteoarthritis Rabbit Model after Subchondral Bone Drilling

✍ LEUNG Kwok Sui • LUI Po Yee Pauline •
CHEUNG Wing Hoi • QIN Ling

📅 1 June 2005

❖ Smith and Nephews plc

The effect of LIPUS to improve the outcome of subchondral bone drilling at different stages of osteoarthritis will be investigated in rabbit model.

We hypothesize that ultrasound may be useful when combined with subchondral bone drilling to direct the differentiation of the marrow mesenchymal stem cells along the lineage of hyaline cartilage instead of fibrocartilage. It may additionally increase matrix synthesis and prevent its degradation by improving the growth factors expression profile for cartilage repair. At early stage of osteoarthritis, LIPUS may reverse its development. One -hundred and twenty-eight New Zealand adult white rabbits will be immobilized for 6 weeks or 12 weeks to develop knee osteoarthritis, followed by subchondral bone drilling. The contralateral limb will served as intact control. After developing different stages of osteoarthritis, they will be randomly divided to study the dose-dependent effect of LIPUS (0, 20 minutes). A ultrasound machine delivering LIPUS that covers the knee joint uniformly will be applied at the indicated dose daily, 5 days/ week for 12 weeks and followed up for another 12 weeks. Changes in the articular cartilage and periarticular structures of knee joint will be examined by radiography, histology (H&E for general morphology and Safararin O for quantification of proteoglycans content) and immunohistochemistry (collgen I, II, X, aggrecan) at different times of the experiment. Function repair will be assessed by non-destructive cartilage elastography, and indentation test. The effect of LIPUS on the expression of TGF-beta, IL-1 and other biochemical factors will be studied to understand its mechanism of action.

(MD04419)

International, Double-Blind, Randomized, Placebo-Controlled Study to Assess the Efficacy and the Safety of 2g/Day of Strontium Ranelate (S12911) versus Placebo Administered for 1 Year

in Asian Women with Postmenopausal Osteoporosis

✍ LEUNG Ping Chung • CHOY Tak Kee Dicky (HK JCC for Osteoporosis Care and Control) • CHAN Wan Kin (Community and Family Medicine)

□ 1 August 2004

❖ Institut De Recherches Internationales Servier

To assess the efficacy and the safety of 2g/day of strontium ranelate (S12911) versus placebo administered for 1 year in Asian women with postmenopausal osteoporosis.

The primary outcome is the relative change from baseline to the end of the spine BMD.

Secondary outcome include safety measure and relative change from baseline to the end of the hip BMD.

Strontium ranelate (S12911) is a new compound formed by an organic acid and 2 atoms of stable strontium. It has been shown *in vitro* and in animals models to act as an inhibitory agent on bone resorption and as a stimulatory agent on bone formation. This new paradigm has been validated in strontium ranelate phase II and phase III studies.

The phase III place-controlled study, called SOTI (Spinal Osteoporosis Therapeutic Intervention), performed in 1,649 Caucasian women with established osteoporosis showed in the group treated with 2g/day of strontium ranelate a relative risk of new vertebral fracture reduced by 41% ($p < 0.001$) over 3 years with an early effect demonstrated after the first year.

(MD04622)

Reconstruction of Damaged Growth Plate with Bioengineered Physisaugmented with Low Intensity Pulsed Ultrasound Application

✍ LEUNG Ping Chung • LEUNG Kwok Sui • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • CHEUNG Wing Hoi • QIN Ling

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

Physeal injuries are serious injuries in children. The successful treatment of growth plate damages continues to be a challenging clinical problem in paediatric orthopaedics. The current modalities for the repair of growth plate defects have limited success and the “functional repair” is seldom achieved.

The transplantation of bioengineered growth plate with full characteristics of normal physis offers a potential solution for this problem. As demonstrated in our previous studies, bioengineered physis up to 8mm diameter could be synthesized *in vitro* and it demonstrated the capacity of cell differentiation and endochondral ossification. The bioengineered tissue was then transplanted in the gap created between the metaphysis and diaphysis of adolescent rabbit tibia by the modified distraction procedures. Continuous growth with growth plate characteristics was detected and no immunological rejection was observed. The transplant became bone 18 weeks post-transplantation.

In the present study, we aim to further enhance the size of bioengineered growth plate to cover the entire cross-sectional area of rabbit tibia. The pellet culture technique will be modified to synthesize a larger growth plate with repeated centrifugations during medium changes, where centrifugations provide mechanical stimulation on the bioengineered growth plate to grow. The development of bioengineered tissues will be further boosted up by

the application of low intensity pulsed ultrasound (LIPUS). LIPUS application has been reported to increase cartilage matrix production and differentiation. We hypothesize that LIPUS promotes the development of bioengineered physes. The findings of this study hold extremely intriguing possibilities for the treatment of growth plate injuries in children and also bone lengthening.

(MD04948)

Establishing Indications for Extracorporeal Shockwave in Treatment of Delayed Bone-Tendon Junction Repair - A Preclinical Study

✍ QIN Ling • LEUNG Kwok Sui • CHEUNG Wing Hoi • LU Hong Bin • GUO Xia*

□ 1 December 2004

❖ CUHK Research Committee Funding (Direct Grants)

Our experimental studies and clinical arthroscopic examinations reveal difficult repair or delay in healing between bone and tendon at the B-T junction, including the delay in restoration of junction fibrocartilage, as compared healing taking place within homogenous tissues such as fracture repair and tendon healing. In the recent years, clinical studies showed that extracorporeal Shockwave (ESW) therapy, which was initially designed for treatment of kidney stone, was an effective non-operative therapy for treatment of musculoskeletal diseases, including fracture delayed and non-union as well as tendinosis 'tennis elbow'.

The purpose of this experimental study is to investigate potential positive effects of ESW in treatment of delayed B-T junction healing using an established partial patellectomy model in rabbits. The scientific evidences to be obtained will help our orthopaedic rehabilitation clinics to develop clinical

indications and protocols of using ESW for treatment of radiographically confirmed delayed union in patients after B-T junction repair surgery. From both the performance and public health perspective, the establishment of such clinical indications will significantly improve treatment results of related conditions so as no further delay for returning to daily work, training and competition or even termination of athletic career.

(MD04533)

Program of Training Professionals in Evaluation of Medicine and Biomaterials Developed for Prevention and Treatment of Osteoporosis, Osteoporotic Fractures, and Osteonecrosis

✍ QIN Ling • YEUNG Hiu Yan • HUNG Wing Yin Vivian • NG Wai Kin • CHEUNG Wing Hoi

□ 1 March 2005

❖ Professional Services Development Assistance Scheme, Commerce, Industry and Technology Bureau, HKSAR Govt

MicroCT and pQCT are popular in many medical and material sciences in western countries, such as USA and Europe for related research and development of both pharmaceutical and non-pharmaceutical products, biomaterials for orthopaedics applications and cardiovascular applications. With support of the Chinese University and Hong Kong Jockey Club in battle against osteoporosis, osteoporotic fractures, and osteonecrosis, we installed pQCT and microCT for research in order to help to reduce the healthcare burden. As we have accumulated much experience in this topic, it is a good time to share with other expertise and hence promote the concept to mainland China and other Asia Pacific regions. The leading

post of Hong Kong in high medical standard can be further consolidated.

The Objectives of this event is to introduce state-of the art peripheral quantitative computed tomography, microCT, and high-resolution MRI, and their evaluation strategies in evaluation of medicine and biomaterials developed for prevention and treatment of osteoporosis, osteoporotic fractures, and osteonecrosis to medical doctors, clinical and material scientists, bioengineers, technologists, postgraduate students and related personnel in Hong Kong, Mainland China, and the regions.

This will help to update their knowledge and technical skills via and international workshop and user meeting.

(MD04722)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

Edition Title/Investigators

2000-01 Low Intensity Pulsed Ultrasound Retained Change of Bone Mineral Content of Complex Tibial Fractures (MD00354)

✍ CHAN Chun Wai* • LEUNG Kwok Sui • TSUI Hon For# • LEE Wing Sze

2000-01 Low Intensity Pulsed Ultrasound Enhanced Bone Mineral Content of Tibial Lengthening (MD00579)

✍ CHAN Chun Wai* • LEUNG Kwok Sui • CHENG Chun Yiu Jack • NG Kin Wah Bobby • LEE Wing Sze • HUNG Wing Yin Vivian

2001-02 A Study of the Potential of a Semi-Purified Total Flavone Extract from Chinese Medicine Hippophae Rhamnoides in Promoting Tendon Healing (MD01092)

✍ CHAN Kai Ming • FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) • FUNG Kwok Pui (Biochemistry) • GAO Jin* • LI Jingxian*

2001-02 To Promote Tai Chi as an Exercise to Enhance the Health Promotion Aspect of Osteoporosis (MD01740)

✍ CHAN Kai Ming • QIN Ling • LI Jingxian (Sports Science & Physical Education)# • HONG Youlian (Sports Science & Physical Education) • LAU Edith Ming Chu (Community and Family Medicine)# • WOO Jean (Medicine & Therapeutics)

2003-04 A Study of Tendon Healing in Sports Injury : The Manipulation of Transforming Growth Factor Beta (TGF-β) on Matrix Deposition (CU03354)

✍ CHAN Kai Ming • FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • ROLF Christer Gustav* • WONG Wan Nar Margaret

2000-01 Re-defining the MRI Reference Level for Cerebellar Tonsil - A Study of 225

	Adolescents - Normal vs Idiopathic Scoliosis (MD00378) ✍ CHAU Wai Wang • CHENG Chun Yiu Jack • GUO Xia • CHAN Y. L.*	2000-01	Osteopenia in Adolescent Idiopathic Scoliosis (AIS): Preliminary Ultrastructural Study (MD00374) ✍ CHENG Chun Yiu Jack • TANG Shengping • GUO Xia • LEE Kwong Man, Simon* • QIN Ling
2000-01	The Implications of Preoperative Somatosensory Evoked Potential (SSEP) in Adolescent Idiopathic Scoliosis Patients (MD00430) ✍ CHAU Wai Wang • FU Lap Kun • GUO Xia • CHENG Chun Yiu Jack	2001-02	Percutaneous Intramedullary Kirschner Wiring for Displaced Disphyseal Fractures in Children (MD99476) ✍ CHENG Chun Yiu Jack • YUNG Shu Hang Patrick • NG Kin Wah Bobby • LAM Tsz Ping
2000-01	"Subacute Synovitis of the Hip in Children" A Distinct Entity? - A Follow-Up Study of 84 Cases (MD99384) ✍ CHENG Chun Yiu Jack • YUNG Shu Hang Patrick • NG Kin Wah Bobby • LAM Tsz Ping	2001-02	Promoting a Safer Household Environment: A Volunteer-Based Home Visit Programme (MD01665) ✍ CHENG Chun Yiu Jack • CIPRA members*
2000-01	An Immunohistochemical Study on Expression of Decorin and Biglycan in Bone of Osteopenic Adolescent Idiopathic Scoliosis Girls (MD00734) ✍ CHENG Chun Yiu Jack • TANG Shengping • GUO Xia • LEE Kwong Man, Simon* • QIN Ling	2002-03	Combination of Extra-Corporeal Shock Wave Therapy and Low Intensity Ultrasound for Inducing Non-Union Healing in a Rabbit Model (MD01503) ✍ CHENG Chun Yiu Jack • GUO Xia* • KWONG S C*
2000-01	Sternocleidomastoid Pseudotumor of Infants (SCMPOI) and Congenital Muscular Torticollis (CMT): The Relation Between Spontaneous Regression and Apoptosis (MD00523) ✍ CHENG Chun Yiu Jack • TANG Shengping • LIU ZQ* • QuanXM* • QIN JZ* • ZHANG DW*	2002-03	Formative Assessment Case Studies (FACS): Establishing Life-Long Learning Skills in Health Science Students (ED01398) ✍ CHENG Chun Yiu Jack • KUMTA Shekhar Madhukar
		2003-04	Combination of Extracorporeal Shock Wave and Low Intensity Ultrasound Therapy - An Alternative Biophysical Treatment of Fracture Nonunion? (MD01999)

- ✍ CHENG Chun Yiu Jack • KWONG S C* • GUO Xia*
- 2003-04 Effect of Extracorporeal Shockwave Treatment on the Delayed Consolidation of Distraction Osteogenesis in Rabbit Tibial Model (MD03814)
- ✍ CHENG Chun Yiu Jack • LEUNG Kwok Sui • KWONG Shek Chuen Kevin* • GUO Xia* • CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)
- 2003-04 Are Estrogen and Vitamin D Receptor Gene Polymorphism Associate with the Occurrence and Growth Abnormality of Adolescent Idiopathic Scoliosis? (MD03960)
- ✍ CHENG Chun Yiu Jack • TANG Leung Sang Nelson (Chemical Pathology) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • GUO Xia*
- 2003-04 Tissue Engineering of Mesenchymal Stem Cell-Calcium Phosphate Ceramic Composite - Study on Application in Spinal Fusion (MD03824)
- ✍ CHENG Chun Yiu Jack • QIN Ling • LEE Kwong Man, Simon* • YEUNG Hiu Yan • HU Yun Yu*
- 2003-04 Are VDR, Era and PTHR1 Genes Associated with the Occurrence as well as Abnormality in Bone Growth and Sexual Maturation in Adolescent Idiopathic Scoliosis? (MD03862)
- ✍ CHENG Chun Yiu Jack • TANG Leung Sang Nelson (Chemical Pathology) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • GUO Xia*
- 2002-03 A Prospective Randomized Study on Two Methods of Mobilization After Flexor Tendon Repair (MD02742)
- ✍ HUNG Leung Kim • WONG Man Wah • HO Pak Cheong • AU Kin Ming* • CHAN Ping Tak*
- 2003-04 Tissue Reactions and Dose Response Characteristics of Electromotive Vancomycin Delivery (MD03471)
- ✍ HUNG Leung Kim • CHAN Chiu Yeung Raphael (Microbiology) • FU Sai Chuen Bruma*
- 2002-03 The Learning Objects Initiative (ED02513)
- ✍ KUMTA Shekhar Madhukar • HART Ian* • CHAN Rita* • Blurton, Craig*
- 2003-04 Aminobisphosphonates and Farnesyl Transferase Inhibitors as Adjuvants in the Treatment of Giant Cell Tumor of Bone (MD03555)
- ✍ KUMTA Shekhar Madhukar • HUANG Lin (Surgery) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • ROSIER R. N.*
- 2000-01 Monteggia Fracture in Children - A Review of 30 Cases (MD00535)
- ✍ LAM Tsz Ping • MA RF* • NG Kin Wah Bobby • CHENG Chun Yiu Jack

- 2000-01 Anterior Spinal Fusion with Halm-Zielke Instrumentation System in Adolescent Idiopathic Scoliosis (MD00788)
✍ LAM Tsz Ping • NG Kin Wah Bobby • CHENG Chun Yiu Jack • MA RF*
- 2000-01 Calcium Intakes in Patients with Adolescent Idiopathic Scoliosis (AIS) (MD00838)
✍ LEE Tak Keung Warren • CHEUNG Siu King (Community and Family Medicine) • LAM See Way Sylvia • LEE Ching Shun Christine* • CHAU Wai Wang • CHENG Chun Yiu Jack
- 2000-01 Reconstruction of Damaged Pylorus with 3-D Chondrocytes Pellet Culture (MD20039)
✍ LEUNG Kwok Sui • LUI Po Yee Pauline • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • CHEUNG Wing Hoi
- 2002-03 Augmentation of Bone Mineral Acquisition in Osteoporotic Bone by Low-intensity Pulsed Ultrasound - A Study with Osteoporotic Goat Model (CU02153)
✍ LEUNG Kwok Sui • CHEUNG Wing Hoi • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • QIN Ling
- 2002-03 Fall and Fractures Prevention Program for the Elderly (MD02439)
- ✍ LEUNG Kwok Sui • CHEUNG Wing Hoi • CHAN Tan Jessica • WONG Josephine* • LAU Herman*
- 2003-04 Effect of Acoustic Pressure Wave on Callus Innervation and Fracture Healing (MD01655)
✍ LEUNG Kwok Sui • GUO Xia* • KEVIN S C Kwong*
- 2003-04 Modification of Home Environmental Hazards for the Elderly (MD03868)
✍ LEUNG Kwok Sui • CHAN Tan Jessica • SZE Pan Ching • LAM Pui Sze • CHEUNG Wing Hoi
- 2003-04 High Frequency, Low Magnitude Vibration Therapy for Preventing Osteoporotic Fracture (MD03361)
✍ LEUNG Kwok Sui • CHEUNG Wing Hoi • QIN Ling • SIU Wing Sum# • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)
- 2003-04 Setting Up Fall Risk Assessment Centres for Community-Dwelling Elderly (MD03791)
✍ LEUNG Kwok Sui • CHAN Tan Jessica • SZE Pan Ching • LAM Pui Sze
- 2001-02 Chinese Medicine Research and Further Development (MD01714)
✍ LEUNG Ping Chung • FUNG Kwok Pui (Biochemistry) • SUNG Joseph Jao Yiu (Medicine & Therapeutics) • HAINES Christopher John (Obstetrics & Gynaecology) •

	SUNG Yn Tz Rita (Paediatrics) • WOO Kam Sang (Medicine & Therapeutics) • CHE Chun Tao (School of Chinese Medicine) • CHAU F T* • TSIM Karl W K* • FONG W F*		Postmenopausal Women with Osteoporosis (MD02656) ✍ LEUNG Ping Chung • CHOY Tak Kee Dicky (HK JCC for Osteoporosis Care and Control)
2001-02	Herbal Formula for Prevention and Treatment of Osteoporosis - A Rat Model (MD01097) ✍ LEUNG Ping Chung • FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) • FUNG Kwok Pui (Biochemistry) • QIN Ling • SHI Yin Yu*	2003-04	Osteoporotic Fractures in Chinese Men: Mr Os Hong Kong (MD03838) ✍ LEUNG Ping Chung • WOO Jean (Medicine & Therapeutics) • WONG Yeung Shan Samuel (Community and Family Medicine) • CUMMINGS Steve* • LANG Tom* • NEVITT Michael C* • STONE Katie* • ORWOLL Eric*
2002-03	A Multicenter, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Zoledronic Acid in the Treatment of Osteoporosis in Postmenopausal Women Taking Calcium and Vitamin D (MD02839) ✍ LEUNG Ping Chung • WOO Jean (Medicine & Therapeutics) • CHOY Tak Kee Dicky (HK JCC for Osteoporosis Care and Control) • WONG Yeung Shan Samuel (Community and Family Medicine)	2003-04	National Institutes of Health - US-China-Japan Research Consortium on Herbal Medicine (MD00555) ✍ LEUNG Ping Chung • FUNG Kwok Pui (Biochemistry) • BUT Pui Hay Paul (Biology) • LEE Ming Yuen (Institute of Chinese Medicine) • FONG Yuet Shim Carmen (Institute of Chinese Medicine)
2002-03	The Prevalence of Vertebral Deformity in Asian Men and Women (MD02449) ✍ LEUNG Ping Chung • WONG Yeung Shan Samuel (Community and Family Medicine)	2000-01	Associated Osteoporosis of the Host Bone in Tibial Lengthening (MD00633) ✍ NG Kin Wah Bobby • HUNG Wing Yin Vivian • CHENG Chun Yiu Jack
2002-03	Comparison of Teriparatide and Calcitonin in the Treatment of	2001-02	Low Intensity Pulsed Ultrasound for Accelerating Bone-tendon Junction Repair (MD01098) ✍ QIN Ling • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • LENG Yang* • WONG Wan Nar Margaret

- 2002-03 Processing and Properties of Hydroxyapatite Coatings on Porous Metal Implants (BL00700)
✍ QIN Ling • LENG Yang* • FU Sai Chuen Bruma* • FUNG Kwok Pui (Biochemistry) • SHI Yin Yu*
- 2002-03 Engineering Titanium Surfaces for Hard Tissue Implants (BL01373)
✍ QIN Ling • LENG Yang*
- 2002-03 Ultrasonic Characterization of the Transient and Inhomogeneous Swelling Behavior and Progressive Degeneration of Articular Cartilage (MD01891)
✍ QIN Ling • ZHENG Yong Ping* • MOW Van C* • LU M H*
- 2002-03 Biophysical Intervention for Enhancing Bone-Tendon Junction Repair during and after Immobilization - An Partial Patellectomy Model in Rabbits (CU02155)
✍ QIN Ling • GUO Xia* • LEUNG Kwok Sui • ZHENG Yong Ping*
- 2002-03 Ultrasound Elastomicroscopy (BL02792)
✍ QIN Ling • LENG Yang*
- 2002-03 Bioactivity Study of Bioceramics Using Transmission Electron Microscopy (BL02906)
✍ QIN Ling • LENG Yang*
- 2002-03 Development of Micro-Finite Element Model for Quantifying Mechanical Properties of Trabecular Bone (BL02993)
- ✍ QIN Ling • GUO Xia* • ZHANG Min* • SHI San Qiang*
- 2003-04 Low Intensity pulsed Ultrasound for Early Restoration of Fibrocartilage Zone and Proprioception in Bone-Tendon Junction Repair - A Partial Patellectomy Model in Rabbits (MD03502)
✍ QIN Ling • CHEN Hong Hui*
- 2003-04 New Born Formation and Tendon Cartilaginous Metaplasia Prevent Postoperative Articular Cartilage Deterioration and Improve Joint Tracking - A Partial Patellectomy Model in Rabbits (CU03342)
✍ QIN Ling • CHAN Kai Ming • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • LEUNG Kwok Sui • ZHENG Yong Ping*
- 2003-04 Vibration Therapy for Preventing Osteoporotic Fracture in Post-menopausal Women (MD03559)
✍ QIN Ling • LEUNG Kwok Sui • CHEUNG Wing Hoi • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)
- 2000-01 Treatment of "Floating Elbow" in Children (MD00960)
✍ TANG Ning • NG Kin Wah Bobby • CHENG Chun Yiu Jack
- 2001-02 The Effect of Glucocorticoid on Human Tendon Explant: The Link with Tendon Rupture (MD01921)

- ✍ WONG Wan Nar Margaret • FU Sai Chuen Bruma* • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • CHAN Kai Ming
- ✍ YEUNG Hiu Yan • LEE Kwong Man, Simon* • CHEUNG Wing Hoi • LAW Lai Pang (Institute of Chinese Medicine)# • TABATA Yasuhiko* • CHENG Chun Yiu Jack
- 2002-03 The Effect of Glucocorticoid on Human Tendon Explant – A Biomechanical Study (MD02366)
- ✍ WONG Wan Nar Margaret • CHAN Kai Ming • FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)
- 2003-04 Clinical Protocol for a Multicentre, Double-Blind, Double-Dummy, Randomized Study of the Analgesic Efficacy and Safety of Valdecoxib Compared to Diclofenac Sodium in Patients Undergoing Knee Arthroscopy Procedure for Anterior Cruciate Ligament Reconstruction (MD03917)
- ✍ YUNG Shu Hang Patrick • TONG Wai Chung Christopher • CHAN Kai Ming • CHAN Tan Jessica
- 2000-01 Culture of Rabbit Chondrocytes Released from Rib Cage on Calcium Phosphate Ceramic and Collagen Sponge (MD98751)

RESEARCH PROJECTS

Development of an Alternative Drug Based on a New Concept for the Treatment of Thrombocytopenia

✍ FOK Tai Fai • YANG Mo • LI Kwai Har Karen
• NG Heung Ling Margaret (Anatomical & Cellular Pathology)

☐ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

To date, there is no ideal treatment for thrombocytopenia. Limited by their undesirable side effects, the platelet-promoting cytokine thrombopoietin (TPO), has remained experimental. We have provided the evidence of serotonin (5-HT) as a growth factor for megakaryocyte (MK) differentiation and platelet formation. The root of polygonum multiflorum thunb (Chinese crude drug “Heshouwu”) is an important ingredient of many popular prescriptions in traditional Chinese medicine (TCM) for promoting “blood production”. Polygonum multiflorum extracts (PME) also inhibits monoamine oxidase (MAO) and thus increases the level of 5-HT. Therefore, we hypothesize that polygonum multiflorum has a promoting effect on thrombopoiesis via inhibition of monoamine oxidase (MAO) to increase 5-HT levels. Based on this hypothesis, this study aims to explore the scientific basis for the hematopoietic role of polygonum multiflorum, which may help develop a new drug for the treatment of thrombocytopenia. Our short-term strategy are: (i) To investigate the mitogenic effect of PME on the ex vivo expansion of CD41+ (MK) cells and CFU-MK (MK progenitor) formation; (ii) To

investigate the effect of PME on platelet-related transcriptional factor NF-E2 and GATA-1, and MAO activities in MK cell lines; and (iii) To analyze the effect of PME on thrombopoiesis and 5-HT levels in a thrombocytopenic mouse model. Our long-term strategy includes: (i) The evaluation of the efficacy of PME on the treatment of thrombocytopenia by a case-controlled clinical study; and (ii) Development of PME as a new drug for the treatment of thrombocytopenia if efficacy is proven in (i). (MD04601)

A Randomized, Double-Blind, Placebo-Controlled Study of the Therapeutic Effect and Safety of a Traditional Chinese Medicine (TCM) for Atopic Dermatitis in Children

✍ HON Kam Lun • LEUNG Ting Fan • LEUNG Ping Chung (Institute of Chinese Medicine)*

☐ 12 November 2004

❖ Health and Health Services Research Fund

Background: Atopic dermatitis (AD) is a common and distressing relapsing skin disease. The mainstay of treatment includes topical corticosteroids use, with its many potential systemic side effects and general phobia by the public. Various traditional Chinese herbs have been tried but effects inconsistent and potential adverse effects concerning. In a recent pilot study of a TCM capsule, we found significant improvement in AD severity scores in children.

Objective: To assess the therapeutic effects and safety of a TCM capsule in children.

Design: Randomised placebo-controlled, double-blind study

Methods: We plan to recruit 60 patients, aged 5 to 18 years, with moderate-to-severe AD from the paediatric dermatology clinic at Prince of Wales Hospital. AD is diagnosed according to Hanifin and

Rajke. Severity is evaluated according to SCORing Atopic Dermatitis (SCORAD) and biochemically with immune markers. Nasal and flexural skin swabs will be cultured for *S. aureus* at each visit. All patients will undergo a 4 to 8-week run-in period and then randomised in a double-blind fashion to TCM or placebo capsules for 12 weeks. Enrolled subjects will be followed 4-weekly for the control of their skin condition.

Outcome: Severity of AD as assessed using SCORAD will be used as the primary outcome. The individual components that constitute SCORAD (extent, pruritus, sleep loss), the details on topical steroid used, the number of doses of oral anti-histamines will be used as a secondary outcome. AD -specific immune markers such as CTACK, and nasal and skin staphylococcal carriage rate will be compared pre- and post-TCM.

(MD04981)

Inflammatory Gene Profiling in Neonates with Maternal Asthma

✍ LEUNG Ting Fan • NG Pak Cheung • LEUNG Tse Ngong (Obstetrics & Gynaecology) • KO Wai San Fanny (Medicine & Therapeutics) • LAM Wai Kei Christopher (Chemical Pathology) • TAM Wing Hung (Obstetrics & Gynaecology) • WONG Chun Kwok (Chemical Pathology)

☐ 1 December 2004

❖ CUHK Research Committee Funding (Direct Grants)

Asthma is one of the commonest chronic illnesses worldwide. Although familial inheritance of asthma and other atopic disorders is a well-known phenomenon, the timing, extent and exact mechanisms leading to this immunomodulation in mother/child pairs are poorly understood. Our

group has recently reported on the reference ranges of a panel of atopy-related chemokines in umbilical cord blood, and that serum macrophage-derived chemokine levels may be increased in newborns who develop wheezing in infancy. The present cross-sectional study will provide important information on the extent of *in utero* priming of fetal allergic inflammatory responses in relation to the presence of maternal asthma. Pregnant women with asthma and those without any atopic disorder will be recruited as the *cases* and *controls* respectively. These results will help to elucidate the inflammatory pathway(s) that is (are) involved in the development of early allergic manifestations. In addition, novel inflammatory markers for childhood asthma and atopy may be discovered through the use of this gene expression study. This project may shed light on whether any specific immunomodulatory agent against cytokines and related pathways may be able to prevent the early development of asthma in high-risk infants with family history of atopy.

(MD04381)

A One-Year, Open-Label, Single Arm, Multi-Center Trial Evaluating the Efficacy and Safety of Oral ICL670 (20mg/kg/day) in Patients Diagnosed with Transfusion-Dependent Iron Overload

✍ LI Chi Kong • CHIK Ki Wai • LEE Vincent • SHING Matthew Ming Kong*

☐ 1 June 2005

❖ Novartis Pharmaceuticals Corporation

This study is carried out to evaluate a new oral preparation for the treatment of iron overload in a population of patients who present with signs of iron overload due to repeat blood transfusions. Entry into the study will be based on the patients showing

the evidence of transfusion induced iron overload. The majority of patients enrolled will be the B-thalassemia major requiring transfusion. Iron overload is caused by the blood transfusions that the patient is incapable of eliminating the iron from the transfused blood, iron thus accumulates in the body or organs such as liver or heart, where it causes complications. The iron chelation therapy prevents the complications arising from iron accumulations. The golden standard used for treatment is deferoxamine, however, this is not considered optimal due to its administration route (subcutaneous) thus interfering the social life of patients. This new oral trial drug is named ICL670 that binds iron in a potent and selective manner. This study is a single-arm, multi-center and an open label trial with 52 weeks treatment period. Eligible patients who fulfill the inclusion and exclusion criteria as stated in the protocol will start their ICL670 treatment with a standard daily dose once a day. This initial dose will be maintained for the 52 weeks treatment period unless the combined evaluation of safety and efficacy markers suggest a dose adjustment. The end-point of the study is the change of serum ferritin which is a commonly used marker for the monitoring of body iron.

(MD04330)

In Vitro Induction of Embryonic Stem Cells into Functional, Multi-Potent Hematopoietic Stem Cells Using a Novel, Chronological Approach Mimicking Normal Embryonic Microenvironments

✍ LI Kwai Har Karen • TSANG Kam Sze Kent (Anatomical & Cellular Pathology) • LAU Tze Kin (Obstetrics & Gynaecology) • Huang Shao Liang*

□ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

Human embryonic stem cells (ESC) have recently been established from preimplantation blastocytes. They have become a novel source of pluripotent stem cells that can be maintained in culture indefinitely and differentiate into cell types of all germ layers. Our hypothesis is that the exposure of ESC to microenvironments of embryonic hematopoiesis is essential for the efficient and normalized induction of ESC to multi-potent and functional hematopoietic stem cells (HSC). In this study, mouse E14 and D3, and human HI ESC lines will be co-cultured (contact and non-contact in transwells) with matrix/stromal cells established from murine and human AGM, fetal liver and bone marrow. Using the appropriate growth factor supports, we shall study the *in vitro* development of the hematopoietic system, using lineage specific markers (including CD34, CD38, CD61, CD41, CD45, CD3, SSEAs, Oct4) and functional clonogenic cells (CFU-GEMM, BFU-E, CFU-GM, CFU-MK). The homing and multi-potent capacity of these ESC-derived HSC will be evaluated by their engraftment in the non-obese diabetic (NOD)/severe immunodeficient (SCID) mouse transplant model. Results obtained from this project would contribute to the much-needed technology for the induction of ESC to a targeted lineage suitable for clinical applications.

(MD04486)

Cardiovascular Complication in Children with Obstructive Sleep Apnoea Syndrome - A Case Control Study

✍ LI Man Chim Albert Martin • WING Yun Kwok (Psychiatry) • SUNG Yn Tz Rita •

ABDULLAH Victor (Surgery) • NG Siu Kwan (Surgery) • CHAN Ho Ming Michael (Chemical Pathology)* • LAU Tak Fai Joseph (Centre for Epidemiology & Biostatistics) • CHAN Dorothy* • LAM Wai Kei Christopher (Chemical Pathology) • FOK Tai Fai

□ 1 January 2005

❖ CUHK Research Committee Funding (Direct Grants)

Childhood obstructive sleep apnoea syndrome (OSAS) is an important and common condition. If it is unrecognised and untreated, OSAS can result in significant morbidity and possibly mortality. Several studies have suggested that systemic hypertension, ventricular hypertrophy and abnormal ventricular diastolic function as documented on echocardiography are common in children suffering from sleep apnoea. However, methodological drawbacks including small sample size, lack of suitable control subjects and selective patient populations make evaluation of many of these studies difficult. Withstanding these limitations, there is a general consensus that childhood OSAS is associated with hypertension and ventricular hypertrophy that may predispose the subject to a higher risk for subsequent cardiovascular adverse events. But the actual prevalence of OSAS-associated hypertension and echocardiographic abnormalities and their correlation with nocturnal respiratory parameters is unclear. There is also a lack of data on the reversibility of such complications after treatment. Our on-going epidemiological study on the prevalence of childhood OSAS in Hong Kong provides the golden opportunity for us to study in greater details the cardiovascular complications in childhood OSAS. Using validated assessment methodologies and standardised sleep-monitoring techniques, we aim to compare ambulatory blood pressure readings and

detailed 3-dimensional Echo parameters between OSAS subjects and normal controls. Repeat assessment will be performed in the OSAS subjects post intervention. We anticipate that the research findings would help to estimate the magnitude of cardiovascular complications in childhood OSAS and guide future healthcare planning with regards to early detection and treatment. This will also foster the development and planning of paediatric Sleep Medicine in Hong Kong.

(MD04990)

A Quantitative Evaluation of a Leukocyte Marker CD64 and Human Inflammatory Cytokines for Diagnosis of Early-Onset (<72 Hours of Life) Neonatal Infection

✍ NG Pak Cheung • LI Kwai Har Karen • FOK Tai Fai

□ 1 August 2004

❖ CUHK Research Committee Funding (Direct Grants)

The Neonatal Team at the Prince of Wales Hospital is one of the world's leading teams for research in diagnostic markers of infection for newborn infants. Recent key publications in this field are listed in the reference section of the proposal (References 1-4).

This study aims to evaluate the usefulness of a neutrophil surface marker (CD64) and a panel of key inflammatory cytokines: interleukin-(IL)-1 β , IL-6, IL-8, IL-10, IL-12p75 and TNF α for early diagnosis of early-onset (<72 hours of age) neonatal infection in term newborn.

Early-onset (<72 hours of life) infection in newborn infants carries a high risk of morbidity and mortality. Early clinical signs and symptoms of infection are often non-specific and subtle, but the progression of the disease process can be alarmingly rapid leading to

irreversible organ damage and death within hours of onset. Identification of early-onset infection is, thus, a major diagnostic problem for neonatal clinicians. Equally difficult is making a correct clinical differentiation between infected and non-infected cases. Continuation of antibiotics for presumptive bacterial infection in non-infected cases, frequently leads to unnecessary and inappropriate treatment. Thus, it is essential to identify a sensitive infection marker (or a set of markers) that will (i) react rapidly to bacterial infection, and (ii) can be reliably used to confirm or to refute the diagnosis of early-onset bacterial infections in newborn infants.

(MD04463)

Effects of Thrombopoietin on Cardio-Protection and Stem Cell Mobilization in Damaged Heart

✍ SUNG Yn Tz Rita • YANG Mo • LI Kwai Har Karen

☐ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

The transplantation of bone marrow cells into the damaged heart has been proposed as a new treatment for heart injury. Haematopoietic growth factors may also have cardio-protective effect. We hypothesize that (1) haematopoietic growth factor thrombopoietin (TPO) has a direct cardiac protection effect on heart damage; and (2) TPO also have a mobilizing effect on bone marrow stem/progenitor cells for cardiac regeneration. In this study, our objectives are (i) To evaluate the effect of TPO on proliferation (MTT assay) of H9C2 cardiomyocytes, anti-apoptosis (Annexin V and caspase 3 assay), and Akt cell survival signaling pathway (western blot); (ii) To investigate the in-vivo effect of TPO in an ischemic heart damage rat model on cardiac function

(Echocardiography), histology (H&E, EM) and apoptosis (TUNEL); and (iii) To study the mobilizing effect of TPO in this rat model by CFU and scal-1 assay. The application of TPO for cardio-protection and stem cell mobilization is a new concept, if proven, could be developed for the treatment of cardiac damage diseases such as ischemic heart attack (MD04681)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
2003-04	<i>In vitro</i> Study of the Mechanism of Angelica Polysaccharide on Platelet Production in Human Haematopoietic Stem Cells (MD03602) ✍ CHIK Ki Wai • YANG Mo • SUNG Yn Tz Rita • LI Kwai Har Karen • FOK Tai Fai
2002-03	Randomised, Controlled Trial of the Use of Colloid and Crystalloid in the Treatment of Hypotension in Preterm Very Low Birth Weight Newborns (MD02796) ✍ FOK Tai Fai • NG Pak Cheung • SO King Woon Alan
2003-04	Mobilization of Endogenous Stem and Progenitor Cells from Bone Marrow for the Repair of Neonatal Hypoxic-Ischemic Brain Damage (MD03469) ✍ FOK Tai Fai • YANG Mo • LI Kwai Har Karen • CHIK Ki Wai

- 2003-04 Prospective, Hospital-Based, Multi-Center Study to Assess the Incidence of Intussusception in Children <2 Years of Age in Hong Kong (MD03530)
✍ LAU Chun Yuen David • YEUNG Chung Kwong (Surgery) • Paul TAM* • KWOK Wing Kin*
- 2003-04 Innate Immunity and Asthma in Chinese Children (MD03742)
✍ LEUNG Ting Fan • TANG Leung Sang Nelson (Chemical Pathology) • WONG Wing Kin Gary • WONG Chun Kwok (Chemical Pathology) • LAM Wai Kei Christopher (Chemical Pathology)
- 2002-03 The Role and Mechanism of Stem Cells in Regenerative Medicine (MD02328)
✍ LI Kwai Har Karen • NG Ho Keung (Anatomical & Cellular Pathology) • CHAN Chung Ngor Juliana (Medicine & Therapeutics) • CHAN Hsiao Chang (Physiology) • SUNG Yn Tz Rita • FOK Tai Fai • LEUNG Po Sing (Physiology)
- 2003-04 Mechanism of a Novel Mannose-Binding Lectin as a Preservation Factor for Human Hematopoietic Stem and Progenitor Cells (MD03711)
✍ LI Kwai Har Karen • OOI Vincent Eng Choon (Biology)
- 2002-03 An Epidemiological Study of Obstructive Sleep Apnoea Syndrome in Hong Kong Chinese Children (CU02161)
- ✍ LI Man Chim Albert Martin • FOK Tai Fai • LAM Chuen Kwong (Surgery) • LAU Tak Fai Joseph (Centre for Epidemiology & Biostatistics) • WING Yun Kwok (Psychiatry)
- 2003-04 Assessment of Cough Frequency in Children with Stable Asthma: Comparison with Lung Function and Other Non-invasive Markers of Airway Inflammation (MD03685)
✍ LI Man Chim Albert Martin • LEUNG Ting Fan • CHAN Fung Ying • SUNG Yn Tz Rita • FOK Tai Fai
- 1998-99 WHO/GSTF Maternity Advice Study (MD98123)
✍ NELSON Edmund Anthony Severn • COWAN S* • MANGIATERRA V* • CAFFERATA M.*
- 2003-04 A Phase III, Double-Blind, Randomized, Placebo-Controlled, Multi-Country and Multi-Center Study to Assess the Efficacy and Safety of Two Doses of GSK Biologicals' Oral Live Attenuated Human Rotavirus (HRV) Vaccine in Healthy Infants (MD03539)
✍ NELSON Edmund Anthony Severn • TAM Siu Lun John (Microbiology)#
- 2001-02 A Multicentre, Randomised, Double-Blind, Controlled Study of Two Corticosteroid Regimens for Treatment of Systemic Hypotension in Preterm Infants (MD01104)

- ✍ NG Pak Cheung • CHOW Chun Bong* • FOK Tai Fai • LAM Wai Kei Christopher (Chemical Pathology)
- 2002-03 A Multicentre, Randomised, Double-Blind, Controlled Study of Oral Erythromycin for Treatment of Gastrointestinal Dysmotility in Preterm Infants (CU02163)
- ✍ NG Pak Cheung • CHENG Fun Bun Augustine (Microbiology)# • CHOW C B* • FOK Tai Fai
- 2003-04 The Use of Proinflammatory and Anti-Inflammatory Cytokines for Early Diagnosis of Systemic Infection in Preterm Infants (MD03519)
- ✍ NG Pak Cheung • LI Kwai Har Karen • WONG Pui On Raymond (Lee Hysan Clinical Research Laboratories) • FOK Tai Fai
- 2003-04 Generation of Cardiomyocytes from Bone Marrow Cells and Their Capacity in Engrafting and Repairing the Infarcted Heart (MD03987)
- ✍ SUNG Yn Tz Rita • SANDERSON John Elsbey (Medicine & Therapeutics)# • LI Kwai Har Karen • YANG Mo • LI Ming (Medicine & Therapeutics) • YI Qi Jian*
- 2002-03 Is the Prevalence of Childhood Asthma Increasing in Chinese Children? (CU02165)
- ✍ WONG Wing Kin Gary • CHEN Yu Zhi* • LEUNG Ting Fan
- 2002-03 A 52-Week Multicenter, Randomised, Double-Blinded, Double-Dummy, Placebo-Controlled Parallel Group Study to Compare the Efficacy and Tolerability of Salmeterol/Fluticasone Propionate Combination (Seretide™) 50/100mcg once Daily in the Morning with Fluticasone Propionate 100mcg Twice Daily and Placebo (Short-acting β_2 -agonist as Required only) Twice Daily, All via the Accuhaler™ as Initial Maintenance Therapy in Mild Asthmatic Subjects (MD02908)
- ✍ WONG Wing Kin Gary • LEUNG Ting Fan
- 2003-04 A Randomized, 2-Period, Multicenter, Double-Blind, Parallel-Group Study Comparing the Effects of 2 Doses of Montelukast Granules and Placebo in the Treatment of Respiratory Symptoms Associated with Respiratory Syncytial Virus-induced Bronchiolitis in Children Aged 6 to 18 Months (MD03878)
- ✍ WONG Wing Kin Gary • LEUNG Ting Fan

RESEARCH PROJECTS

An Investigation of Homocysteine on the Contractile Response of Porcine Resistance Coronary Artery

✍ KWAN Yiu Wa

☐ 2 January 2005

❖ CUHK Research Committee Funding (Direct Grants)

Homocysteine (Hcy) (normal plasma level, 5-10 μ M), a sulphur-containing amino acid, is a reactive intermediary product (due to the free -SH group) of methionine (an essential amino acid supplied by dietary protein) metabolism. The dangers of hyperhomocysteine (hHcy) (>15 μ M) were first recognized in the early 1950s. It has been suggested that the damaging effect is mainly via oxidation of Hcy that occurred in endothelium and vascular vessel wall, and the subsequent generation of reactive oxygen species (ROS: O_2^- , H_2O_2 and OH^\cdot). ROS are produced both intracellularly and extracellularly, and in vascular tissues, most of O_2^- generated is intracellular, and O_2^- undergoes rather selective chemical reactions with the components of biological systems. Moreover, ROS are recognized not only for their potentials to create random havoc in cells but also for participating in signal transduction of growth factors in which mitogen-activated protein (MAP) kinases are important. However, the modulatory effect of Hcy and the possible contribution of O_2^- generated on coronary artery smooth muscle reactivity is scarce. In addition, the role of MAP kinase pathway in mediating the response of Hcy and the beneficial effect of anti-oxidants (N-acetyl-cysteine and

reduced-glutathione) are incompletely characterized. In this study, using different techniques (isometric tension change, patch-clamp electrophysiology and molecular biology), we will determine the modulatory effect of Hcy and its metabolic products (homocystine, homocysteine thiolactone) on background non-selective cation current of single vascular smooth muscle cells of porcine resistance coronary artery. The possible participation of O_2^- generated as well as MAP kinase pathway will also be evaluated.
(MD04919)

Investigation of Pyrrolizidine Alkaloid-Containing Chinese Medicinal Herbs

✍ LIN Ge

☐ 1 January 2005

❖ CUHK Research Committee Funding (Direct Grants)

Pyrrolizidine alkaloids (PAs) are present in a wide variety of plant species. Currently, more than 6000 plants have been found to contain PAs worldwide, among them 49 species are used as plant sources for Chinese medicinal (CM) herbs. Most of naturally occurring PAs are known to induce liver toxicity and tumors in human, and cause a serious health problem through consumption of PA-containing herbal products. Various Western countries have established regulations for the use of PA-containing herbal products. However, there are no systematic investigations on PA-containing CM herbs and no regulations for use of such herbs in Hong Kong and Mainland China. In fact, among 49 known PA-containing CM herbs, 38 were identified by foreign scientists upon studying herbal plants used in their own countries. It is very likely that many more PA-containing CM herbs used in Hong Kong and

Mainland China have not been identified. Furthermore, in CM practice, it is very common to use alternative plant species, which are different from that officially documented, as the plant sources for CM herbs. The usefulness of such alternative plant sources may cause additional use of unknown PA-containing CM herbs.

Therefore, systematic investigations of PA-containing CM herbs and development of biological markers for a rapid assessment of PA intoxication are needed for safer and more effective use of PA-containing CM herbs. In this one-year study, we will focus on the hepatotoxicity of PA-containing CM herbs and establish biological markers for rapid prediction of whether certain PA-containing CM herbs cause potential hepatotoxicity.

(MD04455)

Evaluation of the Anti-Emetic Activity of a Novel Compound in a Ferret Model of Cisplatin-Induced Acute and Delayed Emesis

✍ RUDD John Anthony • XAVIER Emonds-Alt*

□ 6 September 2004

❖ Sanofi-Synthelabo Recherche

The discovery of the anti-emetic action of the 5-HT₃ receptor antagonists lead to the most successful therapy for the treatment of chemotherapy- and radiation-induced sickness in the cancer patient. A Worldwide use of ondansetron and other agents established firstly their highly effective control of 'acute emesis' (i.e. that occurring during the first 24 h), and secondly, revealed that 'delayed emesis' (i.e. that occurring after the first day of treatment) was less effectively managed. The project will investigate the anti-emetic potential of novel compound supplied by Sanofi-Synthelabo Recherche,

France, to antagonize cisplatin-induced acute and delayed emesis in a ferret model.

(MD04766)

Defining the Pathways Involved in Acute and Delayed Chemotherapy-Induced Emesis and the Roles of Tachykinins and Glucocorticoids

✍ RUDD John Anthony

□ 1 October 2004

❖ Merck Sharp & Dohme

Chemotherapy is often associated with severe nausea and vomiting. The project investigates the pathways and mechanisms involved during the acute and delayed phases of emesis and the role of tachykinin systems and glucocorticoids.

(MD04967)

Evaluation of the Anti-Emetic Activity of AMX174, AMX568 and AMX569 in the Cisplatin-Induced Emesis Model in Male Ferrets Following Intraperitoneal Administration

✍ RUDD John Anthony • WARNECK Julie*

□ 1 December 2004

❖ Amedis Pharmaceuticals Limited

The discovery of the anti-emetic action of the 5-HT₃ receptor antagonists lead to the most successful therapy for the treatment of chemotherapy- and radiation-induced sickness in the cancer patient. A Worldwide use of ondansetron and other agents established firstly their highly effective control of 'acute emesis' (i.e. that occurring during the first 24 h), and secondly, revealed that 'delayed emesis' (i.e. that occurring after the first day of treatment) was less effectively managed. The project will

investigate the anti-emetic potential of novel compounds supplied by Amedis Pharmaceuticals Limited, United Kingdom, to antagonize cisplatin-induced emesis in a ferret model.

(MD04829)

Dimerization of Human Prostaglandin E₂ and Thromboxane A₂ Receptors

✍ WISE Helen • CHENG Hon Ki Christopher (Biochemistry)

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

G protein-coupled receptors (GPCRs) are important targets of many therapeutic agents, and initiate cell signalling pathways dependent on the specificity of G protein coupling. Recent technological advances have shown that GPCRs do not necessarily function as single entities, but can form functional complexes with each other to produce homodimers or homo-oligomers. More importantly, GPCRs from different receptor families, or subtypes within the same family, can also function as a heterodimer complex. This novel observation has been used to explain some unusual pharmacology, since the properties of the heterodimer are distinct from those of the individual receptors. This project aims to assess the dimerization properties of two prostanoid receptors: the prostaglandin E₂ subtype receptor (EP₃) and the thromboxane A₂ (TP) receptor. As both these receptors are expressed in platelets and vascular tissue, we will determine if they form heterodimers when expressed in a model cell system, and will monitor cell signalling pathways to look for any unusual pharmacology. Results from this study would be important for further investigations in native cells in which these receptors co-exist in different ratios.

(MD04343)

A Study to Investigate the Mechanisms of the Drug Interaction between Warfarin and Danshen (*Salvia Miltiorrhiza*): Effects on Drug Transport Using Caco-2 Cells

✍ YEUNG Hok Keung John • ZUO Zhong (School of Pharmacy)

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

This study aims to make use of current Caco-2 cell technology for assessing the efficacy of drugs to investigate the mechanisms involved in the clinically important drug interaction between Danshen (*Salvia Miltiorrhiza*) and warfarin. The effects of Danshen, and some of its active components such as tanshinone I, tanshinone IIA and cryptotanshinone on intestinal transport of warfarin will be determined to investigate the pharmacokinetic interactions of these compounds. Results of this study should provide scientific evidence that may be used to improve our understanding on the mechanism(s) of Danshen-warfarin interaction. This will enable awareness by clinicians and the general public in the safe use of Traditional Chinese Medicine (TCM), either alone or in combination with Western medicine.

(MD04897)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
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- 2001-02 The Mechanisms Responsible for the Exaggerated Excitatory Effect of Acetylcholine in the Pulmonary Artery of Spontaneously Hypertensive Rats (MD01107)
✍ KWAN Yiu Wa • GURNEY A M*
SEMPLÉ Hugh A* • LI Xing Fang*
• DAMARAJU Vijayalakshmi*
- 2002-03 The Role of Nitric Oxide and Mitogen-Activated Protein Kinase in Mediating the Inhibition by β_3 -Adrenoceptor Activation of Voltage-Dependent L-type Calcium Channels of Guinea-pig Single Ventricular myocytes (CU02166)
✍ KWAN Yiu Wa • LIU Wing Keung Ken (Anatomy) • TSUI Kwok Wing (Biochemistry)
2002-03 Investigation of Chuanxiong Herbal Materials with GAP Standard (MD02951)
✍ LIN Ge • LI Songlin# • CHUNG Hoi Sing#
- 2002-03 Neural Mediation of Inflammatory Joint Disease (MD02658)
✍ LAM Fu Yuen
2003-04 Study of Hepatotoxic Pyrrolizidine Alkaloid-Containing Chinese Medicinal Herbs (MD03797)
✍ LIN Ge
- 2003-04 Role of Somatostatin in Joint Inflammation (MD03387)
✍ LAM Fu Yuen
2003-04 Investigation of a Taisho Pharmaceutical Co. Ltd. Research Compound to Inhibit Cisplatin-Induced Emesis in the Ferret (MD03483)
✍ RUDD John Anthony
- 2003-04 Interaction between Nitric Oxide and Human Mast Cells (CU03337)
✍ LAU Hang Yung Alaster • HUANG Yu (Physiology) • WONG Chun Kwok (Chemical Pathology)
2003-04 Effect of a Novel Neuropeptide on Emesis Induced by Cisplatin in the Ferret (MD03630)
✍ RUDD John Anthony • SANGER Gareth J*
- 2001-02 Development of TCM-Based Products with Known Active Ingredients and Verified Oral Absorbability (MD01857)
✍ LIN Ge • JONES Robert Leslie • CHOW Hee Lum Albert (School of Pharmacy) • TAM Yun K* •
2003-04 Evaluation of the Anti-Emetic Activity of AMX174 in the Cisplatin-Induced Emesis Model in Male Ferrets Following Oral Administration (MD04389)
✍ RUDD John Anthony • WARNECK Julie*

2002-03 Growth Hormone Secretagogue
Receptors: Cell Signalling and Receptor
Oligomerization (CU02267)
✍ WISE Helen • CHENG Hon Ki
Christopher (Biochemistry)

RESEARCH PROJECTS

Chemical and Biological Characterization of Purified Extracts of Medicinal Mushrooms

✍ CHOW Hee Lum Albert • HO Yee Ping

☐ 1 October 2004

❖ PuraPharm Research Corp. Ltd.

The present project is aimed at developing a set of analytical methods for the standardization and quality control of commercial Lingzhi products. The project will involve the following:

- (1) Extraction of lipophilic constituents from Lingzhi mushroom or other fungi supplied by PuraPharm using conventional solvent extraction, supercritical fluid extraction and column chromatographic methods;
- (2) Isolation and purification of single active components (to be used as reference standards) from lipophilic fractions by chromatographic methods (LC and/or HPLC) and determination of their physicochemical profiles (e.g. spectroscopic characteristics, melting point, solubility, etc);
- (3) Testing of purified actives for specific biological activities;
- (4) Development of HPLC methods for the qualitative and quantitative analysis of lipophilic active fractions extracted from Lingzhi; and
- (5) Application of developed analytical methods for ascertaining the quality of commercially available Lingzhi products.

(MD04904)

Accelerated Stability Studies for Cis-Sulphur Colloid Vial for Injection and Identification of Active Ingredients in Solution A and B

✍ CHOW Hee Lum Albert • LAM Siu Ling • CHAU Ka Yung#

☐ 15 January 2005

❖ Global Medical Solutions Hong Kong Ltd

1. A 6 months stability study of Cis-Sulphur Colloid Vial for Injection at $40 \pm 2^\circ\text{C}$ and relative humidity of $75 \pm 5\%$, two sampling points (time 0 and 6) will be conducted.

The following items are included

- (i) Chemical Assay Method Validation
 - (ii) Appearance and Identification
 - (iii) Microbiological Test
 - (iv) Analysis of Active Ingredient (i.e. Sodium Thiosulphate Anhydrous only)
 - (v) Report Writing
 2. Identification of chloride ion in solution A vial and identification of sodium phosphate monobasic and sodium hydroxide in solution B vial.
 3. Sponsor will be responsible to provide all necessary arrangements, supports, transportation, equipment and information at no cost or charge to CUHK to enable CUHK to perform the Service.
- (MD04605)

Aqueous-Aqueous Emulsion for Microencapsulation of Delicate Proteins for Sustained Release

✍ CHOW Hee Lum Albert • ZUO Zhong • Jun Tuo* • Su Li Ming* • Wu Fei*

☐ 1 April 2005

❖ NSFC/RGC Joint Research Scheme

The primary objective of this proposed research is to develop a novel delivery system that could fundamentally resolve all formidable problems associated with the sustained-release formulation of delicate therapeutic proteins. These problems broadly encompass: a) the poor stability and inactivation of the proteins when being exposed to hazardous conditions during formulation (e.g. organic solvents, cross-linking agents) and after administration to the patient (e.g. body temperature, hydration and pH changes); and b) the burst and/or incomplete protein release from the formulated product. As an effective means to tackle these problems, the present research will employ a newly developed material system termed 'stable aqueous-aqueous emulsion' (SA-AE). This system enables loading of delicate agents into dense polysaccharide glassy particles of uniform size under a condition free of structure-modifying hazards prior to encapsulation in biodegradable polymer microspheres. In addition, the delicate agents are protected by the polysaccharide particles throughout the course of release, as verified by *in vitro* studies using two model proteins (myoglobin and β -galactosidase). We hypothesize that this system offers an inclusive solution for virtually all technical challenges in protein stability and release kinetics. Two therapeutic proteins, namely, granulocyte macrophage colony stimulating factor (GM-CSF) and alpha interferon (α -IFN), which have been extensively used for treating cancer, AIDS and SARS, will be formulated into long-acting dosage forms using the SA-AE technology. Release kinetics, bioactivities, toxicity, pharmacokinetic behaviour as well as therapeutic efficacy of the formulated products will be tested both *in vitro* and *in vivo*. In the long term, the present research will lead to stable,

efficacious, and long-acting injectable products for GM-CSF, α -IFN and other protein drugs with similar stability and release problems.

(MD04857)

Pharmacokinetic and Pharmacodynamic Effects of a Special Buffered Propranolol Formulation for Sublingual Administration

✍ CHOW Sing Sum Moses • ZUO Zhong •
WANG Yan Feng • YIN Qiping •
TOMLINSON Brian (Medicine & Therapeutics)

☐ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

The objective of this study is to prove that a specially formulated buffered propranolol tablet is superior to a conventional propranolol tablet when administered sublingually. This specially formulated tablet is based on our newly developed "buffered sublingual formulation technology" aimed to achieve optimal balance of unionized fraction and drug solubility, two important factors that are critical for rapid absorption across sublingual mucosa. The study will be a randomized, 2-period, 2-sequence cross-over design involving 10-12 healthy male subjects. Each subject will receive 40 mg buffered or conventional propranolol in a crossover manner administered sublingually, followed by swallowing the solubilized propranolol after about 15 minutes. Multiple plasma propranolol concentration as well as heart rate and blood pressure will be obtained post dose. Following administration of 2 formulations, their respective onset and magnitude of peak concentration/effect during sublingual administration as well as the concentration/effect post swallowing will be compared and analyzed using Student's t-test. The results of this study should pave the way to

development of a new convenient therapeutic method for rapid control of acute attacks of atrial fibrillation as well as other urgent cardiac conditions by propranolol (a drug currently used widely only for maintenance therapy by using the conventional formulated tablet). In addition, the results of this study should provide the “proof of concept” that the special “buffered sublingual formulation” technology is suitable to apply to the development of many other ionizable drugs to achieve rapid action sublingually for convenient management of urgent medical conditions in the ambulatory setting.

(MD04500)

Synergistic Interaction between Platinum-Based Antitumor Agents and Demethylcantharidin, a Modified Traditional Chinese Medicine

✍ HO Yee Ping • AU-YEUNG Chik Fun Steve
(Chemistry)

□ 1 November 2004

❖ Research Grants Council (Earmarked Grants)

Cisplatin and carboplatin are valuable valuable platinum-based anticancer drugs that have a broad spectrum of activity against solid tumors. However, therapeutic responses vary among patients, and the emergence of resistance to platinum (Pt) is frequently encountered. Therefore, identification of strategies for enhancing tumor sensitivity to these drugs by circumventing intrinsic and acquired platinum resistance is highly desirable.

Demethylcantharidin (DMC) is a modified structure of cantharidin, which is the active ingredient of “blister beetles”, a traditional Chinese medicine (TCM) that has been used to treat liver, lung and digestive tract tumors. When the two components, namely DMC and a Pt moiety are chemically linked together, the resultant novel “TCM-Pt” compounds

demonstrate excellent preclinical anticancer activity and importantly, able to overcome platinum resistance: a novel mechanism of anticancer action is thus implied.

The drug actions of DMC and cisplatin-type compounds given separately are very different. The aim of this project is to determine whether or not DMC and a Pt-based drug (such as cisplatin or carboplatin) given in combination as separate entities, can induce a synergistic phenomenon; that is, can one drug enhance or potentiate the biological activity of the other. This study will particularly focus on the influence of the combination therapy on cisplatin-resistant cells and to determine the actual role of DMC. This project aims to establish valid strategies for inclusion of DMC in Pt-based chemotherapy for the circumvention of cisplatin resistance

(CU04357)

Co-Operative Study of Safety of Medicines in Children (COSMIC): Scoping Study to Analyse Interventions Used to Reduce Errors in Calculation of Paediatric Drug Doses

✍ LEE Kwing Chin Kenneth • Wong ICK* • Conroy S* • Haines J* • Collier J* • Barber N*

□ 1 February 2005

❖ National Patients Safety Research Programme,
UK Dept of Health

This project aims to identify and evaluate interventions to reduce or prevent dosing errors in neonatal and paediatric patients at all stages of the medicines management process. These interventions will already have been tried and tested in the clinical situation by healthcare professionals from the UK, other parts of Europe or the US.

Representative samples of paediatric medical and pharmacy staff in the UK and experts in EU and the US will be surveyed to identify the maximum number of intervention possible. This will be done using the extensive networks, resources and contacts which the COSMIC team collectively bring to this project.

Methods of data collection will include systematic review of the literature; questionnaire survey of healthcare professionals in all settings where paediatric patients are cared for; semi-structured interviews of staff, on-site observation of 20 interventions for further exploration and testing in wider applications. Final assessment of interventions by an expert panel.

Economic analysis and preparation of protocols to further evaluate the most promising interventions will follow. These will explore transferability, efficacy and economic implications of the application of the interventions to wider UK clinical practice, with a view for further study in the future.

(MD04424)

The Role of 5' - Flanking Region Polymorphisms of CYP2C9 on Warfarin Metabolism in Chinese Patients - Is it the Missing Link?

✍ YOU Hoi Sze Joyce • ZUO Zhong • WAYE Mary Miu Yee (Biochemistry) • CHENG Gregory (Medicine & Therapeutics)

□ 1 February 2005

❖ CUHK Research Committee Funding (Direct Grants)

Background: Despite available data indicate that the allelic frequencies of the functionally defective CYP2C9 variants in the Asian population are significantly lower than Caucasians, Chinese patients required a much lower maintenance dose of warfarin than Caucasian patients. It implies that other

functionally defective polymorphisms of CYP2C9 may also have a significant effect on the phenotype of CYP2C9.

Objective: (1) identify mutation sites within the promoter (5'-flanking) region of CYP2C9 and determine their frequencies in a Chinese population; (2) determine the effects of CYP2C9 genetic polymorphism within 5'-flanking region on the clearance of warfarin.

Methods: Approximately 100 patients receiving stable maintenance dose of warfarin will be recruited at the anticoagulation clinic of the Prince of Wales Hospital. Blood samples will be obtained from each study patient for genotyping of CYP2C9 within the 5'-flanking region and measurement of steady state plasma concentration of S-warfarin. Urine samples will also be collected for assessment of urinary concentration of S-7-hydroxywarfarin.

Significance: The findings of this study will determine the clinical significance of polymorphisms within the 5'-flanking region of CYP2C9 on metabolic clearance warfarin in Chinese patients. The results of this study will provide important information on whether CYP2C9 genotype data can predict the risk for high warfarin sensitivity that leads to high risk of bleeding in Chinese patients.

(MD04361)

Evaluation of Transportation and First-Pass Metabolism of Flavonoids in Small Intestine

✍ ZUO Zhong • LIN Ge (Pharmacology)

□ 1 May 2005

❖ CUHK Research Committee Funding (Direct Grants)

The bioavailabilities of flavonoids, no matter in the form of aglycone or glycosides, were not as high as expected from their favorable lipophilicities. Such

discrepancy is believed to be mainly due to their extensive first-pass metabolism during their absorption in the small intestine. The proposed study is designed to utilize the *in-vitro* human intestinal absorption and metabolic models to interpret the transport as well as the metabolism in the small intestine of 4 structurally related flavonoids belonging to flavonols subgroups, namely Datiscetin, Fisetin, Morin, Myricetin. Their intestinal mucosa transport and preliminary metabolism will be studied by the human intestinal Caco-2 cell monolayer model. In addition, by incubation of the selected flavonoids with pooled human intestinal S9 fraction, the extent of the first-pass metabolites formed, their formation rates and the enzyme responsible for the biotransformation will be delineated. From the results obtained from the above two in-vitro models, a Structure-Activity-Relationship (SAR) will be established for the transportation and first-pass metabolism of flavonoids in small intestine. (MD04576)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

Edition Title/Investigators

2002-03 Development of an *In Vitro* Model for Oral Mucosal Drug Delivery – A Preliminary Investigation (MD02378)
 ✍ CHOW Sing Sum Moses • ZUO Zhong • BURD David Andrew Ross (Surgery) • YIN Qiping • TOMLINSON Brian (Medicine & Therapeutics)

2002-03 A Pharmacokinetic-Genomic Approach for Predicting Herb-Drug Interactions : An Initial Evaluation Using Ginkgo Biloba (CU02180)

✍ CHOW Sing Sum Moses • TOMLINSON Brian (Medicine & Therapeutics) • WAYE Mary Miu Yee (Biochemistry) • ZUO Zhong

2002-03 Novel TCM-Platinum Compounds : New Mechanism(s) of Antitumor Action? (CU02181)

✍ HO Yee Ping • AU-YEUNG Chik Fun Steve (Chemistry)

2001-02 Development of a Ganoderma (Lingzhi) and Coriolus (Yunzhi) Formula as an Anti-cancer Agent (MD01301)

✍ LAU Bik San Clara • ZUO Zhong • CHOW Sing Sum Moses • FUNG Kwok Pui (Biochemistry) • LEUNG Kwok Nam (Biochemistry) • LIN Ge (Pharmacology) • JAMES Anthony Edward (Laboratory Animal Services Centre) • SHAW Pang Chui (Biochemistry) • BUSWELL John Anthony (College Office, SC) • LIEBERMAN Ron*

2003-04 Statin Utilization for Secondary Prevention in Patients with Acute Myocardial Infraction in Hong Kong (MD03424)

✍ LEE Kwing Chin Kenneth • LEE Wing Yan Vivian • TOMLINSON Brian (Medicine & Therapeutics) • CHAN Wai Kwong*

- 2003-04 Co-operative of Safety of Medicines in Children (COSMIC): Scoping Study to Analyse Interventions Used to Reduce Errors in Calculation of Paediatric Drug Doses (MD03642)
✍ LEE Kwing Chin Kenneth • CHAN Yan Keung Thomas (Medicine & Therapeutics)
- 2003-04 Clinical Impact of CYP 2C19 Genetic Polymorphisms on Proton Pump Inhibitors Metabolism (MD03475)
✍ LEE Wing Yan Vivian • LEE Kwing Chin Kenneth • WAYE Mary Miu Yee (Biochemistry) • CHAN Ka Leung Francis (Medicine & Therapeutics)
- 2003-04 Development of an In Vitro Screening Method for Herb-Drug Interaction Involving Glucuronidation - A Preliminary Feasibility Study (MD03746)
✍ YIN Qiping • CHOW Sing Sum Moses • TOMLINSON Brian (Medicine & Therapeutics) • ZHONG Ming Kang* • SHI Xiao Jin*
- 2002-03 Comparison of a Clinical Pharmacist-Managed Anticoagulation Service with Routine Medical Care - Impact on Clinical Outcomes and Healthcare Costs (MD02441)
✍ YOU Hoi Sze Joyce • CHENG Gregory (Medicine & Therapeutics)
- 2003-04 Influence of CYP 2C9 genetic Polymorphisms on Warfarin Metabolic Clearance in Chinese Patients (MD03313)
✍ YOU Hoi Sze Joyce • ZUO Zhong • WAYE Mary Miu Yee (Biochemistry) • CHENG Gregory (Medicine & Therapeutics)
- 2001-02 Absorption of Active Components from Hawthorn and Green Tea - *In vitro* and *In vivo* Relationship (MD01122)
✍ ZUO Zhong • CHOW Sing Sum Moses
- 2002-03 *In-vitro* Evaluation of Glucuronidation of Selected Flavonoids in Gut and Liver (MD02576)
✍ ZUO Zhong • LIN Ge (Pharmacology)
- 2003-04 Evaluation of Transportation and First-Pass Metabolism of Flavonoids in Small Intestine (MD03386)
✍ ZUO Zhong • LIN Ge (Pharmacology)

RESEARCH PROJECTS

Neuroprotective/ Anti-Apoptotic Effects of cGMP/Protein Kinase G (PKG) - Medicated Phosphorylation of BAD and GSK-3 α/β in Cell Culture Models of Alzheimer's Disease

✍ FISCUS Ronald Ray • SHAW Pang Chui
(Biochemistry)

☐ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

During Alzheimer's disease, cortical and hippocampal neurons die of apoptosis, resulting in loss of memory and other neurological problems. Little is known about potential inhibitory pathways that may protect against apoptosis of neurons. Recently, our laboratory showed that two natriuretic peptides, atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP), inhibit apoptotic DNA fragmentation and increase the survival of stressed neural cells, including PC12 cells (Fiscus et al., NeuroReport 12: 185-189, 2001) and N1E-115 and NG108-15 cells (Fiscus, NeuroSignals 11:175-190, 2002). We have identified cGMP/protein kinase G (PKG) as the signaling pathway mediating the protection against apoptosis. Evidence from our currently-funded CERG grant (# CUHK4169/02M) showed (for the first time) that PKG catalyzes phosphorylation of the apoptosis-regulating protein BAD on serine 112 and 155, both *in vitro* and *in vivo*, suggesting that a likely downstream target of PKG is BAD. The present proposed project will further determine the involvement of PKG-mediated phosphorylation of BAD as well as phosphorylation of another potential downstream target, glycogen

synthase kinase-3 α/β (GSK-3 α/β), in anti-apoptotic effects of ANP, BNP, NO (at physiological/non-toxic concentrations) and basal cGMP/PKG in neural cells. Effect of cGMP/PKG on phosphorylation of tau, a target of GSK-3 thought to be involved in pathogenesis of Alzheimer's disease, will also be determined. The resulting data will help to determine the role of cGMP/PKG in the phosphorylation of key apoptosis-regulating proteins, BAD and GSK-3, in neural cells and should give new insight into the potential protective role of this anti-apoptotic pathway in the pathogenesis of Alzheimer's disease.

(MD04582)

Effects of Selective Estrogen Receptor Modulators on Coronary Artery Reactivity in Cholesterol-Fed, Ovariectomized Rabbits

✍ HUANG Yu • VANHOUTTE Paul Michel
Georges* • YAO Xiaoqiang • CHEN Zhenyu
(Biochemistry)

☐ 15 December 2004

❖ Research Grants Council (Earmarked Grants)

Coronary artery disease accounts for one third of all deaths in postmenopausal women. The advantages/disadvantages of hormone replacement therapy (HRT) following menopause are public health issues of major importance, particularly in a society with increasing aged population. The recent large-scale randomized trials of HRT for primary or secondary prevention of heart disease found no overall therapeutic benefit since HRT was actually associated with increased risks of heart attack. Current practice of HRT in postmenopausal women to prevent or treat cardiovascular disease is not justified, thus raising one of key health questions: how can postmenopausal women be protected against

cardiovascular disorders and osteoporosis if HRT is no longer recommended? In seeking to identify estrogen substitutes, selective estrogen-receptor modulators (SERMs) have been developed. Because of their selective estrogen-agonist properties, SERMs can be used to prevent or treat diseases caused by estrogen deficiency, such as osteoporosis, without most of the undesirable effects of estrogen. Conversely, due to their estrogen-antagonist properties, they can be used to treat breast cancer. Thus, SERMs represent a major therapeutic advance for clinical practice. Raloxifene (a 2nd generation SERM, currently used to treat osteoporosis) improves lipid profile and homeostatic parameters in postmenopausal women. It is conceivable that raloxifene and other new generation SERMs, as for natural estrogens, may target the vascular wall and exert an anti-arteriosclerotic role. The possible benefits of SERMs on blood vessel wall could potentially lead to novel therapeutic strategies for the treatment of atherosclerosis and coronary artery disease. However, the actions of raloxifene and other new SERMs on the coronary circulation are incompletely defined, while awaiting the final report from the RUTH study, this proposal is aimed at investigating the actions of raloxifene and idoxifene (another SERM) on coronary artery reactivity upon pre-existing atherosclerosis in cholesterol-fed, ovariectomized rabbits. The primary objective of this proposal is to test our hypotheses that raloxifene or idoxifene therapy improves or prevents high cholesterol diet-induced endothelial dysfunction of coronary arteries following ovariectomy by increased endothelium-derived relaxing factor production, by decreased endothelium-derived constricting factor generation, and by reduced progression of atherosclerotic lesions in hypercholesterolemic rabbits. The proposed study should provide new insight into the mechanisms involved in potential

benefits of SERM therapy on coronary artery function.

(CU04362)

Regulation of Electrolyte Transport in Human Intestinal Epithelia by the Extracellular Calcium-Sensing Receptor

✍ KO Wing Hung

☐ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

Extracellular calcium concentration ($[Ca^{2+}]_o$) exert diverse physiological effects in a variety of tissues, including the parathyroid gland, kidney, brain and intestinal tract, *etc.* These effects are mediated via a calcium-sensing receptor (CaSR), which is a member of G-protein-coupled receptors. The aim of the present project is to investigate the various CaSR agonists on basal and stimulated ion transport in human colonic epithelia using a combined fluorescence and electrophysiological approach. This approach allows us to monitor the effects upon activation of CaSR on the increases in $[Ca^{2+}]_i$ and transepithelial ion transport simultaneously in a polarized epithelium. By using this technique, we shall be able to determine the roles of CaSR on epithelial function in human intestinal cells. The objectives of the project are: (i) to examine the effect of different CaSR agonists upon basal $[Ca^{2+}]_i$ and short-circuit current (I_{sc} ; an index of electrogenic ion transport) in HT-29 monolayers; and (ii) to characterize the signal transduction pathways that allow CaSR to regulate anion secretion by measuring the increase in $[Ca^{2+}]_i$ and anion secretion simultaneously in polarized epithelia.

The information obtained from this study will give us a better understanding of the cellular mechanisms of

CaSR activation with respect to its specific effect(s) on intracellular signaling event(s) and electrolyte transport in human colonic epithelia. In particular, the temporal information of the increases in calcium and anion secretion activated by CaSR is useful in the understanding of the potential roles of this receptor in gastrointestinal physiology.

(MD04751)

Protective Role of Blockade of the Renin-Angiotensin System with Losartan on Pancreatic β -cell Function and Repair and its Relationships with Oxidative Stress in Impaired Glucose Tolerance and Type 2 Diabetes

✍ LEUNG Po Sing • CHAN Chung Ngor Juliana
(Medicine & Therapeutics)

□ 9 October 2004

❖ Merck & Co., Inc.

There is now increasing evidence showing that the exocrine and endocrine pancreas possess an autocrine/paracrine renin-angiotensin system (RAS), which can affect insulin secretion and remodeling of the pancreatic cells. Blockade of the exocrine RAS by Losartan, an antagonist of AT₁ receptor, is effective against cerulein-induced pancreatic inflammation. This may be linked to an inhibition of NADPH oxidase activity. Thus the protective role of Losartan could be mediated by the AT₁ receptor-regulated NADPH oxidase-dependent generation of reactive oxygen species. There is also indirect evidence suggesting that hyperglycemia and increased free fatty acids can lead to increased angiotensin II, which further increases oxidative stress thus reactive oxygen species. The latter can activate intracellular signalling pathways, leading to cellular apoptosis, followed by fibrosis and angiogenesis, finally loss of islet structure and

function. In the LIFE study (Losartan vs atenolol), non-diabetic hypertensive patients with left ventricular hypertrophy were found to have 25% risk reduction in new onset of diabetes compared to patients treated with atenolol. Similarly, in the HOPE study, patients treated with ramipril, an ACE inhibitor, had 24% risk reduction in new onset diabetes compared to placebo in patients with risk factors for cardiovascular diseases. It remains uncertain whether these beneficial effects of RAS blockers on glucose metabolism are due to increased insulin secretion or improved insulin resistance or both.

We thus aims to study the acute and long term effects of Losartan on insulin secretion and islet function and structures, and thence glucose metabolism; the inter-relationships between angiotensin II and oxidative stress induced by elevated blood glucose and free fatty acid, and their response to RAS inhibition. Findings from these experiments will provide a mechanistic insight into the observed clinical benefits of Losartan treatment on incidence of new onset of diabetes. Given the intimate relationships between glucotoxicity and lipotoxicity in the development of metabolic syndrome and cardiovascular complications, these experiments will also provide the rationale for considering using Losartan early in the treatment of metabolic syndrome and glucose intolerance.

(MD04976)

Activation of the Pancreatic Islet Rennin-Angiotensin System: Its Role on Oxidative Stress Induced Pancreatic β -cell Dysfunction in Type 2 Diabetes

✍ LEUNG Po Sing

□ 1 November 2004

❖ CUHK Research Committee Funding (Direct Grants)

Several large clinical trials, such as HOPE, NAVIGATOR and CAPP, have shown that blockade of the renin-angiotensin system (RAS) could reduce the incidence of type 2 diabetes (T2DM) in “high risk” patients with hypertension. In this context, T2DM is due to pancreatic β cell secretory deficiency and/or insulin resistance. A common soil hypothesis linking T2DM and cardiovascular disease is an oxidative stress-induced dysfunction of the β cell and endothelium. Previous studies in patients with hypertension receiving long-term treatment for ACE inhibitors have described an improved first phase of insulin secretion in response to either intravenous or oral glucose administration. In this regard, the pancreas is known to possess a local RAS that performs various activities in the regulation of exocrine and endocrine functions of the pancreas. Apart from its potent vasoconstrictor actions, this local pancreatic RAS may have multiple tissue/organ specific functions including both stimulation and inhibition of cell proliferation; induction of apoptosis; reactive oxygen species generation; influence on hormonal secretion; as well as pro-inflammatory and pro-fibrogenic actions. Recent data have further demonstrated the presence of an islet RAS in the pancreas, which is subject to activation by islet transplantation and T2DM. Such a local islet RAS, if activated, could result not only in the reduction of islet blood flow but also in the direct inhibition of islet insulin secretion, and subsequent deterioration of the beta cell mass. Interestingly, uncoupling protein-2 (UCP-2) is markedly upregulated in islets of ob/ob mice, a model of obesity-induced diabetes, indicating that superoxide-mediated activation of UCP-2 could play an important role in the pathogenesis of β -cell dysfunction and T2DM.

Notwithstanding this evidence for the involvement of the RAS in T2DM, there has been so far a lack of basic scientific data on the protective role of RAS blockade, demonstrable by changes in oxidative stress-induced pancreatic p-cell dysfunction and failure. The present proposed project is therefore designed to study and compare the effects of RAS blockers on oxidative stress-induced changes in the pancreatic β cell function and structure using animal models of T2DM. Results from the proposed project should shed new mechanistic insights into the observed beneficial effects of RAS inhibition in reducing the diabetes incidence in at-risk patients with hypertension in large clinical trials.

(MD04348)

Inhibition of the Pancreatic Renin-Angiotensin System: Its Regulatory Mechanism for Pancreatic Microcirculation, Oxidative Stress and Cytokine-Mediated Inflammatory Response in Pancreatitis

✍ LEUNG Po Sing • IP Siu Po (School of Chinese Medicine)

□ 1 January 2005

❖ Research Grants Council (Earmarked Grants)

A local pancreatic rennin-angiotensin system (RAS) exists, which exhibits exocrine and endocrine activities in the pancreas. This local RAS is responsive to various physiological and pathophysiological conditions. Of particular importance are the expression and localization of key RAS components in the exocrine pancreas, which are subject to upregulation by chronic hypoxia and acute pancreatitis. In this regard, an enhanced sensitivity of angiotensin II-mediated vasoconstriction in pancreatic microcirculation could cause severe ischemia/hypoxia thus the production of oxidative

stress and inflammatory cytokines, leading to pancreatic inflammation and injury. Indeed, recent investigations demonstrated that inhibition of the RAS activation displayed a beneficial role in ameliorating the pancreatic oxidative stress and tissue injury induced in pancreatitis. However, there has been lack of solid evidence for the regulatory mechanism of RAS blockade in pancreatic inflammation and injury. Accordingly, the present study is primarily designed to unravel the regulatory pathways of RAS inhibition involved in pancreatitis-induced pancreatic blood flow, oxidative stress and cytokine-mediated inflammatory reactions. The outcomes of this project should provide a mechanistic insight into the role for pancreatic RAS inhibition in acute pancreatitis as well as systemic inflammatory responses. To this end, future target for a pancreatic RAS by virtue of using selective RAS blocker might provide a novel pathway for the potential treatment of acute pancreatitis and its systemic complications.

(CU04364)

Evaluation of Potential Synergistic Effects of Valsartan Combined with GLP-1 or LAF237 on Pancreatic Islet Function, Endothelial Function and Glucose Tolerance in Type-2 Diabetes Mellitus

✍ LEUNG Po Sing • CARLSSON Per-Ola* • Marc de Gasparo*

📅 1 June 2005

❖ Novartis Institutes for BioMedical Research, Inc.
- Novartis Non-Clinical Study Grant

There is an islet renin-angiotensin system (RAS), whereby angiotensin II (Ang II) induces a marked dose-dependent inhibition of glucose-stimulated insulin release and reduces (pro) insulin biosynthesis

in isolated islets. Blockade of the AT₁ receptor can markedly increase islet insulin release mediated via (pro) insulin biosynthesis and islet blood flow, thus improving glucose-stimulated insulin secretion; meanwhile, its blockade may decrease oxidative stress-induced beta-cell dysfunction and apoptosis in type 2 diabetes mellitus. Previous studies have shown that Ang II decreases outward potassium current and valsartan (AT₁ receptor antagonist) reverses it in diabetes. Valsartan improves glucose utilization in peripheral tissue and reduces gluconeogenesis. Valsartan is a vasodilatory agent, which may increase pancreatic and muscle blood flow and thus promote insulin action like the angiotensin-converting enzyme inhibitor does. Valsartan can also improve endothelial function. Importantly, oxidative stress may be a pathogenic mechanism linking insulin resistance with beta-cell dysfunction and cardiovascular disease. On the other hand, glucagon-like peptide 1 (GLP-1) enhances insulin release and stimulates pro-insulin gene expression. Mice lacking the GLP-1 receptor displayed impaired LV contractility and diastolic function after insulin or epinephrine treatment. Similarly, GLP-1 induced a decrease in contraction amplitude without change in intracellular calcium. In Dahl salt sensitive rats on a high-sodium diet, chronic treatment with GLP-1 attenuated the development of hypertension, reduced proteinuria, improved endothelial function, and decreased renal and cardiac damage. In contrast, GLP-1 was also reported to increase heart rate and blood pressure in rats. This was due to an activation of central sympathetic neurons and adrenal medullary chromaffin cells. In view of this, such clinically significant effects could be prevented by valsartan co-administration. We thus hypothesize that the combination therapy of valsartan and GLP-1 or LAF237 (Dipeptidyl peptidase IV inhibitor) should

have some synergistic effects on stimulating pancreatic islet function, improving insulin sensitivity as well as having cardiac and reno-protective properties.

(MD04711)

The Mechanism of Flow-Induced Vasodilatation in Rat Small Mesenteric Arteries

✍ YAO Xiaoqiang

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

The hemodynamic force generated by blood flow is considered to be the physiologically most important stimulus for the release of nitric oxide (NO), endothelium-derived hyperpolarization factor (EDHF) and prostacyclin (PGI₂), from vascular endothelial cells. These factors then act on the underlying smooth muscle cells, causing vasodilatation and thus lowering blood pressure. Recent study in my lab showed that flow shear stress could trigger a rise in cytosolic Ca²⁺ in cultured rat aortic endothelial cells and depletion of intracellular Ca²⁺ stores could enhance the flow-induced Ca²⁺ influx. Furthermore, our data showed that flow could elicit vasodilatation in isolated rat small mesenteric arteries, and this vasodilatation is Ca²⁺-dependent. Our study also showed that flow-dilatation was caused by release of H₂O₂ from endothelial cells. These experiments suggest that, in rat mesenteric arteries, flow may trigger a Ca²⁺-dependent release H₂O₂ release from endothelial cells. These H₂O₂ may then act on nearby vascular smooth muscle cells, causing vasodilatation. In this proposal, we plan to extend our studies and to study the relationship between Ca²⁺ influx and the flow-induced release of H₂O₂, and to investigate the mechanism of flow-induced

production of H₂O₂. The results from this proposed study should provide important mechanism insight into flow-induced vascular dilatation and blood pressure control.

(MD04865)

Regulation of TRPC3 and TRPC6 Channels by Protein Kinase G Phosphorylation

✍ YAO Xiaoqiang • CHAN Tak Wah Dominic (Chemistry)

□ 1 November 2004

❖ Research Grants Council (Earmarked Grants)

TRPC channels are Ca²⁺-permeable nonselective cation channels that participate in store-operated Ca²⁺ influx. The activity of these channels is regulated by the filling state of intracellular Ca²⁺ stores and/or diacylglycerol and/or Ca²⁺/calmodulin. Recent studies from us demonstrated that the store-operated Ca²⁺ influx is subjected to feedback regulation. This feedback involves the inhibition of store-operated Ca²⁺ influx channels via cGMP/PKG pathway. Our preliminary results suggest that TRPC3 is phosphorylated by PKG *in vitro* and that PKG activation can abolish TRPC3-mediated store-operated Ca²⁺ influx. However, no decisive evidence is available to link direct PKG phosphorylation on TRPC3 proteins to the changes of TRPC3 functions. In this proposal, we hypothesize that TRPC3 may be a direct target for cGMP/PKG-mediated negative feedback inhibition. We will characterize the mechanism of TRPC3 regulation by PKG phosphorylation and we will also extend the study to TRPC6, another TRP isoform that are closely related to TRPC3. TRPC channels are already regarded as promising target molecules in the drug control of hypertension, asthma and chronic obstructive pulmonary diseases. Elucidation of

exact PKG phosphorylation site(s) on TRPC channels and the molecular mechanism of how PKG regulates TRPC channel function would provide crucial new information for rational design of anti-hypertensive and anti-asthma drugs.

(CU04366)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

Edition Title/Investigators

2001-02 Epithelial Cell Biology and Functional Genomics (MD01001)

✍ CHAN Hsiao Chang • CHEW CHENG Siew Boon • CHOW Pak Ham Patricia (Anatomy) • FISCUS Ronald Ray • LEUNG Po Sing • WONG Patrick Yee Ding

2002-03 Development of Globally Marketable Modernized Proprietary Natural Products for Treating Insomnia (MD02645)

✍ CHAN Hsiao Chang • ZHANG Zhi Yan*

2003-04 Investigation of the Role of a Novel Epididymis-Specific Gene, Bin-1b, in Sperm Maturation (CU03365)

✍ CHAN Hsiao Chang • ZHANG Yong Lian*

2003-04 The Role of Epididymis-Specific Defensin, Bin 1b, in Sperm Maturation (MD03885)

✍ CHAN Hsiao Chang • ZHOU CHENXI

2002-03 Protection against Neuronal Apoptosis by the cGMP/protein Kinase G Pathway: Protein Phosphorylation and Quantitation of DNA Fragmentation Using Novel Ultrasensitive CE-LIF Technology (CU02169)

✍ FISCUS Ronald Ray • SHAW Pang Chui (Biochemistry)

2002-03 Mechanisms of Vasorelaxation Induced by the Novel Ca²⁺ Channel Blocker Cilnidipine and Metabolites of Cytochrome P450 in Coronary Vasculature (CU02170)

✍ HUANG Yu • GOLLASCH Maik* • YAO Xiaoqiang

2003-04 Long-Term Effect of Ovariectomy and Raloxifene (SERM) Replacement Therapy on Endothelial Function and on Regulation of Smooth Muscle Ion Channels (CU03366)

✍ HUANG Yu • LAHER Ismail* • YAO Xiaoqiang

2002-03 Stimulatory Effect of Scutellariae Radix (Huangqin) and Its Major Flavonoids on Electrolyte Transport in Rat and Human Colonic Epithelia (CU02171)

✍ KO Wing Hung • HUANG Yu

2003-04 Effect of Scutellariae Radix (Huangqin) and Its Major Flavonoids on Experimental Ulcerative Colitis in Rats (MD03511)

✍ KO Wing Hung

2001-02	Activation of Pancreatic Renin-Angiotensin System: Its Role in the Regulation of Reactive Oxygen Species and Apoptosis in Pancreas (MD01116)	2003-04	Basal Cells as Regulators of Epididymal Principal Cell Functions (CU03371)
	✍ LEUNG Po Sing • IP Siu Po (School of Chinese Medicine)		✍ WONG Patrick Yee Ding
2002-03	Angiotensin-Converting Enzyme Genotype in High-Altitude Populations of Yunnan, China (MD02436)	2002-03	Functional Roles of Trp (Transient Receptor Potential) Channels in Vascular Endothelial Cells (CU02174)
	✍ LEUNG Po Sing • TAM Michael S C • ZHENG Yong Tang* • HUGH Montgomery*		✍ YAO Xiaoqiang
2003-04	The Changes of Expression and Function for Islet Renin-Angiotensin System (RAS) in Experimental Models of Type-2 Diabetes Mellitus: Its Association and Potential Regulatory Mechanism of RAS Blockers for the Protection of Diabetes (MD03430)	2003-04	Functional Role of VRL-2 Channels in Kidney Proximal and Cortical Collecting Duct Cells (MD03786)
	✍ LEUNG Po Sing		✍ YAO Xiaoqiang • HUANG Yu
2002-03	The Role of Organic Anion Transporters (OAT) in the Accumulation of Antifertility Drugs by the Rat Epididymis (CU02268)	2002-03	Subunit Composition, Spatial Distribution and Pharmacological Profiles of GABA-A Receptors in Globus Pallidus Neurons : Correlation with Different Synaptic Inputs (CU02175)
	✍ WONG Patrick Yee Ding		✍ YUNG Wing Ho • YUNG Kin Lam Ken*
		2003-04	The Neurotrophic Action of Secretin in the Developing Cerebellum (MD03619)
			✍ YUNG Wing Ho • CHAN Ying Shing* • CHOW K C Billy* • WANG Jian Jun*

RESEARCH PROJECTS

Epidemiological Survey on the Prevalence and Associated Factors of Suicide Ideation, Life Satisfaction & Quality of Life of Young Rural Residents in Chengdu, China

✍ CHAN Sau Man Sandra • CHIU Fung Kum Helen

📅 1 April 2005

❖ CUHK Research Committee Funding (Direct Grants)

Background: Suicides in China account for 44% of all suicides and 56% of all female suicides in the world, with higher rates of completed suicides in rural areas over urban areas as well as women over men especially in young adults. Suicide ideation is the distal risk factor to future suicides. Quality of Life (QOL) and Life satisfaction are correlates of mental health and suicidal behavior. The epidemiologic profiles of these important public health domains are largely unknown in China.

Objectives: 1) To investigate the prevalence and associated factors of suicide ideation of young rural residents aged 16-34. 2) To investigate the prevalence and associated factors of depressive symptoms of young Chinese rural residents aged 16-34. 3) To investigate the prevalence and associated factors of life satisfaction/QOL of young rural residents aged 16-34. 4) To examine gender difference in the prevalence of suicide ideation, depression, QOL & life satisfaction in young rural Chinese aged 16-34.

Method: Cross-sectional community survey using stratified cluster random sampling to get representative samples of young adults (aged 16-34)

in rural areas of Chengdu from different socio-economic classes. A battery of questionnaire on suicide ideation, psychopathology, social-cultural and socio-economic background, life circumstances, QOL/Life satisfaction will be administered by face-to-face interviews.

Data Analysis: Descriptive statistics will be used to work out the prevalence and mean values of variables under chief domains stratified by categorical demographic variables. Logistic regression model will be used to predict categorical membership (such as suicide ideators vs non-ideator; depressed as non-depressed) with other domains as independent variables.

(MD04585)

An International, Multicenter, Large Simple Trial to Compare the Cardiovascular Safety of Ziprasidone and Olanzapine

✍ CHUNG Wai Sau Dicky • MO Yi Man Flora • Pang Edwin* • Wong Yip Chau*

📅 15 December 2004

❖ Pfizer Corporation Hong Kong Limited

This is an observational study on schizophrenic patients' health outcomes related to two atypical antipsychotic drugs. The study is a post-marketing (Phase IV), Large Simple Trial (LST) with open-label, 1:1 random assignment of ziprasidone or olanzapine to patients with schizophrenia.

We will estimate prospectively the relative incidence among patients on ziprasidone and olanzapine of all-cause mortality; non-suicide mortality; mortality due to suicide; cardiovascular mortality and mortality due to sudden death during the study period. Patients, who are considered to be benefited from atypical antipsychotic drugs, will be recruited from psychiatric clinics and hospitals. Approximately

18,000 patients will be included in the study over the world. Our goal is to recruit about 30 patients from the catchment areas of New Territories East Cluster in Hong Kong. Subjects' vital status, continued use of assigned study drug, and whether the patient is hospitalised during the course of the study, will be recorded through normal clinical practice follow-up with the treating physician. The maximum duration of exposure to the study drug for an individual subject and the maximum follow-up will be one year. No additional blood tests or investigation are needed. Only medical records and other documentation are required to verify the above safety outcomes.

(MD04621)

A Two Year Study of the Progression of Cognitive Decline and Its Association with Proinflammatory Genotypes in Chinese Elderly with Prodromal Alzheimer's Disease

✍ LAM Chiu Wa • TANG Leung Sang Nelson
(Chemical Pathology)

☐ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

As the aging population increases, Alzheimer's disease (AD) has become one of the most disabling disorders worldwide. Recent advances have brought insight into the pathological mechanisms leading to the development of AD. For the past few years, a composite of genetic, physical and lifestyle factors have been identified as associated with AD. As multiple factors are involved, the identification of specific high risk groups for early intervention will be of special clinical value.

This project aims to study the progression of cognitive deterioration in Chinese elderly with prodromal AD with special reference to potentially

remediable genetic risk factors. A group of cognitively high risk individuals, subjects with questionable dementia, would be recruited and their cognitive function monitored regularly for 2 years. For the specific genetic risk factors, the investigator team has recently identified significant association between AD and some genetic factors with propensity for increased inflammatory response. In the present study, elderly recruited would be classified with reference to their polymorphisms for relevant pro-inflammatory genes. The rates of cognitive decline will be compared. If a faster rate of cognitive decline or conversion to AD is found with subjects having pro-inflammatory genotypes, this would reaffirm the significance of inflammatory reactions in the influencing the clinical progression of AD. The findings will hopefully add support for the selection of early intervention with anti-inflammatory agents in genetically and cognitively at risk individuals to prevent the development of symptomatic AD.

At present, cognitive performance and cognitive function of over 100 subjects with questionable dementia and 100 cognitive intact control elderly have been assessed at the baseline. Six months follow up reassessment is currently underway. Further longitudinal follow up with a longer observation period will help to evaluate if genetic predispositions in inflammatory response will lead to a faster rate of cognitive impairment in susceptible individuals./PART II

(MD04887)

To Establish a Functional Enhancement Program for the Improvement of Emotional and Functional Well Beings of Demented Elders

✍ LAM Chiu Wa • LUI Wing Cheong Victor* •
CHAN Sau Man Sandra • KO Flora* • LEUNG
Pui Yiu Vivian*

□ 1 January 2005

❖ S.K. Yee Medical Foundation

Demented elders, depending on the severity of illness, suffer from different forms of functional disabilities. The perception of progressively deteriorating function greatly affects their mood state and quality of life. Not uncommonly, demented subjects will react to the functional disabilities with significant depression and even self harm attempts. The current proposal aims to develop a functional enhancement program (FEP) for the demented subjects with mood disturbances. The main objective of the program is to develop an operational manual with practice guidelines focusing on improving functional deficits that are particularly distressing. It is anticipated that with enhancement in functional abilities, mood state and emotional well being could be improved. The FEP manual could then be used to train health care workers for the benefits of more demented elders with mood disturbances. The study will be implemented in two phases. In the first phase, the project team will design specific training activities for demented elders with different functional deficits. The protocol of a FEP targeted on the training of specific areas that was found to be most distressing and contributory to adverse mood state. Pilot study will be carried out to determine the optimal schedule and mode of training. In the second phase, the FEP will be carried out to demented subjects with mood disturbances attending the psychogeriatric services of the New Territories East Region of Hong Kong. It is estimated that about 200 subjects would benefit from the program in 2 years. To evaluate the effects of FEP on emotional and functional well beings of

the demented elders, pre- and post- treatment assessment on mood, behavior, functional status and severity of dementia will be carried out. A follow up assessment will also be carried out 3 months after completion of the FEP to determine if the therapeutic effects are sustained. At the end of the evaluation, practice guidelines for the FEP incorporating experience of the actual implementation will be derived. A training manual will be developed for further use by health workers caring for demented elders with mood disturbances.

(MD04494)

An Outcome Evaluation Study of Postnatal Depression Early Intervention Program

✍ LEE Tak Shing Dominic • LOK Hung Ingrid
(Obstetrics & Gynaecology) • YIP Shing Kai
Alexander (Obstetrics & Gynaecology) •
CHUNG Kwok Hung Tony (Obstetrics &
Gynaecology)

□ 1 June 2005

❖ O & G private fund

This is a prospective longitudinal follow-up study of 323 consecutive women who are identified as at risk of postnatal depression in a postnatal depression early intervention program in the Prince of Wales Hospital. The early intervention involves proactively identification of women who are at risk of postnatal depression, and early treatment of depression and management of psychosocial difficulties using a graded care approach. All recently delivered women are invited to participate this programme. To evaluate the effectiveness of the early intervention programme in treating women with postnatal depression, women who were screened high on both the EPDS and GHQ over a six-month period in 2004 will be invited to the study. Participants will be

enquired by the research nurse in a semi-structured manner. The depressive symptomatology as well as psychosocial difficulties at 6 and 12 months postpartum will be examined. Baseline sociodemographic, depressive symptomatology and outcome measures will also be examined by comparing with those of a historical cohort of postpartum women who scored high on the GHQ/EPDS double test. We hope that such an effectiveness evaluation will open door to a randomized controlled trial study which would eventually provide the empirical evidence needed to inform policy maker and service provider.

(MD04678)

Diffusion Weighted Magnetic Resonance Imaging Correlates of Depression after Acute Ischemic Stroke in Chinese Population

✍ TANG Wai Kwong • WONG Ka Sing Lawrence (Medicine & Therapeutics) • LAM Wai Man Wynnie (Diagnostic Radiology & Organ Imaging) • UNGVARI Gabor Sandor

□ 1 December 2004

❖ Research Grants Council (Earmarked Grants)

Stroke-related depression, a type of vascular depression, is of major public health concern. Computer tomography (a relatively old imaging technique with lower resolution) studies on poststroke depression (PSD) did not yield consistent findings on the relationship between the location of infarcts (areas of dead brain tissue due to a lack of blood supply) and PSD. The only large-scale study on this subject examined Caucasian patients, failed to separate acute and old infarcts, and did not use precise methods to measure the size of infarcts. No large-scale studies have been carried out on Magnetic Resonance imaging (MRI) (a relatively new imaging

technique with higher resolution), correlates of PSD in Chinese or other Asian populations.

The aim of this study is to evaluate the MRI correlates of PSD in 600 Chinese patients with first or recurrent stroke who receive treatment in the Acute Stroke Unit of the Prince of Wales Hospital over 24 months. The MRI examination, which can differentiate between recent and old infarcts, will be performed within the first 7 days admission. Three months after the index stroke, a psychiatrist will interview all participants and identify PSD. In addition, a host of demographic and psychosocial variables, clinical and MRI characteristics will be examined. MRI and other variables will be compared between depressed and non-depressed patients in order to identify the characteristics of infarcts contribute to the development of PSD.

(CU04369)

A Pilot Study on the Safety and Efficacy of a Traditional Chinese Medicine Formula (益腦素) in Vascular Dementia

✍ TANG Wai Kwong • CHIU Fung Kum Helen • UNGVARI Gabor Sandor

□ 1 April 2005

❖ CUHK Research Committee Funding (Direct Grants)

In traditional Chinese medicine (TCM) dementia is part of the broader “feeble-mindedness” category. Dementia is a comprehensive term characterized by disturbance of higher cognitive function. Its pathogenesis is explained by exhaustion of kidney essence, consumption of brain marrow and mental dysfunction. Vascular dementia (VaD) is the second most common cause of dementia in the elderly. There is no definitive medical or surgical treatment for VaD, although several drug classes,

including TCM have been used for the symptomatic treatment of VaD. The aim of the present project is to examine the safety, feasibility and efficacy of a TCM formula (益腦素) in patients with VaD. 益腦素 contains Folium Ginkgo 銀杏葉, Radix Astagali 黃耆, Cortex et Radix Polygalae 遠志, Rhizoma Acori Tatarinowii 石菖蒲, and Radix Salviae Miltiorrhizae 丹參. Sixty patients will enter this double blind, randomized, placebo-controlled trial, and half of them will receive 益腦素 while the rest will receive placebo for 12 weeks. Patients' cognitive function and the possible drug side effects will be recorded and compared.

(MD04333)

Herbal Treatment of Primary Insomnia in the Elderly

✍ WING Yun Kwok • FONG Yat Yuk Samson • YU Wai Man Mandy • LEUNG Ping Chung (Orthopaedics & Traumatology) • WONG Yeung Shan Samuel (Community and Family Medicine)

□ 1 May 2004

❖ Institute of Chinese Medicine

Sleep problems in the elderly are very common. Epidemiological surveys showed that 23 to 33% of individuals aged 65 and above complain their sleep. The elderly tend to go to bed early at night and wake up early in the morning. Their sleep-wake cycles are fragmented. We investigated the prevalence of sleep problems in 1034 noninstitutionalized old people (age >70) locally and found out that 75% of them reported occasional or persistent sleep disturbance and 38% reported themselves suffering from insomnia. Sleep disturbance has been associated with poorer quality of life, disproportionate use of sleeping pills and even

increased morbidity and mortality. However, there is no perfect treatment for sleep disturbance especially primary insomnia. In recent years, there has been a resurgence of interest in alternative or complementary medicine, both locally and internationally. Therefore, the institution of the Chinese Medicine at the Chinese University of Hong Kong developed a herbal formula to treat primary insomnia. The purpose of this study is to evaluate the effects of the herbal formula (安神茶) among Chinese elderly with primary insomnia over a period of 3 months. We will recruit the subjects from the Jockey Club Center for Osteoporosis Care and Control (JCCOCC). All the male elderly in the JCCOCC for the follow-up study will be interviewed by the sleep questionnaire to screen for insomnia and SAS. Forty-five subjects with insomnia symptoms will be recruited into the study. There will be two phases of clinical trial: an initial open study and a randomized double blind controlled trial. The efficacy of the formula will be measured by Actiwatch objectively and subjective sleep recording. (MD03909)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
2003-04	Suicide in Non-Elder Population in Hong Kong: A Psychological Autopsy Study (CU03373) ✍ CHAN Sau Man Sandra • CHIU Fung Kum Helen

2001-02	"Life Clinic", 3-Tier Coordinated Service Model, Joint Project on Prevention of Elderly Suicide (MD01324) ✍ CHIU Fung Kum Helen • LAM Chiu Wa	2003-04	Economic Reform and People's Well-Being in China: An Inter-Disciplinary Study (MD03928) ✍ LEE Tak Shing Dominic • HSIAO William* • KLEINMAN Arthur* • YIP Winnie*
2003-04	Association of Pro-Inflammatory Genotypes and Progress of Cognitive Decline in Prodromal Alzheimer's Disease (MD03506) ✍ LAM Chiu Wa • TANG Leung Sang Nelson (Chemical Pathology) • CHIU Fung Kum Helen	2003-04	Paternal Postpartum Depression in Hong Kong Chinese (MD03600) ✍ LEE Tak Shing Dominic • YIP Shing Kai Alexander (Obstetrics & Gynaecology)
2001-02	A Mutli-Centre Efficacy Trial of Naltrexone Maintenance Therapy in Hong Kong (MD01462) ✍ LEE Tak Shing Dominic • CHEUNG Kin Leung Ben# • LEUNG Shun Pun* • WONG Chi Keung* • CHAN Ronald* • LAM Ming	2003-04	A Supplementary Drug Abuse Monitoring System (MD03512) ✍ LEE Tak Shing Dominic

RESEARCH PROJECTS

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
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2002-03	Translation and Validation of Two Disease-Specific Instruments in Chinese Patients with Coronary Heart Disease (MD02421)
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✍ LOPEZ Violeta • THOMPSON David Robert (The Nethersole School of Nursing)

2003-04	Exploring Hong Kong Public Awareness of Coronary Heart Disease (MD03668)
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✍ LOPEZ Violeta • CHAN Choi Wan (The Nethersole School of Nursing)#

RESEARCH PROJECTS

Development of a Validated and Reliable Quality of Life Tool Specific to Children with Urinary Incontinence

✍ BOWER Wendy Fiona • YEUNG Chung Kwong

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

Until recently the paradigm ‘quality of life’ (QoL) has been associated more with children facing life-threatening diseases than those with organic or functional disorders. In children with bladder dysfunction the psychological impact of continence problems has been measured, but to date there has been no tool to allow evaluation of QoL. A general and holistic assessment of the impact of incontinence on affected children is needed in order to ensure that therapy addresses not only signs and symptoms but issues that are important to the patient. A tool that reliably measures relevant aspect of quality of life can be used as a treatment outcome measure, particularly when symptoms take a long period to resolve, and often quantifies the benefits of intervention. The ideal tool would be age-appropriate, child-completed, cross-culturally comparable, easy and speedy to complete, valid, and reliably able to measure response to treatment in different diagnostic groups. The aim of this research is to develop such a paediatric QoL measurement tool.

The study will be conducted in six phases and take approximately 14 months to complete. The tool development and testing will involve children and

clinicians from at least ten countries, making this a multi-centre and multicultural project. The new QoL measure will be translated into two other languages and analysed for cultural nuances. After modification the definitive tool will be tested for reliability and sensitivity on 300 children before and after treatment of their incontinence.

(MD04858)

Cytotoxic Effect of *Pteris Semipinnata* L on Human Colorectal Cancer Cells

✍ CHEN Gong George • LEE Fung Yee Janet • Nianci Liang*

□ 1 March 2004

❖ CUHK Research Committee Funding (Direct Grants)

Pteris semipinnata L (PsL) is a Chinese traditional herb, which has been used to treat variety of inflammatory conditions such as hepatitis, enteritis and snake bite (1). Recently, several chemical compounds have been identified from the ethanolic extract of the PsL. Some of these compounds are able to inhibit the growth of tumor cells, including gastric adenocarcinoma cells (MGC-803), lung adenocarcinoma cells (SPC-A-1), human promyelocytic leukemia cells (HL-60) and nasopharyngeal carcinoma cells (CNE-2Z), liver adenocarcinoma cells (BEL-7402, HepG2). Further studies reveal that PsL-induced cell arrest is associated with reduced DNA topoisomerase, abnormal activation of mitogen activated protein kinase, decreased Bcl-2 expression and high levels of Bax, c-Foc and c-Jun. However, the effect of PsL on human colon cancer cells has not yet been investigated. The aim of this pilot study is to test whether PsL will affect the growth of human colorectal cancer cells and if so, to examine possible

molecules involved. We also wish to determine which constituent extracted from PsL offers the significant effects against tumor cells. For this purpose, we have purified several different compounds from PsL, including 5F and 4F.

(MD03581)

Expression of Estrogen Receptors and the Peroxisome Proliferators-Activated Receptor Gamma in Thyroid Cancer

✍ CHEN Gong George • VAN HASSELT Charles Andrew • VLANTIS Alexander Chris • TSE Man Kit Gary (Anatomical & Cellular Pathology)

□ 15 March 2005

❖ CUHK Research Committee Funding (Direct Grants)

Evidence shows that estrogen plays a role in the development of thyroid cancer by promoting the proliferation of thyroid cells. The mitogenic and regulatory effect of estrogen is mediated through two closely related nuclear receptors, estrogen receptors (ER) α and β . ER α is thought to be associated with promoting cell proliferation and ER β with retarding cell proliferation. ER α signaling can be inhibited by ER β in target tissues. The ratio of ER α to ER β thus appears to be a critical factor in determining cell proliferation in estrogen-responsive cells. The activation of peroxisome proliferator-activated receptor gamma (PPAR γ) is known to retard cell growth and proliferation. Interestingly, the activation of PPAR γ can inhibit the expression of ER α -related genes and cell proliferation, suggesting that there is an interaction between PPAR γ and ER α . However, exactly how the ratio of ER α to ER β affects the growth and proliferation of thyroid cells is unknown. We hypothesize that the alteration in the

ratio of ER α to ER β contributes to the proliferation and growth of thyroid cancer tissue. The proposed study is to examine the expression of PPAR γ , ER α , ER β and other relevant molecules in human thyroid cancer tissues and cells.

(MD04322)

Effect of Hypoxia-Reoxygenation and Preconditioning on the Release of Nitric Oxide and Endothelium-Derived Hyperpolarizing Factor from the Coronary Endothelium during Heart Surgery

✍ HE Guo Wei

□ 1 January 2005

❖ CUHK Research Committee Funding (Direct Grants)

Hypoxia-reoxygenation (H-R) or ischemia/reperfusion injury to the heart is a major problem in open heart surgery. During open heart surgery (including heart transplantation), the heart is arrested (hypoxia/ischemia) and protected by cold cardioplegic (or organ preservation) solutions. When the heart is resuscitated, it is subjected to H-R (ischemia-reperfusion) injury.

Others and we have demonstrated that both NO and EDHF are important components in either porcine or human arteries. NO is probably the most important mediator for maintaining the vascular tone and EDHF serves as back up for NO although it also plays a role in maintaining the basic tone. The alteration of NO under H-R has been observed to be related to many mechanisms such as modulation of a cGMP mechanism. The alteration of EDHF during H-R has been less studied and the results are contradictory. Further, it has been proposed that the addition of L-arginine, the precursor for NO, may partially prevent coronary functional damage but the

restoration of the EDHF-mediated function must be through other mechanisms such as potassium channel openers or cytochrome P450-monooxygenase metabolite such as EETs.

We have recently demonstrated 1) that the release of NO is different in various arteries and veins; 2) that hypoxia (at O_2 5.7 ± 0.8 mmHg) significantly reduces the EDHF-mediated relaxation in both large and micro coronary arteries when NO is blocked; 3) that hypoxic preconditioning (PC)/potassium channel openers may restore the EDHF-mediated relaxation in coronary arteries; and 4) that the mechanism of PC in the coronary artery may involve mitochondrial K_{ATP} channel. In this proposal, we hope by using multiple methods to investigate heart surgery-related H-R, we will be able to explore the following aspects: 1) the alteration of release of NO and the effect of supplementation of NO donors; 2) the alteration of release of EDHF and the mechanism; and 3) the effect of PC on the release of NO and EDHF. We expect that with the knowledge derived from this proposed project, the effect of H-R on the most important function of the coronary endothelium (release of NO and EDHF to maintain adequate coronary tone) and the mechanism during open heart surgery will be better understood and eventually new methods will be developed to protect the cellular function in order to further improve the operative results of the open heart surgery including heart transplantation.

(MD04318)

A Placebo-Controlled, Double-Blind, Randomized, Parallel-Group Study of the Efficacy and Safety of Dapoxetine in the Treatment of Men With Premature Ejaculation

✍ NG Chi Fai • CHENG Chi Wai • WONG Yim Fong Annie • NG Chi Wa* • Li Miu Ling* • Wu Pui Hing*

□ 26 April 2005

❖ Johnson & Johnson (Hong Kong) Limited

Adult patient who suffered from premature ejaculation (PE), with 75 % of the intravaginal ejaculatory latency times (IELT) less than 2 minutes, for more than 6 months, will be included for the study. After performing safety evaluation and giving informed consent to the subject, those eligible subjects will then be randomized to receive either placebo, or Dapoxetine 30mg or 60mg for 12 weeks. The total study time will be approximately 18 weeks. The patient will be instructed to take the assigned study drug on a on-demand basis, before sexual intercourse. The subject is required to complete a report form about the circumstances of ejaculation, duration of intercourse and the satisfactory about the sexual experience. The subject will attend the follow-up visit every 4 week during the study for efficacy and safety evaluation.

(MD04342)

Prevalence and Risk Factors of Metabolic Bone Disease after Gastrectomy for Gastric Cancer

✍ NG Enders Kwok-wai • CHEUNG Ka Yin • LAW Sheung Wai (Orthopaedics & Traumatology) • LEUNG Kwok Sui (Orthopaedics & Traumatology) • TANG Leung Sang Nelson (Chemical Pathology)

□ 1 November 2004

❖ CUHK Research Committee Funding (Direct Grants)

Gastrectomy is the main modality of treatment for gastric cancer. It is well known that gastrectomy is

associated with osteomalacia, osteoporosis or a combination of both. The loss in bone mass increases the risk of fracture. However, local data on the severity of bone disorders among gastrectomised patients is lacking. We aim to measure the prevalence of metabolic bone disease after gastrectomy for stomach cancer in our locality and to determine the risk factors associated with severe form of osteopenia, by measuring the bone mineral density and biochemical markers of bone metabolism.

(MD04996)

Investigation of the Metabolic and Neuroendocrine Response in the Fetal Goat to Open and Minimally Invasive Intrauterine Surgery

✍ SHI Yimin • YEUNG Chung Kwong • BOWER Wendy Fiona • CHEN Hui# • CLARKE Simon Andrew# • Xiang Bo*

□ 1 September 2004

❖ CUHK Research Committee Funding (Direct Grants)

The major obstacle affecting the outcome of fetal surgery is the onset of premature labour. This may be due to fetal stress resulting from the surgical intervention. The fetal response to surgical stress, by either open or minimally invasive surgery, (keyhole) has not yet been examined.

Aims :

To investigate the fetal response to fetal surgery

To confirm the reduction in stress offered by keyhole surgery on a fetus.

Hypothesis :

1. That a fetus does produce a stress response to surgery
2. That a fetus produces a reduced response to

minimally invasive surgery when compared to open surgery.

Materials and Methods :

18 fetal goats will have drips inserted into an artery in their necks. This will be carried out by opening the uterus and directly accessing the fetal neck under general anaesthetic. The fetuses will be replaced into the uterus, carefully monitored and supported to ensure survival for 7 days. They will then undergo a second operation. This will be either open fetal surgery by a direct incision on the uterus or by placing instruments and a videocamera inside the uterus through small holes. A third set of fetuses will have no intervention and will act as controls. All 'surgical' fetuses will have an incision made on the lower part of their back to simulate an operation. They will be nursed to recovery and have daily sampling of various markers in their blood that indicate the response of the body to the stresses of surgery.

(MD04943)

The Development of the Cantonese Lexical Neighborhood Tests in Noise (CLMTM) - An Outcome Measurement Instrument for Children with Hearing Impairment

✍ TONG Chi Fai Michael • LEE Tan (Electronic Engineering) • YUEN Chi Pun • VAN HASSELT Charles Andrew

□ 2 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

Objective

To date, there are very few validated open-set recognition measures (in pre-recorded format) to evaluate the speech recognition abilities of the Cantonese-speaking hearing-impaired pediatric

population using hearing aids and/ or cochlear implants. Sentence testing instrument is even unavailable. Without validated speech recognition tools, it is very difficult to objectively evaluate the performance change of hearing impaired children after receiving medical, surgical, and re/habilitation intervention including middle ear management, hearing aid fitting and cochlear implantation. There is an urgent need to develop such sensitive outcome measurement instruments that can (1) effectively evaluate the performance level and (2) objectively document the intervention efficacy, of this clinical group.

Materials and Methods

Based on the lexical neighborhood activation model (Luce, 1986; Luce & Pisoni, 1988), the Cantonese CHILDES language database (Fletcher, et al. 2000) will be used to generate two new pre-recorded spoken word recognition measures (1) the Cantonese Lexical Neighborhood Word Tests in Noise-CLNTN-monosyllable and CLNTN -disyllable, and (2) the Cantonese Lexical Neighborhood Sentence Test in Noise (CLNTN-sentence). For CLNTN -monosyllable and CLNTN disyllable, eight lexically “easy” wordlists (high frequency words with few phonemically similar neighbors) and eight lexically “hard” word lists (low frequency words with many phonemically similar neighbors) will be constructed in each test. For the CLNTN-sentence, 20 lists of sentences will be constructed from lexically “easy” words and 20 lists of sentences will be constructed from lexically “hard” words. A total of 100 children, 40 with normal hearing, and 60 hearing-impaired children with severe to profound sensorineural hearing loss using hearing aids and/ or cochlear implants will participate in the study. The performance of the three subtests - CLNTN-monosyllable, CLNTN-disyllable and CLNTN-sentence will be evaluated in four

signal-to-noise ratios: 0dB, +5dB, +10dB and +15dB. The percent correct scores from each of these measures will be transformed into rationalized arc-sine units to homogenize the variances. Weighting factors will be applied in order to achieve list equivalency between test lists within each subtest. CLNTN is expected to provide a speech recognition performance measure of individual hearing impaired children under noise environment, and to prevent ceiling and basement effects in statistical measurement - signal-to-noise ratio (SNR) for 50% correct speech recognition (SNR-50). As a clinical measurement tool, CLNTN will provide guidelines for interpreting a difference (the critical difference) between two SNR-50 scores observed between different conditions for the same individual for testing. The cumulative distributions of differences between pairs of SNR-50 scores will be obtained using a second order polynomial fitting for determining the critical difference.

Preliminary Results

A predecessor for CLNTN - the Cantonese Lexical Neighborhood Tests (CLNT), which is a test-in-quiet version of the monosyllable and disyllabic subtests, was evaluated in 15 severe to profound hearing impaired children using hearing aids or cochlear implants. The results were presented at the Fourth Congress of Asia Pacific Symposium on Cochlear Implant and Related Sciences (Yuen et al, 2003). The results revealed that word recognition performance was consistently higher on CLNT-disyllable than CLNT-monosyllable word lists. Lexically “easy” words were recognized correctly more often than lexically “hard” words in CLNT-disyllable, while no significant difference in performance between them was observed in CLNT-monosyllable. No significant difference in performance was observed among different words lists within the same category of “easy” and “hard”

words in both tests. Inter-list equivalencies were therefore achieved. These results from this study strongly suggest that CLNT and the upcoming CLNTN will become valuable clinical tools for objectively evaluating the speech recognition performance of the pediatric hearing impaired population.

(MD04359)

Molecular Regulation of Bak by HPV16E6 and E7 in Laryngeal Cancer

✍ VAN HASSELT Charles Andrew • CHEN Gong George • VLANTIS Alexander Chris • TSANG King Yin Raymond

□ 15 December 2004

❖ CUHK Research Committee Funding (Direct Grants)

Human papillomavirus type 16 (HPV 16) is a causative agent for human laryngeal and cervical cancer. HPV 16 contributes to neoplastic progression predominantly through the action of two of its viral oncoproteins, namely E6 and E7. We have established two laryngeal cancer cell lines transfected with HPV16 E6 and E7 respectively. Both cell lines were found to be less sensitive to apoptotic stimuli than controls, which was consistent with our previously published work where we showed that there was an increase of anti-apoptotic nuclear factor-kappaB in human laryngeal cancer tissue. We further demonstrated that E6 down-regulated the expression of Bak protein in laryngeal cancer cells by 100 folds. Such an obvious decrease in pro-apoptotic Bak is deemed to contribute to the uncontrolled growth of cancer cells. In order to prevent or reverse this pathological process, further studies are needed to detail the interaction between E6 and Bak. We propose to

clone the promoter region of Bak and find out regulatory components in this region. If possible, we also plan to examine whether E6 can interact one or more these regulatory components in laryngeal cancer cells.

(MD04481)

The Functional Inhibition of NF KappaB in Squamous Epithelial Cells Infected with HPV 16 Promotes Apoptosis

✍ VLANTIS Alexander Chris • CHEN Gong George • VAN HASSELT Charles Andrew • CHAN Kay Sheung Paul (Microbiology)

□ 1 December 2004

❖ CUHK Research Committee Funding (Direct Grants)

People infected with human papillomavirus 16 (HPV 16) have an increased chance of developing carcinoma. E6 and E7 are known to be the main viral oncoproteins of HPV 16 that lead to the uncontrolled growth of infected cells. A variety of cell proliferation and growth molecules are altered by E6 and E7. A common feature of these molecules is that they are governed by the transcription factor NF-kB. Our recent study indicated a positive correlation between E7 and p65, a subunit of NF-kB, in laryngeal cancer tissues. The study also suggested that NF-kB is constitutively activated in those laryngeal cells infected with HPV 16. These findings are in line with those of studies performed on cervical cancer that was positive for HPV 16. These results have prompted us to hypothesize that inactivating NF-kB will have an inhibitory effect on tumour development and growth by promoting apoptosis. Apoptosis is suppressed by high levels of NF-kB. Our proposed study will test our hypothesis by using different strategies to inactivate NF-kB in

human epithelial cells infected with HPV 16, and in human epithelial cells that express HPV 16 oncoproteins E6 or E7. We will examine whether the function of cells is altered after inactivation of NF-kB.

(MD04925)

Efficacy of Conventional Acupuncture Therapy Versus Overnight Acupuncture-Point Transcutaneous Electrical Nerve Stimulation (ACU-TENS) Therapy for Children with Severe Primary Nocturnal Enuresis: A Clinical and Neurophysiological Comparative Study

✍ YEUNG Chung Kwong • LEUNG Ping Chung (Orthopaedics & Traumatology) • CHAN Yu Leung (Diagnostic Radiology & Organ Imaging)# • Tong Kai Yu*

□ 1 December 2004

❖ CUHK Research Committee Funding (Direct Grants)

Primary nocturnal enuresis (PNE), or bedwetting, is a common disorder affecting 5-10% of children by age 7. It is associated with bladder dysfunctions, arousal disturbance and/or a derangement of nocturnal antidiuretic hormone (ADH) secretion, causing in common a mismatch of nocturnal urine production in excess of the bladder capacity during sleep at night, with a simultaneous failure to wake up in response to a full bladder. Recent studies observed an elevated arousal threshold and a reduced prepulse inhibition (PPI) of startle in enuretic children, suggesting a relationship between brainstem dysfunction and nocturnal enuresis. However, the relationship between the underlying brainstem and bladder dysfunctions in enuretic patients, and their possible implications on treatment outcome, has remained unclear. Currently, the results of

long-term desmopressin therapy, the treatment of choice, are less than satisfactory with only about 60% patients responding initially and only 19% remaining dry after cessation of therapy using an intention-to-treat analysis. In contrast, reports of traditional Chinese acupuncture has claimed overwhelmingly positive results, with efficacy ranging from 76% to 98%, although its use in children is restricted by fear of needling and the time limitation for daily application. The aim of this study is to evaluate the efficacy of a non-invasive treatment modality, viz. overnight acupuncture-point transcutaneous electrical nerve stimulation (ACU-TENS) therapy, versus conventional acupuncture for children with severe PNE. The underlying brainstem and bladder functions will be assessed using PPI of startle, sleep arousal threshold, brainstem evoke potential, functional magnetic resonance imaging (fMRI) during bladder stimulation, voiding diary, ultrasound and urodynamic studies respectively, and correlated with the treatment outcome.

(MD04900)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
2003-04	Natural History of the Elimination Syndrome of Childhood (MD03818)
	✍ BOWER Wendy Fiona • YIP Shing Kai Alexander (Obstetrics & Gynaecology) • YEUNG Chung Kwong

- 2003-04 A Study of Paracrine Factors Involved in Keratinocyte-Melanocyte Interaction in a Laser Induced Model (MD03529)
✍ BURD David Andrew Ross • POON Kwok Man#
- 2003-04 The Design and Development of a Novel Bio-Interactive Electro-Chemical Wound Dressing Incorporating the Physical Vapour Deposition of Nanoscale Silver Ions (MD03739)
✍ BURD David Andrew Ross • IP Margaret (Microbiology) • LAM Wai Kei Christopher (Chemical Pathology) • POON Kwok Man#
- 2003-04 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), a Tobacco-Specific Carcinogen, Regulates Apoptotic Molecules via a Nuclear Factor Kappa B-Dependent Pathway (CU03390)
✍ CHEN Gong George • YIM Ping Chuen Anthony • MOK Shu Kam Tony (Clinical Oncology) • WARNER Timothy D.*
- 2003-04 Cytotoxic Effect of Pteris Semipinnata L on Human Colorectal Cells (MD03565)
✍ CHEN Gong George • LEE Fung Yee Janet • LIAN Nianci*
- 2000-01 A Multi-Centered, Randomized, Controlled Trial Comparing Standard Oesophagectomy versus Primary Chemo-Irradiation without Surgery as the Treatment for Squamous Oesophageal Cancer (CU00084)
✍ CHUNG Sheung Chee Sydney • CHAN Chi Wai Angus • GRIFFITH
- James Francis (Diagnostic Radiology & Organ Imaging) • KWOK Po Yin Samuel • LEONG Heng Tat • LEUNG Sing Fai (Clinical Oncology) • ONG Lina Lilian# • LI Ka Wah Michael
- 2001-02 The Interaction between Endothelium and Smooth Muscle/Cardiac Myocytes During Heart Surgery and Clinical Significance (MD01127)
✍ HE Guo Wei
- 2003-04 Function of Potassium Channels in the Coronary / Pulmonary Arteries during Heart / Lung Surgery (CU03383)
✍ HE Guo Wei • HUANG Yu (Physiology) • YAO Xiaoqiang (Physiology)
- 1997-98 Prospective Study on the Relationship of Central Venous Pressure and Blood Loss During Hepatectomy (MD96217)
✍ LAI Bo San Paul • CHUI Po Tong (Anaesthesia & Intensive Care) • LEOW Chon Kar# • LAU Wan Yee Joseph
- 2001-02 Isolation and Characterisation of the Nitrite Reductase Gene of Helicobacter Pylori and Its Role in Gastric Carcinogenesis (MD01126)
✍ NG Enders Kwok-wai • CHAN Chiu Yeung Raphael (Microbiology) • CHENG Fun Bun Augustine (Microbiology)# • LEUNG Wai Keung (Medicine & Therapeutics) • LING Kin Wah Thomas

- (Microbiology) • SUNG Joseph Jao
Yiu (Medicine & Therapeutics)
- 2003-04 Surveillance of Bleeding Peptic Ulcers Using Wireless Capsule Endoscopy (CU03382)
✍ NG Enders Kwok-wai • CHAN Ka Leung Francis (Medicine & Therapeutics) • SUNG Joseph Jao Yiu (Medicine & Therapeutics) • WONG Kin Hung Simon
- 2002-03 IMASH - Intravenous Magnesium Sulfate in Aneurysmal Subarachnoid Hemorrhage (Does Intravenous Magnesium Sulfate Improve Clinical Outcome?) (CU02183)
✍ POON Wai Sang • CHAN Matthew Tak Vai (Anaesthesia & Intensive Care) • LAM Ming Kuen Joseph • BOET Ronald
- 2003-04 A CT Decision-Making Tool for Mild Head Injury (CU03386)
✍ POON Wai Sang • CHAN Yu Leung (Diagnostic Radiology & Organ Imaging)# • LEUNG Clarence Hin Shuen • CAMERON Peter Alistair (Accident and Emergency Medicine Academic Unit)# • YU Ly Mee Ashley (Centre for Clin. Trials & Epidemiological Research)# • ZHU Xian Lun Cannon
- 2002-03 The Establishment of the Chinese Rhinitis Symptom Utility Index (RSUI) (MD02323)
✍ VAN HASSELT Charles Andrew • TONG Chi Fai Michael • LO Suk
- Yee Phoebe • WOO Kong Sang John • LAM Chuen Kwong • LEE Ching Chyi (Decision Sciences and Managerial Economics) • REVICKI Dennis*
- 2003-04 Estradiol Inhibits Apoptosis by Promoting the Expression of Metallothionein II and NF-kappaB in Human Thyroid Cancer Cells (CU03387)
✍ VAN HASSELT Charles Andrew • VLANTIS Alexander Chris • CHEN Gong George • CHERIAN M. George* • LEUNG Chi Hang Bertrand
- 2002-03 The Nuclear Localization of NF Kappa B and p53 in Laryngeal Squamous Cell Carcinoma Infected with HPV16 (MD02687)
✍ VLANTIS Alexander Chris • CHEN Gong George • VAN HASSELT Charles Andrew
- 2003-04 NF kappaB is Involved in Resistance to Apoptosis in Squamous Epithelial Cells Infected with HPV 16 (MD03419)
✍ VLANTIS Alexander Chris • CHEN Gong George • VAN HASSELT Charles Andrew
- 2001-02 Children's Continence Care Centre (MD01896)
✍ YEUNG Chung Kwong • BOWER Wendy Fiona • SIT K Y Frances* • YEW Siu Yin*
- 2003-04 Efficacy of Acupuncture Versus Standard Therapy for Children with Primary

- | | | | | |
|---------|--|--|---------|--|
| | Nocturnal Enuresis and the Implications of Brainstem and Bladder Functional Changes (CU03389) | | 2001-02 | Homocysteine, Oxidant Stress and Vein Graft Failure: Interactions with Diabetes and Hypercholesterolaemia and Novel Approaches to Therapy Using Gene Transfer in a Porcine Model (MD01133) |
| | ✍ YEUNG Chung Kwong • LEUNG Ping Chung (Orthopaedics & Traumatology) • BOWER Wendy Fiona | | | ✍ YIM Ping Chuen Anthony • ELAREFI Ahmed Abdalla • HE Guo Wei • JEREMY Jamie* • NEWBY Andrew C* • WAN Song |
| 2003-04 | A Longitudinal Study on Primary Nocturnal Enuresis in Hong Kong Children (MD03452) | | 2002-03 | Role of Angiogenesis in Mediating the Inhibitory Effect of the External Stent on Porcine Vein Graft Thickening (MD02883) |
| | ✍ YEUNG Chung Kwong • CHAN Wai Fung Anita# • SIHOE Dart Yin Jennifer* • SHIT Kam Yee Frances* • MAK Kwok Hang* | | | ✍ YIM Ping Chuen Anthony • WAN Song • JEREMY Jamie* • BAKER Andrew* • ELAREFI Ahmed Abdalla |
| 1995-96 | Video Assisted Thoracic Surgery (MD92192) | | | |
| | ✍ YIM Ping Chuen Anthony | | | |

RESEARCH PROJECTS

Cost-Effectiveness Analysis of Oral Paracetamol and Ibuprofen for Treating Pain after Soft Tissue Limb Injuries: Double-Blind, Randomized, Controlled Trial

✍ GRAHAM C A • MAN Shin Yan • WOO Wing Keung • RAINER Timothy Hudson • JACOBS Philip* • Lam Peggo K W*

📅 1 November 2004

❖ CUHK Research Committee Funding (Direct Grants)

Background: Paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen are commonly used oral analgesics in emergency departments (ED) not only in Hong Kong but throughout the world. There are no large-scale (n>100), prospective, randomised studies comparing paracetamol with ibuprofen in the management of acute soft tissue injury. As paracetamol is cheaper than most NSAIDs, may be as effective in the management of acute pain and possibly with fewer adverse effects, a large-scale, randomised, controlled trial is needed to answer questions of relative analgesic efficacy, safety and cost-effectiveness. Previous comparative studies on NSAIDs have been done in this unit and have suggested equivalence between two NSAIDs and paracetamol, but numbers were small and drug doses were modest.

Objective: To compare the efficacy, safety and cost between oral ibuprofen and paracetamol in pain control for acute soft tissue injuries in an ED setting

Design: Prospective, double-blind, randomised controlled trial with three arms: oral paracetamol

with placebo; oral ibuprofen with placebo; paracetamol and ibuprofen in combination

Participants: 783 subjects having sustained isolated soft tissue limb injury without significant fracture presenting to the ED of Prince of Wales Hospital

Main outcome measures: Pain relief profiles of paracetamol, ibuprofen and the combination of both; adverse effect profiles of paracetamol, ibuprofen and the combination of both; overall cost effectiveness of paracetamol, ibuprofen and the combination of both from the perspective of the healthcare provider.

(MD04974)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
2002-03	Plasma Nucleic Acids as a Non-Invasive Marker of Severity in Acute Coronary Syndrome (MD02581) ✍ RAINER Timothy Hudson • LO Yuk Ming Dennis (Chemical Pathology) • WOO Kam Sang (Medicine & Therapeutics) • CAMERON Peter Alistair#
2003-04	Investigation into Circulating Nucleic Acids in Patients with Stroke (CU03402) ✍ RAINER Timothy Hudson • LAM Wai Man Wynn (Diagnostic Radiology & Organ Imaging) • LO Yuk Ming Dennis (Chemical Pathology) • METREWELI Constantine (Diagnostic Radiology & Organ Imaging)# • WONG Ka

Sing Lawrence (Medicine &
Therapeutics)

RESEARCH PROJECTS

Needs Assessment of Male Hong Kong Clients of Female Sex Workers in Shenzhen and Serving Male Hong Kong Clients in Shenzhen - A Pilot Study

✍ LAU Tak Fai Joseph • FENG Tiejian*

📅 1 April 2004

❖ Shenzhen Centre for Disease Control and Prevention

A pilot study to assess the needs of female sex workers working in Shenzhen and their clients in terms of HIV prevention.

(SS04395)

An Extended Study of the Understanding the Adolescent Project (Primary)

✍ LAU Tak Fai Joseph • LAU Man Chun Mason

📅 1 July 2004

❖ Education & Manpower Bureau, HKSAR Government

The Education Manpower Bureau introduced the Understanding the Adolescent Program (UAP) to primary school students. The UAP (primary) was developed for the purposes of early detection and early prevention of social/psychological problems in the primary school setting. In the last 3 years, a research project has been commissioned to the Centre for Epidemiology and Biostatistics to assess feasibility and effectiveness of the UAP screening/intervention package in primary schools. The first UAP primary school cohort of positively screened students (n = about 390) has been

randomized into the intervention and the control groups and has been followed up for the last 3 years. A booster program is proposed to be offered to the intervention group students at this transition junction may therefore facilitate these positively screened students to perform better in secondary schools. Baseline and post-program measurement for both the control and intervention groups will be obtained in July, 04 and July, 05 respectively. The effectiveness of the booster program will be evaluated by comparing the changes of the two groups of students.

(SS04773)

Love Teeth Campaign 2004-05 Effectiveness Evaluation Survey

✍ LAU Tak Fai Joseph • TSUI Hi Yi • CHAN Mei Wah (School of Public Health)

📅 1 September 2004

❖ Oral Health Education Unit, Department of Health, HKSAR Government

The project consists of a cross-sectional survey on 1200 Hong Kong respondents to investigate knowledge, perceptions, awareness and behaviors that are related to gum health and plaque. Significance of healthy gums and white teeth will be assessed and compared. Prevalence of gum disease will also be investigated. Factors predicting gum disease and protective behaviors such as regular check up and use of dental floss etc. will also be identified. The first survey will also serve as the baseline study of an evaluation exercise for a “love-teeth” campaign, to be launched by the Department of Health. A second and a third survey will compare any differences in awareness, knowledge and behaviors of the general public, as

well as assessing the exposure and perceived impacts of the campaign.
(SS04976)

Development of Electronic Screening Tool for the Understanding the Adolescent Project in Secondary Schools

✍ LAU Tak Fai Joseph • LAU Man Chun Mason

☐ 1 October 2004

❖ Social Welfare Department, HKSAR Government

To develop and to replicate a computer software for screening of students under the UAP in secondary schools. To provide training, technical support services relating to the application of the computer software, and to conduct a trial-run application under the UAP in secondary schools in the 2004/05 school year and a full-scale application in the 2005/06 school year.

(SS04920)

Data Classification for the Understanding the Adolescent Project in Secondary Schools in 2004/05

✍ LAU Tak Fai Joseph • LAU Man Chun Mason

☐ 1 November 2004

❖ Social Welfare Department, HKSAR Government

To identify students who are in need of primary preventive programme from a maximum of 300 secondary schools participating in the Understanding the Adolescent Project (UAP) based on the data generated from the Hong Kong Student Information Form - Student Form (HKSIF-S) and Hong Kong Student Information Form - Teacher Form

(HKSIF-T). To provide the Social Welfare Department with the identification results by individual school and by gender.

(SS04799)

Refinement of CD-ROM of Hong Kong Student Information Form under the Understanding the Adolescent Project (Primary)

✍ LAU Tak Fai Joseph • LAU Man Chun Mason

☐ 4 February 2005

❖ Education & Manpower Bureau, HKSAR Government

The project was commissioned by the Education xx to develop a CD-ROM as well as a process to implement data collection by using the Hong Kong Student Information Form that was developed by the Centre, which was designed for screening of potentially-at-risk primary school students. Positively screened students will be invited to join the Understanding the Adolescents Program, a primary prevention program which has now been used by over 300 primary schools in Hong Kong. The CD-ROM will automate the screening process for participating schools. It also allows The Education and Manpower Bureau to capture new research data on a massive scale. This new commission is to update and to refine the afore-mentioned CD-ROM.

(ED04759)

Influenza Vaccination Coverage and Self-Reported Reasons for Not Receiving Influenza Vaccination among Community-Dwelling Elderly Aged 65 or Above

✍ LAU Tak Fai Joseph • KIM Jean Hee

☐ 21 February 2005

❖ Centre for Health Protection, Department of Health, HKSAR Government

Influenza is a highly infectious disease that commonly results in large outbreaks in which the elderly population is at disproportionate risk of infection and mortality. The objectives of the proposed study are to investigate the prevalence of influenza vaccination and factors that are associated with influenza vaccination among 1100 Chinese-speaking community-dwelling elderly residents of Hong Kong who are of age 65 and older: (1) The prevalence of vaccination in the last 1, 3, and 12 months, as well as intent to vaccinate in the next 12 months. (2) To examine the demographic, socioeconomic, logistical or attitudinal factors associated with whether or not the respondent vaccinated against influenza and their future intent to do so.

(MD04879)

Needs Assessment and Benchmark Study of Male Hong Kong Clients of Female Sex Workers in Shenzhen and Female Sex Workers Who Have Been Serving Male Hong Kong Clients in Shenzhen

✍ LAU Tak Fai Joseph • TSUI Hi Yi

☐ 1 March 2005

❖ Council for the AIDS Trust Fund

The present study aims to investigate the needs and HIV-related behaviors of Hong Kong males patronizing female sex workers (FSW) in Shenzhen and those FSW serving Hong Kong male clients in Shenzhen. The study will be carried out in ShaTsui, Shenzhen, which is a popular red-light district for commercial sex among Hong Kong males. A total of 250 Hong Kong male clients of FSW and 250

FSW serving Hong Kong men will be interviewed. Anonymous structured questionnaire will be used to collect data.

(SS04312)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
2001-02	Understanding Adolescent Project 4 (ED01367) ✍ LAU Tak Fai Joseph • LEUNG Kit Sang (School of Public Health)# • LAU Man Chun Mason
2002-03	Evaluation of the Adolescent and family Counselling Service (SS02390) ✍ LAU Tak Fai Joseph • LEUNG Kit Sang (School of Public Health)# • LAI Yee Ching Kelly (Psychiatry) • LAU Man Chun Mason
2002-03	Consultancy Project for CK Life Sciences Development Inc. (MD02992) ✍ LAU Tak Fai Joseph • XU Liying (School of Public Health)#
2002-03	Surveillance and Intervention Research for Different Communities in Hong Kong (MD02369) ✍ LAU Tak Fai Joseph • KIM Jean Hee
2003-04	Clinical Data Management and Medical Statistics Functions for CK Life Sciences Development Inc. (MD03532)

- ✍ LAU Tak Fai Joseph
- 2003-04 Prospective Randomized Study on the Therapeutic Gain for the Nasopharyngeal Carcinoma Patients (MD03576)
- ✍ LAU Tak Fai Joseph • XU Liying (School of Public Health)#
- 2003-04 The Impact of Calcium Intake on Blood Pressure and Prevalence of Hypertension: A Pilot Cross-Sectional Study of Older Chinese Subjects in Hong Kong (MD03385)
- ✍ LAU Tak Fai Joseph • CHAN Yan Keung Thomas (Medicine & Therapeutics) • KWOK Chi Yui Timothy (Medicine & Therapeutics) • WOO Jean (Medicine & Therapeutics)
- 2003-04 The Production of CD-Rom of Hong Kong Student Information Form Under the Understanding Adolescent Project in Primary Schools (ED03821)
- ✍ LAU Tak Fai Joseph • LAU Man Chun Mason
- 2003-04 Baseline Study on Needs and Risks of Women Attending STD Clinics in Hong Kong (MD03489)
- ✍ LAU Tak Fai Joseph
- 2003-04 A Randomized, Controlled Study to Evaluate the Relative Efficacy of Using the Voluntary Counseling & Testing (VCT) Approach & the Information Distribution Approach to Reduce HIV-Related Risk Behaviors among Hong Kong Male Cross-Border Truck Drivers (MD03908)
- ✍ LAU Tak Fai Joseph • KIM Jean Hee • TSUI Hi Yi

RESEARCH PROJECTS

BRE - Investigation of Its Roles in Death Receptor Signaling, Human Cancers and Its Primary Function

✍ CHUI Yiu Loon

□ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

BRE (brain and reproductive expressed), a highly conserved protein in evolution, is a cytoplasmic binding protein of TNF-RI, which is a ubiquitous receptor for a potent pleiotropic cytokine, TNF-Activation of TNF-RI initiates a number of signaling pathways that regulate apoptosis. We have shown that over-expression of BRE can inhibit apoptosis. Furthermore, we have demonstrated that BRE not only binds to TNF-RI, but also to Fas. Over-expression of BRE in cell lines reduced apoptotic response to death receptor activation, as well as to stress stimuli, suggesting that BRE exerts its antiapoptotic effect through inhibition of the mitochondrial apoptotic machinery. Using siRNA to knock down the endogenous BRE expression level, we have shown that the physiological antiapoptotic role of BRE is specific to the death receptor stimulation. However, the mitochondrial inhibitory mechanism of the death receptor-binding BRE remains unknown. We propose to investigate whether BRE affects the death receptor signaling cascades known to modulate mitochondria-dependent apoptosis, such as the phosphoinositide-3OH kinase (PI3K) and MAPK pathways. Our preliminary study also revealed an association between anomalous BRE transcription and kidney cancer.

We seek to further this observation by investigating BRE protein expression in a larger number of human kidney cancer using the matched tumor / normal tissue pairs. An animal tumor model will also be established to probe the underlying mechanism for such an association. We believe that understanding the function, and the mechanism by which BRE works will shed new insight into the control of apoptosis, and development of some human cancers. (MD04756)

Prevalence and Pathophysiological Properties of Antibodies to Guanosine Triphosphate in Systemic Lupus Erythematosus

✍ LIM Pak Leong • LEUNG Tze Ming • WONG Kong Chiu (Medicine & Therapeutics)

□ 1 October 2004

❖ CUHK Research Committee Funding (Direct Grants)

Systemic lupus erythematosus (SLE) is a chronic and debilitating disease found commonly in Hong Kong and globally, especially in young women, but little is known about its etiology. However, antibodies to double-stranded DNA (dsDNA) are strongly associated with the disease and are increasingly regarded as important players in the pathogenesis. We recently found that some of these antibodies are not truly specific for dsDNA due to a flaw in a method (dsDNA ELISA) used commonly for their detection. This flaw has not been noted previously and we suspect that some of the antibodies thus misidentified may just be as common and important in SLE as the anti-dsDNA antibodies. One such antibody that we found and focus on in this proposal is specific for the guanine base (or guanosine) in the DNA molecule. We found that this particular antibody actually recognizes guanosine-triphosphate

(GTP) rather than guanine or guanosine itself, and that it could penetrate a certain type of human cells we keep in culture in our laboratory, suggesting it may be induced by substances other than DNA and it may be biologically important. We want to know more about such antibodies, including how prevalent these are in our SLE patients, how they might be generated, and what biological functions they might have. The knowledge gained will be very useful to rheumatologists, immunologists and cell biologists. (MD04634)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
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2002-03	Functional Studies of a Putative Peroxisomal Regulating Gene, BRE - Its Roles in Cellular Survival, Immune System and Tumorigenicity (CU02090) ✍ CHUI Yiu Loon • CHAN Yeuk Hon John* • CHING Kar Keung • LEE Ka Ho Kenneth (Anatomy)
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2003-04	Investigation of <i>BRE</i> as a Gene Affecting Tumor Growth and Metastasis (MD03382)
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✍ CHUI Yiu Loon • CHING Kar Keung

2002-03	Crystallisation of a Carrier-Specific Antibody and Its Reconstruction as a Bona Fide Antibody Fragment (CU02092)
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✍ LIM Pak Leong • SUTTON Brian*

2003-04	Development of Specific Immunotherapeutics and Rapid Immunodiagnostics for Severe Acute Respiratory Syndrome (CU03527)
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✍ LIM Pak Leong • CHAN Kay Sheung Paul (Microbiology) • LEUNG Tze Ming • TAM Siu Lun John (Microbiology)#

RESEARCH PROJECTS

Colourful and Bright Fruits and Vegetables Project - Creating a Supportive Eating Environment for New Generation

✍ HO Man • LEE Albert (Community and Family Medicine) • KEUNG Mei Wan • Chow Chun Pong*

☐ 1 June 2005

❖ Health Care & Promotion Fund

Insufficient consumption of fruits and vegetables is identified by the World Health Report 2002 to be one of the top five leading global disease burden risk factors. The aims of this project is to help primary school children in Hong Kong adopt a habit of eating

enough fruits and vegetables by creating a supportive school eating environment to enhance awareness, change behaviour and support good practices. An integrated approach, entailing improved school eating policies and environment, training of teachers and parents, involvement of family and community, along with a comprehensive nutrition education programme and the active participation of students will be used to achieve the aims. It is an 18-months pilot project in which 11 primary schools of around 20,000 students, parents and teachers will benefit from the project. After that, the deliverables of the project will become valuable resources and experience for the benefits of potentially all schools in Hong Kong to create a bright and healthier new generation.

(MD04397)

RESEARCH PROJECTS

Transcriptional and Functional Regulation of TBX3 in Retina Formation

✍ HE Mingliang • KUNG Hsiang Fu • PENG Ying* • RAO Yi*

📅 1 December 2003

❖ Research Grants Council (Earmarked Grants)

T-box (Tbx) genes play an essential role in organogenesis during embryonic development. TBX3 is a vital molecule, since firstly it causes Ulnar-mammary syndrome (UMS) in patients heterozygous for apparent loss-of-function alleles; and secondly, it causes inhibition of cell senescence, and facilitation of cell transformation through myc/ras-p19^{ARF}-p53 pathway. Accumulated data has shown that TBX3 is a downstream target of BMP4. However, how BMP4 regulates the function of TBX3 is unclear. We have recently demonstrated that TBX3 represses gene transcription in mammalian cells and in *Xenopus* embryos (He et al, 1999), and inhibits ventral retina formation (Wong et al., 2002). We recently cloned 13-kb genomic DNA containing the first open reading frame (ORF) of Xtbx3 and 5'-flanking sequence, and we identified a 420-bp region with strong promoter activity in the retina precursor cells of *Xenopus* embryos, which contains conserved API and E2F1 binding sites. We also discovered that E2F1 can act as a transcription repressor that is independent of pRB to repress TBX3 promoter in culture cells, and isolated TBX3 interacting proteins, which can block the TBX3 transcription repression activity.

In this study, we intend to extend our previous work to further characterize TBX3 promoter and identify

the elements responsible for retina formation. Moreover, we will elucidate its role and relationship with other molecules (BMP4, jun/fos, E2F1, pRB) in the BMP4-pRB-p53 signaling pathway. Finally, we will characterize the common as well as distinct functions of TBX3 and TBX2 for retina formation. The principles garnered from this study should lead to a better understanding the mechanism of retina formation, Lunar-mammary syndrome, and human cancer.

(BS03524)

The Mechanisms of a Novel HCC-associated Oncogene (HCAO) in Hepatocellular Carcinogenesis

✍ HE Mingliang • KUNG Hsiang Fu • LI Tsai Ping*

📅 1 January 2005

❖ Research Grants Council (Earmarked Grants)

Liver cancer is one of the most frequent and malignant diseases worldwide, especially in Hong Kong and China. The molecular mechanisms of hepatocarcinogenesis are poorly understood. We previously identified a hepatocellular carcinoma (HCC) associated oncogene (HCAO), which is highly expressed in HCC tissue specimens and HCC cell lines but not expressed in normal liver tissues. We recently revealed that HCAO is a transcriptional repressor/co-repressor and identified a portable repressor domain. Our preliminary data also showed that silencing HCAO expression by shRNA or overexpression of dominant-negative (DN) HCAO in HCC line (BEL7404) blocked tumor formation in nude mice. One of the possibilities of the inhibition of tumor formation by shRNA or DN-HCAO may be a consequence of elevated p16^{INK4a} expression.

We propose to extend our current study to further characterize the role and mechanism of HCAO in cell proliferation, cell division, cell cycle control, apoptosis, and tumorigenesis. We will investigate the signaling pathways mediated by HCAO, especially focus on HCAO/p16^{INK4a}/pRB pathway. We will also identify the interacting proteins of HCAO and characterize their functions in hepatocarcinogenesis. Knowledge gained from this study should lead to a better understanding the mechanism of hepatocarcinogenesis and may result in discovery of new therapeutic targets for HCC.

(BL04361)

Development of Interfering RNA Agents to Inhibit SARS Associated Coronavirus Infection and Replication

✍ HE Mingliang

□ 1 March 2005

❖ Research Fund for the Control of Infectious Diseases - Health, Welfare and Food Bureau

Severe acute respiratory syndrome (SARS) recently emerged as a human disease associated with pneumonia. The virus spread to more than 30 countries and caused disease in more than 8100 patients across five continents, including Hong Kong this year. A novel coronavirus (SCoV) was identified as the etiological agent of SARS, and the virus causes a similar disease in cynomolgous macaques. We have developed siRNAs targeting on the conserved replicase 1A region, which blocked SCoV infection and replication (He et al, JAMA, in press). Although the precise functions of other four structure genes (S, E, M, and N) have not been well characterized, it is proposed that they are important for host cell entry and virion morphogenesis and release. All the four structural genes have unique

roles in the structure, infection and replication of the SARS-CoV. Therefore, we propose that they are also potentially good targets for gene silencing by siRNAs. Furthermore, since these siRNAs are targeting different SARS genes, when combined together, they would have synergistic effects. Here we propose (1) to design more siRNAs to knock-down the four structural genes; (2) to test their effects in the inhibition of SARS infection and replication in vitro in the monkey kidney (FRhk-4 cells) cell culture system; (3) to elucidate their half-life and dose response; (4) test the potential combinational synergistic antiviral effects of different siRNA; (5) to test the potential synergistic effect of siRNA in combination with other known therapeutic agents; and (6) to develop recombinant Adenovirus (rAd) gene delivery system for the expression of shRNAs to combat SARS coronavirus infection.

(BL04674)

Molecular Basis of MAD1 Mitotic Checkpoint Functions in Mammalian Cells

✍ KUNG Hsiang Fu • Jin Dong Yan*

□ 1 September 2000

❖ Research Grants Council (Earmarked Grants)

Cell cycle checkpoints in eukaryotes are highly conserved regulatory pathways that ensure the orderly and faithful progression of critical events. Checkpoints arrest the cell cycle in response to damage, thereby either providing time for repair or inducing apoptosis to eliminate unrepairable cells. Loss of checkpoint results in genetic instability, which is a hallmark of cancers. In addition to DNA checkpoints, there exists a mitotic checkpoint, which prevents onset of anaphase until all chromosomes are properly aligned. Recently, we have identified and characterized human MAD1, a central component of

the mitotic checkpoint. The proposed studies are designed to investigate the molecular basis of MAD1 functions in mammalian cells. Specifically, we will isolate and characterize isotypes and subtypes of human and mouse MAD1, analyze the MAD1 promoter and its regulatory elements, compare MAD1 expression profiles in normal and checkpoint-defective cells, define the phenotypes induced by forced overexpression of MAD1, identify and characterize the upstream regulator (p53 as one candidate) and downstream effector (CDC20 and related proteins as candidates) of MAD1, and investigate the integration of MAD1 functions with the programs of cell proliferation and cell death (apoptosis). These studies will provide novel insights into checkpoint control as well as the anti-proliferative mechanisms of checkpoint-targeting chemotherapeutic agents.

(BL00921)

Study of a Novel Pathway that Links Small G Protein to Neuronal Differentiation-Regulation of the Neuronal cdc-2-like Kinase by Chimaerin

✍ KUNG Hsiang Fu • CHING Yick Pang*

📅 31 December 2001

❖ Research Grants Council (Earmarked Grants)

Neuronal cdc2-like kinase (Nclk) has been shown to play an important role in neuronal differentiation, neuro-cytoskeleton dynamics, and neurite extension. Aberrant of Nclk activity has been implicated in a number of neurodegenerative diseases including Alzheimer's disease. Nclk consists of a catalytic subunit, called cyclin dependent protein kinase 5 (Cdk5), and a 25 kDa regulatory subunit derived proteolytically from a 35 kDa neuronal-specific protein, called neuronal Cdk5 activator (Nck5a). Although Cdk5 protein exists ubiquitously, Nclk

activity can only be found in brain because of the restricted expression of Nck5a. This suggests that Nck5a is the crucial modulator for the Nclk activity. Since little is known about the regulation of Nclk, we therefore perform a search for proteins that specifically interact with the p35 activator. Using the yeast two-hybrid screen approach, several proteins have been discovered in a human brain cDNA library. One of the isolated clones encodes a partial sequence of chimaerin, which is a GTPase-activating protein (GAP) specific for the GTPase Rho family members Rac and Cdc42. The Rho family of GTPases is well documented for their involvement in cell growth, proliferation, and change in morphology. To dissect the pathway regulated by this specific interaction, we will introduce specific proteins, such as chimaerin, Nck5a, Cdk5a, Rac, Cdc42, Rho, PAK and their mutants, into neuronal and fibroblast cells by microinjection and liposome-mediated transfection. Biochemical analysis will also be performed to investigate how chimaerin binds to Nclk and how this interaction affects their enzymatic activities. These studies will define the regulation of Nclk by chimaerin, which may have an impact on understanding the pathogenesis of Alzheimer's disease.

(MD01519)

Molecular Basis for the Telomere Dysfunction and Anti-Tumor Activities of a C-terminal Polypeptide of Human Telomerase Reverse Transcriptase (hTERTC27)

✍ KUNG Hsiang Fu • WONG Chun Yu Benjamin* • LIN Chia Mi Marie*

📅 1 December 2003

❖ Research Grants Council (Earmarked Grants)

The C-terminus of telomerase reverse transcriptase (hTERT) has been shown to participate in the nuclear translocation of TERT through interaction with the 14-3-3 proteins. Recent studies have also suggested that it may play a role in the telomere maintenance. To characterize the function of the C-terminus of hTERT in telomere maintenance and tumorigenesis, we have constructed a plasmid expressing the C-terminal 27 kDa polypeptide of hTERT (hTERT C27) and showed that the expression of this polypeptide alone causes a defect of telomere maintenance in hTERT positive HeLa cells. In this application, we will further elucidate the underlying mechanisms, characterize the corresponding structure domains, identify the hTERT C-terminus interacting proteins, and finally we will test the anti-tumor activity of hTERT C27 in vivo in animal models of solid tumors. Information gained from this study will significantly enhance our knowledge regarding the role of the C-terminus of hTERT in tumorigenesis and in telomere maintenance. Furthermore, this suggests a new strategy for cancer therapy by the induction of telomere dysfunction in cancer cells without affecting the telomerase enzymatic activity. (MD03854)

Functional Characterization of Makorin-2 and Its Interacting Proteins in *Xenopus* Embryonic Development

✍ KUNG Hsiang Fu • PENG Ying* • HE Mingliang • LIN Chia Mi Marie* • CHEN Zhu*
• ZHANG Qing Hua* • HUANG Qiu Hua*

☐ 30 May 2004

❖ NSFC/RGC Joint Research Scheme

The highly orchestrated process of blood cell development and homeostasis is termed “hematopoiesis”. Understanding the biology of

hematopoiesis is important to developing improved treatments for hematologic malignancies, congenital disorders, chemotherapy-related cytopenias, and blood and marrow transplants. Our team has previously cataloged the expressed sequence tags (ESTs) from cDNA libraries of CD34+ Hematopoietic Stem/Progenitor Cell populations (Zhang et al., 2000) and identified over three hundred novel genes. One of the genes, HSPC070 (also named Makorin-2), contains domains implicated in protein-protein interactions and ubiquitin ligase activity. More importantly, microinjection of the mRNA encoding human makorin-2 into the *Xenopus* embryos produced tadpole with enhanced hematopoiesis and suppressed neural development. Our laboratory has cloned the *Xenopus* homologue of Makorin-2 (Xmakorin-2) and confirmed its biological activity in *Xenopus* hematopoiesis and neural development. The present proposal seeks to characterize the functions of Xmakorin-2 and to identify its interacting proteins in *Xenopus* neurogenesis and hematopoiesis. We will further study their roles in *Xenopus* embryonic development by gain of function and loss of function studies, and identify the signal transduction pathways involved in the regulation of hematopoiesis/neurogenesis by constructing various mutant genes. Information gained will significantly enrich our understanding of the molecular mechanisms that regulate hematopoiesis and neurogenesis.

(BL03394)

Characterizing the Role of PI3K Signaling Cascade in *Xenopus* Neural Induction

✍ KUNG Hsiang Fu • PENG Ying* • LIN Chia Mi Marie*

☐ 1 January 2005

❖ Research Grants Council (Earmarked Grants)

Our laboratory has a long term interest in studying the roles of BMP4 and FGF in the regulation of *Xenopus* neural development. Recently, we found that phosphatidylinositol 3-kinase (PI3K) is an important neural induction signal and that over-expression of PI3K in *Xenopus* embryos can produce double heads phenotype in tadpoles. In this project, we aim to further characterize the role of PI3K signal cascade in neural induction. To achieve this aim, we plan to conduct experiments to identify and characterize the neural induction signals upstream and downstream of PI3K, in particular the Akt and GSK signaling molecules, and to elucidate the target neural genes. In addition, the potential cross talks between PI3K and Wnt signals in the regulation of *Xenopus* neural development will be examined. Information gained from this study will enhance our understanding of the complex system of neural-promoting and neural-blocking factors, and how they activate the neurogenic genes or genes that regulate neural development.

(BL04767)

Research and Development of a New TCM-Based Antidepressant

✍ KUNG Hsiang Fu • KONG Lingdong • LU Xiaobo

📅 16 March 2005

❖ Hong Kong Jockey Club Institute of Chinese Medicine Limited

Depression, a common psychological disease normally associated with other diseases, severely influences patients' physical and mental health. The mechanism that causes depression is very complex. Depression is always associated with disorders of central nervous system, neuronal-endocrine system, and immune system. Currently available commercial drugs usually only act at one effective site and very often come with undesirable side-effects. Clinically, there is no ideal drug for anti-depression. However, cocktail drugs based on traditional Chinese medicine (TCM) theory have been promising in treating some mental diseases, such as depression therapies. Therefore, it is time now to develop new antidepressant drugs with high safety and efficacy from traditional Chinese drugs using modern molecular biology techniques. Objective of this project is to obtain solid data for the application of new TCM drug for clinical trial in accordance with the FSDA Application in China which will lead to the issuance of a license for clinical trial.

(MD04822)