

RESEARCH PROJECTS

Evaluation of Nitrous Oxide in the Gas Mixture for Anesthesia

✍ CHAN Matthew Tak Vai • GIN Tony

☐ 1 July 2003

❖ CUHK Research Committee Funding (Direct Grants)

There are some compelling reasons to question the routine use of nitrous oxide (N₂O) during anesthesia. Despite being the first anesthetic drug introduced, and still widely used, there is sufficient doubt as to the risk-benefit profile. Previous experiments suggested that N₂O exposure impairs methionine synthetase and consequently DNA production. Therefore, potential immunosuppression, anemia and hyperhomocystinemia associated with N₂O may increase wound infection, sepsis and cardiac morbidity. This is most likely to be a problem with sick patients after long (>2 hours) surgical exposure. We plan to compare the incidence of adverse outcomes after anesthesia with and without N₂O. We will also correlate the plasma folate and homocysteine concentrations with adverse anesthetic outcomes. When considering its widespread use in more than 75% of all surgery around the world, any difference in outcome would have major implications for healthcare delivery.

(MD03569)

External Cephalic Version for Breech Presentation : A Randomised Controlled Trial of Anaesthetic Interventions

✍ KHAW Kim Sun • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Tak Yeung (Dept of Obstetrics & Gynaecology) • NGAN KEE Warwick Dean

☐ 1 December 2003

❖ Research Grants Council (Earmarked Grants)

Breech presentation places a fetus at increased risk from vaginal delivery, and the outcome is improved by planned caesarean delivery. External cephalic version (ECV) would substantially reduce the need for cesarean delivery, which is associated with increased maternal morbidity. ECV converts breech to cephalic presentation through application of external force over the maternal abdomen. Success rates ranged from 35-86%, and factors limiting further attempts include maternal discomfort, and obstetrician's concerns of fetal injury from using excessive force.

Regional anaesthesia has been shown to improve success rates of ECV, although the mechanism by which it helps is uncertain, and may be (1) analgesia, or (2) muscle relaxation of the abdomen. The issue is whether analgesia or muscle relaxation is more important for ECV. This is crucial because if it is just analgesia, then less invasive methods such as intravenous (3) analgesia may produce comparable analgesia, and thus success rate as good as regional anaesthesia.

Although it has been suggested that a greater force may have been applied during ECV under regional anaesthesia thus potentially risking fetal injury, there is no published literature to scientifically address this controversy. This issue will be answered in our study.

Our objectives in this prospective randomized blinded control study are to compare the outcome and effects of using (A) intravenous analgesia or (B) spinal anaesthesia for primary and reattempts of ECV

at term. Secondary objectives are comparisons of the effects on the fetus, mechanical forces used, pain and side effects during ECV. The conclusion will define the role of using IV analgesia and spinal anaesthesia for ECV, and establish guidelines that are not available in current literature.

(CU03405)

The Effect of Vasopressor Choice on Fetal Acid-base Status During Spinal Anaesthesia for Emergency Caesarean Section

✉ NGAN KEE Warwick Dean • KHAW Kim Sun
• LAU Tze Kin (Dept of Obstetrics & Gynaecology)

□ 30 June 2004

❖ Research Grants Council (Earmarked Grants)

Spinal anaesthesia is commonly used for Caesarean section because it avoids the dangers of general anaesthesia in pregnancy. However, it has potential side effects, particularly hypotension which has been associated with fetal acidosis. This may be exacerbated by the use of ephedrine, the standard recommended vasopressor, to maintain maternal blood pressure. Our previous work in elective cases showed that fetal acidosis was decreased by the use of alpha agonists such as phenylephrine and metaraminol. However, the clinical significance of this finding is uncertain in patients having planned elective Caesarean sections in which neonatal outcome is normally expected to be good regardless of the anaesthetic technique used. The current proposal is an extension of our previous work to emergency cases. In emergency Caesarean section: 1) The optimal vasopressor has not been investigated and 2) Biochemical differences in outcome may be more clinically important in the face of pre-existing fetal compromise.

This study will be a prospective, randomized double-blinded controlled trial of phenylephrine (alpha agonist) versus ephedrine (standard control drug) used to maintain maternal blood pressure during spinal anaesthesia for emergency Caesarean section. The main outcome measurement will be neonatal acid-base status, specifically umbilical arterial and venous blood gases and lactate and glucose concentrations. Secondary clinical outcomes that will also be assessed will include neonatal Apgar scores and admission to and progress in the neonatal intensive care unit. The results will provide important information on the optimum management of haemodynamic changes during regional anaesthesia in emergency Caesarean section and thus will have implications for the practice of obstetric anaesthesia.

(CU03406)

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 (Dept of Psychology) • YEUNG Chung Kwong (Dept of Surgery) • LAI Yee Ching Kelly (Dept of 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*
- 2000-01 Evaluation of Two Traditional Chinese Medicine Formulations for the Treatment of the Metabolic Syndrome Regarding Cardiovascular Function and Insulin Sensitivity (CU00134)
✍ CRITCHLEY Lester Augustus Hall • CHAN Chung Ngor Juliana (Dept of Medicine & Therapeutics) • THOMAS Neil G (School of Pharmacy)# • TOMLINSON Brian (Dept of Medicine & Therapeutics)
- 2001-02 Evaluation of Ginseng on Indices of Chronic Stress in Patients with the Metabolic Syndrome (MD01618)
✍ CRITCHLEY Lester Augustus Hall • THOMAS Neil G (School of Pharmacy)# • CRITCHLEY Julian A J H (Dept of Medicine & Therapeutics)#
- 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 (Dept of Medicine & Therapeutics) • LAM Wai Man Wynnie (Dept of Diagnostic Radiology & Organ Imaging) • ARIFI Ahmed A (Dept of Surgery)* • LEE Anna • GIN Tony
- 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 The Effects of Maternal Oxygen Therapy during Emergency Caesarean Section (CU02060)
✍ KHAW Kim Sun • NGAN KEE Warwick Dean • ROGERS Michael Scott (Dept of Obstetrics & Gynaecology) • TAM Wing Hung (Dept of Obstetrics & Gynaecology) • WANG Chi Chiu (Dept of Obstetrics & Gynaecology)
- 2001-02 Randomized Controlled Trial of Remifentanyl at Induction of General Anaesthesia for Caesarean Section (MD01465)

	✍	NGAN KEE Warwick Dean • MA Kwok Chiu (Dept of Paediatrics) • LEE Bee Beng* • KHAW Kim Sun • WONG Sum Yee April • GIN Tony	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*					
2001-02	A	Comparative	Traditional	Dose-response Study of Ropivacaine and Bupivacaine for Epidural Analgesia in the First Stage of Labour (MD01631)			
	✍	NGAN KEE Warwick Dean • LEE Bee Beng • KHAW Kim Sun					

RESEARCH PROJECTS

Multivariate Dependencies Approach in the Prognostic Modelling of Microarray Data Based on CGH Information in Hepatocellular Carcinoma (HCC)

✉ ZEE Chung Ying Benny • WONG Nathalie (Dept of Anatomical & Cellular Pathology) • LEUNG Wai Tong Thomas (Dept of Clinical Oncology)#

☐ 1 September 2003

❖ Research Grants Council (Earmarked Grants)

Hepatocellular Carcinoma (HCC) is a common cancer in Hong Kong and Southeast Asia. Accurate prediction of outcome for patients with HCC would improve patient management, refining treatment options to target population, and permitting more efficient use of resources. In order to obtain a good prognostic model, clinical outcome data alone may not be adequate. The recent development of DNA microarray technology has enabled a quantification of thousands of genes in a single assay. A set of genes may encode proteins required for a particular function and contribute to the prognosis of HCC. However, few studies have taken into account the multivariate nature and potential interaction among the genes during prognostic modeling. The objectives of this project are: 1) to develop prognostic models using gene expression information from DNA microarray data in addition to the clinical prognostic factors for HCC patients; 2) to customize and expand on the statistical methods for the analysis of DNA microarray data.

One of the difficulties in the modeling process is that the number of potential prognostic factors generated

from microarray data, together with other commonly used patient characteristic, increase the dimension of the problem to the extent that conventional statistical methods may not be appropriate. In order to deal with the problem of information overflow in the analysis of microarray data, we developed a multivariate dependencies approach. This approach is based on information from the Comparative Genomic Hybridization (CGH) analysis together with a robust principal-component analysis for dimension reduction of the microarray data to avoid computational difficulties and potential outliers and violation of model assumptions when we are working with high-dimensional data matrix. For the prognostic model, the potential interaction among the genes will be assessed using statistical methods with favorable properties for managing interaction effect. They include regression, recursive partitioning and neural networks. Some of these methods are computer intensive approaches requiring fast computer processing and specific algorithm tailored to the microarray data structure. Statistical and methodological development in this project will make a contribution to the area of quantitative bioinformatics, particularly in the analysis of microarray data with high dimension and with small to moderate sample size.

(CU03469)

Protocol Development for the Safety and Efficacy of Influenza Treatment of PRB Pharmaceuticals

✉ ZEE Chung Ying Benny

☐ 1 November 2003

❖ PRB Pharmaceuticals Inc.

Contract to Development a Randomized Clinical Trial Protocol for Patients with Influenza.

(MD03662)

TCM Research Protocol Review

✍ ZEE Chung Ying Benny

☐ 15 November 2003

❖ Integrated Chinese Medicine Holding Ltd.

Protocol Review for the TCM Research for The House of Yin Yang Holding Limited.
(MD03938)

Protocol Development for a Randomized Clinical Trial to Evaluate the Safety and Efficacy of Letrozole in the Treatment of Premenopausal Women with Hormone Receptor Positive Breast Cancer

✍ ZEE Chung Ying Benny

☐ 1 January 2004

❖ Novartis (Singapore) Pte Ltd

Objectives:

To design a study protocol to evaluate the safety and efficacy of letrozole in the treatment of premenopausal women with hormone receptor positive breast cancer;

To develop a data management plan and provide statistical advice on analysis of the Study

(MD03379)

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"

✍ ZEE Chung Ying Benny

☐ 1 March 2004

❖ PRB Pharmaceuticals Inc.

Planning and documentation:

Design case-report form

Design trial database

Develop data checking programs

Design laboratory test logistic

Verify completeness of the database (patients, visits, pages, and modules)

Verify autoencoding

Verify SAE reconciliation

Complete database quality control (including CRF to database sampling)

Prepare randomization list

Unblind the project database and generate the unblind listing

Designing tables and listings

Program and test tables and listings for general reports

Create and verify derived datasets for reporting

Generate tables and listings

Generate interim study report

Programming specifications and quality control test plans for tables/listings/graphs/analyses

Tables/listings/graphs

Document all SAS codes used in their production

Data management

To ensure that data entry and processing occurs in an ongoing fashion

Collect CRF from centers

Enter CRF to computer

Data Validation

Reconciliation of Serious Adverse Experiences (SAEs)

All laboratory data will be received, stored, verified and incorporated into the trial database.

Review Database for Completeness: CUHK will ensure that the subjects in the database accurately reflect the subjects enrolled in the study.

Finalize Data Extracts: CUHK will verify that the extraction programs have properly extracted the correct data to the specified format and that the extracted data accurately reflects the data in the project database.

Finalize SAE Reconciliation: CUHK will ensure that any discrepancies resulting from the reconciliation of the SAE database and the project database have been identified and addressed.

Statistical Report

Provide discussion on design and methods used in the analysis

Results

Sponsor will be responsible to provide additional supports, transportation, equipment and information at no cost or charge to CUHK to enable CUHK to perform the Service if necessary.

(MD03637)

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

Edition	Title/Investigators
2002-03	Multivariate Dependencies Approach in the Prognostic Medelling of Microarray Data Based on CGH Information in Hepatocellular Carcinoma (HCC) (MD02412) ✍ ZEE Chung Ying Benny • WONG Nathalie (Dept of Anatomical & Cellular Pathology) • JOHNSON Philip*
2002-03	Hong Kong Emesis Registry (MD02596) ✍ ZEE Chung Ying Benny

RESEARCH PROJECTS

Interleukin-10 Gene Polymorphisms in Malignancies Associated with Infectious Agents in Hong Kong

✉ CHAN Bik Wan • CHAN Wing Yee • LEI Ieng Kit Kenny (Dept of Clinical Oncology)

☐ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

A link between cancer and inflammation has long been postulated. It is known that some people launch a stronger inflammatory reaction to infections than others. Genetic variability in the ability to produce a key immune system protein, IL-10 has not been determined in the general population or patients with infectious disease in Hong Kong. We propose to study 1) The frequency of various polymorphisms of the IL-10 gene, including some that have not been examined previously, in the general population in Hong Kong, 2) The relationship of these polymorphisms to IL-10 production and compare them with the Western data, 3) The frequency of different IL-10 polymorphisms in cancer patients and in non-cancerous individuals with EBV or HP infections. As EBV and HP infect most of the population, it is not possible to watch over all infected individuals. By identifying polymorphisms associated with predisposition to the cancers, those at risk could be identified and watched closely. Early detection of cancer usually means more chance of cure.

(CU03408)

Genomic Aberrations of Squamous Cell Carcinoma of Larynx Associated with Tumor Progression

✉ CHAN Bik Wan • LO Wing Ip Anthony • TSANG King Yin Raymond (Dept of Surgery)

☐ 1 December 2003

❖ CUHK Research Committee Funding (Direct Grants)

Squamous cell carcinoma (SCC) of larynx is the most common malignancies in the heterogeneous group of SCC of head and neck (HNSCC). Earlier stage of the tumor is associated with better survival. A wide spectrum of morphological changes of tumor is paralleled by accumulation of chromosomal aberrations. Genetic studies on HNSCC using cytogenetic analysis, and especially comparative genomic hybridization (CGH), showed that a number of chromosome regions consistently demonstrated chromosomal aberrations.

Using CGH analysis, it is possible to obtain comprehensive information of genome-wide chromosomal aberrations associated with tumor progression such as staging, histological grades and prognosis. Such data may assist in identifying biological prognostic parameters that could in the future be used as a basis for patient counseling and therapeutic decisions. It may also help to identify important steps in carcinogenesis.

However, until now research has been concentrated on oral cavity tumor rather than larynx, although the latter comprise the majority of HNSCC. Knowledge of chromosomal abnormalities in this subgroup of HNSCC and clinical relevance of the genomic aberrations are relatively limited.

This study proposes to investigate the genome-wide chromosomal aberrations in SCC of larynx by means of CGH analysis. By comparing the genomic

aberrations identified in different stages of tumor, we intend to identify changes in chromosomal abnormalities associated with progress of tumor.

(MD03328)

Comprehensive Characterization of Common Amplicons in Nasopharyngeal Carcinoma

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

□ 1 September 2003

❖ Research Grants Council (Earmarked Grants)

Our comprehensive genome-wide studies have defined multiple tumor suppressor loci on chromosomes 3p, 9p, 11q, 13q, 14q and 16q and identified several critical genes involving in NPC tumorigenesis. These studies have also revealed recurrent amplification of multiple chromosomal regions, including 1q, 3q, 8q, 11q, 12, 17q and 20q in NPC. We hypothesize that the oncogenes in these regions are critical targets for activation in initiation and progression of NPC. In the present proposal, we aim to delineate the common amplicons in NPC genome and thereby to identify the NPC-associated oncogenes. By using the high-density genomic arrays containing 3000 BAC clones, copy number aberrations will be systematically investigated throughout the genome of a large panel of NPC samples at high-resolution. The comprehensive approaches will characterize the recurrent amplicons in NPC genome and identify the chromosomal aberrations correlated with disease status and tumor progression. We will also focus our effort on the identification and characterization of the target oncogene(s) on the most frequent amplification region. Quantitative analysis of the copy number

and expression level of all genes/transcripts within the amplicon core will identify the candidate oncogene(s) implicated in NPC tumorigenesis. Studies of oncogenic properties of this target gene in nasopharyngeal epithelial cells will confirm its critical roles in NPC development. The results will contribute to a much better understanding of the molecular pathogenesis of NPC. The oncogenes identified in this study will be target(s) for the development of more effective diagnostic strategies and anticancer therapeutics for this common Asian cancer.

(CU03410)

Antitumor Effects of Histone Deacetylase Inhibitors in Epstein-Barr Virus-positive Nasopharyngeal Carcinoma

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

□ 1 September 2003

❖ CUHK Research Committee Funding (Direct Grants)

Epigenetic alterations including DNA methylation and histone modification play important roles in the tumorigenesis of human cancers. Current studies of antisense or drugs targeting for these molecular events show promising results for the development of efficient therapeutic strategies. Inhibitors of histone deacetylase (HDAC) induce histone acetylation and reactive expression of cellular genes including several important tumor suppressor genes (e.g. *p21*) in cancer cells. *In vitro* and *in vivo* studies have demonstrated potent antitumor activities in human cancers. These compounds inhibit proliferation, induce apoptosis, and/or cell differentiation in cancer cells but not in normal cells. HDAC inhibitors are also to activate the EBV lytic genes in

EBV-associated cancers and induction of the lytic form of EBV infection could potentially result in death of the tumor cell. Based on these exciting findings, we hypothesize that the HDAC inhibitors are potential anticancer drugs for NPC and these compound have significantly higher antitumor effect in the EBV-positive tumors than that of the EBV-negative tumors. In the present study, we aim to evaluate the anticancer effect of histone deacetylase (HADC) inhibitors on the EBV-positive and -negative nasopharyngeal carcinoma cells and to assess the global effect of HDAC inhibition on the expression of viral and cellular genes in this cancer.

(MD03393)

The Role of Pif1 DNA Helicase Homolog in Telomere Maintenance and Chromosome Stability in Mammalian Cells

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

□ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

Telomere is an important nucleoprotein structure protecting the ends of the chromosomes and maintaining chromosome stability. Dysfunction of the telomere is thought to be important in the aging process and cancers. Telomerase, the enzyme that add telomere to chromosome ends during DNA replication, has long been regarded as one important way of telomere maintenance. Recently, there is experimental evidence suggests the presence of alternative pathways involving recombination and some other mechanisms. Pif1 DNA helicase was identified in yeast and 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 maintenance of mammalian cells. We have cloned the human and mouse homologs of Pif1. The study will be carried out in two directions: Firstly, inducible expression studies of Pif1 in mammalian cells will allow telomere function to be followed through time in human and mouse cell culture models; and secondly, the yeast two-hybrid system will be employed to study the interaction of Pif1 with other proteins in order to provide further information about this alternative pathway of telomere maintenance. It is anticipated that the study of telomere function and the understanding of the alternative pathway will provide further insight into the aging and cancer process. These results would generate potential targets for drug discovery and rational therapeutic design.

(CU03411)

Isolation of Oligodendroglioma-associated Tumor Suppressor Genes on Chromosome 1p36.3

✉ NG Ho Keung

□ 1 March 2004

❖ CUHK Research Committee Funding (Direct Grants)

Oligodendroglioma is a primary brain tumor that usually affects adults. Unlike other gliomas that are mostly non-responsive to chemotherapy, oligodendroglioma shows remarkable sensitivity to chemotherapeutic treatment. Oligodendroglioma is also characterized by a high incidence of loss of chromosomal arms 1p and 19p, suggesting that these chromosomes carry critical tumor suppressor genes (TSGs) involved in the oncogenesis of oligodendroglioma. Recent studies have shown that

allelic loss (i.e. single copy loss) of 1p is a predictor of chemosensitivity in oligodendroglioma. This finding raises the possibility, for the first time, that genetic marker such as 1p loss may be used in guiding decision on treatment of oligodendroglioma at diagnosis. Although the role of chromosome 1p in chemosensitivity is unknown, the identification of target gene on 1p would provide insights into the tumorigenesis of oligodendroglioma and the molecular basis of chemosensitivity in glioma. We have employed microsatellite analysis to study allelic deletion of 1p and have identified three commonly deleted regions on 1p36.3 in oligodendroglioma. We hypothesize that these regions harbor critical TSGs and biallelic inactivation of these genes is involved in oligodendroglioma development. In this project, we propose to identify the target genes on 1p36.3 using an approach based on the 2-hit model for inactivation of TSGs. The specific aims are: 1) to refine the deletion regions on 1p36.3 and to determine the breakpoints in oligodendroglioma carrying 1p36.3 deletion. 2) to identify genes, CpG islands and promoter regions within the refined deletion regions using bioinformatics tools, and 3) to detect transcript expression changes, somatic mutations, promoter hypermethylation and allelic loss of candidate genes within the deletion regions. Our systematic screening of the complete list of genes in these deletion regions using combined molecular techniques will target the candidate genes on 1p36.3 that are involved in oligodendroglioma. The outcome of this project will provide insights into the molecular pathogenesis of oligodendroglioma, the molecular basis of chemosensitivity and the development of more precise markers for prognosis and better monitoring of chemosensitivity in oligodendroglioma.

(MD03543)

Identification of Multiple Tumor Suppressor Genes on Chromosome 8p21-23.1 in Medulloblastoma

✉ PANG Chung Sean Jesse • NG Ho Keung • POON Wai Sang (Dept of Surgery)

☐ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

Carcinogenesis is a multi-step process in which accumulative genetic alterations, involving inactivation of tumor suppressor genes and activation of oncogenes, lead to uncontrolled cell growth. The short arm of chromosome 8 (8p) is a frequent site of deletions in a variety of human cancers suggesting that 8p carries critical tumor suppressor gene(s). Our group has also identified 8p deletion as one of the common events in the development of medulloblastoma, a childhood brain malignancy. Finer deletion mapping revealed high frequency of deletion at 8p22-23.1 and multiple interstitial deletions at 8p12-8p21. These regions share overlapping areas with deletion regions described in other tumors. More important, a novel region of homozygous deletion was identified at 8p23.1 in medulloblastoma. On the basis of these findings, we hypothesize that these deletion regions harbor critical tumor suppressor genes involved in medulloblastoma. The objectives of this proposal are to identify the putative tumor suppressor gene(s) located on 8p21-23.1 and to elucidate their biological significance in the tumorigenesis of medulloblastoma. This project will screen four known putative tumor suppressor genes (PINX1, LZTS1, DLC1 and N33) and the known and predicted genes that lie in the homozygous deletion region located on 8p21-23.1 for their involvement in medulloblastoma. These genes will be examined for transcript expression patterns, somatic mutation, promoter hypermethylation and

allelic loss. Combined data of these analyses will provide strong indication for the candidacy of tumor suppressor genes. Such genes will be further evaluated for their functional effects on growth, apoptosis and tumorigenicity. This project will provide insights into the tumor suppressor role of chromosome 8p in the molecular pathogenesis of medulloblastoma and other human cancer carrying 8p loss and the potential discovery of novel targets for treatment of medulloblastoma.

(CU03414)

SOCS-1 Hypermethylation in Gastric Cancer, Intestinal Metaplasia and Tumor Suppressor Effect of SOCS-1 in Gastric Cancer

✉ TO Ka Fai • LEUNG Wai Keung (Dept of Medicine & Therapeutics) • CHAN Ka Leung Francis (Dept of Medicine & Therapeutics) • CHAN Wing Yan Michael (Dept of Medicine & Therapeutics)#

□ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Gastric cancer remains the world second most common and highly fatal malignancy. It is estimated that more than 600,000 patients died from gastric cancer each year. *H. pylori* infection is implicated as an important etiological factor and gastric cancer appears evolved from inflammation to pre-cancerous lesion and invasive cancer. Upregulation of cytokine-signaling pathway is common in inflammation and recent studies supported that activation of such pathway, namely IL (interleukin)-JAK/STAT, is linked to malignancy. Moreover, a negative regulator of the cytokine-signaling pathway - SOCS-1 is silenced by gene hypermethylation and is a candidate tumor

suppressor gene in liver cancer. Based on our pilot study, we hypothesises that SOCS-1 may also functioned like tumor suppressor in gastric cancer. We aim to demonstrate the up-regulation of this cytokine-signaling pathway in human gastric cancer tissues and determine the methylation status of SOCS-1 gene in both gastric cancer and its precancerous lesion. The tumor suppressor effect of SOCS-1 will be investigated by transfection study. The results would enhance our understanding of gastric carcinogenesis and provide further insights between inflammation and carcinogenesis. By targeting therapy against such pathway, it opens new treatment strategies for this common fatal disease.

(MD03826)

Characterisation of Genomic Amplicons in Hepatocellular Carcinoma : Targeting Candidate Genes by Array-CGH, Transcriptional Profiling and Functional Study

✉ WONG Nathalie • CHAN Yuen Yee • LAI Bo San Paul (Dept of Surgery) • ZEE Chung Ying Benny (Faculty of Medicine (Planning Office))

□ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

Hepatocellular carcinoma (HCC) is a highly malignant tumour that is prevalent in China including Hong Kong. Correlative analysis of cytogenetic findings with clinical pathologic phenotypes suggested a number of amplicon loci in association with poorer clinical features, particularly drug resistance, metastasis and aggressive tumour variants. While genomic amplification represents one of the major molecular mechanisms by which tumor-promoting oncogenes can be activated, the causative genes in HCC amplicons remained mostly undefined. The aim of this work is to systematically

characterize clinically relevant HCC amplicons for their underlying target genes by the high throughput microarray technology. Using a high-density cDNA array, we propose to elucidate candidate genes, at the genomic DNA level, by the array-based comparative genomic hybridization (CGH). A simultaneous expression array analysis on the same sample, at the RNA level, will also be performed to assess the parallel transcriptional changes, which will be correlated with copy number gains determined from array-CGH in integrative analysis. Potential genes identified will be prioritized according to their significance in primary HCCs and clarified for functional importance in cell lines. Our underlying hypotheses are (1) chromosome amplification can activate oncogene(s) or cancer-related gene(s) critical to the progression of HCC; (2) the intrinsic genetic alterations associated with DNA amplification will lead to an increased gene(s) dose and up-regulation of gene(s) expression. The identification of target genes in amplicon loci could provide basis for future development of biomarkers for the prognosis of HCC.

(CU03467)

Characterization of Drug Resistance Phenotype in Hepatocellular Carcinoma in-vitro Models

✉ WONG Nathalie

☐ 1 April 2004

❖ CUHK Research Committee Funding (Direct Grants)

Hepatocellular carcinoma (HCC) is a highly malignant tumor that is prevalent in China, including Hong Kong. Doxorubicin and analogues are widely used first-line chemotherapeutic agents and has been shown to prolong patient survival with improvement in disease-related symptoms. However, the clinical

behavior of HCC patients in response to doxorubicin and analogues can be variable, and patients often develop drug resistance during the course of treatment. This may be attributed to the difference in genetic properties of the disease. Whilst molecular studies on HCC have indicated recurring sites of genetic alterations, information on drug resistance related genes has been minimal. The goal of our study is to enhance our understanding on the genetic changes that confer cellular chemo-resistance to doxorubicin. To model this insensitive response, we have established doxorubicin-resistant sub-lines through prolonged doxorubicin exposure to HCC cell lines during the past 24 months. These doxorubicin-resistant sub-lines have an elevated IC50 by 12 to 135 folds when compared to their corresponding parental lines. Cell lines represent the ideal resource for our study, since it would not have been possible to utilize surgical tissues. In responding patients, the effect of doxorubicin will not have provided viable cells for genetic and expression analysis, while in non-responding patients curative surgery will unlikely have been offered. We plan to employ the cDNA microarray technology and CGH to the study of deregulated genes and genomic anomalies involved. The insensitivity to doxorubicin in human HCC cell lines is expected to reflect upon the response found in patients. Knowledge of the molecular targets will represent valuable information and provide basis for future research on areas such as pharmacological intervention and development of combined adjuvant chemotherapeutic agents.

(MD03589)

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

Edition	Title/Investigators	Year	Title
2002-03	Interleukin-10 Gene Polymorphisms in Malignancies Associated with Infectious Agents in Hong Kong (MD02338) ✉ CHAN Wing Yee • WHITNEY Bruce Montfort (Hong Kong Cancer Institute)# • LEI Ieng-Kit Kenny (Dept of Clinical Oncology)*	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 (Dept of Clinical Oncology) • TO Ka Fai • TSUI Kwok Wing (Biochemistry)
2000-01	Evaluation and Characterization of a New Composite Biocompatible Skin Graft Incorporated on the Noedermis of Integra in Experimental Burn Wounds (CU00153) ✉ LIEW Choong Tsek • CHAN Sun Yin Eric (Dept of Surgery)# • LAM Ping Kuen (Dept of Surgery)# • LI Hiu Ming (Pathology Teaching Laboratory)	2002-03	High-resolution Array-based Comparative Genomic Hybridization for Diagnosis for Distant Metastases in Nasopharyngeal Carcinoma (MD02640) ✉ LO Kwok Wai • TO Ka Fai • HUI Bik Yu
2002-03	The Investigation of Multiple Mutations in Hepatocellular Carcinoma (CU02066) ✉ LIEW Choong Tsek • LAI Bo San Paul (Dept of Surgery) • LAU Wan Yee Joseph (Dept of Surgery) • LI Hiu Ming (Pathology Teaching Laboratory) • WONG Nathalie	2002-03	Molecular Genetics of Mucopolidosis II (MD02358) ✉ LO Wing Ip Anthony • TANG Leung Sang Nelson (Dept of Chemical Pathology)
2001-02	Characterization of the RASSF1A Gene in Nasopharyngeal Carcinoma (MD01010) ✉ LO Kwok Wai • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute) • TO Ka Fai • TSUI Kwok Wing (Biochemistry)	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 (Dept of Medicine & Therapeutics)# • HOU Jian* • LEI Ieng Kit Kenny (Dept of Clinical Oncology) • LO Kwok Wai • TSANG Kam Sze Kent

- 2002-03 Studies on the Possible Association of ApoE and Receptor Genes with Vascular Dementia in Hong Kong Chinese (CU02069)
 ✉ NG Ho Keung • BAUM Lawrence William (Dept of Medicine & Therapeutics) • CHAN Yu Leung (Dept of Diagnostic Radiology & Organ Imaging) • CHIU Fung Kum Helen (Dept of Psychiatry) • PANG Chi Pui Calvin (Dept of Ophthalmology and Visual Sciences) • WONG Ka Sing Lawrence (Dept of Medicine & Therapeutics)
- 2002-03 High-resolution Genomic Profiling of Medulloblastomas Using Array-based Comparative Genomic Hybridization Analysis (MD02423)
 ✉ NG Ho Keung • HUI Bik Yu • LO Kwok Wai
- 2000-01 Genetic Mechanism of Malignant Progression in Low-grade Astrocytomas (MD00421)
 ✉ PANG Chung Sean Jesse • NG Ho Keung
- 2002-03 Identification of the Medulloblastoma-associated Tumor Suppressor Genes on Chromosome 8p22-23.1 (MD02330)
 ✉ PANG Chung Sean Jesse • NG Ho Keung
- 2002-03 Molecular Alterations in Normal Looking Nasopharyngeal Epithelia - Implication in the Molecular Carcinogenesis of Nasopharyngeal Cancer (NPC) (CU02071)
 ✉ TO Ka Fai • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute) • LO Kwok Wai
- 2001-02 Chromosomal Aberrations in Hepatocellular Carcinoma: A Comprehensive Elucidation by Spectral Karyotyping and Comparative Genomic Hybridisation (MD01044)
 ✉ WONG Nathalie • LAI Bo San Paul (Dept of Surgery) • LEUNG Wai Tong Thomas (Dept of Clinical Oncology)#
- 2002-03 Characterizing Drug Resistance Pattern in Doxorubicin Insensitive Hepatocellular Carcinoma (CU02097)
 ✉ WONG Nathalie • JOHNSON Philip James (Dept of Clinical Oncology) • LAI Bo San Paul (Dept of Surgery) • ZEE Chung Ying Benny (Faculty of Medicine (Planning Office))
- 2002-03 Characterization of Common Chromosome 19 Aberrations in Hepatocellular Carcinoma (MD02999)
 ✉ WONG Nathalie • CHAN Yuen Yee
- 2002-03 Hepatocellular Carcinoma Research Group: Clinical Applications of Functional Genomics (MD02380)
 ✉ WONG Nathalie • LAI Bo San Paul (Dept of Surgery) • POON Y C Randy* • MOK Shu Kam Tony (Dept of Clinical Oncology) • TO Ka Fai • LIEW Choong Tsek • POON Chuen Wai (Dept of

Medicine & Therapeutics) •

JOHNSON Philip J*

RESEARCH PROJECTS

A Study of Carcinogenicity of Estrogen in Prostatic Cells

✉ CHAN Leung Franky

☐ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Epidemiological and animal studies have demonstrated that estrogens are carcinogenic and play an important role in the development of breast and uterine cancers in females. Growing evidences have suggested that estrogens might play a dual role in the initiation and promotion in prostate carcinogenesis. This hypothesis is based on the fragmented bodies of evidences as shown in experimental animal studies and *in vitro* studies of cultured cells. These evidences are summarized as follows: (1) functional estrogen receptors are highly expressed in the rodent and human prostates, suggesting that estrogens can exert direct actions on this gland; (2) direct effects of estrogen on the prostate gland, which may be mediated via estrogen receptors, can be demonstrated in various hormone-induced animal models of prostate cancer and benign prostatic hyperplasia; (3) wide spectrum of pathological lesions, including squamous metaplasia, dysplasia, carcinoma and altered growth of stromal tissues, can be induced in prostates by high levels of exogenous estrogens; (4) perinatal exposure to estrogen in male rodents can lead to permanent alteration in prostatic development and differentiation; (5) estrogens and their metabolites are genotoxic carcinogens and microtubule disrupting agents. However, up to now there is no direct experimental

evidence proving that estrogens are responsible for the initiation of prostate cancer. In order to test the validity of this hypothesis whether estrogens and their carcinogenic metabolites could initiate the prostate carcinogenesis, we used a spontaneously immortalized normal rat prostatic epithelial cell line, NRP-152, which is negative for estrogen receptors, as an *in vitro* model to evaluate whether the natural estrogen 17 β -estradiol (E_2) could initiate the neoplastic transformation in this cell line. The NRP-152 cell line, which was spontaneously immortalized and clonally derived from the dorsolateral prostate of a Lobound-Wistar rat, is an androgen-dependent and non-tumorigenic cell line that retains a normal basal cell phenotype. We expect that through these proposed studies it would help to better understand the role of estrogen in the initiation of prostate cancer.

(MD03875)

Developmental Controls of Axon Patterning in the Retinofugal Pathway of Mouse Embryos

✉ CHAN Sun On

☐ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

In the mouse, retinal axons undergo several changes in fiber arrangement from the optic nerve to the optic tract. These changes in fiber organization are essential for development of normal pattern of neural connections in the visual system. The developmental mechanisms that control such fiber order changes in the mouse retinofugal pathway are the focus of this study. We will investigate the functions of two molecules, sialylated neural cell adhesion molecule (PSA-NCAM) and CD44, which are known to regulate axon growth and provide guidance information to growing axons, on patterning

the fiber orders in the mouse retinofugal pathway. Preliminary findings suggest that PSA-NCAM and CD44 may be involved in formation of partial retinotopic order in the optic tract and crossing of retinal axons at the midline of the chiasm, respectively. In this proposal, we investigate the functions of these molecules and their interactions with extracellular matrix molecules on patterning the axon orders in brain slice preparations of the retinofugal pathway. Changes in partial decussation pattern, age-related order and segregation of axons from dorsal and ventral retina in the chiasm and the tract will be determined after perturbing normal functions of PSA-NCAM or CD44. Furthermore, we will determine whether the fiber order in the optic tract is essential to the formation of retinotopic termination in the visual relay nuclei. Changes in termination patterns of retinal axons in the target nuclei of perinatal mice that have received an early intraventricular injection of PSA-NCAM antibody in utero will be examined. Results of these experiments will provide important insights in to mechanisms that govern axon routing in decision regions of the visual pathway and show how these fiber orders contribute to the map formation in the mammalian visual system.

(CU03417)

Is Abnormal Sacral Neural Crest Cell Migration to the Gut Involved in Aganglionosis : An Investigation Using an Animal Model for Hirschsprung's Disease

✉ CHAN Wood Yee • ALAN J. Burns*

☐ 1 December 2003

❖ Research Grants Council (Earmarked Grants)

Hirschsprung's disease (HD) is the most common type of gastrointestinal motility disorder in the

newborn and is also the most common cause of neonatal obstruction of the colon. The most prominent feature of HD, abnormal dilatation of a segment of the terminal colon, is attributed to a lack or a reduction of parasympathetic enteric ganglia, the neurons and glia of which are both derived from the neural crest during development. Hence, it is generally believed that HD is a developmental disorder related to the abnormal development of neural crest cells. Recent studies on avian embryos have indicated that neural crest cells derived from the sacral level of the neural tube (developing central nervous system) migrate along different pathways and then contribute a significant number of enteric neurons to the hindgut, the region of the gut where aganglionosis is usually detected in the HD patients. In order to establish the role of the mammalian sacral neural crest in enteric ganglia formation in the hindgut, we propose to map the normal spatio-temporal migration of sacral neural crest cells and to determine the anomalies in sacral neural crest cell migration in an animal model for studying HD. We will also investigate the possibility of restoring normal sacral neural crest migration by tissue transplantation.

(CU03418)

Does Deletion of Male Accessory Sex Glands Produce Heritable Changes in Spermatozoa?

✉ CHOW Pak Ham Patricia • ANNE Ferguson-Smith* • O Wai Sum*

☐ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

The production of healthy offspring is the determinant factor in evolutionary success. Male mammals have evolved a complex system of reproductive structures made up of gametes, ducts

and glands that are collectively called the accessory sex glands. Successful artificial intervention of the reproductive process seems to suggest that procreation can be achieved by gametes alone. Thus it is commonly thought that apart from realizing such trivial missions as transferring gametes, attracting the opposite sex or blocking insemination by a second male, accessory sex glands in the male are largely dispensable. However, our past studies provide evidence that non-exposure of sperm to secretions of these glands predisposes to abnormalities in development of embryos such that pregnancy may terminate at any time. Recently the revelation of parental genomic instability and its unfavourable consequence on embryo development has caught the attention of reproductive biologists. Even though modification can be inflicted without altering the structure of genes, the outcome is heritable. Genomic imprinting is the process whereby epigenetic marks are added to chromosomes in such a way that parental alleles are expressed unequally in the offspring. Are accessory sex glands evolved in the male to help stabilize spermatozoan genome? We propose to test this by studying the effects of deletion of these glands on methylation status and expression of some well-studied imprinted genes in sperm and embryo in an *in vivo* rodent model.

(CU03419)

The Role of a Novel TNF- α Modulator Gene (BRE) in Acute Hepatitis

✉ LEE Ka Ho Kenneth • CHAN John* • CHING Kar Keung (Clinical Immunology Unit) • CHUI Yiu Loon (Clinical Immunology Unit)

☐ 31 December 2003

❖ Research Grants Council (Earmarked Grants)

Hepatitis is one of the major diseases affecting Asia. It is very difficult to treat and the exact molecular mechanism involved is still not fully understood. Hepatitis could be induced by a variety of viral and chemical agents and we have used carbon tetrachloride (CC14) to induce acute hepatitis in mice. We discovered a gene called *BRE* that is normally expressed at low levels in the liver and that it could be strongly up-regulated following CC14 insult. We also found that TNF α is correspondingly up-regulated with *BRE*. It is generally acknowledged that TNF and related cytokines play a major role in the pathogenesis of both chemical and viral induced hepatitis - a crucial role in liver inflammation, hepatocyte proliferation, differentiation and apoptosis. Previously, we have established that *BRE* could modulate the effects of TNF α by binding to the juxtamembrane domain of TNFR1. Because of the relationship between *BRE* and TNF, we hypothesized that *BRE* may play an important modulating role in hepatocyte survival, proliferation and death during the acute phase of hepatitis. In this research proposal, we aimed to: (1) determine the inter-relationship between *BRE*, TNF and TNFR1 expressions during acute and chronic hepatitis; (2) establish whether *BRE* is capable of modulating NF κ B and Ap-1 transactivation by TNF α in hepatocytes; and (3) determine the ability of *BRE* to protect the liver from CC14 induced injury. If the outcome of the proposed experiments is positive, then *BRE* could be a potential target for therapeutic drugs in the treatment of liver diseases.

(CU03421)

The Mechanism of Increased Susceptibility to Retinoic Acid Teratogenicity in Diabetic Pregnancy

✉ SHUM Sau Wun Alisa • COPP A J* • WANG

Chi Chiu (Dept of Obstetrics & Gynaecology)

☐ 1 December 2003

❖ Research Grants Council (Earmarked Grants)

The aim of this study is to determine the mechanism that underlies the increased susceptibility of embryos of diabetic mothers to develop malformations, following exposure to the vitamin A bioactive metabolite retinoic acid.

Maternal diabetes is associated with increased risk of spontaneous abortion and congenital malformations in the offspring. Although it is clearly evident that diabetic embryopathy is the result of multifactorial interactions, few attempts have been made to investigate the association between diabetic embryopathy and other factors, such as dietary or drugs intake during pregnancy. We have recently established a mouse model to test the possibility of interaction between maternal diabetes and retinoic acid, a common drug with well-known teratogenic properties. We find that following *in utero* exposure to retinoic acid, embryos of diabetic mice are significantly more susceptible than embryos of non-diabetic mice in developing caudal regression syndrome, a defect that is highly associated with diabetic pregnancy in humans (Chan et al. (2002) *Diabetes* 51:2811-2816). To further investigate the mechanism of this increased susceptibility to malformation, the specific objectives of this proposal are to determine whether maternal diabetes affects: (1) the uptake of retinoic acid into the embryo; (2) the synthesis and metabolism of retinoic acid; (3) the transduction of retinoic acid signal in the embryo.

Results of this study will provide important information on the fundamental processes that are disturbed in diabetic embryopathy, and pave the way for deriving preventive measures.

(CU03397)

Personality Traits and Substance Abuse - A Case/Control Association Study on Receptor Gene Polymorphisms in Chinese Psychostimulant Users

✉ STADLIN Alfreda • LEUNG Yiu Kin Freedom
(Dept of Psychology)

☐ 1 August 2003

❖ CUHK Research Committee Funding (Direct Grants)

Ketamine, 3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy') and methamphetamine (METH, 'ice') are psychostimulants that are widely abused in the world. In Hong Kong, ketamine, MDMA and METH are popular recreational drugs, particularly used by young people in the 'rave' parties/discos. Prevalence for ketamine and MDMA use in Hong Kong has dramatically escalated over the last few years. With its emerging popularity also in China, their use causes a great concern to the Hong Kong community.

At present, a number of candidate genes have been shown to be associated with certain personality traits and the risk of substance abuse. They include the DRD4 genes associated with opioid-dependence and 'novelty seeking' behavior; the 5-HT1B, MAO-A, and GABAA γ 2 genes linked to alcoholism and antisocial behavior as well as the DRD2 gene linked to 'harm avoidance' and 'novelty seeking' behavior and severe alcoholism, polysubstance abuse, cocaine addiction and smoking. COMT and 5-HTTPR polymorphisms were also shown to be associated with 'harm avoidance' behavior and alcoholism. At present, the genetic factors linking the personality traits and psychostimulant use has not yet been explored. This study aims to establish an association between the aforementioned genetic markers of personality trait and psychostimulant use.

Self-report measures of ‘novelty seeking’ and ‘harm avoidance’ behavioral traits will be conducted in 200 ketamine, MDMA and/or METH users and 20 age- and sex-matched controls recruited from various social service agencies in Hong Kong. DNA will be obtained from these subjects and genotyped using the PCR-RFLP technique. The correlation between gene variants, personality traits and the pattern/extent of drug use can perhaps act as predictors of drug-taking behavior, thus will aid in the development of better behavioural therapies for the treatment and prevention of psychostimulant use.

(MD03520)

Characterization of the Metabolic Events Associated with Ocular Enlargement in the Black Moor Goldfish

✉ YE W Tai Wai David • TSANG David Sau Cheuk (Biochemistry)

☐ 1 November 2003

❖ CUHK Research Committee Funding (Direct Grants)

In most animals, the eyes stop enlarging once its growth reaches a certain volume. The basic mechanism for this phenomenon is unknown. Black Moor goldfish is a mutant strain of goldfish (*Carassius auratus*) in which the eyes keep on expanding in size as the fish grows older, resulting in eyes as large as 4 ml in volume, while the volume of the common goldfish does not grow larger than 0.4 ml. Our previous studies found that the eyes of Black Moor goldfish possessed few morphological abnormalities apart from a thinner retina and being myopic. More recently, we detected a close association between ocular volume and high concentration of lactic acid in the aqueous and vitreous humour of the Black Moor goldfish. This

relationship was not observed in the common goldfish. In this study, we intend to analyze the mechanism associated with ocular enlargement, particularly the metabolic pathways leading to the concentrations of lactic acid and the parameters to be determined include glucose, lactic acid, hexokinase and phosphorylase in the eyes and blood of Black Moor goldfish and common goldfish. A thorough understanding of the metabolic events associated with continuous eye expansion in Black Moor goldfish should help to delineate the underlying mechanisms responsible for the giant eyes in this strain of goldfish as well as providing further insights into myopia.

(MD03750)

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

Edition	Title/Investigators
2000-01	An Expression and Functional Study of a Prostatic Secretory Protein of 94 Amino Acids in Normal and Neoplastic Rat Prostate Glands (CU00131) ✉ CHAN Leung Franky
2002-03	Gene Expression Analysis of an Orphan Nuclear Receptor, Estrogen Receptor-related Receptor (ERR), and Its Isoforms in Human Prostate Cancer (MD02345) ✉ CHAN Leung Franky • CHEN Shiuan*
2002-03	The Roles of Cell Adhesion Molecules on Patterning Axon Orders in the

	Retinofugal Pathway of Mouse Embryos (MD02573) ✉ CHAN Sun On	Ribosome-inactivating Proteins (MD02326) ✉ KWONG Wing Hang • NG Tzi Bun (Biochemistry) • LEE Ka Ho Kenneth
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 Cloning, Sequencing and Biological Characterization of an Immunomodulatory Fungal Protein (CU00125) ✉ LIU Wing Keung Ken • NG Tzi Bun (Biochemistry)
2002-03	The Roles of DOC-2/Dab2 in Cortical Development (MD02775) ✉ CHAN Wood Yee • YEW Tai Wai David	2000-01 Genes and Heroin Addiction in the Chinese Population: Association Studies on Receptor Gene (MD98904) ✉ STADLIN Alfreda • LEE Tak Shing Dominic (Dept of Psychiatry) • TANG Leung Sang Nelson (Dept of Chemical Pathology) • LOH El-Wui* • CHEN Chih Ken* • CHAN Pui* • CH'IENT James*
2001-02	A Study on the Use of Sertoli Cells to Promote Retinal Ganglion Cell Regeneration (MD01017) ✉ CHO Yu Pang Eric	2001-02 Glial Immune Response After METH ('Ice') or MDMA ('Ecstasy') Treatment (MD01546) ✉ STADLIN Alfreda • CHANG Chuen Chung Ryamong* • FENG Zhe Hui*
2002-03	Does Deletion of Male Accessory Sex Glands Produce Heritable Changes in Spermatozoa? (MD02605) ✉ CHOW Pak Ham Patricia • O Wai Sum* • FERGUSON-Smith A*	2001-02 Cellular Mechanisms of Neuronal Loss During Aging (MD01023) ✉ YEW Tai Wai David • CHAN Wood Yee
2002-03	Offspring of Males without Accessory Sex Glands, Are They Different? (MD02930) ✉ CHOW Pak Ham Patricia	
1999-00	Effects of Ribosome-inactivating Proteins on Motor and Ganglionic Neurons (BL97043) ✉ KWONG Wing Hang	
2002-03	Cellular Mechanism of the Neurotoxicity of Type 1 and Type 2	

RESEARCH PROJECTS

Regulation of Prolactin and Prolactin Receptor Gene Expression

✉ CHAN King Ming • CHENG Hon Ki
Christopher

☐ 1 January 2004

❖ CUHK Research Committee Funding (Direct Grants)

Prolactin (PRL) is a pituitary polypeptide hormone with many important physiological functions in vertebrates. PRL is expressed in numerous extra-pituitary sites in mammals, beyond lactation different bioregulatory functions including immune response, osmoregulation, angiogenesis, development, hair-growth, etc, are related to PRL. Results from this study using goldfish model will provide useful information on the regulation of PRL to exert its different biological functions in general. Most studies on PRL in fish are related to its role in freshwater adaptation migrated from seawater, such as retention of ions and control of Na⁺-K⁺ ATPase, however the basic physiological role of PRL in freshwater fish is not well characterized. Hormonal regulation of gfPRL gene expression in the pituitary will be carried out. We are also interested in the regulation of gene transcription of the gfPRL gene promoter. Seasonal profiles of PRL gene expression in the pituitary and PRL receptor (PRLR) gene expression in different tissues will be investigated; hormonal regulation of PRLR and PRL gene expression *in vivo* will also be examined. Using goldfish as a vertebrate model, the information obtained will be useful in delineation the role and physiological functions of PRL.

(MD03342)

Bioassay-guided Isolation, Characterization, and Mechanistic Study of the Bioactive Components from *Paeonia Lactiflora*, *Sophora Flavescens*, *Oldenlandia Diffusa* and *Scutellaria Barbata* for the Anti-proliferative Effect on Human Hepatoma Cells In Vitro and

✉ FUNG Kwok Pui • KONG Siu Kai
(Biochemistry) • MAK Thomas Chung Wai
(Dept of Chemistry) • TSUI Kwok Wing •
WAYE Mary Miu Yee

☐ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

The main objective of the present research is to identify the *in vitro* and *in vivo* anti-proliferative efficiency and the action mechanisms of four TCM on human hepatoma cells (HepG2 cells): the root of *Paeonia lactiflora*, the root of *Sophora flavescens*, the whole plant of *Oldenlandia diffusa* and the aerial part of *Scutellaria barbata*. Then, guided by the results of antitumor activity, we will isolate, purify and characterize the bioactive components in these four TCM. We will also study the probable circumvention of multidrug resistance of these four TCM and their active components and the mechanisms involved using multidrug-resistant hepatoma cells (HepG2/DR cells) *in vitro* and *in vivo*. Combined treatment is another important aim of this project. We hope to develop a scientific-based strategies in studying the anti-proliferative efficiency on hepatomas cells (HepG2 cells and HepG2/DR cells) when more than two of these TCM are used in combination in one prescription. Since the most common adverse side effects of conventional anti-tumor drugs to the host is cardiotoxicity, the probable toxic effect of the herbs and their active

components, in single or combined treatment, on the heart and liver of the HepG2-cells-bearing mice will be examined. The results of this research are expected to provide a scientific basis for clinical usage of these TCM and the identification of new potential compounds leading to safe and effective drug development for the treatment of hepatoma.

(CU03399)

Functional Characterization of a Novel SNF2/SW12-like Gene and Its Role in Drug Resistance

✉ KWOK Tim Tak

□ 1 November 2003

❖ CUHK Research Committee Funding (Direct Grants)

Cancer is one of the leading “death-causing-diseases” in Hong Kong and in many other countries. The common ways of cancer therapy include chemotherapy while the outcome is not always satisfactory. Development of anticancer drug resistance in cancer cells is believed to be one of the major causes for treatment failure. The mechanisms that led to drug resistance are complicated and some of those are still not clear. Therefore, the study of identification and characterization of drug resistance associated genes is important and is of potential benefit to cancer patients including those prevalent in Hong Kong. In the course of examining the doxorubicin resistance in human cancer cells, a novel gene was found to be over-expressed in cells demonstrated drug resistance and the gene appeared to be regulated by tumor suppressor p53 gene. The aim of this study is to investigate the biological function and the regulation of this novel gene. In addition to have a greater understanding of the function of this novel gene, the results from the

proposal will be useful in the development of better drugs or strategies in cancer therapy.

(MD03421)

Effect of Flavonoids on the Initiation and Promotion of Breast Carcinogenesis

✉ LEUNG Lai Kwok • CHAN Leung Franky
(Dept of Anatomy)

□ 1 April 2004

❖ CUHK Research Committee Funding (Direct Grants)

Many polyphenolic compounds can be isolated from plant foods, and they have various pharmacological properties that may be applicable in preventive medicine. Since estrogen and some environmental toxicants have been implicated in the etiology of breast cancer, we propose to evaluate the inhibitory actions of flavonoids and other dietary phytochemicals towards the enzymes involved in the metabolism of estrogen and environmental toxicant. Flavonoids were shown to be agonists of estrogen receptor (ER) with various potencies, and they also displayed inhibitory effects on cytochrome p450 enzymes and detoxifying enzymes involving in the estrogen and toxicant metabolism. Because these properties could affect carcinogenesis in the breast, in this proposal we have divided our investigation into *in vivo* and *in vitro* studies. Cell culture models are employed to address the regulatory mechanisms of these enzymes. Animal models are used to address the flavonoid effect on estrogen metabolism. The overall aim is to assess flavonoids as natural alternatives for the chemoprevention of breast cancers.

(MD03933)

Promoter Analysis of Chicken Acetylcholinesterase Gene

✉ WAN Chi Cheong David • TSIM Wah-keung Karl (Biochemistry)#

☐ 1 September 2003

❖ Research Grants Council (Earmarked Grants)

Acetylcholinesterase (AChE, EC 3.1.1.7.) is a major enzyme of vertebrate neuromuscular junctions and cholinergic synapses responsible for the rapid hydrolysis of acetylcholine released from the nerve terminals. This enzyme has been shown to play a key role in the synaptogenesis of cholinergic nerves, myogenic differentiation and in the pathologically of many neurological diseases such Alzheimer's disease and muscular dystrophy. In many organisms, AChE is encoded by a single gene, however, multiple polymorphic forms of AChE have been shown differentially expressed in the brain and muscle cells. Recently, we have cloned an approximately 8 kilobases of genomic DNA fragment from chicken, which is upstream of the start site of cDNA encoding chicken AChE. In the present studies, we propose to determine whether this ~ 8kb DNA fragment participates in the regulation of AChE gene and to dissect the promoter elements in this DNA in the control of synaptogenesis of cholinergic nerves in the brain and the myogenic differentiation in muscle. The results obtained should provide insight into the role of AChE in the pathophysiology of neurological diseases.

(CU03311)

Study of the Function of the HBX Gene of Hepatitis B Virus Using the Tetracycline-inducible System

✉ WAYE Mary Miu Yee

☐ 15 September 2003

❖ CUHK Research Committee Funding (Direct Grants)

Hepatocellular carcinoma has been associated with the expression of the hepatitis virus X (HBX) protein. The long term goal of this research is to characterize fully the functions of HBX protein to facilitate diagnosis and perhaps prevention of hepatocellular carcinoma.

Our laboratory has developed a cultured mouse cell line stably transfected with an inducible HBX recombinant construct. We propose to use this stable cell line to test the following hypotheses: 1. Induction of HBX expression in cells can lead to an increase in oncogenic properties of a hepatocyte. 2. The expression of HBX can activate transcription of cellular genes (including protooncogenes such as c-myc and c-jun).

To test these hypotheses, we propose a study with the following specific aims:

To characterize cell lines of pseudonormal mouse hepatocytes stably transfected with an inducible HBX gene using flow cytometry assay.

To determine what genes are switched on at different stages of induction of the HBX gene using DNA microarray analyses and two-dimensional gel electrophoresis.

(BL03958)

Establishment of a SARS Coronavirus Protein/Peptide Library and an Antibody Library as Common Platforms for Biological and Medical Applications

✉ 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 (Dept of Biology) • TAM Siu Lun John (Dept of Microbiology) • TSUI Kwok Wing • WAN Chi Cheong David • WONG Kam Bo (Biochemistry)

□ 30 September 2003

❖ RGC Special Grants for Severe Acute Respiratory Syndrome (SARS) Research

Severe Acute Respirator Syndrome Coronavirus (SARS-CoV) has been isolated and identified as the primary agent associated with Severe Acute Respirator Syndrome (SARS). SARS-CoV imposes one of the largest social economic burdens on the affected communities. There is no specific treatment for SARS, and to date, control of SARS-CoV infection by vaccination is not available. Analysis of the genomic sequence of SARS-CoV indicates that the genomic organization of SARS-CoV is similar to that of other coronaviruses but it is phylogenetically distinct from all the known coronaviruses. SARS-CoV is approximately 30Kb in length with 11 open reading frames. In order to facilitate biological and medical research on SARS-CoV, we plan to construct an expression library consisting of peptides/proteins of the SARS-CoV and to establish an antibody library consisting of polyclonal, monoclonal, and single-chain variable fragment (ScFv) antibodies against various viral proteins of SARS-CoV. We plan to make use of the *in vitro* site-specific recombination system that allows easy transfer of clones to different expression systems. These libraries of viral proteins and antibodies would contribute open platforms and made available to investigators who are interested to do further research

on SARS related projects. This open architecture would facilitate further research on SARS-CoV essential for the development of sensitive diagnostic reagents and efficacious therapeutic agents.

(CU03536)

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

Edition	Title/Investigators
1990-91	Comparative Endocrinology of Prolactin, Growth Hormone, and Their Receptors (BP88031) ✉ CHENG Hon Ki Christopher • NG Tzi Bun • WONG Chun Cheung (Dept of Physiology)
2001-02	Molecular and Functional Characterization of Ghrelin and Its Receptors in Seabream (BL01149) ✉ CHENG Hon Ki Christopher • WOO Norman Ying Shiu (Dept of 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	Functional Roles of Type II Angiotensin Receptor in Pancreatic Endocrine Cells (BL01792) ✉ CHEUNG Wing Tai

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|---------|--|---------|--|
| 2001-02 | Mechanistic Study of Anti-tumour Effect of Natural and Synthetic Saponins (MD01668)
✉ FUNG Kwok Pui | 2002-03 | Induction of Anticancer Drug Resistance in Human Cancer Cells by Chronic Exposure to Growth Factors (MD02989)
✉ KWOK Tim Tak |
| 2002-03 | Effect of Antisense Oligodeoxynucleotide of Glucose Transporter 5 on Human Breast Tumor (MD02302)
✉ FUNG Kwok Pui | 2002-03 | The Role of 14-3-3 Epsilon in Calmodulin-mediated Signaling Pathway (MD02361)
✉ LEE Cheuk Yu • FUNG Kwok Pui • TSUI Kwok Wing • WAYE Mary Miu Yee |
| 2001-02 | Signaling Mechanisms Underlying the Effects of Apolipoprotein E on Cell Proliferation and Apoptosis (BL01438)
✉ HO Yuanyuan • FUNG Kwok Pui | 2002-03 | Effect of Baicalein on Hormone-responsive MCF-7 Tumor (MD02487)
✉ LEUNG Lai Kwok • CHEN Zhenyu (Biochemistry) • CHAN Leung Franky (Dept of Anatomy) |
| 2002-03 | Identification and Characterization of Apolipoproteine Polymorphism-Induced Variation of Cell Function Involved in Atherosclerosis (CU02274)
✉ HO Yuanyuan • FUNG Kwok Pui • WAYE Mary Miu Yee | 2002-03 | The Role of FHL Proteins in Cell Cycle Regulation (MD02379)
✉ TSUI Kwok Wing |
| 2002-03 | Characterization of the Glucose Transport-modulating Effects of Anti-epileptic Compounds (MD02769)
✉ HO Yuanyuan • FUNG Kwok Pui • FOK Tai Fai (Dept of Paediatrics) • FUNG Lai Wah Eva (Dept of Paediatrics) | 2002-03 | Natural Inhibitors Against HIV-1 Integrase (MD02467)
✉ WAN Chi Cheong David • NG Tzi Bun |
| 2001-02 | Functional Analysis of a Novel Gene Over-expressed in Doxorubicin Resistant Human Cancer Cells (MD01024)
✉ KWOK Tim Tak • CHEUNG Wing Tai • KONG Siu Kai (Biochemistry) | 2002-03 | Characterization of a RING-H2 Finger Protein, ANAPC11, the Human Homologue of Yeast Apc11p (BL02860)
✉ WAYE Mary Miu Yee • ZIMMERMANN Rene* • CHAN Hei (Biochemistry) |

RESEARCH PROJECTS

Investigation of the Differences in the Concentrations and Molecular Characteristics of DNA in the Plasma and Serum of Healthy Subjects

✍ CHAN Kwan Chee • LO Yuk Ming Dennis

☐ 1 January 2004

❖ CUHK Research Committee Funding (Direct Grants)

The presence of cell-free nucleic acids in the circulation has opened up new possibilities for medical diagnosis. Plasma and serum are the two most commonly used specimens for clinical biochemical analyses. However, there is a lack of consensus on whether plasma or serum should be used for molecular diagnostic purposes such that results from different groups could not be compared directly. This is a major hurdle to the further development of this field.

Rational choice of samples depends on the understanding of the fundamental differences of serum and plasma DNA, namely, concentration and molecular size. We have previously shown that EBV DNA molecules in the plasma of nasopharyngeal carcinoma patients are short fragments of approximately 180 bp. Our finding suggests that the release of tumor-derived DNA may be closely related to apoptosis.

We hypothesize that the release of circulating DNA in healthy subjects is also related to apoptosis. Thus, the size of *plasma* DNA would be around 180 bp. On the other hand, DNA would be released from nucleated cells into the fluid compartment during blood clotting due to the mechanical damage of cell

membrane. As a result, the DNA concentration of *serum* would be higher than that of plasma and the size of serum DNA would be longer than plasma DNA.

In this project, we plan to study the concentration and size distribution of DNA in the plasma and serum of healthy control subjects. The resulting information would be important in rational choice of sample for clinical molecular analysis.

(MD03988)

Origins of Circulating mRNA in Maternal Plasma

✍ CHIU Wai Kwun Rossa • LO Yuk Ming Dennis
• LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Tse Ngong (Dept of Obstetrics & Gynaecology) • CHAN Ho Ming • NGAN KEE Warwick Dean (Dept of Anaesthesia & Intensive Care)

☐ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Circulating nucleic acids have been an area of active research in recent years. To date, the reported applications of the analysis of nucleic acids in plasma or serum are wide-ranging and include cancer diagnosis, monitoring and prognostication, non-invasive prenatal diagnosis, trauma assessment, and transplant monitoring. Initially, much research focused on the detection of circulating DNA. However, recently, circulating RNA has also emerged as a marker with much potential. Tumour-derived and fetal-associated mRNA species have been demonstrated in the plasma of cancer patients and pregnant women, respectively. These findings have opened up the possibility of non-invasive gene expression profiling and may ultimately be useful for the management of

malignancies or the prenatal diagnosis of genetic conditions. Recently, we have demonstrated that some of the mRNA species detectable in maternal plasma are placental derived and they are cleared rapidly post-partum. We have studied the mRNA concentrations of human placental lactogen, human chorionic gonadotrophin, and corticotrophin releasing hormone. We have demonstrated that the mRNA concentrations positively correlated with the protein expression levels. We have further shown that the concentration of CRH mRNA is elevated in the plasma of preeclamptic pregnant subjects. These findings confirm the utility of maternal plasma mRNA analysis for the monitoring of fetomaternal well-being. In order to expand the potential utility of maternal plasma mRNA analysis, in this study, we propose to explore whether pregnancy-associated circulating mRNA from tissue sources other than the placenta could be detected in maternal plasma. We plan to investigate two main sources: (1) the central nervous system; and (2) the fetus.

(MD03839)

Non-invasive Prenatal Diagnosis of β -thalassaemia through Maternal Plasma Analysis: A Multi-centre Collaborative Study

✍ CHIU Wai Kwun Rossa • CHAN Li Chong* • CHUI David H.K.* • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Tse Ngong (Dept of Obstetrics & Gynaecology) • LO Yuk Ming Dennis

☐ 15 December 2003

❖ Research Grants Council (Earmarked Grants)

β -thalassaemia is one of the most common inherited disorders of the world and is particularly prevalent in Southeast Asia, including Hong Kong. β -thalassaemia is caused by the defective synthesis of

the β -globin chains of haemoglobin. The severest form, namely β -thalassaemia major, is a condition where survival is dependent on regular blood transfusions and iron chelation therapy. Prenatal diagnostic programmes have been implemented in many regions, including Hong Kong. At present, prenatal diagnosis is performed by methods such as amniocentesis and chorionic villus sampling that are associated with a small but finite risk of fetal loss. Recently, circulating fetal DNA has been found to exist in maternal plasma and thus, has opened up the possibility of non-invasive prenatal diagnosis. Based on fetal DNA analysis in maternal plasma, we have recently developed an assay for the specific detection of the most common β -thalassaemia mutation in Southeast Asians. The approach has been found to be effective in the exclusion of β -thalassaemia major in a small series of at-risk pregnancies. The aim of the current proposed study is to extend on the promising results of the initial study by developing additional assays for the prenatal detection of other β -thalassaemia mutations and to perform large-scale evaluation of this safer prenatal diagnostic approach through the collaboration of several regional prenatal diagnostic centres.

(CU03395)

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

✍ LAM Ching Wan

☐ 1 September 2003

❖ Research Grants Council (Earmarked Grants)

The incidence of sporadic basal cell carcinomas (BCCs) in Hong Kong has increased three-fold from

1990 (0.32 in 100,000) to 1999 (0.92 in 100,000). In our previous studies, we have collated data suggesting that the genetic alterations occurring in sporadic BCCs among Chinese may be etiologically different from those of the Caucasian population. This evidence includes: (1) the lack of p53 ultraviolet signature mutations in sporadic BCCs among Chinese; (2) the common SMOOTHENED mutation in sporadic BCCs among Chinese is not an ultraviolet radiation-induced mutation and occurs with 5-fold higher frequency in Chinese BCCs than Caucasian BCCs; (3) the absence in Chinese with sporadic BCCs of loss of heterozygosity (LOH) of the PATCHED gene at chromosome 9q22.3, while in sporadic BCCs of Caucasians, LOH on chromosome 9q22.3 is the most frequent genetic alteration; (4) the finding of a new LOH site in sporadic BCCs in Chinese; (5) 10-fold higher percentages of pigmented BCCs in Chinese than Caucasian BCCs; and (6) the prevalence of arsenic-associated BCCs in Chinese populations. Because of these differences, we envisage that analysis of sporadic BCCs in Chinese will reveal genetic subsets of BCCs that are not common in BCCs in Caucasians-subsets that will inform our diagnostic and therapeutic strategy for this disease. We now propose to perform a comprehensive genome-wide study to identify additional LOH sites in Chinese. We will overcome the problem of having only a small amount of DNA available for a whole genome scan of LOH sites by using a recently established, innovative method-high-density single-nucleotide polymorphism arrays. Because the oncogenic pathway in BCCs, the sonic hedgehog pathway, is activated irrespective of ethnicity and genetic alterations in BCCs, the finding of new genetic alterations in sporadic BCCs promises to further our understanding of the role of this signaling pathway in human carcinogenesis. Importantly, our increased understanding of the

molecular basis of sporadic BCCs will benefit the 1.2 billion population by helping us design and instigate correct measures for the prevention of BCCs in Chinese.

(CU03472)

Roles of Mitogen Activated Protein Kinases and Transcription Factor NF- κ B Controlling the Recruitment, Inflammatory Mediator Release and Apoptosis of Human Mast Cells in Allergy

✉ LAM Wai Kei Christopher • WONG Chun Kwok

□ 1 September 2003

❖ Research Grants Council (Earmarked Grants)

Allergic diseases such as asthma and allergic rhinitis are prevalent and have been increasing in Hong Kong. Mast cells, the key effector cells of immediate allergic reactions, can be activated by allergens to accumulate at sites of immediate hypersensitivity and release an array of inflammatory mediators, such as histamine and inflammatory cytokines. This project aims to elucidate the intracellular signal transduction regulating mast cell recruitment, inflammatory mediator release and apoptosis in allergic inflammation. We plan to study (1) Roles of mitogen activated protein kinases (MAPK) and transcription factor NF- κ B on (i) chemotaxis, (ii) expression of adhesion molecules: intercellular adhesion molecule (ICAM)-1, -3 and β_2 -integrin, and (iii) expression and release of inflammatory mediators including histamine, tumor necrosis factor (TNF)- α , interleukin (IL)-6, IL-8, IL-18, and eotaxin, by a human leukemia mast cell line, HMC-1 cells. (2) Role of MAPK and NF- κ B in dexamethasone and sodium salicylate-induced apoptosis of HMC-1 cells. (3) Effects of various activators, including tumor necrosis factor- α , stem cell factor, platelet activating

factor and interleukin-18, and inhibitors of MAPK(e.g. SB 203580 and PD 098059) and NF- κ B (e.g. MG-132) on recruitment, degranulation, cytokine release, and dexamethasone and sodium salicylate-induced apoptosis of HMC-1 cells. Elucidation of the intracellular control mechanisms of mast cell chemotaxis, and release of inflammatory mediators and apoptosis will be useful for the development of novel effective and specific therapeutic strategies for treating allergic inflammation. (CU03473)

Intracellular Signal Transduction Mechanisms Mediating the Induction of Adhesion Molecule and Cytokine Expression in the Co-culture of Human Eosinophils and Epithelial Cells

✉ LAM Wai Kei Christopher • WONG Chun Kwok

☐ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Allergic diseases such as asthma are prevalent and reaching epidemic proportions in Hong Kong and worldwide. Eosinophils are the principal effector cells of allergic inflammation, characterized by an accumulation and infiltration of eosinophils in tissues mediated by chemokine eotaxin, and adhesion molecules on epithelial cells and endothelium. The interaction of eosinophils and epithelial cells can induce inflammatory mediator, cysteinyl leukotrienes and enhance eosinophil degranulation through CD18-dependent adhesion. The objective of the project is to study intracellular signal transduction mechanisms mediating the induction of adhesion molecule and cytokine expression in the co-culture of human eosinophils and epithelial cells. We plan to

study: (1) Effects of various activators including tumor necrosis factor (TNF)- α , platelet activating factor, interleukin (IL)-3, 5, 18 and granulocyte-macrophage colony-stimulating factor on (i) expression of inflammatory cytokines including IL-6, TNF- α , IL-12, IL-18, and chemokine including regulated upon activation normal T cell expressed and secreted, monokine induced by interferon- γ , monocyte chemoattractant protein-1, IL-8 and interferon-inducible protein-10, and (ii) expression of adhesion molecule intercellular adhesion molecule (ICAM)-1, vascular cell adhesion molecule (VCAM)-1 and CD18 on human eosinophils and bronchial epithelial BEAS-2B cells in co-culture of eosinophils and BEAS-2B cells; and (2) relationship between the activation of nuclear factor (NF)- κ B, c-Jun amino-terminal kinases (JNK) and p38 mitogen-activated protein kinase (MAPK), and the expression of adhesion molecules and cytokines in co-culture of eosinophils and BEAS-2B cells. Results of this basic study may provide a biochemical basis for the development of a target for therapeutic intervention in the treatment of allergic inflammation. (MD03552)

Quantitative Analysis of Plasma Viral and Host RNA in Severe Acute Respiratory Syndrome

✉ LO Yuk Ming Dennis • CHIU Wai Kwun Rossa • LEE Nelson (Dept of Medicine & Therapeutics)* • NG Pak Cheung (Dept of Paediatrics) • POON Lei Lit Man* • TAM Siu Lun John (Dept of Microbiology)

☐ 15 August 2003

❖ RGC Special Grants for Severe Acute Respiratory Syndrome (SARS) Research

In this project, we hope to achieve the following objectives:

To develop a robust RNA extraction protocol for the detection and measurement of severe acute respiratory syndrome (SARS)-coronavirus and host-derived mRNA in the plasma of SARS patients;

To document the variation of plasma viral RNA concentration during the course of infection;

To investigate the prognostic implication of plasma viral loads;

To compare the difference in plasma viral loads in paediatric and adult SARS patients;

To document the variation of plasma host-derived mRNA concentration during the course of infection and its potential prognostic impact.

The project may result in novel diagnostic and prognostic tests for SARS.

(CU03508)

Molecular Analysis of Placental RNA in Maternal Plasma

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

□ 15 December 2003

❖ Research Grants Council (Earmarked Grants)

In this project, we plan to perform a quantitative analysis of circulating RNA in maternal plasma, with the following objectives:

1) To show that mRNA is released from the placenta into maternal plasma;

2) To show that such circulating placental mRNA is stable enough for diagnostic use;

3) To show that the concentration of such circulating placental mRNA correlates with gestational parameters and other non-invasive biochemical or molecular markers.

These data will provide the first quantitative data regarding circulating fetal RNA in maternal plasma.

This development will open up a new approach for the non-invasive investigation of fetal gene expression which may improve our understanding of fetomaternal physiology and may form the basis for new assays for assessing pregnancy-associated pathologies.

(CU03474)

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

✍ LO Yuk Ming Dennis • CHIM Siu Chung Stephen • LEUNG Tse Ngong (Dept of Obstetrics & Gynaecology) • CHIU Wai Kwun Rossa • LAU Tze Kin (Dept of Obstetrics & Gynaecology)

□ 20 December 2003

❖ CUHK Research Committee Funding (Direct Grants)

With the discovery of circulating fetal DNA in maternal plasma, the prenatal determination of fetal RhD blood group status and sex-linked disorders can now be achieved by the molecular analysis of maternal peripheral blood. Such non-invasive approaches also hold promise for diagnosing other antenatal complications and diseases that involve quantitative aberrations of fetal DNA in maternal plasma, such as pre-eclampsia, antepartum haemorrhage, preterm labour, and fetal Down syndrome. However, as the quantification of fetal DNA concentration in maternal plasma in these studies depends on Y-chromosome sequences, the application is limited to pregnancies conceived with male fetuses. Addressing the long-sought goal for a gender-independent fetal DNA marker, we plan to

study the epigenetics of the maspin (SERPINB5) gene, the expression of which is up-regulated in the placenta regardless of the fetal sex during late pregnancy. We hypothesize that (1) the cytosine residues in the CpG sites of the maspin promoter are unmethylated in the placenta for expression to occur; and that (2) this unmethylated maspin promoter can be detected in maternal plasma. By testing these hypotheses in our proposed study, we aim to develop a fetal DNA marker useful for diagnosing disorders that occur in late pregnancy.

(MD03364)

A Centre for the Study of Fetal Nucleic Acids in Maternal Plasma

✉ LO Yuk Ming Dennis • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Tse Ngong (Dept of Obstetrics & Gynaecology) • WONG Hing Nam Ivy* • CANTOR Charles* • HUANG H M Tim*

□ 1 March 2004

❖ RGC Central Allocation • Supplementary Funding for RGC Central Allocation

The development of approaches for the non-invasive prenatal analysis of fetal DNA and RNA is a long-sought goal in human genetics. Our original discovery of fetal nucleic acids in maternal plasma has enabled non-invasive prenatal diagnosis which can be performed simply through the analysis of a maternal peripheral blood sample. Biologically, these discoveries have opened up a new field of investigation. Through this project, we plan to set up a virtual research Centre and to launch a multidisciplinary study of the biology of fetal DNA and RNA in maternal plasma. We plan to use state-of-the-art genomic technologies, including microarrays and mass spectrometry, to achieve many

of our goals. On the fetal DNA front, we plan to elucidate the origin of circulating fetal DNA, its molecular characteristics (e.g. size), and to develop new methods which would allow us to robustly distinguish fetal from maternal DNA, even down to a single base level. We hope also to develop generic fetal DNA markers which can be used irrespective of the gender and genetic makeup of the fetus. On the fetal RNA front, we plan to elucidate its biological characteristics and to develop a collection of RNA markers which can be robustly detected in maternal plasma and to explore their potential diagnostic applications. It is hoped that this project will ultimately bring us closer to the realisation of routine non-invasive prenatal diagnosis and to unveil many of the biological mysteries of circulating fetal nucleic acids.

(MD03672)

To Develop a Clinical Prognostic Profile for Severe Disease Course in SARS with Serum Cytokines Measurements and Genomic Markers - A Retrospective Case Control Study

✉ TANG Leung Sang Nelson • CHAN Kay Sheung Paul (Dept of Microbiology) • HUI Shu Cheong David (Dept of Medicine & Therapeutics) • LAM Wai Kei Christopher • TO Ka Fai (Dept of Anatomical & Cellular Pathology) • WONG Chun Kwok

□ 1 September 2003

❖ RGC Special Grants for Severe Acute Respiratory Syndrome (SARS) Research

The recent outbreak of severe acute respiratory syndrome (SARS) in Hong Kong poses a big impact to the health care system. More than 80% patients recovered while the others suffered a severe disease leading to respiratory failure, ICU admission. In

short, there is a marked heterogeneity in the course of disease and we hypothesize that the difference in disease course and outcome are partly determined by differences in intensity of host reaction toward the infection. Our previous investigation in the 1997 H5N1 influenza outbreak showed that patients who died of the disease had lymphoid depletion associated with marked elevation of circulating concentrations of cytokines, including interleukin-6, Interleukin-2 receptor and interferon-gamma. There are many features in common between H5N1 infection and SARS. It is likely that hypercytokinemia and its associated systemic and local effects play a key role in the lung damage and disease outcome in SARS. Recent studies also showed that genetic variations in immune system related genes were determinants of disease course and mortality in DAI or ARDS subsequent to systemic sepsis and shock. These genomic polymorphisms account for the variation of the intensity of immune reaction of individuals against a pathogen and they will be studied here together with circulating cytokines levels as prognostic markers for SARS infection.

(CU03507)

Study of Predisposition Genes Underlying IgA Nephropathy and Their Genetic Interactions

✉ TANG Leung Sang Nelson • SZETO Cheuk Chun (Dept of Medicine & Therapeutics) • TO Ka Fai (Dept of Anatomical & Cellular Pathology) • MAC-MOUNE LAI Fernand (Dept of Anatomical & Cellular Pathology) • LI Kam Tao Philip (Dept of Medicine & Therapeutics)

☐ 21 June 2004

❖ CUHK Research Committee Funding (Direct Grants)

IgA nephropathy is most common primary glomerulonephritis affecting our population. The pathogenesis is related to deposition of IgA immune complex in the glomeruli and leading to subsequent mesangial proliferation and glomerular damages. Although the etiology of this disease is not well understood, a genetic predisposition is clearly evident from clinical observations. Therefore, this project aims at further our knowledge about the genetic susceptibility of this disease

Previous experiments reported that the disease might be related to defects in different systems. There is an enhanced production of IgA molecules which is also defectively glycosylated. The mesangial cells in the glomeruli may also produce receptors result in deposition of IgA. Several candidate genes in these systems had been associated with predisposition for IgAN.

We will examine the genetic predisposition in our patient samples. Although moderate number of candidate IgAN predisposition gene had been reported, the interaction between these different genes had not been explored in depth. Understanding of how these genes interact in IgAN patients will enhance our ability to identify patients at risk and will also in the long run allow more precise prediction of prognosis in patients.

(MD03407)

Elucidation of Nitric Oxide Mediated Mechanisms Controlling the Recruitment and Apoptosis of Human Eosinophils in Allergic Inflammation

✉ WONG Chun Kwok • LAM Wai Kei Christopher • FISCUS Ronald Ray (Dept of Physiology)

☐ 1 October 2003

❖ 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 accumulation and delayed apoptosis of eosinophils in inflammatory sites. Their degranulation results in the release of cytotoxic proteins including eosinophil cationic protein (ECP) causing tissue damage. Asthmatic patients have elevated levels of exhaled nitric oxide (NO). Inducible NO synthase (iNOS) is upregulated in airways of asthmatics to promote allergic inflammation. The project aims to elucidate the putative role of NO in regulating eosinophil recruitment and apoptosis in allergic asthma. We plan to study: (1) Effects of inflammatory factors including tumor necrosis factor (TNF)- α , platelet activating factor (PAF), interleukin (IL)-18 and chemokine eotaxin on (i) activation of NOS, nuclear factor kappa B (NF- κ B), and mitogen-activated protein kinases (MAPK), (ii) kinetics of NO synthesis and release, (iii) apoptosis, (iv) adhesion to epithelial cells, (v) chemotaxis, and (vi) expression of very late antigen-4 (VLA-4) and intercellular adhesion molecule-1 (ICAM-1) of eosinophils, and (vii) expression of E-selectin, ICAM-1 and vascular cell adhesion molecule (VCAM)-1 and NO production of human epithelial BEAS-2B cells; (2) Effects of non-specific inhibitor of NOS, *N*^ω-nitro-L-arginine methyl ester (L-NAMA), selective iNOS inhibitor, 1400W, and NO donor, S-nitroso-N-acetylpenicillamine (SNAP) or 3-morpholinosydnonimine (SIN-1) on (i) chemotaxis, (ii) apoptosis and (iii) expression of VLA-4 and ICAM-1 on eosinophils. The above studies will be useful for the elucidation of pathogenic mechanisms, development of new markers for diagnosis and

monitoring, and design of new therapeutic strategies for treating allergic inflammation.
(MD03943)

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

Edition	Title/Investigators
2002-03	Quantitative Analysis of Size Distribution of Plasma Epstein-Barr Virus DNA in Nasopharyngeal Carcinoma and Lymphoma Patients (MD02447) ✉ CHAN Kwan Chee • LO Yuk Ming Dennis • CHAN Anthony Tak Cheung (Dept of Clinical Oncology) • LEI Ieng-Kit Kenny (Dept of Clinical Oncology)*
2002-03	Quantitative Analysis of Circulating Mitochondrial DNA (MD02310) ✉ CHIU Wai Kwun Rossa • LO Yuk Ming Dennis • RAINER Timothy Hudson (Accident and Emergency Medicine academic unit)
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
2002-03	Production of Nitric Oxide, Soluble Thrombomodulin, Soluble Adhesion Molecules, and Interleukin-18 in

- Systemic Lupus Erythematosus Patients with Renal Disease (MD02791)
 ✎ LAM Wai Kei Christopher • LI Kwok Ming Edmund (Dept of Medicine & Therapeutics) • WONG Chun Kwok
- 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)
- 2001-02 Development of Genomic Strategies for the Non-invasive Detection of Down Syndrome (MD01862)
 ✎ LO Yuk Ming Dennis • CHIU Wai Kwun Rossa • LAU Tze Kin (Dept of Obstetrics & Gynaecology)
- 2001-02 Molecular Characterization of Circulating Epstein-Barr Virus DNA in Nasopharyngeal Carcinoma Patients (MD00534)
 ✎ LO Yuk Ming Dennis • CHAN Anthony Tak Cheung (Dept of Clinical Oncology)
- 2002-03 Molecular Characterization of Circulating Epstein-Barr Virus DNA in Nasopharyngeal Carcinoma Patients (CU02086)
 ✎ LO Yuk Ming Dennis • CHAN Anthony Tak Cheung (Dept of Clinical Oncology) • TO Wai Hei Edward*
- 2002-03 Development of a Maternal Plasma RNA Marker for Preeclampsia (MD02565)
 ✎ LO Yuk Ming Dennis • NG Kai On# • LEUNG Tse Ngong (Dept of Obstetrics & Gynaecology) • CHIU Wai Kwun Rossa • LAU Tze Kin (Dept of Obstetrics & Gynaecology)
- 2002-03 Treatment and Diagnosis of Severe Acute Respiratory Syndrome (MD02397)
 ✎ LO Yuk Ming Dennis
- 2000-01 Enhanced Expression of a Novel Gene BRE That May Modulate Steroid Metabolism in Adrenal Gland and Testis (MD00669)
 ✎ PANESAR Nirmal Singh • CHAN John Y H*
- 2001-02 Is Thyrotoxic Periodic Paralysis Resulted from a Calcium Ion Channelopathy? (MD01035)
 ✎ TANG Leung Sang Nelson • CHOW Chun Chung Francis (Dept of Medicine & Therapeutics) • COCKRAM Clive Stewart (Dept of Medicine & Therapeutics) • YAO Xiaoqiang (Dept of Physiology)
- 2002-03 Establish a Diagnostic Laboratory for Inherited Metabolic Diseases in Hong Kong (MD02558)
 ✎ TANG Leung Sang Nelson • FOK Tai Fai (Dept of Paediatrics) • LAM Wai Kei Christopher • CHEUNG Kam Lau (Dept of Paediatrics) • HUI Joannie (Dept of Paediatrics)

2002-03 Genotypic Determinants of Circulating Levels of Proteins in the GH-IGF Axis in Chinese (MD02607)

✉ TANG Leung Sang Nelson • TO Ka Fai (Dept of Anatomical & Cellular Pathology) • MAC-MOUNE LAI Fernand (Dept of Anatomical & Cellular Pathology) • CHAN Lung Wai*

Interleukin-18 Mediated Recruitment of Eosinophils in Allergic Inflammation (MD02884)

✉ WONG Chun Kwok • LAM Wai Kei Christopher

2002-03 Intracellular Signal Transduction for Tumor Necrosis Factor- α and

RESEARCH PROJECTS

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

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

☐ 1 September 2003

❖ Roche Hong Kong Limited

Primary Objective: To demonstrate that the combination of capecitabine and oxaliplatin is at least equivalent to the combination of 5FU and LV and oxaliplatin in terms of time to tumor progression or death in patients previously untreated by systemic therapy for advanced or metastatic colorectal cancer.

Secondary Objectives: (1) To evaluate and compare the efficacy (overall survival, overall response rate, time to response, duration of response, and time to treatment failure) in the two treatment groups; (2) To evaluate and compare the safety profiles of the two treatment groups; (3) To evaluate and compare perceived treatment convenience and satisfaction with treatment in the two treatment groups; (4) To evaluate and compare medical care utilization in the two treatment groups.

(MD03467)

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

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

☐ 1 May 2004

❖ Merck Pharmaceutical Ltd.

This study is a phase III randomized, open-label, multi-center study of Irinotecan and Cetuximab vs. Irinotecan as second-line treatment in patients with metastatic, EGFR-positive colorectal carcinoma with primary endpoint of determining whether overall survival is prolonged in subjects with metastatic, epidermal growth factor receptor (EGFR)-positive colorectal cancer treated with Cetuximab in combination with Irinotecan compared with Irinotecan alone as second-line therapy following treatment with a fluoropyrimidine/oxaliplatin-based, non-Irinotecan containing regimens. It is a multi-center study with the target number of 1300 in total.

(MD03817)

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

✉ MA Buig Yue Brigitte • CHAN Anthony Tak Cheung • MOK Shu Kam Tony • YEO Winnie

☐ 1 September 2003

❖ Metabasis Therapeutics, Inc.

Hepatocellular Carcinoma (HCC) is a common cancer in Hong Kong as well as other Asian countries. Most patients presented in advanced stage and are not

suitable for surgical resection. Systemic chemotherapy has not been successful because of resistance of HCC to most cytotoxic agents. MB07133, a HepDirect prodrug of cytarabine (araC), is being used to target araCMP specifically to the liver. AraC is an analog of deoxycytidine, which is transported into cells via nucleoside transporters and phosphorylated to the active metabolite cytarabine-5'-triphosphate (araCTP) by nucleoside and nucleotide kinases. HepDirect cytarabine offers the potential to improve effectiveness of araC in the liver by specifically targeting much higher concentrations of araCTP to cytochrome P450 isoenzyme 3A4 (CYP3A4) expressing HCC cells. HepDirect cytarabine is therefore predicted to have increased anti-tumor activity in the liver compared with araC, and to be less toxic to the extra-hepatic hemopoietic system, reducing the dose-limiting myelosuppression seen in human after administration of araC. This trial aims to document dose limiting toxicity and pharmacokinetics of MB07133 in patients with unresectable hepatocellular carcinoma. (MD03679)

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

✉ 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)

☐ 1 March 2004

❖ CUHK Research Committee Funding (Direct Grants)

Nasopharyngeal carcinoma (NPC) is common in Hong Kong where radiotherapy (RT) is the main treatment. Patients who developed metastatic disease often receive first-line platinum-based chemotherapy, however, response duration is brief and survival remains poor. Our team has shown that the epidermal growth factor receptor (EGFR) is expressed in over 70% of NPC and is associated with poor prognosis following radical RT. Subsequently, we have demonstrated in a phase II trial that targeting EGFR with a monoclonal antibody (cetuximab) has clinical activity in combination with carboplatin in patients with metastatic NPC refractory to platinum-chemotherapy. ZD1839 is a potent small molecule inhibitor of the EGFR tyrosine kinase (TK) that has clinical activity in patients with cancers of the lung and head-and-neck (non-NPC). It can also potentiate the anti-tumor activity of chemotherapy and radiation in preclinical models of various cancers. In NPC cell lines, ZD1839 inhibits growth and enhances the cytotoxic effects of platinum and 5-fluorouracil. This study investigates if ZD1839 can augment the anti-tumor activity of some of the chemotherapeutic agents with known clinical activity in NPC: gemcitabine, cisplatin. Second, the optimal sequencing of chemotherapy and ZD1839 administration will be examined, and third, any correlation between ZD1839 activity and expression level of EGFR in NPC cell lines will be evaluated. This study will form the basis of future clinical trials using ZD1839 in treating patients with NPC.

(MD03347)

A Randomized, Double-blind, Placebo-controlled, Phase III Study of Oxalipatin/5-fluorouracil/leucovorin with PTK787/ZK 22584 or Placebo in Patients with Previously Treated Metastatic Adenocarcinoma of the Colon or Rectum

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

□ 1 April 2004

❖ Novartis Pharmaceuticals (HK) Ltd

Chemotherapeutic options for patients who have failed irinotecan-based first-line chemotherapy are limited. The use of an oxaliplatin/5-FU/LV regimen in patients progressing during or after an irinotecan-based therapy is supported by results of a phase III trial which patients who failed first-line irinotecan/5-FU/LV therapy showed evidence of a favorable outcome with higher overall response rate when treated with second-line oxaliplatin/5-FU/LV (Achille 2001). Oxaliplatin/5-FU/LV (“FOLFOX4” regimen) was shown to be superior as a second-line therapy in a randomized, 3-arm, phase III trial comparing oxaliplatin/5-FU/LV (FOLFOX4) to 5-FU/LV to oxaliplatin alone (Rothenberg 2003). PTK787/ZK 222584 is a potent and orally active inhibitor of VEGF-R tyrosine kinases (Wood 2000). Data from the monotherapy study CPTK787 0103/98077 which enrolled 21 patients with colorectal cancer metastatic to the liver who were previously treated with at least 1 prior therapy revealed a median time to progression of 2.8 months and a median overall survival of 9.2 months. These encouraging results in this refractory group of patients suggest that PTK787/ZK 222584, when given in addition to chemotherapy, may enhance the activity of chemotherapy alone. The purpose of this prospective, multinational, randomized, double-blind, placebo-controlled, parallel group, phase III study is to compare treatment with oxaliplatin/5-FU/LV + PTK787/ZK 222584 to oxaliplatin/5-FU/LV + placebo in patients with previously treated metastatic adenocarcinoma of the colon or rectum whose disease has recurred or progressed, during or within 6

months following treatment with irinotecan in combination with a fluoropyrimidine. The 1250 mg continuous once daily dose and schedule of PTK787/ZK 222584 in combination with oxaliplatin/5-FU/LV (FOLFOX4) has been selected as the treatment regimen (de Gramont 2000). (MD03899)

An Open Label, Randomized, Multicenter, Phase II Study to Determine the 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

✉ MOK Shu Kam Tony • POON Annette Ngar
Ying

□ 1 September 2003

❖ Roche Hong Kong Limited

The current study is an open label, multicenter, parallel group, phase II study to investigate the dose responsiveness of RO 50-3821 in anemic patients with stage IIIB or IV NSCLC receiving first or second line antineoplastic therapy. Safety, efficacy and PK data will be obtained throughout the study. The primary variable of this trial will be based upon Hb values. Approximately 42 centers are anticipated for this study and at least 210 patients are to be randomized in six treatment groups (low, medium and high) in two schedules (q1 wk, q3 wk), with 3 doses in each schedule. All patients will receive the study medication for 12 weeks in total. (MD03528)

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

✉ MOK Shu Kam Tony

☐ 1 November 2003

❖ Schering-Plough Research Institute

This study is a phase 3, multicenter, randomized, double-blind, placebo-controlled study of WBRT versus WBRT plus temozolomide for the treatment of subjects with brain metastases from non small cell lung cancer. All subjects will receive standard treatment for brain metastases defined as WBRT administered for 10 days over a two weeks period at 3Gys/day for a total of 30 Gys. In addition to WBRT, subjects will be randomly assigned to receive the study drug (temozolomide or placebo). Study drug will be administered at 75mg/m² PO daily on days 1-14 during WBRT followed by an additional 7 days after completion of WBRT (total of 21 days of study drug). Following the 21 days of study drug treatment, there will be a 7 days rest period. Following completion of the 7 day rest period and the day 28 tumor assessment, subjects may be treated according to the investigator's discretion (including chemotherapy, best supportive care, etc). No further CNS radiotherapy is permitted until radiologic CNS progression and clinical neurological (CNOS) progression are established.

(MD03309)

Open-Label Single-Arm Phase 2 Study of ALIMTA in Patients with Advanced Non-Small Cell Lung Cancer Who Have Had Prior Chemotherapy

✉ MOK Shu Kam Tony • LAM Kwok Chi

☐ 1 January 2004

❖ Eli Lilly (Asia) Inc.

This is a multicenter, single arm, open-label Phase 2 study of single agent ALIMTA in patients with advanced NSCLC who had prior chemotherapy. It is anticipated that a total of 186 qualified patients will be enrolled in this study. In order to qualify for response assessment according to RECIST criteria, patients will be required to have at least unidimensionally measurable disease. All patients will receive treatment with ALIMTA. Patients who have no hematologic and nonhematologic toxicity in Cycle 1 that exceeds predefined levels will receive ALIMTA at 800 mg/m² starting with Cycle 2.

(MD03542)

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)

✉ MOK Shu Kam Tony • ZEE Chung Ying Benny (Faculty of Medicine (Planning Office)) • YAU Sau Han • POON Annette Ngar Ying • KOH Chun • WONG Tze Ming

☐ 1 April 2004

❖ CK Life Sciences Development Inc.

HCC is a common fatal malignancy. Patients with unresectable HCC who have either failed or are ineligible for chemotherapy and/or treatment modality are candidates for supportive care only. There is no standard therapy that can consistently induce tumor response or prolong survival. Given the short duration of survival the primary objective of any form of therapy is to relieve symptom and improve quality of life.

The project is a Phase II randomized, open label, single center study assessing and comparing the

quality of life of patients with inoperable HCC taking trial drug CKBM-01 (formulated Chinese herbal product) vs Tamoxifen (anti- estrogen drug). A total number of 60 patients will be recruited.

(MD03455)

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

✉ MOK Shu Kam Tony • LAM Kwok Chi • HO Wing Ming • CHAN Chung Sau • CHAK Yin Mui Karen

□ 1 May 2004

❖ AstraZeneca Hong Kong Limited

This is a multicenter study using Iressa in patients with locally advanced or metastatic recurrent non-small cell lung cancer. The primary endpoint is to compare overall survival between ZD1839 and docetaxel. Time to progression and quality of life of patients would also be evaluated.

(MD03803)

An Open-label Phase Iia Trial Evaluating the Safety and Efficacy of EPO906 as Therapy in Patients with Advanced Local or Metastatic Gastric Cancer

✉ YEO Winnie • LAM Kwok C* • POON Annette*

□ 1 July 2003

❖ Novartis Pharmaceuticals (HK) Ltd

Primary objective is to determine the objective

response rate (CR, PR) of EPO906 administered I.V. weekly at 2.5mg/m² for three weeks followed by one week off in patients with locally advanced or metastatic gastric cancer.

Secondary Objectives:

(1) To determine the duration of objective tumor response in patients with complete response (CR) or partial response (PR) in this patient population.

(2) To determine the time to disease progression (TTP) in this patient population

(3) Overall survival.

(4) To investigate the safety and tolerability of EPO906 administered at this dose and schedule to this patient population.

(5) To evaluate blood pharmacokinetics of EPO906 after a single dose and multiple doses.

(6) To study tumor-specific mutations and compare gene expression changes in tumor cells with blood cells and plasma for biomarker development.

(7) To perform pharmacogenetic analyses with blood (when available) from patients treated with EPO906.

(MD03307)

Predictors of Lymphedema and Quality of Life in Breast Cancer Patients Undergoing auxiliary Lymph Node Dissection

✉ YEO Winnie • ZEE Chung Ying Benny (Faculty of Medicine (Planning Office)) • MAK Suzanne* • LEE Idy* • HO Fung Ping* • TSE Suet Mun*

□ 1 May 2004

❖ Health & Health Services Research Fund, Hospital Authority

This study is a matched case-control study. It is designed to evaluate potential factors associated with moderate to severe lymphedema for breast cancer

patients who have had an axillary lymph node dissection, to determine if there is a correlation between arm circumference measurements and subjective perception of severity of lymphedema, to investigate the degree of interference of lymphedema on patient's quality of life, as well as which patient and treatment characteristics are associated with the various degree of interference with quality of life.
(MD03999)

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

Edition Title/Investigators

2001-02 Studies on Anti-tumour Effect of M225, a Monoclonal Anti-epidermal Growth Factor Receptor Antibody, on Nasopharyngeal Carcinoma (MD01039)
✉ CHAN Anthony Tak Cheung • JOHNSON Philip James • POON Chuen Wai (Dept of Medicine & Therapeutics) • TO Ka Fai (Dept of Anatomical & Cellular Pathology)

2002-03 A Randomized Phase II Study of Concurrent Cisplatin-radiotherapy with or without Neoadjuvant Chemotherapy Using Taxotere and Cisplatin in Advanced Nasopharyngeal Carcinoma (MD02726)
✉ CHAN Anthony Tak Cheung • MOK Shu Kam Tony • LEUNG Sing Fai • TEO Peter* • HUI Edwin P* • LAM Kwok C* • KAM K Michael* • CHIU K W* • KWAN Wing H*

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 (Dept of Medicine & Therapeutics) • TO Ka Fai (Dept of Anatomical & Cellular Pathology)

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

2000-01 Randomized, Double-blind, Placebo-controlled Trial of Primary Prophylaxis with Recombinant Human Thrombopoietin (rhTPO) Administered to Patients Receiving DHAP Chemotherapy for Recurrent or Refractory Intermediate-grade or High-grade non-Burkitt's, non-Hodgkin's Lymphoma (NHL) (MD20067)
✉ LEI Ieng Kit Kenny • LEUNG Wai Tong Thomas# • HUI Pun

2001-02 Impact on Salivary Gland Function by Intensity-modulated Radiation Therapy in Treatment of Nasopharynx Cancer: A Prospective Randomised Trial (MD01041)

- ✎ LEUNG Sing Fai • CHEUNG Kin Yin • KAM Koon Ming Michael • TEO Man Lung Peter
- 2002-03 Identification of Changes in Protein Expression Patterns in Nasopharyngeal Carcinoma in Response to Anti-Epidermal Growth Factor Drug Cetuzimab (C225) (MD02776)
- ✎ MA Buig Yue Brigitte • POON Chuen Wai (Dept of Medicine & Therapeutics) • LO Kwok Wai (Dept of Anatomical & Cellular Pathology) • PANG Ting Kai Ronald • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute) • CHAN Anthony Tak Cheung
- 2000-01 A Double-blind Placebo-control Randomized Study of the Efficacy of Chinese Herbal Medicine in Reduction of Cytotoxic Chemotherapy-induced Toxicity (CU00109)
- ✎ MOK Shu Kam Tony • JOHNSON Philip James • YEO Winnie • ZEE Chung Ying Benny (Faculty of Medicine (Planning Office))
- 2000-01 A Phase I/II Open Label Study of T138067-sodium in Patients with Advanced Surgically Unresectable Hepatocellular Carcinoma (MD20061)
- ✎ MOK Shu Kam Tony • JOHNSON Philip James
- 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)
- ✎ MOK Shu Kam Tony • JOHNSON Philip James • ZEE Chung Ying Benny (Faculty of Medicine (Planning Office))
- 2001-02 A Phase II Study of Sequential Administration of Irinotecan and Cisplatin Combination Followed by Docetaxel in Treatment of Advanced Non-small Cell Lung Cancer (MD01922)
- ✎ MOK Shu Kam Tony
- 2001-02 Phase II Trial of Gemcitabine-carboplatin-paclitaxel as Neo-adjuvant Chemotherapy for Operable Non-small Cell Lung Cancer (MD01571)
- ✎ MOK Shu Kam Tony • WONG Tze Ming • LAM Kwok Chi
- 2002-03 Kinetic of Plasma HBV-DNA Following Transarterial Chemo-embolization: a Potential Tumor Marker for HCC (MD02993)
- ✎ MOK Shu Kam Tony • ZHONG Sheng# • LEUNG Wai Tong Thomas# • LEE Conrad*
- 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 (Faculty of Medicine (Planning Office))
- 1997-98 High Dose Adjuvant Chemotherapy and Peripheral Stem Cell Transplant for High Risk Breast Cancer Patients (MD95266)
 ✍ YEO Winnie • KWAN Wing Hong • TEO Man Lung Peter • LEUNG Wai Tong Thomas# • SUEN Wang Ming Michael (Dept of Anatomical & Cellular Pathology) • KING Wing Keung Walter (Dept of Surgery)
- 1997-98 Randomized Trial of Tamoxifen versus Placebo for the Treatment of Inoperable Hepatocellular Carcinoma (MD97169)
 ✍ YEO Winnie • JOHNSON Philip James • LEUNG Wai Tong Thomas#
- 2001-02 Detection of Mitochondrial DNA Mutation in Tumour and Peripheral Blood (Cell-free) of Patients with Hepatocellular Carcinoma (MD01045)
 ✍ YEO Winnie • JOHNSON Philip James • ZHONG Sheng#
- 2001-02 Open-label, Multicenter, Randomized, Controlled Study of IM or Oral Exemestane (Aromasin^R) in Postmenopausal Women with Advanced Breast Cancer (ABC) Having Progressed on Tamoxifen (MD01739)
 ✍ YEO Winnie • HO Wing M* • KWAN Wing H*
- 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)
 ✍ YEO Winnie
- 2002-03 A Randomized, Double-blind, Parallel-Group Study Conducted Under In-house Blinding Conditions to Determine the Efficacy and Tolerability of Aprepitant for the Prevention of Chemotherapy-induced Nausea and Vomiting Associated with Moderately Emetogenic Chemotherapy (MD02388)
 ✍ YEO Winnie • POON Annette* • LAU S M June*
- 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)
 ✍ YEO Winnie • MOK Shu Kam Tony • LAM Kwok Chi • HO Wing Ming • ZEE Chung Ying Benny (Faculty of Medicine (Planning Office)) • CHAN Anthony Tak Cheung • LEUNG Wai Tong Thomas# • JOHNSON Philip James

RESEARCH PROJECTS

Effects of Soy Isoflavones Supplementation on Cognitive Function in Chinese Postmenopausal Women : A Double-blind Randomized Controlled Trial

✉ HO CHAN Suzanne • CHAN Sui Yin Agnes (Dept of Psychology) • HO Yee Ping (School of Pharmacy) • WOO Jean (Dept of Medicine & Therapeutics) • ZEE Chung Ying Benny (Faculty of Medicine (Planning Office))

☐ 1 August 2003

❖ Research Grants Council (Earmarked Grants)

The menopause is associated with a dramatic decline in circulating estrogen concentrations. Among the many reported menopausal related symptoms, psychological symptoms, including memory loss, are among the most noted complaints in Chinese climacteric women. Estrogen deficiency has been proposed as among the causes for age-related cognitive decline in menopausal women.

Studies have suggested that estrogen replacement therapy (HRT) may be effective in improving cognitive function in postmenopausal women. However, the use of HRT is low in the Asian countries, including Hong Kong. There are women in whom HRT is contraindicated, and there are concerns for the HRT-associated risks. Recent laboratory, animal and limited human studies have suggested that isoflavonoid phytoestrogens, with the highest concentration in soy foods, seem to have a positive effect in cognitive function. However, the hypothesis is still speculative.

This study proposes to investigate the effects of soy isoflavone supplement on cognitive functioning as

compared to placebo in Chinese postmenopausal women. It is hypothesized that isoflavone supplement will be beneficial in the promotion and preservation of cognitive function, and the overall quality of life.

Soy food is traditionally part of the Asian diet. If proven effective, the provision of alternative methods to HRT will be an important breakthrough for women who cannot or choose not to take HRT. The significance of this work lies in the potential of a simple dietary intervention that is culturally and traditionally acceptable. Thus the proposed study would have potential great clinical as well as public health impact.

(CU03471)

Adolescent and Adult Soy Intake and Breast Cancer Risk in Chinese Pre-menopausal Women

✉ HO CHAN Suzanne • WOO Jean (Dept of Medicine & Therapeutics) • CHU Chiu Wing Winnie (Dept of Diagnostic Radiology & Organ Imaging) • YEO Winnie (Dept of Clinical Oncology) • TANG Leung Sang Nelson (Dept of Chemical Pathology) • LAU Tak Fai Joseph (Centre For Epidemiology & Biostatistics)

☐ 1 March 2004

❖ World Cancer Research Fund International Grant

Hong Kong has experienced an increase in breast cancer (BC) incidence over the past 10 years, particularly in younger women. A one-and-half fold increase is noted in the age group 45 to 59 years. The increase may be partially attributable to changes in lifestyle factors, particularly pattern of dietary intake and physical activity.

Case-control studies have shown soy food intake in early life may reduce risk of BC, particularly among pre-menopausal women (Wu 2002; Lee, 1990).

However, recall bias on information obtained after the disease diagnosis is an important limitation for case-control study. Some researchers have begun investigations of mammographic density (Jakes, 2002) which has been shown to be associated with the development of BC.

This study proposes to investigate both cross-sectionally, and longitudinally the relation between soy food intake and mammographic density in a population-based sample of premenopausal women aged 38 to 48 years. The study aims to investigate whether high intake of soy protein, in particular soy protein, in particular soy isoflavones, reduces the risk breast pattern / density. The mean soy protein intake ranging from the mean $1.39 \pm 0.75\text{g/d}$ in the first intake quartile to $19.21 \pm 10.66\text{g/day}$ in the 4th intake quartile observed in a recent study would provide an adequate variation for testing the research hypotheses. The study will relate adolescent and adult soy food intake to mammographic density pattern / in the cross-sectional study, and changes in the longitudinal study, taking into account relevant genetic, health and lifestyle confounding factors.

(MD03666)

Provision of Population Health Survey - Second Module on Cardiovascular Disease and Risk Factor

✉ HO CHAN Suzanne • WOO Jean (Dept of Medicine & Therapeutics)

☐ 1 May 2004

❖ Dept of Health, HKSAR Government

A territory-wide study of cardiovascular disease risk factor prevalence was carried out in 1995. A repeat of such a survey nine years later would give some indication of the effectiveness of preventive measures,

if disease prevalence or risk factor prevalence were shown to have fallen.

This is a contract service for Department of Health (DH) for assessing the health status of the Hong Kong population. The study aims to determine the prevalence of ischaemic heart disease and stroke; to determine the prevalence of cardiovascular risk factors; and to compare the findings with those from the Hong Kong Cardiovascular Risk Factor Prevalence Study conducted in 1995.

About 1,600 subjects, approximately 200 subjects from each of the eight sex and age groups (15-24,25-44,45-64,65-84 years) will be generated at random by the Department of Health based of the participant list of the First Module.

Participants will be screened for coronary heart disease with the use of Rose angina questionnaire, which is a screening tool in initial telephone contact. They will be invited to attend designated centres for blood tests on lipid profile (Total cholesterol, HDL, LDL, VLDL, triglycerides) and blood glucose.

Both questionnaire and blood results will be reviewed by a medical doctor (specialist in internal medicine). Subjects found to have abnormal response or results would be recommended to consult a doctor and a referral note and blood results will be given to them.

(MD03481)

21st Century Hong Kong, a Health Promoting Society: A Territory Wide Community Participation in Promoting Health

✉ LEE Albert • CHENG YAM Fung Khing Frances

☐ 20 July 2003

❖ Hong Kong Health Education and Health Promotion Foundation

In 2000, the Quality Education Fund has granted

HK\$8.86 million to Centre for Health Education and Health Promotion to develop a comprehensive health education program implementing the concept of Healthy Schools. The aims are: (1) To provide training in Health Promotion and Health Education to train school-related workers; (2) To establish a district based task force of teachers, parents, students, health and social services professionals, administrators, and community leaders working in partnership to promote school health through curricular and extra-curricular activities. This task force is charged with the challenge of developing core values, visions, goals and activities that would provide a new direction for health education within the district; (3) To conduct research in health promotion and health education, school health surveillance and evaluation; (4) To publish journals, textbooks, periodicals and newsletters in health education and health promotion; (5) To provide consultancy services in health education and health promotion for the school community.

Although the funding support from QEF ended on June 30, 2003, the concept needs to be ongoing. The project will be further developed to promote quality education and quality primary health care which is in line with health care reform to promote preventive medicine, and also education reform in promoting healthy lifestyles and active living.

(MD03863)

Professional Development Program for Primary Care Practitioners

✍ LEE Albert • CHENG YAM Fung Khing Frances • 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)

□ 2 October 2003

❖ HEP Foundation • Matching Contribution (PSDAS) • Professional Services Development Assistance Scheme, Commerce, Industry and Technology Bureau, HKSAR Government

The project aims at enhancing the professional development of local primary care practitioners. A 10-month Professional Certificate course in primary care included a series of seminars, workshops which will be held to enhance the health professionals in understanding the concept of primary health care, the role of different professionals, and the skills in delivering quality and structured primary health care. Clinical attachment in the community settings will also be arranged to let candidates experience the delivery of primary health care in the local community. A web page, containing clinical quizzes and discussion forum, will be established to facilitate self-learning. At the end of the project, a 2-day international conference will be organized to update the knowledge of local primary care practitioners on the latest trend of primary health care.

(MD03795)

Development of a Template for a Teachers' Short Course on Health Promoting Schools

✍ LEE Albert • CHENG YAM Fung Khing Frances

□ 20 December 2003

❖ World Health Organization

A template for a teacher's short course on health promoting schools is proposed to address the need for a practical capacity building intervention to

accelerate expansion of health-promoting schools in the Western Pacific Region. Currently, there have been some models for successful partnerships between Ministries of Health and Ministries of Education for pilot projects but many of these are of limited scale and are not able to impact on large populations of school children within a country.

Four day training of trainers workshop at the campus of The Chinese University of Hong Kong with field visits and other experiential learning activities. It is aimed to develop a regional teacher's training short course on health-promoting schools. The course will cover curriculum development and trainers training workshop on a regional teacher's training on health promoting schools with selected countries [Kiribati, Lao PDR, Papua New Guinea, Tuvalu, Viet Nam].

A study tour for participants will be organize to visit a health education resource centre and interact with other stakeholders in health promoting schools such as community leaders, school administrators, teachers and children. An interactive website for participants in the trainers training workshop will be set up to enable continuing dialogue and interaction as the regional teacher's training course is adopted at country level. Evaluation in the form of the trainers participation in their own home country.

(ED03431)

Kwai Tsing Healthy City and Safe Community Project

✉ LEE Albert • CHENG YAM Fung Khing Frances • FUNG Wing Yan (Centre for Health Ed. & Health Promotion) • WONG Wing Suen (Centre for Health Ed. & Health Promotion)

☐ 1 January 2004

❖ Kwai Tsing District Council

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 Kwai Tsing 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

(MD03346)

Evidence Based Primary Care: Management Guidelines for Osteoarthritis in Primary Care Setting

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

☐ 1 February 2004

❖ GlaxoSmithKline Limited

The Family Medicine Unit of Department of Community and Family Medicine, Chinese University of Hong Kong, would like to establish an ad hoc committee to review the recent developments in the field and update the recommendations. The committee would follow the principles of evidence-based medicine as used in the process of making clinical decisions. This guideline will address the appropriate use of drugs in the primary care treatment of patients with osteoarthritis. It does not consider therapies other than drug treatment. General practitioners / family physicians must use

their professional knowledge and judgement when applying guideline recommendations to the management of individual patients. They should note the information, contraindications, interactions, and side effects contained in the *MIMS Annual Hong Kong*.

(MD03823)

Programme for Extended Courses on "Health Promoting School" to School Heads and Teachers

✍ LEE Albert • CHENG YAM Fung Khing Frances

□ 2 June 2004

❖ Curriculum Development Institute, Education and Manpower Bureau

To provide a series of 1 day workshop for Principals and Teachers of Primary and Secondary Schools for the summer of 2004.

The series of training workshop is an extended course to the one conducted last summer. This extended course serves to bring the whole picture of the concept of "Health Promoting School" in perspective. (ED03838)

A Randomized Controlled Trial to Evaluate the Credibility of a Sham Placebo Acupuncture Design

✍ TANG Jinling

□ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

The randomized controlled trial is scientifically the most rigorous method for evaluating the efficacy of medical interventions. Sham acupuncture as a placebo control in a randomized trial helps to

implement blinding and reduce observer biases that may arise due to the observers' knowledge of the treatment patients receive. As acupuncture is a procedural treatment, it is particularly difficult to design satisfactory placebo acupuncture. Five different designs have been proposed and used in clinical trials. Among these different designs, a normal acupuncture needle being inserted at non-acupuncture or irrelevant acupuncture points (acupoints) and with moderate needling manipulation seems to provide a promising placebo procedure. However, the credibility of this placebo design has not been properly evaluated against the requirements of a placebo: no specific therapeutic effect and mimics the real treatment so that those involved in the trial cannot tell the difference. We thus design a randomized controlled cross-over trial to evaluate the credibility of the minimal acupuncture as a placebo control in clinical trials of acupuncture.

(MD03557)

Assessment of Toxic Air Pollutant Measurements in Hong Kong - An Extended Study

✍ WONG Tze Wai • LAU Kai Hon Alexis* • LOH Kung Wai Christine*

□ 1 October 2003

❖ Environmental Protection Department, HKSAR Government

This study aims to characterize the composition, toxicity, possible sources and trends of PM_{2.5} both in Hong Kong and its neighbouring area, to evaluate the health and economic impacts of current and projected pollution levels of PM_{2.5}, to consider whether tighter PM objectives would be appropriate for Hong Kong, and if so, broadly assess practicable control options that can help achieve compliance of the tighter objectives.

(The part to be conducted by CUHK: Determination of the health impacts of PM_{2.5} both under its current and projected pollution levels.)

(MD03450)

Improving General Practitioners' Interviewing Skills in Managing Patients with Common Psychiatric Problems in Primary Care: A Randomized Clinical Trial

✉ WONG Yeung Shan Samuel • LEE Albert • WONG Chi Wai

☐ 1 March 2004

❖ CUHK Research Committee Funding (Direct Grants)

Although almost 60% of mental health care is provided in primary care settings, primary care practitioners fail to recognize up to two thirds of the emotional disorders manifested by their patients. Previous studies showed that training can increase the sensitivity of primary care physicians to mental health problems. Moreover, training can improve physicians' communication skills, leading to greater patient disclosure of sensitive psychosocial information and better detection of emotional distress. In one study, two four-hour interactive workshops changed primary care physicians' behaviour and communication skills in diagnosing and managing depression.

In this study, a randomized control trial will be conducted to explore the effect of a four 2-hour Depression and Anxiety Education Program for general practitioners on their interviewing behaviour and diagnostic ability when consulted by patients presented with depression or generalized anxiety disorders. The outcome measures will include: change of their behaviour and communication skills measured by standardized checklists (completed by

standardized patients and trained interviewers during interviews and video tapes). Improvement of their management skills for depression and anxiety (assessed from the standardized patients' records and reviews of video tapes).

The objectives are as follows:-

1. To investigate the effectiveness of a brief education program to improve physicians' ability to diagnose and manage depression and generalized anxiety disorders in primary care
2. To see if such brief education program improve physicians' interviewing behaviour and communication skills

Results from the study will provide evidence for the effectiveness of a brief training course for general practitioners. It will help to provide important information for future development of higher training for general practitioners in handling psychosocial issues in primary care.

(MD03945)

Male Lung Cancer, Occupational Exposures and Smoking - A Case-control Study in Hong Kong

✉ YU Tak Sun Ignatius • TSE Lap Ah • WONG Tze Wai

☐ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

Lung cancer is the leading cause of deaths among men in Hong Kong for decades. Only half of the lung cancer cases among Hong Kong Chinese males could be attributable to smoking. Occupational lung carcinogens account for a substantial proportion of lung cancers in industrialized countries, but the relationship between occupational exposures and lung cancer has not been properly studied in Hong Kong.

The present study will investigate the associations between occupational exposures to various potential lung carcinogens and lung cancer after taking into consideration the effects of other potential risk factors - smoking , diet, residential radon exposure, cooking fume, etc. We shall interview 1,000 to 1,200 newly diagnosed male lung cancer cases and an equal number of age-matched controls without lung cancer, selected from among hospital patients as well as an equal number of controls from the general population using a standardized questionnaire. Information on their lifetime occupational history, smoking habits, passive smoking exposures, diet history, previous diseases, cooking fumes exposure, etc. will be obtained. By comparing the differences in occupational exposures between cases and controls, we shall be able to document the occupational hazards that are important in the causation of lung cancer among males in Hong Kong. Interactions between occupational exposures and smoking will also be explored.

This study will provide the necessary information on the burden of occupational hazards on lung cancers among the general male population in Hong Kong. Such information will guide future strategies for improving population health and saving medical resources.

(CU03460)

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

Edition Title/Investigators

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 (Dept of Medicine & Therapeutics) • YU Jimmy C. (Dept of Chemistry)

2001-02 Development of Food Frequency Questionnaire and Database for Assessing Soy Isoflavones Intake in the Chinese Population (MD01047)

✍ HO CHAN Suzanne • CHEN Zhenyu (Biochemistry) • WOO Jean (Dept of Medicine & Therapeutics)

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 (Dept of Medicine & Therapeutics) • WOO Jean (Dept of Medicine & Therapeutics) • CHAN Sieu Gaen • HO Sin Yee Stella (Dept of Diagnostic Radiology & Organ Imaging) • LAM Wai Kei Christopher (Dept of Chemical Pathology) • AHUJA Anil Tejbhan (Dept of Diagnostic Radiology & Organ Imaging)

2002-03 A Study of Informal Caregivers and Association of Caregiving Status with Health and Quality of Life (MD02923)

✍ HO CHAN Suzanne • WOO Jean (Dept of 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 (Dept of Psychology)
- 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 (Dept of Psychology)
- 2001-02 Testing the Effectiveness of an
Intervention Programme in Reducing
Non-urgent Utilization of Accident and
Emergency Services: Pilot Study to
Analyse the Feasibility and Develop the
Framework of the Intervention
(MD01314)
✍ LEE Albert • CHENG YAM Fung
Khing Frances
- 2002-03 Improving the Services Standard of
Rehabilitation Personnel (MD02556)
✍ LEE Albert • TSANG Kwong Ka •
CHENG YAM Fung Khing Frances
- 2002-03 In-service Teacher Development Courses
on Moral and Civic Education for
Principals and Teachers of Primary and
Secondary Schools for the 2002-2004
School Years (Category: Health/Drug
Education) (ED02318)
✍ LEE Albert • CHENG YAM Fung
Khing Frances
- 2002-03 Development of Health Promoting
Schools: Intensive Course for School
Teachers (MD02657)
✍ LEE Albert • CHENG YAM Fung
Khing Frances • YUEN Suk Kwan
(Centre for Health Ed. & Health
Promotion) • HO Man (Centre for
Health Ed. & Health Promotion) •
AU Wing Yan Grace (Centre for
Health Ed. & Health Promotion)#
- 2001-02 A Study on the Prevalence, Brain Pain
Centre Activity, Psychological Stress and
Quality of Life of Subjects with the
Irritable Bowel Syndrome (IBS)
(MD01046)
✍ TANG Jinling • CHAN Ka Leung
Francis (Dept of Medicine &
Therapeutics) • LAU Edith Ming
Chu# • LEE Albert • LEUNG Chi
Ming (Dept of Psychiatry) • SUNG
Joseph Jao Yiu (Dept of Medicine &
Therapeutics) • CHAN Cynthia Shiu
Yee • WU Che Yuen Justin (Dept of
Medicine & Therapeutics)
- 2002-03 Development and Analysis of Primary
Care Prescribing Database (MD02322)
✍ WONG Chi Wai • CHAN Cynthia
Shiu Yee
- 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*

- 2002-03 Air Pollution and Respiratory Diseases in Primary Health Care (MD01938)
✍ WONG Tze Wai • WUN Yuk Tsan Kyran Patrick# • YU Tak Sun Ignatius • TAM Wai San Wilson
- 2001-02 Postmenopausal Evaluation And Risk Reduction with Lasofoxifene (PEARL) (MD01823)
✍ WONG Yeung Shan Samuel • WOO Jean (Dept of Medicine & Therapeutics) • LEUNG Ping Chung (Dept of Orthopaedics & Traumatology) • CHAN Wan Kin (HK JCC for Osteoporosis Care and Control)
- 2002-03 Record on Satisfaction of Patients with Actonel 35mg Once-A-Week (MD02804)
✍ WONG Yeung Shan Samuel • CHOY Tak Kee Dicky (HK JCC for Osteoporosis Care and Control) • WOO Carrie (HK JCC for Osteoporosis Care and Control)#
- 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

RESEARCH PROJECTS

Cardiac Energetics in Thalassaemic Patients and Its Relationship with Total Body and Cardiac Iron Overload: An *in vivo* ³¹P Magnetic Resonance Spectroscopy and Magnetic Resonance Imaging Study

✍ CHAN Yu Leung • CHIK Ki Wai (Dept of Paediatrics)

☐ 1 September 2003

❖ CUHK Research Committee Funding (Direct Grants)

Beta-thalassaemia major is the most common transfusion dependent anaemia in Hong Kong with iron-overload in the body being the most important complication of the chronic blood transfusion treatment. Cardiomyopathy, occurring in 15% of these patients from the adverse effect of excessive iron on energy production in myocardial cells, is the leading cause of death in beta-thalassaemia major. The chelation treatment of iron-overload has been conventionally monitored by measuring the total body iron status, - there being no safe technique available to estimate the cardiac iron. The finding of a dissociation of cardiac iron-overload and body iron-overload in a recent study has however generated issues regarding the appropriate investigation to estimate the risk of iron toxicity, which is necessary for determining the chelation regimen. As the decision on the appropriate investigation for these patients would depend on knowing the relationship of cardiac iron-overload and total body iron-overload, and the effect of the cardiac iron overload on the physiology and function of the heart, we propose to take advantage of the recent

technological advances in magnetic resonance to non-invasively study the cardiac energetics by using³¹ phosphorous magnetic resonance spectroscopy, and the cardiac iron-status and function by cardiac magnetic resonance imaging.

(MD03426)

The Effect of Rigid Underarm Brace on the Correction of Spinal Curve in Idiopathic Adolescent Scoliosis during Sleeping

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

☐ 1 May 2004

❖ CUHK Research Committee Funding (Direct Grants)

In assessing the compliance of orthotic treatment for Adolescent Idiopathic Scoliosis (AIS), the commonly accepted methods are to ask the family if the orthosis is being used and to visually inspect for signs of wear. However, in routine clinical practice, the effectiveness of bracing is judged using standing X-ray films. There are few studies about the effect of orthosis on the scoliotic spine in lying positions where the axial gravitational effect on the spine is eliminated. Would the rigid spinal orthosis really work in sleeping hours?

With the introduction of MRI, it becomes possible to study how the orthosis performs in different recumbent positions in a non-invasive fashion. This study is the first to assess in details how bracing can correct the spinal curvature of AIS patients in three conventional anatomical planes during recumbent positions. With the use of MRI, the degree of rotational deformity in AIS can be accurately measured in a three-dimensional manner. The

results will enable better understanding of the effect of bracing to the AIS patients during bedtime. The result, no matter it shows significant effect of bracing at bedtime or not, will provide evidence base for the current practice of full-time treatment protocol with long-hour bracing. Furthermore, if bracing is effective in spinal correction during bedtime, a preferred recumbent position might be found to maximize its effect.

(MD03341)

Radio-frequency Ablation for Better Quality of Life

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

□ 1 April 2004

❖ S.K. Yee Medical Foundation

Minimal invasive treatment as alternative to radical or conventional surgery for treatment of carcinoma are becoming more attractive simply because of improvement in technology, reduced side effect including morbidity and mortality. Most patients can receive treatment in an out-patient or day care setting.

Radio-frequency (RF) ablation has become more popular in the west as imaging-guided ablation method. It is relatively low cost and low toxicity. It is able to kill the tumour cell in a controlled fashion (coagulative necrosis).

Many part of body can be potentially treated by RFA without major side effect. In the past the clinical application of RFA focused at liver. However, the potential use and safety in other part of the body needed to be established, such as breast, kidney or bone tumour. RFA is also useful in control local tumour growth and to improve quality of life of

patient suffered from inoperable carcinoma and terminal care.

(MD03435)

Prevention and Treatment of Ischaemic Stroke by Endovascular Stenting of Intracranial Vascular Stenosis

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

□ 1 May 2004

❖ S.K. Yee Medical Foundation

Ways in which the project is of direct benefit to the poor and sick:

1. A screening program will be arranged for patients presenting with minor stroke despite appropriate medication for stroke management and prevention. Screening is by means of non-invasive brain scanning with magnetic resonance imaging, to detect for presence of blood vessel narrowing within the brain.

2. Narrowed brain vessels of the stroke patients will be widened with artificial reconstruction of the blood vessel by a non-surgical and minimally invasive stenting procedure. After the treatment procedure the patients can be protected from suffering a major stroke which will likely lead to death or severe morbidity.

Aims:

3. To provide a screening program for stroke patients to detect narrowing of brain vessels.

4. To provide a stenting treatment procedure to widen narrowed brain vessels of stroke patients to prevent to occurrence of a major stroke.

5. To protect stroke patients from the danger of death from a major stroke and the suffering of severe morbidity as a result of major stroke.

6. To decrease the incidence of major stroke in the society and thereby reduce the medical expenses of the society on stroke management.

7. To accumulate experience of stenting procedure to enhance knowledge of stroke management and to refine procedure techniques.

Implementation plans and work schedule:

8. Application of ethics approval of the project (approved in December 2002).

9. Application of funding (current exercise).

10. Commencement of screening program to detect narrowed brain vessels (upon funding allocation).

11. Installation of an image signed network system to allow a precise navigation system for the stenting procedure.

12. Commencement of the performance of stenting treatment procedures and a clinical and radiological follow up program.

13. Evaluation of treatment outcomes after treatment of 30 patients.
(MD03571)

Irradiated Normal Brain Tissue after Arteriovenous Malformation Radiosurgery (CU00104)

✉ CHAN Yu Leung • CHIU Kwok Wing Samuel (Dept of Clinical Oncology) • LAM Ming Kuen Joseph (Dept of Surgery) • YEUNG Ka Wai David*

2001-02 Clinical and MRI Evaluation of Skeletal Changes and Growth in Well Chelated Thalassaemic Patients: Comparison of Oral Chelator with Desferrioxamine (MD01507)

✉ CHAN Yu Leung • CHIK Ki Wai (Dept of Paediatrics) • HA Shau Yin* • OOI Gaik Cheng*

2002-03 Combined Static-dynamic MR Urography for Congenital Urinary Tract Obstruction in Children before and after Corrective Surgery (MD02950)

✉ CHU Chiu Wing Winnie • YEUNG Chung Kwong (Dept of Surgery)

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

Edition Title/Investigators

2002-03 Glemoid Bone Loss in Recurrent Shoulder Dislocation: Quantification with Computer Tomography and Magnetic Resonance Arthrography (MD02513)

✉ ANTONIO Gregory • GRIFFITH James Francis

2000-01 Turbo Spectroscopic Imaging Evaluation of Dose-response Relationship in

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

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

RESEARCH PROJECTS

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

✉ BAUM Lawrence William • NG Ho Keung
(Dept of Anatomical & Cellular Pathology)

☐ 1 November 2003

❖ CUHK Research Committee Funding (Direct Grants)

Alzheimer's disease (AD) is a common cause of death and disability. Anti-inflammatory drugs and anti-oxidants help prevent AD. Because curcumin, an extract of the herb *geung wong* which is widely used as a food coloring, has anti-inflammatory and anti-oxidant effects, it was recently tested in AD animal models. Curcumin reduced amyloid plaque deposits, inflammation, and oxidant damage in brain, and also reduced memory loss. There are several possible mechanisms: lowering cholesterol, which may inhibit amyloid production; reducing inflammation, which may block immune damage to neurons; anti-oxidation, which may block direct neuron damage; chelating metals, which may reduce metal-induced amyloid aggregation; inhibiting kinases which transduce amyloid toxicity; and reducing secretion of Apolipoprotein E (ApoE), since ApoE can induce amyloid formation.

I propose to test the latter three mechanisms. Our preliminary study used changes in the curcumin absorbance spectrum after adding metal ions to measure the affinity of curcumin for metals. I propose to test the ability of curcumin to inhibit metal-induced amyloid aggregation *in vitro* by using 0.2 micron filters to trap aggregates. Three

proline-directed kinases, JNK, GSK3 β , and CDK5, transduce amyloid neurotoxicity. Curcumin inhibits JNK. To test whether curcumin also inhibits GSK3 β , and CDK5, I will expose cells to curcumin and amyloid, immunoprecipitate JNK, GSK3 β , and CDK5, and measure their activity. Curcumin inhibits prenylation, which is required to release ApoE from glia in the brain. We will test whether curcumin inhibits ApoE secretion by cultured cells. These results may yield insights into AD pathogenesis and lead to new AD drugs.
(MD03921)

The Relationship Between Erectile Dysfunction and Endothelial Dysfunction in Chinese Type 2 Diabetes Patients

✉ CHAN Chung Ngor Juliana • CHAN Nor Norman (Dept of Community and Family Medicine)# • TONG Peter Chun Yip

☐ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

In men with type 2 diabetes, there is a very high prevalence of erectile dysfunction which contributes to decreased quality of life. The underlying cause of this complication is complex and may involve several components including vascular, hormonal, psychological and pharmacological. Identification of these factors would help to determine the most appropriate therapies. The vascular endothelium plays an important role in maintaining vascular integrity and endothelial dysfunction has been associated with diabetic vascular complication. Whether endothelial dysfunction plays a key role in erectile dysfunction in diabetes remains unclear. Although animal data are suggestive, no studies in humans have addressed this problem directly. We

therefore plan to initiate this study to investigate whether endothelial dysfunction is associated with erectile dysfunction in type 2 diabetic men. In addition, there is growing evidence that the endogenous nitric oxide synthase inhibitor, asymmetric dimethylarginine (ADMA), plays an important role in endothelial dysfunction in many disease conditions, including diabetes. We plan to investigate the determinants of erectile dysfunction in diabetic men and whether elevated ADMA occurs in endothelial dysfunction in diabetic men with erectile dysfunction.

(MD03790)

Olmesartan Reduces Incidence of Endstage Renal Disease in Patients with Type 2 Diabetic Nephropathy Trial (ORIENT)

✉ 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

□ 20 January 2004

❖ Sankyo Pharmaceutical Company

Type 2 diabetes is the leading cause of end stage renal disease (ESRD) both locally and on a world wide basis. Epidemiological and randomized clinical studies have confirmed that Chinese and Japanese type 2 diabetic patients have increased risk for developing ESRD compared to Caucasian populations. There are now studies showing that treatment with angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) have renoprotective effects independent of their blood pressure reducing effects. Furthermore, preliminary studies also suggest that inhibition of the rennin angiotensin system (RAS) using dual therapy of ACE inhibitors and ARB reduced proteinuria more

effectively than single agent for similar blood pressure reduction. The dual therapy was well tolerated with minimal effects on hyperkalaemia or blood pressure. In this landmark Japan-Hong Kong multicentre randomized double-masked, placebo-controlled, study, 400 type 2 diabetic patients with nephropathy and renal impairment established on ACE inhibitors will be randomised to receive either Olmesartan, an ARB or placebo over a 5-year period. The primary endpoint is death or ESRD defined as need for dialysis or doubling of baseline plasma creatinine. Half of these patients will be recruited from Hong Kong and half will be from Japan. The results of this study will have major health care implications in light of the growing epidemic of type 2 diabetes in Asia and the predilection for Asian population to develop ESRD.

(MD03356)

Prevalence of Diabetes and Metabolic Syndrome in Hong Kong Adolescents

✉ CHAN Chung Ngor Juliana • TONG Peter Chun Yip • OZAKI Risa • QING Qiao* • TUOMILEHTO Jaakko*

□ 1 March 2004

❖ Hong Kong Foundation for Research and Development in Diabetes

There is now a burgeoning epidemic of diabetes and metabolic syndrome on a worldwide basis. Much of this increase will occur in Asia and the increase is mainly found in the young to middle-aged population. This is in turn due to the rising prevalence of obesity in childhood which is associated with a constellation of risk factors. The pathogenesis of metabolic syndrome involves genetic, lifestyle, intra-uterine and environmental factors. Using a cluster-sampling method, 2000 adolescents aged between 11 and 18

years were recruited to undergo clinical and biochemical assessments to estimate the prevalence of metabolic syndrome including glucose intolerance, dyslipidemia, high blood pressure, albuminuria and obesity. These results will be jointly analysed by the project team and the world renowned epidemiological group in Finland, led by Prof Jaakko Tuomilehto. Finding from this study will provide important sight into the magnitude of the problem and also generate hypothesis for further testing in our attempt to understand the etiologies of this public health problem and thus, design interventional measures.

(MD03932)

A Population-based Study on the Prevalence of SARS-associated Coronavirus Infection in Hong Kong

✍ CHAN Ka Leung Francis • CHAN Kay Sheung Paul (Dept of Microbiology) • Douglas G ALTMAN* • LAU Tak Fai Joseph (Centre For Epidemiology & Biostatistics) • McCARTHY Noel* • NG Pak Cheung (Dept of Paediatrics) • SUNG Joseph Jao Yiu • WONG Wing-sze* • WU Ka Lun Alan • YU Ly-mee* • LO Su Vui*

□ 1 September 2003

❖ RGC Special Grants for Severe Acute Respiratory Syndrome (SARS) Research

The aim of this study is to investigate the prevalence of antibody to SARS-associated coronavirus infection in the general population of Hong Kong. The proportion of seropositive individuals in the population who is asymptomatic or had atypical or mild illness will be assessed. The result will provide clues to the possible risk factors for the disease, which may uncover the distribution and the mode of transmission of the virus. The proposed

study will set the ground for the future follow-up study on the seropositive subjects. A follow-up study on the seropositive subjects would help obtain important information about the persistence of antibody to SARS-associated coronavirus in the population following infection and/or possible immunization. Such information will shed light on the future formulation of hypotheses on the pathogenetic mechanisms of the disease.

(CU03532)

Preventing NSAID-associated Ulcer Bleeding for High-risk Patients: From Cyclooxygenase-2 to Therapeutics

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

□ 30 September 2003

❖ Research Grants Council (Earmarked Grants)

The incidence of bleeding peptic ulcer is 5 to 10 times higher in Hong Kong than in western countries. About 50% of the cases are induced by nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs are commonly used worldwide for the treatment of arthritis, painful conditions and, recently, prevention of colorectal cancer. However, NSAIDs are also notorious for its stomach toxicity. NSAIDs damage the stomach by inhibiting cyclooxygenase (COX), the key enzyme in prostaglandin synthesis. Recently, two isoforms of COX, COX-1 and COX-2, were identified. COX-1 produces prostaglandins that maintain the Integrity of the stomach barrier. In contrast, COX-2 is normally absent in the stomach but is induced at sites of inflammation e.g. arthritis. This finding has led to the development of NSAIDs selective for COX-2 as 'stomach-safe' painkillers (COX-2 selective NSAIDs). However, our recent study showed that among patients with a recent

history of ulcer bleeding who took a COX-2 selective NSAID, the risk of recurrent bleeding is still considerable. The objectives of this proposal are to:

1. study whether COX-2 has any significant contribution to prostaglandin synthesis at the previously damaged mucosal barrier; and
2. define an effective strategy for the prevention of NSAID-associated ulcer bleeding in high-risk patients.

(CU03455)

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

✉ CHAN Ka Leung Francis • LEE Yuk Tong • LEUNG Wai Keung • WU Che Yuen Justin • HUNG Cheung Tsui • HUI Aric Josun • WONG Wai Sun

□ 23 June 2004

❖ AstraZeneca Hong Kong Limited

The aim of the study is to investigate the effect of esomeprazole 20 mg o.d. versus placebo for up to 26 weeks for the prevention of gastric and/or duodenal ulcers in patients using low-dose SAS. This is a 26 weeks, randomised, double-blind, parallel-group, two-armed placebo controlled trial studying the effect of esomeprazole 20mg o.d. for the prevention of gastroduodenal lesions, erosive esophagitis and upper gastrointestinal symptoms in patients receiving low doses of ASA (75-325 mg daily). Male or female patients 60 years, with no active/current gastric and/or duodenal ulcer, whom are HP -ve and are at

moderate to high risk of developing gastroduodenal ulcers while taking low-dose ASA.

(MD03325)

A Multinational Phase 2 Study of LY582563 in the Treatment of Patients with Chronic Hepatitis B Viral Infections

✉ CHAN Lik Yuen • HUI Yui • SUNG Joseph Jao Yiu

□ 1 July 2003

❖ Eli Lilly (Asia) Inc.

This study (PDAC) is a Phase 2, double-blind, multicenter study of three oral treatment regimes in patients who are chronically infected with hepatitis B virus (HBV). Approximately 252 patients (20 from our center) will be enrolled. After enrollment and written informed consent, patients will be randomized to one of two LY528563 doses (5mg or 10mg daily) or lamivudine (100mg daily). Patients will be treated for 24 weeks. Follow-up interval will range from 1 to 4 weeks with clinical and laboratory assessments for evaluation of the hepatitis status as well as safety. Following drug discontinuation at week 24, the patients will be observed for 12 weeks and will then be offered the opportunity of participate in the extension study (PDAE) if there is evidence of hepatitis relapse. Patients enrolled into the extension phase of the study will be continued on the study medication that they were assigned to in this study (PDAC) in a blinded fashion until the data of PDAC is analysed and the optimal dose is selected.

(MD03640)

A Study on the Serum and Hepatic Viral Dynamics in Chronic Hepatitis B Patients Treated

**by Pegylated Interferon and Lamivudine
Combination Therapy**

✉ CHAN Lik Yuen

□ 1 November 2003

❖ CUHK Research Committee Funding (Direct Grants)

On anti-viral treatment of chronic hepatitis B, some patients who have negative serum HBV DNA at the end of treatment experience hepatitis relapse after cessation of treatment. This is believed to be related to the persistence of HBV DNA inside the hepatocytes in the form of closed covalent circular (ccc) DNA. This project aims to investigate the relationship of intrahepatic and serum HBV DNA with treatment response. An open-labeled, randomized study of pegylated interferon and lamivudine combination versus lamivudine monotherapy has been conducted in our center and it is expected to finish by October 2003. Serial serum samples and liver biopsy specimens of selected patients have been saved in -70°C freezer. HBV DNA in the serial serum samples during and after treatment as well as total intrabepatic HBV DNA will be measured by TaqMan real-time PCR assay, which can detect HBV DNA at a range of 10^2 to 10^9 copies/ml. The level of cccDNA will be measured by quantitative PCR using specific primers and quantified against a standard curve calibrated using serial dilution of a plasmid containing cccDNA donated by Prof. Stephen Locarnini of Victorian Infectious Disease Research Laboratory, Australia. The HBV DNA levels in the serum and liver among treatment responders and non-responders will be compared to detect any cutoff that can differentiate the two groups. The results of this study will improve the understanding of viral activity of chronic hepatitis B patients undergoing anti-viral treatments

and are important in the design of future treatment strategies.

(MD03584)

**A Study of Virodynamics in the Treatment of
Chronic Hepatitis B by Pegylated Interferon and
Lamivudine Combination**

✉ CHAN Lik Yuen • SUNG Joseph Jao Yiu •
ZEUZEM Stefan* • MIHM Ulrike*

□ 1 January 2004

❖ Germany/Hong Kong Joint Research Scheme

Chronic hepatitis B is the commonest cause of liver cirrhosis and hepatocellular carcinoma in Hong Kong. Since 1999, we have started an open-labeled, randomized (1:1) trial of pegylated interferon alfa-2b plus lamivudine combination treatment versus lamivudine monotherapy in the treatment of HBeAg positive chronic hepatitis B. The interim analysis of the first 40 patients showed that 75% of patients on combination treatment can achieve virological response (HBeAg seroconversion and negative HBV DNA) at the end of treatment and 50% remained so at 24 weeks after the cessation of treatment. Previous virodynamics studies have shown a biphasic viral reduction in the use of nucleoside analogues to treat chronic hepatitis B. An early phase of rapid reduction in HBV DNA reflects the inhibition of viral replication and clearance of hepatitis B virus in the blood, while a delayed slower reduction in HBV DNA reflects the clearance of hepatitis B virus inside the liver. This viral dynamics model provides important information including viral half-life and half-life of infected cell, which may be useful to predict response to anti-viral treatment. The viral dynamics of interferon and the combination of interferon and lamivudine has never been studied. Understanding of the viral dynamics will be

important for the refinement of treatment regime, decision of treatment duration and prediction of treatment response of this effective combination treatment. In this study, the pattern of serial HBV DNA reduction and the relationship between the viral dynamics and the treatment response will be studied.
(MD03949)

A Randomized, Double-blind Trial of Telbivudine (LdT) versus Lamivudine in Adults with Decompensated Chronic Hepatitis B and Evidence of Cirrhosis

✉ CHAN Lik Yuen • HUI Yui • WONG Wai Sun
 □ 1 May 2004
 ❖ Idenix Pharmaceuticals, Inc

This is a Phase III, randomized, double blind, multicenter study of treatment with telbivudine versus treatment with lamivudine, in adults with decompensated chronic hepatitis B. Approximately 240 eligible patients will be randomly assigned (1:1) to one of the following two treatment groups:

Group A: LdT 600 mg + lamivudine placebo PO daily x 104 weeks

Group B: LdT placebo + lamivudine 100 mg PO daily x 104 weeks

The primary efficacy endpoint is a composite endpoint called “Clinical Response” which is defined as HBV DNA < 10⁴ copies/mL AND ALT normalization AND improvement or stabilization in CTP score. During the study period, the investigator should continue with routine healthcare measures for the enrolled patients, including surveillance for HCC, according to the prevailing local standard of care. HCC surveillance and other routine healthcare modalities are not part of this study.

(MD03850)

A Randomized Controlled Trial to Evaluate the Safety and Efficacy of the Medtronic AVE ABT-587 Eluting Driver Coronary Stent in De Novo Native Coronary Artery Lesions

✉ CHAN Wai Man Wilson • YU Cheuk Man • KUM Chi Chiu Leo • WU Eugene Brian*

□ 1 August 2003

❖ Medtronic Bakken Research Center B.V.

One of the major limitations of percutaneous transluminal coronary angioplasty (PTCA) is restenosis, which occurs in 20% to 40% of patients. The loss of luminal diameter resulting in restenosis is primarily due to two mechanisms: elastic recoil of the vessel and neointimal hyperplasia. Coronary stenting reduces restenosis compared to balloon angioplasty alone by preventing acute elastic recoil. However, stents provoke increased neointimal hyperplasia with a consequent increase in late luminal loss. Despite novel new stent designs, restenosis still occurs in > 15% cases and a lot higher in more complex cases. Recently, drug eluting stents with stents coated with anti-proliferative agents have been shown to reduce both neointimal hyperplasia and in-stent restenosis dramatically.

This study is a phase III study demonstrating the safety and efficacy of the Driver Coronary Stent coated with a new anti-proliferative agent.

Patients with symptomatic ischemic heart disease due to stenotic lesions of native coronary arteries that fulfil the inclusion/exclusion criteria, will be recruited after informed consent. These patients will be randomised into 1 of the 2 treatment groups, either implanted with a stent coated with or without the anti-proliferative agent.

After the procedure, the patients will have the clinical follow-up at 30th day and 9th month after the stent

implantation, and also telephone follow-up at 6th month, 12th month and annually thereafter up to 5 years. This is a global study, the first 600 consecutive patients will have the angiographic follow-up at 8th month.

(MD03716)

Catheter Based Interventions for Patients with Symptomatic Peripheral Vascular Disease

✉ CHAN Yat Sun Joseph • YU Cheuk Man • CHAN Wai Man Wilson

□ 1 April 2004

❖ S.K. Yee Medical Foundation

Patients with peripheral vascular disease involving extracranial carotid arteries, renal arteries or peripheral vascular vessel supplying upper and lower limbs suffer from significant morbidity and mortality. At present the mainstay of treatment re surgical operations and catheter based peripheral vascular interventions. This group of patient usually has multiple medical problems and risk factors and significant increase peri-operative risk. Catheter based peripheral vascular interventions, on the other hand will potentially reduce incidence of these complications. The aim of the project is to provide a funding to cover the equipment costs pertained to catheter based peripheral interventions for patients with significant peripheral vascular disease who cannot afford to pay for the equipment cost.

(MD03998)

A Randomised, Multi-centre, Double-blind, Double-dummy, 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 the Treatment of Type 2 diabetic Subjects (Phase IIIa)

✉ CHOW Chun Chung Francis • COCKRAM Clive Stewart • CHAN Wing Bun* • OZAKI R* • SO W Y*

□ 20 July 2003

❖ Novo Nordisk Asia Pacific Pte Ltd

This is a 6-month extension of a double-blind, double-dummy, multi-center, 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:

1. 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}.
2. 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.

(MD03614)

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

✉ CHOW Chun Chung Francis • OZAKI Risa • MA Ching Wan Ronald

□ 1 December 2003

❖ Novo Nordisk Asia Pacific Pte Ltd

The purpose of this trial is to document BIAsp 30 as a novel, safe, effective and simple way to initiate insulin therapy in patient with type 2 diabetes and in a setting as close to daily clinical practice as possible

The design of this trial attempts to replicate current clinical practice as close as possible yet taking advantage of the improved pharmacodynamic profile of BIAsp 30. The trial will explore the potential benefits of BIAsp 30 as a simple and safe yet more effective way to initiate insulin treatment in poorly controlled type 2 patients.

Subjects who are inadequately control on their current OAD regimen will be recruited for the trial. They will be randomised to 2 groups; OAD group and BIAsp group. The former group will continue with the current OAD regime while the latter will continue with their current OAD therapy plus once daily BIAsp 30 injection (dinner)

The treatment goals for all subjects randomized in this trial are:

1. fasting or pre-prandial plasma glucose: 4.4 – 6.1 mmol/l (79-110mg/dl)
2. post prandial plasma glucose: 4.4-8.0mmol/l (79-144mg/dl)

After 12 weeks of treatment (at Visit 5), subjects in the BIAsp group will be split into two groups.

1. If $HbA_{1c} > 8.5\%$ OR $7\% \leq HbA_{1c} \leq 8.5\%$ but $FPG > 7\text{mmol/l}$ (126mg/dl), these subjects will increase BIAsp 30 dosing from once daily (before dinner) to twice daily (before breakfast and before dinner):
2. If $HbA_{1c} < 7\%$ OR $7\% \leq HbA_{1c} \leq 8.5\%$ and $FPG \leq 7\text{mmol/l}$ (126mg/dl), these subjects will continue with once daily BIAsp 30 (before dinner) and their OAD(s).

This design will make the transition to insulin treatment as simple as possible as subjects will start with only one injection a day and it will allow for an assessment of the number of subjects where BIAsp o.d. at dinner time are sufficient to reach treatment targets.

(MD03744)

An International, Randomised, Open-labelled Parallel Group Four Months Comparison of Basal Bolus Treatment with Insulin Aspart Including NPH and Biphasic Insulin Aspart Formulations in Subjects with Types 2 Diabetes

✉ CHOW Chun Chung Francis • OZAKI R* • MA C W Ronald* • CHAN W B*

□ 15 January 2004

❖ Novo Nordisk Asia Pacific Pte Ltd

Primary Objective:

To show that the glycaemic control as measured by HbA_{1c} of BIAsp 70/70/30 or BIAsp 50/50/30 is non-inferior to that of basal bolus treatment with insulin aspart (IAsp) including human isophane insulin (NPH) after four months treatment; where BIAsp 70/70/30 is Biphasic Insulin Aspart 70 administered with breakfast and lunch and Biphasic Insulin Aspart 30 administered with dinner and BIAsp 50/50/30 is Biphasic Insulin Aspart 50 administered with breakfast and lunch Aspart 30 administered with dinner.

Secondary Objectives:

1. To compare the glycaemic control as measured by the 8-point blood glucose profile of BIAsp 70/70/30 or BIAsp 50/50/30 with that of basal bolus treatment (IAsp + NPH) after four months treatment.

2. To compare the incidence of hypoglycaemic episodes of BIAsp 70/70/30 or BIAsp 50/50/30 with that of basal bolus treatment (IAsp + NPH) after four months treatment
3. To compare the safety profiles of BIAsp 70/70/30 or BIAsp 50/50/30 with those of basal bolus treatment (IAsp + NPH) as measured by the incidence of adverse events after four months treatment
4. To compare changes in body weight and vital signs of BIAsp 70/70/30 or BIAsp 50/50/30 with that of basal bolus treatment (IAsp + NPH) after four months treatment
5. To compare BIAsp 70/70/30 or BIAsp 50/50/30 with basal bolus treatment (IAsp + NPH) with respect to Treatment Satisfaction of the subjects after 4 months treatment

(MD03708)

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 Patients with Atrial Fibrillation

✍ FUNG Wing Hong • SANDERSON John Elsby
• CHAN Yat Sun Joseph • KUM Chi Chiu Leo
• WONG Tai Hung John • LAM Yat Yin*

☐ 10 January 2004

❖ Sanofi-Synthelabo (Singapore) Pte. Ltd

Atrial fibrillation (AF) affects over 1% of the population. The most powerful risk factors for developing AF are systemic hypertension and advancing age, which lead to vascular events of all kinds. The current approach to antithrombotic management in Atrial fibrillation, which depends heavily on oral anticoagulation, is inadequate, serving the needs of only a minority of those at risk. Based

on the new understanding of the role of antiplatelet agents against thrombosis associated with stasis, and powerful evidence of the additive effects of antiplatelet combinations, clopidogrel plus ASA is the most promising new therapy to be evaluated. As a result, the ACTIVE study, which included three separate but related trials have been designed with the following objectives:

- (1) To evaluate whether clopidogrel plus aspirin is superior to aspirin alone and non-inferior to standard oral anticoagulant therapy in preventing vascular events in patients with atrial fibrillation
- (2) To evaluate whether blood pressure lowering with irbesartan is superior to placebo in preventing vascular events in patients with atrial fibrillation
- (3) To evaluate the safety of clopidogrel plus aspirin in patients with atrial fibrillation
- (4) To evaluate the safety of irbesartan in patients with atrial fibrillation

This study aims to yield clinically relevant results that will immediately affect practice, with the potential to reduce disability and death in thousands of otherwise productive people each year.

(MD03400)

A Study on Nonalcoholic Steatohepatitis (NASH) in Hong Kong

✍ HUI Yui • CHAN Lik Yuen • CHAN Ka Leung Francis • CHOW Chun Chung Francis • WONG W S Vincent* • SO Wing Yee*

☐ 1 January 2004

❖ Hong Kong Society of Gastroenterology

Nonalcoholic steatohepatitis (NASH) is increasingly being recognised as an important cause of chronic liver injury and cirrhosis in the West. Studies in recent years establish clearly the strong association between NASH and the metabolic syndrome that is characterised by insulin resistance, type II diabetes, hyperlipidemia and obesity. It is a disease that may progress from inflammation through increasing

hepatic fibrosis to cirrhosis and hepatic decompensation. There is already evidence in the West of increasing prevalence of NASH, its complications and the associated health burden. Few studies have been carried out in the Far East to investigate the clinical significance of NASH, let alone its management. There is however circumstantial evidence to suggest that NASH may become an increasingly important cause of liver disease in the near future in Hong Kong. With our Westernised life style and rising prevalence of diabetes and metabolic syndrome, we have an increasing number of people with risk factors for NASH. To fully evaluate the clinical significance of NASH in our population, we propose the following studies: 1. a retrospective follow up analysis of histological progression of steatosis and steatohepatitis in paired liver biopsy samples. 2. a prospective study on patients with biopsy-proven NASH to delineate the natural history of the disease in Chinese. We expect that the studies will yield sufficient data on the clinical, laboratory and histological aspects of the disease to provide valuable information for the management of such patients in our locality in future.

(MD03702)

The Role of Cyclooxygenase-2 in Liver Fibrosis and the Potential of Misoprostol as an Anti-fibrotic Agent

✉ HUI Yui • CHAN Lik Yuen • CHENG Sze Lok# • LEUNG Wai Keung • SUNG Joseph Jao Yiu

☐ 1 March 2004

❖ Research Grants Council (Earmarked Grants)

Liver fibrosis is the wound-healing response of liver to chronic injury, which if persistent can lead to

cirrhosis and liver failure. It is the common disease process linking chronic hepatitis to liver cirrhosis, regardless of the primary cause of liver disease. There is currently no effective anti-fibrotic therapy that could successfully stop or prevent progression of fibrosis to cirrhosis. Cell culture experiments showed that arachidonic acid cascade is an important signaling mechanism in cells responsible for liver fibrosis. Inhibition or augmentation of this cascade can therefore potentially alter the progression of liver fibrosis. Cyclooxygenase-2 (COX-2) is one of the key enzymes in the cascade and prostaglandins are the catalytic products of this enzyme. We aim to investigate the role of COX-2 and prostaglandins in the process of liver fibrosis by several animal experiments. The effects of COX-2 inhibitor and misoprostol (a prostaglandin analogue) in rats with liver fibrosis will be investigated. Furthermore, transgenic mice that over-express COX-2 in liver will be tested for susceptibility to liver fibrosis. Results of this project will provide guidance on future clinical research on effect of COX-2 inhibitors and misoprostol in patients with chronic hepatitis and cirrhosis. Ultimately this may lead to the development of a successful anti-fibrotic agent.

(CU03446)

Prevalence of Respiratory Symptoms, Common Respiratory Disease, Atopy and Bronchial Hyperresponsiveness in Elderly Chinese Living In Hong Kong

✉ KO Wai San Fanny • HUI Shu Cheong David • WOO Jean

☐ 1 July 2003

❖ Hong Kong Lung Foundation

Respiratory symptoms are common in the general population with significant morbidities worldwide.

Most of the epidemiological data on population respiratory symptoms have derived from survey of school children or general population due to the ease of sampling. There is however, limited data available in the elderly subjects.

A study conducted in Hong Kong in 1991 to 1992 on the elderly, aged 70 yrs or over, found respiratory symptoms were common and reported by 56% of the subjects. A self-reported disease of chronic bronchitis, asthma, and emphysema were noted by 7%, 5% and 2% respectively. The prevalence of airway hyperresponsiveness at that time was 28.5%. Studies found that respiratory symptoms vary in different part of the world. However, it is not sure whether the prevalence of respiratory symptoms, common chronic respiratory diseases and objective measurements of atopic status like bronchial hyperresponsiveness and skin atop in the elderly changes with time.

In this survey, we aim to assess the prevalence of respiratory symptoms, common chronic respiratory diseases, atop and bronchial hyperresponsiveness in the Chinese elderly population living in Hong Kong. Changes in these parameters over time and predictors for respiratory symptoms will also be investigated. Prevalence of respiratory symptoms and common respiratory diseases will be assessed by telephone survey. Prevalence of atopic status and bronchial hyperresponsive will be assessed by skin prick test, total serum IgE and eosinophil levels in blood and bronchial challenge test.

As a result of decreasing birth rate and increasing life expectancy, the population in Hong Kong has been aging steadily. With the growing and aging population, it is important to have better understanding of the health status of the elderly for planning of healthcare resources. We hope that with more information, the lung health of the elderly will

be better looked after by proper arrangement of healthcare resources.

(MD03741)

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

✉ KWOK Chi Yui Timothy • LAM Chiu Wa (Dept of Psychiatry) • WOO Kam Sang • ZEE Chung Ying Benny (Faculty of Medicine (Planning Office))

☐ 1 November 2003

❖ CUHK Research Committee Funding (Direct Grants)

Background

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. We therefore propose to perform a pilot randomized placebo controlled trial to determine the effectiveness of oral vitamin B₁₂ and folate supplements in preserving cognitive function of older subjects with dementia.

Subjects and Method

100 mild to moderate dementia patients aged 60 years or more are recruited from psychogeriatric outpatient and memory clinics. All subjects have blood taken for plasma homocysteine and serum vitamin B₁₂, folate, creatinine, complete blood count, thyroid function test, and VDRL. Those with serum vitamin B₁₂ <150pmol/l, serum creatinine >250 μ mol/l, hypothyroidism and syphilis are excluded.

Mattis Dementia Rating Scale, Mini mental state examination, (MMSE), the Chinese version of the

Neuropsychiatric Inventory and Cornell scale for depression in dementia will be performed.

The subjects are stratified into low and high levels of MMSE groups before randomization. The supplement subjects will be prescribed one methylcobalamin 1 mg capsule and one folic acid 5 mg capsule daily. The placebo group subjects will be prescribed two placebo capsules of identical appearances daily. Acetylcholinesterase inhibitors are allowed if they have been taken at the maintenance dose for more than three months.

All subjects will then be reviewed in the same clinics at six months when all the measurements will be repeated.

(MD03611)

Chemoprevention and Treatment of Gastric Cancer by Peroxisome Proliferator-activated Receptor γ Ligands: An *in vivo* Study

✉ LEUNG Wai Keung • CHAN Wing Yan Michael# • TO Ka Fai (Dept of Anatomical & Cellular Pathology) • CHAN Ka Leung Francis • SUNG Joseph Jao Yiu

☐ 1 September 2003

❖ CUHK Research Committee Funding (Direct Grants)

Gastric cancer is one of the leading causes of cancer related death worldwide and it is estimated that more than 600,000 patients died from this disease each year. The need to identify an effective chemopreventive strategy is obvious. Despite the intense interest in the elucidation of the role of *H. pylori* eradication in the chemoprevention of gastric cancer, there is currently insufficient data to support that *H. pylori* eradication could prevent gastric cancer development. Other agents, particularly vitamin supplements, have also been used with conflicting

results. Peroxisome proliferator-activated receptor (PPAR) γ is a member of the nuclear hormone receptor superfamily that binds to DNA response element and regulates the expression of other target genes. Cell line studies including our previous study show that activation of PPAR γ results in growth inhibition and induction of apoptosis of gastric cancer cells. In this study, we seek to evaluate the chemopreventive and therapeutic effect of PPAR γ ligands *in vivo*. The effects of PPAR γ activation on the growth of two animal models of gastric cancer will be determined. Moreover, the gene expression profiles of these tumors before and after treatment with PPAR γ ligands will be examined by cDNA expression array to elucidate the underlying mechanism of cancer prevention and treatment. Results from this study will possibly open up new therapeutic options on the chemoprevention and treatment of human gastric cancer.

(MD03832)

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

✉ LEUNG Wai Keung • CHAN Ka Leung Francis • HUNG Cheung Tsui • WONG Wai Sun

☐ 1 May 2004

❖ Celltech R & D Limited

CDP870 is an anti-TNF, humanized Fab' fragment-polyethylene glycol (PEG) conjugate, that is manufactured in *E. Coli*. This is a phase III

multi-national, multi-center, open label, 52 week study to assess the safety and efficacy of CD870, in the treatment of patients with active Crohn's disease who have previously completed studies CDP870-031 or CDP032. The aim of this study is to assess the long term safety and efficacy of chronic therapy with CDP870.

(MD03369)

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

✉ LEUNG Wai Keung • CHAN Ka Leung Francis
• HUNG Cheung Tsui • WONG Wai Sun

□ 1 May 2004

❖ Celltech R & D Limited

CDP870 is an anti-TNF, humanized Fab' fragment-polyethylene glycol (PEG) conjugate, that is manufactured in E. Coli. This is a phase III multi-national, multi-center, open label, 52-week safety study to assess the safety of re-exposure after a variable interval and subsequent chronic therapy with the CDP870, in the treatment of patients with active Crohn's disease who have previously been withdrawn from studies CDP870-031 or CDP870-032. The aim of this study is to provide a chance for patient who may have benefit from CDP870.

(MD03548)

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

✉ LEUNG Wai Keung • CHAN Ka Leung Francis
• HUNG Cheung Tsui • WONG Wai Sun

□ 1 May 2004

❖ Celltech R & D Limited

This is a phase III multi-national, multi-centre, double blind placebo-controlled 26-week study that evaluates the safety and efficacy of CDP870, a new anti-TNF antibody, in the treatment of active Crohn's disease. CDP870, a new anti-TNF, humanized antibody Fab' fragment-polyethylene glycol (GEG) conjugate. In total, 604 of patients will be enrolled. The primary endpoint is percentage of patients with clinical response at weeks 6 and 26.

(MD03937)

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 • TAM Lai Shan •
TOMLINSON Brian • BENZIE Iris F F*

□ 1 September 2003

❖ 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 diseases

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 24-week 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 azathiopine were recruited, and they will be randomized to receive active atreatment or placebo in additional to their current drugs.

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

(MD03646)

The Expression of Human Bone Morphogenetic Protein-4 in *Pichia Pastoris* and the Effects of Site-directed Mutagenesis on Its Expression and Function

✉ LI Ming

□ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Bone Morphogenetic Proteins (BMPs) are a subgroup of TGF-beta gene super-family. They were identified as a group of growth factors that play important roles in growth, differentiation and repair of a wide variety of tissues. BMPs have been demonstrated to induce ectopic bone-formation in human/various animal species. Previous 30 years studies on BMPs with animal models and human clinical trials have demonstrated that BMPs are valuable molecular tools for regenerating bone, accelerating bone fracture healing.

Active hBMPs were expressed in Chinese hamster ovary, which, however, is an expensive system with the disadvantages of low expression level and high cost. According to recent research reports and our previous studies, *E coli* has been used as a cheaper system for BMPs' expression, however, the produced recombinant BMPs are inactive. Renaturation of the inactive BMPs, if successful, is time-costly and expensive too.

Recently, a powerful *Pichia pastoris* expression system has been developed as a unique system for producing high level of recombinant protein yet active. It is the only system that offers not only the benefits of *E coli* (high level expression, easy scale-up and inexpensive) but also the advantages of expression in a eukaryotic system (protein processing, folding, & posttranslational modifications). The flexibility of *Pichia* expression system makes it an ideal tool for production of functional recombinant protein for laboratory research as well as for industrial applications.

Therefore, we propose to produce recombinant hBMP-4 in *Pichia pastoris* and the effects of site-directed mutagenesis on its expression and biological function will be investigated.

(MD03888)

Purification and Cloning of the Novel Muscle Healing Protein(s) that Enhances Muscle Repair and Regeneration

✉ LI Ming • SANDERSON John Elsby • LEE Ka Ho Kenneth (Dept of Anatomy)

☐ 1 November 2003

❖ Research Grants Council (Earmarked Grants)

One of the most challenging problems in muscular skeletal trauma is the limited capacity of regeneration of damaged skeletal muscle fibres after injury and the inevitable replacement by fast growing fibrous tissue compromising function. To date, there is no effective therapeutic measure available in clinical practice.

In our previous studies, we have identified and partially purified a protein fraction, probably containing muscle healing protein(s), ranging from 35-50 kDa containing about 15 different proteins from rat red muscle aqueous extract that enhanced the proliferation and differentiation of cultured myoblast (C2C12) and promoted skeletal muscle repair and regeneration in the rat model. N-terminal sequencing data of this fraction in conjunction with functional testing in myoblast culture system have excluded 5 abundant proteins and 2 less-abundant proteins. Further Heparin affinity chromatography has excluded another 4 proteins from being the candidate of the unknown muscle healing protein (MHP). Currently the myogenic fraction with about 4 proteins are under investigation.

In this research proposal, we will further isolate, identify, clone and express this novel MHP. The functions of the expressed recombinant MHP will be studied *in vivo* using our established rat model.

There is far-reaching clinical application in providing a new approach for the treatment of skeletal muscle injuries. With the local injection of exogenous muscle healing protein, it will significantly increase the local concentration to such a level that the satellite cells, previously quiescent, could be triggered to proliferate and fuse with previously injured muscle fibers during the repair process or completely replace them by forming new myotubes.

(CU03450)

Salvage of Ischemic/Infarcted Myocardium by Dagencao Induced Rapid Angiogenesis and Myogenesis and Its Development

✉ LI Ming • SANDERSON John Elsby • YU Cheuk Man • LEE Ka Ho Kenneth (Dept of Anatomy) • CHEUNG N M Edmund*

☐ 1 March 2004

❖ Funding from Industrial Sponsors • University-Industry Collaboration Prog.: Matching Grant for Joint Research, ITF, Innovation & Tech. Commission

Recently, we discovered an extract of a plant-Dagencao (ECD) that showed potent dual effects on stimulating rapid growth of new vessels & myogenesis in animal models. In this proposal, we propose to further isolate the active compounds from ECD, to investigate its salvaging effects on ischemic myocardium and to further develop its potential use for the treatment of ischemic heart disease. The project will be divided into three main stages. The main work in stage one will be focused on the collection of Dagencao from Guizhou from July to September according to the growth condition of particular year and making active organic extract (ECD).

The second stage of this project is the further isolation of the active components (acECD) from ECD that can induce rapid angiogenesis and myogenesis using bioassay-guided fractionation strategy.

The third stage is mainly involved in evaluation of the treatment effects of the acECD on ischemic heart disease/heart infarction. Heart infarction animal models will be used to evaluate the effects of acECD-induced neovascularization and cardiomyogenesis. Both morphological and functional evaluations of the treated animals will be conducted. The mechanism of cardiac myocyte regeneration will be investigated using proteomic and functional genomic subtraction strategies.

All data obtained from above experiments will be analyzed using bioinformatics and associated DNA and protein databases to elucidate the possible mechanism of acECD induced angiogenesis and cardiomyogenesis in skeletal muscles and in heart muscles.

(MD03801)

Identification of Tumor-specific Glycoforms of Serum Proteins from Patients with Early Hepatocellular Carcinoma by Differential Lectin Affinity Chromatography and Quantitative Proteomic Profiling

✉ POON Chuen Wai • CHAN Anthony Tak Cheung (Dept of Clinical Oncology) • LAI Bo San Paul (Dept of Surgery) • LEE Chi Yan Conrad (Dept of Clinical Oncology)# • MOK Shu Kam Tony (Dept of Clinical Oncology) • JOHNSON Philip James (Dept of Clinical Oncology)

☐ 1 September 2003

❖ Research Grants Council (Earmarked Grants)

Hepatocellular carcinoma (HCC) is a serious health problem in Hong Kong and China. As tumor cells have different glycosylation machinery, we hypothesize that identification of tumor-specific glycoforms should improve the specificity of a protein tumor marker. This hypothesis has been supported by our previous studies showing that identification of fucosylated/hyposialylated glycoforms can improve the diagnostic value of serum AFP. HCC-specific glycoforms of other serum proteins have also been reported. Instead of investigating one single protein at a time, this proposed project is aimed to identify HCC-specific glycoforms through comprehensive profiling of serological glycoproteins. Because protein glycosylation structures are highly diversified, we will focus at specific types of glycosylation structures alteration of which have been previously shown to be tumor-related such as fucosylated *N*-glycan. Serum glycoproteins carrying a specific type of carbohydrate side chains will be first purified with differential lectin affinity chromatography, followed by quantitative proteomic profiling. Comparing serum glycoprotein profiles of patients with early HCC and those of patients with CLD will identify a panel of HCC-specific glycoforms. Finally values of their serum levels in the diagnosis of early HCC will be assessed. Ultimately, this proposed study will lead to the discovery of a panel of potential glycoprotein tumor markers for early detection of HCC.

(CU03466)

Identification of Serum Proteomic Patterns for the Prediction of Tumor Recurrence in Patients with Hepatocellular after Curative Resection

✉ POON Chuen Wai • LAI Bo San Paul (Dept of Surgery) • CHAN Anthony Tak Cheung (Dept of Clinical Oncology)

□ 1 May 2004

❖ CUHK Research Committee Funding (Direct Grants)

Hepatocellular carcinoma (HCC) accounts for more than 90% of all primary liver cancer. It is a serious health problem in Hong Kong and China. Surgery is the only potentially curative treatment. However, the 5-year recurrence rate and 5-year survival rate of HCC patients received curative resection are about 50% and 30%, respectively. Identification of the patients with high risk of recurrence after curative resection should allow provision of intensive preventive treatment. 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 and bioinformatic analyses. Our recent pilot study has also demonstrated that both diagnostic and prognostic proteomic patterns are present in the sera of the NPC patients. The merit of SELDI-TOF mass spectrometry-based assay is that it is of a protein chip format, high-throughput and readily adoptable by clinical practice. By combining our clinical oncology, surgery and proteomics expertise, in this grant application we propose to perform a pilot study to identify the prognostic proteomic patterns in sera of the HCC patients before and after curative resection. With the use of the SELDI-TOF protein chip technology, this proposed project is aimed to:

To identify the proteomic patterns in preoperative sera of HCC patients received curative resection for the prediction of recurrence and survival;

To examine the changes of the prognostic proteomic features/patterns that are identified from the Objective 1 and 2 in serial serum samples collected within one year before the tumor recurrence.

(MD03631)

A Study of Sympathetic Activity and Cardiac Hypertrophy and Dysfunction in Hypertensive Chronic Renal Failure Patients

✉ SANDERSON John Elsby • WANG Yee Moon Angela • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging)#

□ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Cardiac hypertrophy is one of the most important determinants of mortality in chronic renal failure patients. However, management strategies to reduce the progression of cardiac hypertrophy in these patients remain extremely limited. Nearly 90% of our dialysis patients had severe LVH, indicating that treatment of this complication should be initiated much earlier than before patients progress to end stage renal failure. Drugs that interfere with the rennin-angiotensin system, although have been shown to reduce left ventricular mass index, are virtually contraindicated among patients with moderate to severe degree of renal failure. Beta-blockers have been shown to be beneficial post-myocardial infarction and in chronic heart failure and reduce mortality. Carvedilol, a non-selective β beta-blocker with α 1-receptor antagonist activity, not only has protective effect on the myocardium but also protects against glomerulosclerosis in rat remnant kidney model even at non-hypotensive doses, possibly also via sympatho-inhibitory effect and may be an effective treatment for LVH in chronic renal failure patients. Our own study demonstrated a reduction of symptom score, improvement of NHYA class and an increase in left ventricular ejection fraction in heart failure patients treated with beta-blockers. Moreover, greater blood pressure lowering effect, reduction in

LV end-diastolic dimension and normalization of the mitral E wave deceleration time was observed with carvedilol than metoprolol. Carvedilol but not metoprolol significantly decreases both systemic and cardiac norepinephrine spillover and myocardial collagen production. Hence, this study is important in that we evaluate the efficacy of non-selective adrenergic receptor blockade, carvedilol in retarding the progression of cardiac hypertrophy and myocardial fibrosis as well as preserving systolic and diastolic function and possibly preserving residual renal function in hypertensive chronic renal failure patients as compared to calcium channel blockers. This part of the study will provide important insights into the neurohumoral mechanisms of cardiac hypertrophy in chronic renal failure patients and will have important therapeutic implications for the management of hypertensive chronic renal failure patients.

(MD03350)

Screening of Colorectal Neoplasm in Chinese

✍ SUNG Joseph Jao Yiu • LEUNG Wai Keung • TO Ka Fai (Dept of Anatomical & Cellular Pathology) • LAM Wai Man Wynn (Dept of Diagnostic Radiology & Organ Imaging) • CHAN Ka Leung Francis • YEUNG Deacons*

☐ 1 August 2003

❖ Supplementary Funding for RGC Central Allocation

Colorectal cancer (CRC) is the second leading cause of cancer death around the world. In recent years, the incidence of CRC has been rising at an alarming rate in SE Asian countries including Hong Kong. Our previous studies have revealed that among Hong Kong Chinese, there is an exceptionally high CRC incidence in the young population, and a significant

proportion of these have germline mutation in cancer susceptibility gene. While well-established national guidelines for CRC screening are available in the US and UK, very few data are available in Asia. The recent developments of new imaging modalities (virtual colonography) and molecular diagnostic methods (stool tumor markers) open new horizons for non-invasive screening of CRC.

The aims of this project are: (1) To evaluate MR colonography as a screening test for CRC; and (2) To study the detection of aberrant DNA methylation as a diagnostic tool for CRC screening. The team consists of expertise from different disciplines (Physicians, Radiologist and Pathologists) from CUHK.

(MD03767)

Genotypes of Pro-inflammatory Cytokines (IL-1 β , TNF- α and IL-10) Associated with Pre-malignant Gastric Lesions

✍ SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • CHUNG Sheung Chee Sydney (Dept of Surgery) • LEUNG Wai Keung • NG Enders Kwok-wai (Dept of Surgery) • TO Ka Fai (Dept of Anatomical & Cellular Pathology)

☐ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

H. pylori is widely recognized as an important triggering factor in the development of gastric cancer yet only a small proportion of infected subjects develop the disease. Recent studies revealed that host genetic makeup regulating cytokines production is correlated with risk of gastric cancer development. Certain genotypes of IL-1 β , TNF- β and IL-10 are more commonly found in gastric cancer patients. We hypothesize that these genotypes are associated with pre-malignant gastric lesions and determine the

progression (or regression) of the gastritis cascade with time. To address these questions, we propose to study 1. Pro-inflammatory genotypes of IL-1 β , TNF- β and IL-10 and pre-malignant gastric lesions in first degree relatives of gastric cancer patients and 2. Progress/regression of pre-malignant gastric lesions and pro-inflammatory genotypes of IL-1 β , TNF- β and IL-10. These studies are built on ongoing project supported by RGC (CUHK4061/01M) in the study of histology and cell kinetic changes in pre-malignant gastric lesions with cyclo-oxygenase inhibition (Study1) and the 5-year follow-up data of an interventional study of chemoprevention of gastric cancer after eradication of *H. pylori*. Unlike existing evidence which is based upon case-control studies and cross-sectional observation, these studies will provide prospective data from randomized studies. The results of these studies will provide important insight into the host susceptibility of *H. pylori*-related gastric cancers.

(CU03436)

Randomized Studies on the Use of a Recombinant Human Trefoil Factor (ITF) in the Prevention and Healing of Aspirin-induced Gastric Mucosal Injuries in Human Subjects

✉ SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • LEUNG Wai Keung • LAU Yun Wong James (Dept of Surgery)

☐ 1 December 2003

❖ The GI Company, Inc

We propose two double blinded placebo-controlled studies in which healthy volunteers between the ages of 18 to 45 will be recruited. A baseline endoscopy will be performed to ensure a normal upper gastrointestinal tract at trial entry.

The first study aims to determine the mucosal protective effect of ITF against aspirin-induced mucosal injury along the upper gastrointestinal tract in humans. After a control endoscopy on day 1, volunteers are required to take aspirin 900mg twice daily before meals for 3 days. Along with aspirin, they are randomized to take ITF of its equivalent placebo for 7 days. Serial endoscopies are then performed on day 4 and 8. The primary outcome is mucosal damage expressed in number of hemorrhagic or non-hemorrhagic erosions along esophagus, stomach and duodenum recorded separately. A single experienced endoscopist blind to the assigned treatment will be assigned to perform all the examinations to ensure consistency of findings. The secondary outcome is adverse events during the course of treatment.

The second study aims to determine if ITF heals artificially created gastric ulcers in volunteers receiving aspirin. At baseline endoscopy, 8 antral floor biopsies will be taken in a straight line 1 cm from the pylorus to create mini-ulcers. Volunteers will then be asked to take aspirin 900 mg twice daily for three days to induce mucosal injury. Each biopsy would be at least 1 cm apart. Volunteers are also started on day 1: ITF per oral or its equivalent placebo for 14 days. Endoscopy will be performed under sedation on day 4 and 15 of each treatment group. Similarly, mucosal damage (in numbers of erosions) will be serially recorded. Biopsy induced mini-ulcer is recorded healed if no defect in mucosa was visible on endoscopy.

(MD03304)

The Role of Cyclooxygenase (COX)-2 Overexpression in Gastric Carcinogenesis: A Transgenic Mouse Model

✉ SUNG Joseph Jao Yiu • LEUNG Wai Keung •
CHENG Sze Lok# • FU Yuangen# • CHUN Wu
Kai* • XU Li* • WANG Xin*

□ 1 December 2003

❖ NSFC/RGC Joint Research Scheme

Gastric cancer is the second most common cause of cancer related death in China and in the world. Recently, overexpression of cyclooxygenase-2 (COX-2) has been detected in gastric cancer but whether COX-2 expression initiates or simply promotes gastric cancer development remains undermined. We propose to examine the role of COX-2 overexpression in gastric carcinogenesis by using a transgenic mouse model. The incidence of gastric tumor development in transgenic mice exposed to carcinogen will be compared to wild type mice. Moreover, the effect of specific COX-2 inhibitor in preventing gastric tumor development will be determined. The molecular mechanism underlying COX-2 expression in gastric cancer development will be explored by cDNA microarray and proteomics study. The results of this study will bring new insight into the role of COX-2 overexpression in gastric carcinogenesis as well as the potential therapeutic use of COX-2 inhibitor in chemoprevention of human gastric cancer.

(MD03968)

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

✉ SUNG Joseph Jao Yiu • LAU Yun Wong James
(Dept of Surgery)

□ 17 June 2004

❖ Novo Nordisk Asia Pacific Pte Ltd

It is a parallel group, randomised, multi-centre, multi-national, placebo-controlled, and double-blinded trial on efficacy and safety. The trial duration is 42 days (range 42-46 days) starting at first trial product administration. The aim of the study is to determine the treatment success of activated recombinant factor VII(rFVIIa) in patients with advanced cirrhosis and active variceal bleeding at endoscopy despite standard pharmacological treatment and further evaluations of efficacy and safety of rFVIIa. Treatment success is defined as control of acute bleeding, prevention of clinically significant rebleeding, and prevention of death in the five-day trial period after first trial product administration (FTPA).

(MD03518)

Messenger RNA Expression of Glomerular Podocyte Components in the Urinary Sediment of Patients with Acquired Proteinuric Diseases

✉ SZETO Cheuk Chun

□ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

The podocyte slit diaphragm is an important glomerulus filtration barrier. Mutations of the podocyte slit diaphragm proteins such as nephrin and podocin lead to congenital nephrotic syndrome. The relationship between the gene expression of podocyte proteins and acquired kidney diseases has not been studied in great detail, partly because current methodology involve invasive tests such as kidney biopsy. Since viable podocyte has recently been identified in human urinary sediment, we propose a

study to examine the gene expression of podocyte in urinary sediment, a novel non-invasive technique for studying kidney diseases. We plan to study 40 subjects of proteinuric renal diseases and 10 healthy controls. Messenger RNA will be extracted from the urinary sediment, and gene expression of podocyte will be determined by reverse transcription and real-time quantitative polymerase chain reactions. The podocyte gene expression will be compared between patients with various diagnoses and degree of renal impairment. The present project will establish a scientific basis for further large-scale study. The measurement of urinary messenger RNA expression may represent a simple and non-invasive method clinical practice in the risk stratification and monitoring of patients with proteinuric kidney diseases.

(MD03748)

Treatment of Early Immunoglobulin a Nephropathy by Angiotensin Converting Enzyme Inhibitor - A Randomized Controlled Trial

✍ SZETO Cheuk Chun • LI Kam Tao Philip* • YU Wai Yin Alex*

□ 1 July 2004

❖ Aventis Pharma Ltd.

The treatment of IgA nephropathy (IgAN) with normal renal function and minimal proteinuria is unknown. Since angiotensin-converting enzyme (ACE) inhibitors reduce proteinuria and retard the rate of decline of renal function in chronic proteinuric nephropathies, including IgA nephropathy, it would be logical to use ACE inhibitor even when proteinuria is minimal. The objective of the present study is to evaluate the efficacy of the ACE inhibitor ramipril in the treatment of early IgA nephropathy. We plan to study 60 IgAN patients with normal renal

function and minimal proteinuria (less than 0.5 gram/day). They will be randomized to either ramipril 5 mg daily or no treatment, and then followed for 5 years. Primary end points of the study are development of hypertension, development of proteinuria ≥ 1 g per day, and 20% decline in creatinine clearance. Our study will give important information on the therapeutic efficacy of early initiation of ACE inhibitor in the treatment of IgAN.

(MD04749)

A Sibling-based Study of the Molecular Genetics of Hypertension-application of Microarray-based DNA Chip Technology

✍ TOMLINSON Brian • THOMAS Neil G (School of Pharmacy)# • YANG Michael*

□ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

Essential hypertension is caused by the interaction of environmental and genetic factors. Hypertension is common (about 18% of the adult population) in Hong Kong Chinese and is responsible for considerable morbidity and mortality. Recent advances in molecular biology and genetic linkage methods have resulted in the identification of several genes associated with hypertension or the pathophysiological mechanisms related to the susceptibility to hypertension. In our previous work comparing hypertensive and normotensive populations, supported by the Research Grants Council we have begun preliminary investigations into the genetic epidemiology of primary hypertension in both population and family (siblings) studies and have identified a number of single nucleotide polymorphisms (SNPs) that appear to modulate blood pressure. Utilization of microarray-based DNA chip technology will enable

us to accelerate our investigations by not only reducing the time involved with genotyping these SNPs, but should also reduce the cost. Following patenting of the chip, this technology would then be available to other investigators to help meet the needs of a number of potential collaboration from around the region. This study will provide the proof of concept for the high throughput screening of hypertension-related disease gene SNPs and provide data essential for our understanding of the pathogenesis of hypertension in these Chinese subjects.

(CU03438)

An Open-label, Randomized, Multi-centre, Phase IIIb/IV, Parallel Group Study to Compare the Efficacy and Safety of Rosuvastatin and Atrovastatin in Subjects with Type IIa and IIb Hypercholesterolaemia

✉ TOMLINSON Brian • YU Cheuk Man • KO T C Gary*

☐ 1 December 2003

❖ AstraZeneca Hong Kong Limited

This is a randomised, multi-national, multi-centre, open-label, 2 arm-parallel study comparing rosuvastatin 10mg daily or atorvastatin 10 mg daily in subjects with primary hypercholesterolaemia at high risk for cardiovascular disease. Subjects will be randomised to receive 12 weeks of open-label treatment with either rosuvastatin 10 mg od or atorvastatin 10 mg od in 2:1 ratio. Subjects will be assessed at weeks 0 and 12. After the 12 week study period, if rosuvastatin is not yet available commercially, subjects may continue, on rosuvastatin treatment in an optional extension period.

The primary objective of the study is to compare the efficacy of rosuvastatin 10 mg with atorvastatin 10

mg by assessment of the percentage of subjects who reach EAS LDL-cholesterol target goals after 12 weeks of therapy.

The secondary objectives of the study are:

To compare the efficacy of rosuvastatin 10 mg with atorvastatin 10 mg by assessment of the percentage of subjects who reach EAS total cholesterol treatment goals after 12 weeks of therapy.

Percentage change in LDL-cholesterol, total cholesterol, HDL-cholesterol and triglyceride from pre-dose (week 0) and 12 weeks will be performed separately for the switched and the naïve patients.

To compare rosuvastatin 10 mg with atorvastatin 10 mg after 12 weeks of treatment with respect to the incidence and severity of adverse events and abnormal laboratory values.

The primary objective of the optional extension study is to assess the long-term safety of rosuvastatin.

(MD03656)

Oxidative Stress and Insulin Resistance in Hong Kong Chinese with Thalassaemia Minor

✉ TONG Peter Chun Yip • CHAN Chung Ngor Juliana • CHAN Yu Leung (Dept of Diagnostic Radiology & Organ Imaging) • HO Chung Shun (Dept of Chemical Pathology) • LAM Wai Kei Christopher (Dept of Chemical Pathology) • NG Heung Ling Margaret (Dept of Anatomical & Cellular Pathology)

☐ 1 November 2003

❖ Research Grants Council (Earmarked Grants)

Diabetes mellitus is a common chronic disease affecting about 10% of our general population. Impaired glucose uptake in target organs following insulin stimulation, a condition known as insulin resistance, is a key feature in the development of the disease. Thalassaemias are characterized by the

deficient synthesis of the globin chains of the haemoglobin and are common in southern Chinese. In Hong Kong, up to 8.5% of the population are carriers of thalassaemia genes. For those who are homozygous for thalassaemia, abnormal glucose tolerance and diabetes mellitus are common. Insulin resistance has been shown to precede the development of diabetes in these patients. Given that both conditions share the common feature of insulin resistance, it is plausible that there may be a clustering of these conditions in susceptible subjects.

In a hypothesis-generating study, we demonstrate that normal glucose tolerant subjects with thalassaemia minor and a family history of diabetes are insulin resistant and have raised marker for chronic inflammation as compared to those without thalassaemia minor. Furthermore, there are significant associations between insulin resistance and liver function test only in individuals with thalassaemia minor. These results suggest that thalassaemia minor may impose an additional burden on glucose metabolism in subjects with a genetic predisposition of diabetes.

The mechanisms for these associations are not well defined. Reduced survival of microcytic red blood cells may lead to a higher turnover of iron. Iron, being a highly reactive species, may generate free radicals and cause an increase level of oxidative stress. These highly reactive free radicals may induce low-grade inflammation and contribute to the insulin resistance state.

In this proposal, we hypothesize that the development of insulin resistance in subjects with thalassaemia minor is related to increased oxidative stress secondary to iron overload. We propose to examine the relationships between thalassaemia minor, insulin resistance, iron overload and oxidative stress. Individuals with thalassaemia minor will be recruited from the registry for α - and β -thalassaemias at the

Prince of Wales Hospital. Non-thalassaemic sibling of the same family will be studied for comparison. Anthropometric parameters, metabolic profiles, insulin resistance indices, iron status and oxidative stress level will be determined. The results will enhance our understanding of the interactions between two common diseases among Hong Kong Chinese. The knowledge acquired from this study will provide the foundation for designing novel therapeutic strategies in targeting oxidative stress in the management of insulin resistance.

(CU03439)

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

✉ WONG Ka Sing Lawrence • LEUNG Wai Hong Thomas • HUI Andrew Che Fai • MOK Chung Tong Vincent • LIANG K S Eric*

□ 1 August 2003

❖ AstraZeneca Hong Kong Limited

The study is double-blind, randomized, placebo controlled with parallel groups carried out on a multicenter basis to assess the efficacy and safety of i.v.NXY-059 in acute ischemic stroke. The planned total number of subjects is 1550 included at approximately 150 centers. Subjects with acute ischemic stroke without intracerebral hemorrhage or other intracerebral pathology indicating another diagnosis (as determined by a baseline Computerized Tomography CT) or Magnetic Resonance Imaging (MRI) scan) and a total NIHSS score of 6 or greater will be eligible for randomization.

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 EOI, Discharge Assessment, 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 demonstrate the efficacy of NXY-059 compared to placebo in subjects with acute ischemic stroke by the statistical testing of global disability as measured by the modified Rankin Scale (mRS) at last rating; and second by the statistical testing of neurological recovery as measured by the change from baseline in the total National Institute of Health Stroke Scale (NIHSS) at last rating.

Secondary objectives of the study are: (1) To explore the efficacy of NXY-059 compared to placebo on global disability, functional and neurological recovery as measured by the mRS and BI at the Discharge Assessment (Day 7 if subject remains hospitalized), Day 30, Day 90 and last rating, and total NIHSS and change from baseline in NIHSS at 24 hours, EOI, Discharge Assessment and Day 90. (2) To evaluate the effects of NXY-059 in comparison to placebo on the ability of the subjects to perform activities of daily living (ADLs), mobility and hand function as measured by the SIS-16 and the domain scores for communication, memory and thinking, emotional function and social participation, respectively, of the Stroke Impact Scale (SIS) at Day 90 in subjects with acute ischemic stroke. (3) To evaluate the effects of NXY-059 in comparison to placebo on subjects self-reported health status and health-related quality of life respectively, using the EQ-5D instrument at Day 90 in subjects with acute ischemic stroke. (4) To evaluate the safety and tolerability of NXY-059 compared to placebo in subjects with acute ischemic stroke. (5) To

characterize the pharmacokinetics of NXY-059 in subjects with acute ischemic stroke. (6) To evaluate the effects of NXY-059 compared to placebo on residence/location of care of subjects with acute ischemic stroke during the 90-day follow-up period.

(MD03486)

The Significance of Microembolic Signals and New Cerebral Infarcts on the Progression of Neurological Deficit in Acute Stroke Patients with Middle Cerebral Artery Stenosis

✉ WONG Ka Sing Lawrence • CHAN Yu Leung
(Dept of Diagnostic Radiology & Organ Imaging)
• LAM Wai Man Wynn (Dept of Diagnostic Radiology & Organ Imaging)

□ 1 September 2003

❖ Research Grants Council (Earmarked Grants)

The pathophysiology of stroke is somewhat different in Chinese, with predominantly intracranial large artery atherosclerosis rather than extracranial atherosclerosis in Caucasians. Our previous RGC-supported research has documented about 50% of acute stroke patients in Hong Kong had usually diffuse intracranial large artery disease. Another RGC-funded study provides evidence that on-going artery-to-artery embolisation, as detected by the number of microembolic signals (MES) detected by transcranial Doppler, (1) correlates with the number of acute infarctions on diffusion-weighted magnetic resonance imaging (DWI), (2) predicts the risk of having progressing stroke and (3) recurrent stroke/transient ischaemic attack. Our data provide evidences that in Chinese patients, on-going embolisation may be one of the causes of progressing stroke. The results of this study may provide another window for the treatment of acute ischaemic

stroke by investigating and effective treatment for on-going thromboembolism.

(CU03440)

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

✉ WONG Ka Sing Lawrence • MOK Chung Tong Vincent • YEUNG Hon Ming Jonas

☐ 6 October 2003

❖ Schering-Plough Research Institute

This study is designed to assess the efficacy of 3 doses of SCH 420814 vs placebo over a 6-week period in treating the motor signs and symptoms of Parkinson's disease.

The doses selected for this study are 5mg, 25mg, and 100mg once daily vs placebo. These doses were chosen the basis of *in vitro*, animal toxicology, and preliminary unaudited human safety data.

This is a Phase 2, multicenter, placebo-controlled, randomized, double-blind study of SCH 420814 in subjects with idiopathic, mild Parkinson's disease to be conducted in conformance with Good Clinical Practices, Approximately 240 subjects will be enrolled from about 30 sites.

The study will be divided into 3 periods: Screening visit (6 weeks), double-blind treatment period (6 weeks) and follow-up period (4 weeks). A separate 12-month extension study (P03376) will enroll subjects who complete the 6-weeks treatment period and who agree to participate.

Endpoints: (1) Mean change from baseline to endpoint at the 1 hour postdose time point in UPDRS score, Part III (motor score). (2) Mean change from baseline in Part II of the UPDRS. (3) Mean change

from baseline in Parts I and IV of the UPDRS. (4)

Time to initiation of a dopamine agonist or L-dopa.

(MD03427)

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

✉ WONG Ka Sing Lawrence • MOK Chung Tong Vincent • YEUNG Hon Ming Jonas

☐ 1 December 2003

❖ Schering-Plough Research Institute

This study is designed to assess the safety and tolerability of 25 mg dose of SCH 420814 as monotherapy, or as an adjunct to a D2 agonist/L-dopa, in subjects with idiopathic early Parkinson's disease who completed the 6-week double-blind Protocol No.P02541.

The 25 mg dose of SCH420814 was chosen on the basis of pharmacokinetic/pharmacodynamic data from previous studies. These data suggest that a dose of 25 mg once a day should generate sufficient plasma concentrations in >90% of subjects to occupy 50% of the receptors for 8to 9.5 hours. Owing to the long treatment duration of this study and progressive nature of the disease, subjects will be allowed to increase their dosing to BID and then add a dopaminergic agent (either a dopamine D2 agonist or L-dopa).

This is a Phase 2, multicenter, open-label, 12-month extension study of SCH 420814 in subjects with idiopathic Parkinson's disease to be conducted in conformance with Good Clinical Practices. Approximately 220 subjects will be enrolled.

Endpoints: (1) Assessment of safety and tolerability in Parkinson's subjects, with and without concomitant L-dopa or a dopamine agonist, using

adverse event data, laboratory test results, vital signs, ECG results, and UPDRS scores; (2) Time to dose increase; (3) Proportion of subjects who require a dose increase; (4) Time to initiation of adjunct therapy (dopamine agonist or L-dopa); (5) Proportion of subjects who required the addition of a dopaminergic medication (MD03583)

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

✉ WONG Ka Sing Lawrence • LEUNG Thomas WH* • HUI Andrew CF* • MOK Chung Tong Vincent* • LIANG K S Eric*

☐ 1 December 2003

❖ Sanofi-Synthelabo (Singapore) Pte. Ltd

Atrial fibrillation (AF) affects over 1% of the population and is much more common in the elderly. AF leads to formation of thrombus in the left atrium, which can dislodge into the systemic circulation. About 15% of all strokes are directly attributable to AF, and in those over 80 years AF is the single leading cause of major stroke. The most powerful risk factors for developing AF are systemic hypertension and advancing age, which lead to vascular events of all kinds. Thus, AF is a very powerful marker for development of stroke, myocardial infarction and other vascular events that reduces the quality & duration of life. OAC therapy & ASA therapy have both been shown to reduce risk of vascular events in AF patients, however, current guidelines recommend OAC

treatment, which has risk of bleeding, for most of the patients.

The current approach to antithrombotics management in AF which depends heavily on oral anticoagulation is inadequate. As a result, ACTIVE A & W has been designed to look at whether

Warfarin is effective against stroke but problematic Clopidogrel plus ASA potentially equivalent to warfarin and superior to ASA

Potential for less bleeding

In addition, most AF patients are having high blood pressure. In a recent large trial of antithrombotic therapy. No lower limit to the benefits of blood pressure lowering has ever been shown, and lower blood pressure is associated with a lower risk of cardiovascular events throughout the whole range of physiological pressures. There is very good reason to test a moderate level of blood pressure lowering with irbesartan, as adjunctive therapy, in AF patients. As a result, ACTIVE I has been designed for to test the following hypotheses;

High Blood Pressure is an important cause of AF

High prevalence of poorly treated hypertension

Blood pressure lowering even below currently accepted normal range may be beneficial

Based on the new understanding of the role of antiplatelet agents against thrombosis associated with stasis, and powerful evidence of the additive effects of antiplatelet combinations, clopidogrel plus ASA is the most promising new therapy to be evaluated. The ACTIVE study is aimed to allow this evaluation.

To evaluate whether clopidogrel plus aspirin is superior to aspirin alone and non-inferior to standard oral anticoagulant therapy in preventing vascular events in patients with atrial fibrillation

To evaluate whether blood pressure lowering with irbesartan is superior to placebo in preventing vascular events in patients with atrial fibrillation

To evaluate the safety of clopidogrel plus aspirin in patients with atrial fibrillation

To evaluate the safety of irbesartan in patients with atrial fibrillation

(MD03774)

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

✉ WONG Ka Sing Lawrence • MOK Chung Tong Vincent • DAI Lok Kwan David

☐ 20 April 2004

❖ Sanofi-Synthelabo (Singapore) Pte. Ltd

This is a randomized, multicountry, multicenter, double-blind, parallel-group, placebo-controlled phase III study that examines the efficacy on cognitive function and global decline of xaliproden in patients with mild-to-moderate dementia of the Alzheimer's type. Xaliproden (SR57746A) is a nonpeptide compound that possesses neurotrophin-like activities. It reduces the histological, neurochemical, and functional deficits in a variety of experimental models of neurodegeneration making it a potential disease-modifying treatment for Alzheimer's disease (AD). Subjects of male and female outpatients having probable AD according to NINCDS/ADRDA and DSM-IV criteria MMSE between 16-26 are recruited. Subjects will be administered 0.25 or 0.5 mg of xaliproden or placebo orally each day. Primary objective is to assess the efficacy on cognitive function and global decline of xaliproden in comparison to placebo in patients with mild-to-moderate AD. It will be measured psychometrically by Alzheimer's Disease

Assessment Scale Cognitive subset (ADAS-cog) and Clinical Dementia Rating Scale (CDR). Secondary efficacy is 1. to assess the effect of xaliproden on the annualized rate of progression of hippocampal and whole brain atrophies as measured by MRI; 2. to evaluate the effect of xaliproden on functional decline, behavioural symptoms and healthcare resource utilization; 3. to evaluate the long-term safety and tolerability of one dose of xaliproden; 4. to document plasma concentrations of xaliproden. Secondary efficacy is measured using MMSE, ADCS-ADL, NPI and RUD. The total duration is approximately 21 months, with a screening period of 1 month and followed by a treatment period of 18 months.

(MD03610)

A Quality Website for Healthy Ageing in Hong Kong

✉ WOO Jean • KWOK Chi Yui Timothy

☐ 1 August 2003

❖ Sir Murray MacLehose Trust Fund

This website will be first of its kind in Hong Kong. The intended users are firstly the older people in Hong Kong, secondly the family members of older people, and finally the care professionals related to elderly care. The website will present information which is applicable to Hong Kong people. Special considerations will be made for older people with impaired vision and limited computer and language skills, by using audiovisual aids. The content will include the following:

- (1) Preventive strategies against disease in old age: osteoporosis, dementia, strokes, ischaemic heart disease, under nutrition;
- (2) Common medical conditions in old age and their management, e.g. diabetes mellitus, hypertension,

arthritis, blindness, deafness, dementia, depression, incontinence, falls;

- (3) Comprehensive catalogue of health and social services available to older people in community;
- (4) Residential services: private and subvented homes for older people with all range of disabilities.

The website will achieve the following objectives:

- To promote healthy ageing in Hong Kong;
- To improve older people's understanding of medical and social problems of old age;
- To assist family members and care professionals to look after older people with disease or disabilities;
- To provide a platform for publicly funded as well as voluntary organizations involved in aged care to disseminate information;
- To foster closer collaborations among the organizations involved in aged care.

(MD03815)

A Multicentre, Double-blind, Double-dummy, Randomized, Controlled Trial Comparing the Efficacy and Safety of the Vira-38^o versus Oseltamivir in Patients with Acute Influenza

✍ WOO Jean • ZEE Chung Ying Benny (Faculty of Medicine (Planning Office))

□ 1 March 2004

❖ PRB Pharmaceuticals Inc.

Contract for carrying out a randomized clinical trial for patients with influenza.

(MD03974)

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

✍ 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*

□ 1 January 2004

❖ Sanofi-Synthelabo (Singapore) Pte. Ltd

Fondaparinux sodium is a synthetic antithrombotic drug. It is being evaluated in the prevention and treatment of the thromboembolic disease from venous or arterial origin. The current study (EFC 3197), OASIS 5 - UA/NSTEMI is proposed to compare efficacy and safety of a 2.5mg o.d. injection of fondaparinux with enoxaparin (twice daily 1 mg/kg s.c.) in patients with Non STEMI/UA Acute Coronary Syndrome(ACS).

This is an international, randomized, double-blind, controlled, parallel group study. Approximately 16,000 patients will be recruited in 600-700 centres worldwide, 8,000 patients in the fondaparinux treatment and 8,000 in the enoxaparin arm.

The Investigators will detail the study to subjects presenting to hospital with symptoms suspected to represent an ACS, and will complete the consent process.

Randomization will be performed centrally by an interactive voice response system (IVRS) within 24 hours of the onset of the most recent episode of symptoms. In order to satisfy the double blinding, patients will receive double dummy administration of either fondaparinux and placebo-enoxaparin or enoxaparin and placebo-fondaparinux. Visually matching syringes will be used for fondaparinux, enoxaparin and placebo.

The duration of treatment for the fondaparinux group will be 8 days or until hospital discharge if earlier; 2-8 days or until clinically stable for the enoxaparin group. Follow up visit are scheduled at Day 30+5, Day 90+7 and Day 180+14.

Patients will be allowed to undergo PCI or CABG if this is the standard practice or the clinical situation requires this intervention. Specific Investigational Drug will be provided for the PCI in order to ensure double-blindness during PCI.

Special attention will be paid to renal function of patients as renal impairment may be responsible for overdosing and, consequently, induce bleeding complications.

The primary outcome is the first occurrence of Death, Myocardial infarction and Refractory ischemia up to Day 9.

Patients may discontinue from the study drug at any time, and in any case in which emerging effects are of such a nature that the risk/benefit ratio is unacceptable to the individual subject.

This trial will be coordinated at the Canadian Cardiovascular Collaboration Project Office, (CCC PO) at the Population Health Research institute at McMaster University, Hamilton, Canada. 25 AMI patients will be recruited from PWH.

(MD03332)

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

✉ WOO Kam Sang • YU Cheuk Man • CHAN Wai Man Wilson • CHAN Yat Sun Joseph • WU E B*

□ 1 April 2004

❖ Organon

This is a randomised, controlled, parallel group, multi-center, multinational study of fondaparinux vs. control (double-blind) and a partial 2x2 factorial study evaluating GIK vs control in patients with ST segment elevation acute myocardial infarction (STEMI). Randomized within 24 hours of the onset of symptoms.

Fondaparinux versus Control

Primary efficacy objective: To evaluate whether fondaparinux is superior to control (UFH or placebo) in preventing death or recurrent MI up to day 9 in patients with ST segment elevation acute myocardial infarction (STEMI).

Secondary efficacy objectives: 1) To evaluate whether a beneficial effect of fondaparinux compared to control in preventing death or recurrent MI is sustained up to day 30, 90 and 180. 2) To evaluate whether fondaparinux is superior to control in preventing death, recurrent MI and refractory ischemia up to day 9.

Safety objective: To evaluate the safety of fondaparinux compared with control in terms of server & hemorrhage up to day 9.

GIK versus Control

Primary efficacy objective: To evaluate whether GIK is superior to control (usual care alone) in preventing the composite of death or nonfatal cardiac arrest up to day 30.

Secondary efficacy objectives: 1) To evaluate GIK versus control by evaluating the components of the composite of death or nonfatal cardiac arrest separately up to day 30. 2) To evaluate whether a beneficial effect of GIK infusion in preventing the composite of death or nonfatal cardiac arrest is sustained up to day 180.

(MD03460)

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

✉ 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*

□ 24 May 2004

❖ Novartis Pharmaceuticals (HK) Ltd

Idiopathic or functional constipation is a common disorder, affection up to 20% of the population depending on demographic factors, the sampling situation and the definitions used. Constipation is a collective term used by the patient to imply that stools are too hard, too infrequent or too difficult to pass. Based on an epidemiological study in US, there were 2.5 million annual physician visits for this problem.

Treatment of constipation is usually based on increased dietary fiber and supplementation with bulking agents, exercise, and habit training. However, results have been far from satisfactory. Majority of patients use non-bulking laxatives on a regular basis without medical supervision. Chronic use of non-bulking laxatives is often inappropriate, and may lead to side effects such as dependency and progressive tolerance, electrolyte imbalance, and, for the anthraquinones, melanosis coli. In addition, stimulant laxatives may damage the myenteric plexus, resulting in cathartic colon. A more appropriate approach to the therapy of constipation consists of physiologically stimulating intestinal motility.

Tegaserod (HTF919) is an aminoguanide indole compound and a member of a new class of subgroup-selective 5-hydroxytryptamine (5-HT) agonists. Activation of 5-HT₄ receptors triggers the release of neurotransmitters from the enteric nerves, which stimulates contractility and peristalsis. (MD03414)

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 Acute ST-segment Elevation Myocardial Infarction Receiving Fibrinolytic Therapy

✉ 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*

□ 1 July 2003

❖ Aventis Pharm Limited (Aventis-HK) sanofi-aventis group

Primary Objective:

The primary objective of the study is to determine whether enoxaparin (30mg IV bolus, then 1mg/kg subcutaneous q 12 h x 8 days) compared to unfractionated heparin (60 unit/kg IV bolus, then 12 unit mg/hr x 48 hours, to be adjusted by APTT level) will reduce the composite endpoint of all-cause mortality and non-fatal myocardial re-infarction within 30 days after randomization in patients with acute ST-segment elevation myocardial infarction within 6 hours after onset, and who are eligible to receive fibrinolytic therapy. (Proposed recruitment:

50 AMI from PWH; 25 AMI each from AHNH & NDH respectively).

Secondary Objectives:

The secondary objectives of the study are to determine a) whether enoxaparin compared to unfractionated heparin will reduce the composite endpoint of all-cause mortality, non-fatal myocardial re-infarction, and myocardial ischemia leading to urgent revascularization within 30 days after randomization in patients with acute ST-segment elevation myocardial infarction, who are eligible to receive fibrinolytic therapy. b) whether enoxaparin compared to unfractionated heparin will reduce the composite endpoint of all-cause mortality, non-fatal myocardial re-infarction and non-fatal disabling stroke within 30 days after randomization in patients with acute ST-segment elevation myocardial infarction, who are eligible to receive fibrinolytic therapy.

Tertiary Objectives:

The tertiary objectives of the study are to determine a) whether enoxaparin compared to unfractionated heparin will reduce the incidence of severe congestive heart failure alone or in combination with all-cause mortality and non-fatal myocardial reinfarction within 30 days after randomization. b) whether enoxaparin compared to unfractionated heparin will reduce the incidence of all-cause mortality, non-fatal myocardial re-infarction, non-fatal disabling stroke, and myocardial ischemia leading to urgent revascularization alone or in combinations at 48 hours (inclusive) and at 8 days after randomization.

(MD03404)

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

✉ YU Cheuk Man • KONG Shun Ling • YIP Wai Kwok Gabriel • LAM Y Y* • YU Eugene*

□ 1 September 2003

❖ Merck Sharp & Dohme (Asia) Ltd

This is a multi-center, double-blind, randomized, parallel group study to evaluate the effects of two doses of losartan (50 mg and 150 mg) on morbidity and mortality in patients with symptomatic congestive heart failure and intolerant of ACE inhibitor treatment.

Primary objective is to compare the effects of losartan 50 mg with losartan 150 mg with respect to the composite event rate of all cause death and/or hospitalization for heart failure in patients with symptomatic heart failure (NYHA II-IV) who are intolerant of treatment with angiotensin converting enzyme (ACE) inhibitors.

(MD03316)

The Benefit of Biventricular Pacing Therapy in Heart Failure Patients with Narrow QRS Complexes Who Had Systolic Mechanical Asynchrony by Echocardiography

✉ YU Cheuk Man • SANDERSON John Elsby • FUNG Wing Hong

□ 1 September 2003

❖ CUHK Research Committee Funding (Direct Grants)

Heart failure (HF) is the leading cause of cardiovascular morbidity and mortality despite established cocktail of pharmacological therapy. The development of biventricular packing becomes the mainstay of therapy for HF patients with wide

QRS complex which signifies the presence of electromechanical delay and asynchronous contraction of the heart. In such patients, the use of biventricular pacing has been shown to improve contractile function, HF symptoms, quality of life and exercise capacity, by our local work as well as by multicenter studies. In addition, our previous work has found that there is favorable reduction of heart size, called reverse remodeling.

Despite the convincing benefits of biventricular pacing, non-responders of therapy were observed in about one-third of patients received biventricular pacing. Our group is the earliest which explained that non-responders are due to the absence of mechanical asynchrony on echocardiography. In fact, the latter method was developed in our echo-lab and was found to be highly sensitive and specific to predict responders of pacing therapy. Our recent study also found that mechanical asynchrony is in fact evident in cardiac patients with normal QRS duration. Based on this background, the current proposal will assess the role of biventricular pacing in patients with narrow QRS complex with co-existing evidence of mechanical asynchrony by echocardiography. It will assess the potential benefit of pacing on reverse remodeling, cardiac function and clinical parameters.

(MD03394)

Predictors of Response To Cardiac Resynchronization Therapy (PROSPECT)

✉ YU Cheuk Man • FUNG Wing Hong • ZHANG Qing*

☐ 6 May 2004

❖ Medtronic Inc.

Currently, the majority of heart failure patients who qualify for and received a CRT or CRT+ICD device

feel better than before their implant. However, there are some patients who do not improve after the implant. Medtronic is sponsoring a research study called the Predictors of Response to Cardiac Resynchronization Therapy (PROSPECT) to help identify patients who will feel better after receiving a CRT or CRT+ICD device.

The “PROSPECT” study is a prospective worldwide, non-randomized, multi-center clinical trial. In this study, patients with symptoms of heart failure (i.e. the ability of heart to pump is reduced) and indicated for implantation of an CRT or CRT+ICD device will be included. Patient participation is completely voluntary, if the patient chooses to participate, and informed consent form and an Authorization to Use and Disclosure Health Information Form need to be sign. The doctor will collect the health information before the implant, during the implant, and at 1 month, 3 months, 6 months and every 6 months after implant until study closure. From the time of the initial implant attempt, any overnight hospitalization information will be collected. The tests done during baseline, implant and follow-up, included echocardiogram 12 Lead ECG, Six minute hall walk, QoL Questionnaire, Patient Global Assessment and device check; none of the tests done are experimental and may be done as part of standard care to assess the heart function or in receiving a CRT or CRT+ICD device.

There will also be 2 sub-studies, the BNP sub-study and the Troponin sub-study. The objective of the sub-studies is to evaluate whether pre-CRT BNP & Troponin values can prospectively identify patients more likely to respond to CRT.

(MD03718)

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

Edition Title/Investigators

2002-03 A Pilot Study of Curcumin for Treating Alzheimer's Disease (MD02910)

✉ BAUM Lawrence William • WOO Jean • KWOK Chi Yui Timothy • LAM Chiu Wa (Dept of Psychiatry) • CHIU Fung Kum Helen (Dept of Psychiatry) • ZEE Chung Ying Benny (Faculty of Medicine (Planning Office)) • CHOW Sing Sum Moses (School of Pharmacy)

2002-03 Use of Software for Design of DNazymes (MD02506)

✉ BAUM Lawrence William

2002-03 DNazymes against SARS Coronavirus (MD02700)

✉ BAUM Lawrence William

2001-02 Diabetes Mellitus, Obesity and Cardiovascular Risk Factors in Hong Kong Adolescents (MD01055)

✉ CHAN Chung Ngor Juliana • COCKRAM Clive Stewart • NG Chor Yin# • TONG Peter Chun Yip • WONG Wing Kin Gary (Dept of Paediatrics)

2001-02 A Multicentre, Double-blind, Randomised, Placebo- and Active-controlled Parallel Study to Evaluate the Glucose and Lipid-altering

efficacy and Safety of L-410198 in Patients with Type 2 Diabetes (MD01943)

✉ CHAN Chung Ngor Juliana • TONG Peter Chun Yip • SO Wing Yee

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*

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 (Dept of 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 (Dept of Anatomical & Cellular Pathology)

- 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 (Dept of Surgery) • CHUNG Sheung Chee Sydney (Dept of Surgery) • TO Ka Fai (Dept of 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
- 2001-02 Prevention of Ulcer Bleeding in High-risk Patients: Is the Enthusiasm for COX2 Selective NSAIDs Justified? (MD01406)
 ✉ CHAN Ka Leung Francis • LEUNG Wai Keung • SUNG Joseph Jao Yiu • LUK Yiu Wing* • LAI Moon Sing* • LEUNG King Sun Vincent*
- 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 Viral Factor of HbeAg Seroconversion in Chronic Hepatitis B (MD02532)
 ✉ CHAN Lik Yuen • CHAN Ka Leung Francis • SUNG Joseph Jao Yiu • HUI Y*
- 2002-03 Salt Sensitivity of Blood Pressure in Chinese: the Role of Neurohormones and Genetic Factors (MD02917)
 ✉ CHAN Yan Keung Thomas • CHAN Chung Ngor Juliana • THOMAS Neil G (School of Pharmacy)# • TOMLINSON Brian
- 2002-03 Effects of COX-2 inhibitors on Leukemic Cells (MD02613)
 ✉ CHENG Gregory
- 2001-02 Multi-centre, Multinational, Open-labelled, Randomised, Parallel, Controlled Trial in Type 2 Diabetic Subjects Inadequately Controlled on Repaglinide, to Compare the Efficacy and Safety of Repaglinide Combined with Bedtime NPH Insulin versus Twice Daily NPH Insulin (MD01661)
 ✉ CHOW Chun Chung Francis • COCKRAM Clive Stewart • MA Ronald* • OZAKI R*
- 2001-02 A 24-Week, Open, Controlled, Randomized, Multinational, Multicenter,

	Phase IIIb Clinical Study to Investigate the Efficacy and Safety of Lantus [®] Insulin Analogue (Once Daily at Bedtime) Plus Amaryl [®] (Glimepiride) and NPH Basal Insulin (Once Daily at Bedtime) Plus Amaryl [®] in 440 Patients with Type 2 Diabetes Mellitus Who Fail Good Metabolic Control with Oral Antidiabetic Drugs (OADs) (MD01709)	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)	<p>✍ CHOW Chun Chung Francis • CHAN Wing Bun* • OZAKI R*</p>
	✍ CHOW Chun Chung Francis • COCKRAM Clive Stewart • SO W Y* • OZAKI Risa • CHAN Wing Bun	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)	<p>✍ CHOW Chun Chung Francis • CHAN Wing Bun* • OZAKI R*</p>
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)				<p>✍ CHOW Chun Chung Francis • COCKRAM Clive Stewart • FUNG Wing Hong • CHAN W* • CHAN Wing Bun • SO Wing Yee • CHAN N* • MA R*</p>
		2002-03		Psychosocial Stress and Neurohormonal Regulation in the Pathogenesis of Young Onset Type 2 Diabetes (MD02517)	<p>✍ COCKRAM Clive Stewart • CHAN Chung Ngor Juliana • NG Chor Yin# • TONG Peter Chun Yip</p>
		2000-01		The Effects of Nasal Continuous Positive Airway Pressure on Platelet Activation, Fibrinolysis and Activities of the Sympathetic Nervous System and Renal Kallikrein-kinin System in Obstructive Sleep Apnoea (CU00147)	<p>✍ HUI Shu Cheong David • CHENG Gregory</p>
2002-03	A Six-month, Multi-centre, Open, Randomised, Parallel Safety and Efficacy Comparison of Actrapid [®] Produced by the Current Process and Human Insulin with the Same Formulation as Actrapid [®] , Produced by the NN729 Process in Subjects with Type 1 Diabetes on a Basal/Bolus Regimen (MD02572)				<p>✍ CHOW Chun Chung Francis • OZAKI R* • CHAN Wing Bun*</p>
		2001-02		The Effects of Nasal Continuous Positive Airway Pressure Treatment on Cardiac Structure, Function and Cardiac	

- Natriuretic Peptide Levels in Obstructive Sleep Apnoea (MD01436)
 ✍ HUI Shu Cheong David • SANDERSON John Elsby
- 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
- 2002-03 A Comparison of the Effectiveness of Treatment with Symbicort® Turbuhaler® (budesonide/formoterol; 160/4.5 mcg) Single Inhaler Therapy and Seretide Diskus (salmetero/fluticasone; 50/100, 50/250 or 50/500 mcg) plus Ventoline (salbutamol) as Needed in Steroid-treated Adult and Adolescent Asthmatic Subjects -- A Randomized, Open, Parallel-group, Phase IIIB, Multicentre, 12-month Study (MD02588)
 ✍ HUI Shu Cheong David • HO Wai Mun • CHAN Pui Shan • KO Wai San Fanny* • FOK Pui Chu Joan* • TONG Mabel* • CHAN Chio Ho Michael*
- 2000-01 Quality of Life and Handicap of Stroke Survivors in Hong Kong (MD20055)
 ✍ KWOK Chi Yui Timothy • WOO Jean • KAY Li Chi Richard • YU Ly Mee Ashley (Centre for Clin. Trials & Epidemiological Research)# • LEUNG Kwok Fai* • Lo Raymond*
- 2001-02 A Comparative Study of the Long-term Outcomes of Two Orthopaedic Services with and without Geriatric Liaison in Older Hip Fracture Patients (MD01886)
 ✍ KWOK Chi Yui Timothy • WOO Jean • LAU Edith Ming Chu (Dept of Community and Family Medicine)# • LEUNG Ping Chung (Dept of Orthopaedics & Traumatology)
- 2002-03 Mr Os (Hong Kong) - The First Cohort Study on Osteoporosis in Chinese Men (CU02101)
 ✍ KWOK Chi Yui Timothy • LAM Wai Kei Christopher (Dept of Chemical Pathology) • LEUNG Ping Chung (Dept of 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 (Dept of Psychiatry)
- 2002-03 A Randomized, Controlled Trail of
Resistance Exercise in Improving Insulin
Sensitivity in Old Age Home Resident
(MD02806)
✉ KWOK Chi Yui Timothy • CHAN
Chung Ngor Juliana • WOO Jean •
LAU Edith Ming Chu (Dept of
Community and Family Medicine)#
- 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
(Dept of Anatomical & Cellular
Pathology) • CHUNG Sheung Chee
Sydney (Dept of Surgery) • NG
Enders Kwok-wai (Dept of Surgery)
• SUNG Joseph Jao Yiu • YU Jun#
- 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
Leung Francis • HUNG Cheung
Tsui
- 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
(Dept of Anatomical & Cellular
Pathology) • CHAN Ka Leung
Francis • SUNG Joseph Jao Yiu
- 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 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 II, Randomized,
Partially-blinded Study to Evaluate the
Safety, Tolerability, Pharmacokinetics

- and Antiviral Activity of 12 Weeks of Treatment with Clevudine (10mg, 30mg or 50mg QD) in Patients Infected with Hepatitis B Virus (MD02682)
 ✉ LEUNG Wai Yee Nancy • CHAN Lik Yuen
- 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
- 2002-03 A Randomized, Double-blind Trial of LdT (Telbivudine), versus Lamivudine in Adults with Compensated Chronic Hepatitis B (MD02314)
 ✉ LEUNG Wai Yee Nancy • YIU C H Desmond*
- 2001-02 Endothelial Dysfunction as an Early Index of Atheromatous Disease in Systemic Lupus Erythematosus and Its Association with Markers of Oxidative Stress and Inflammatory Mediator (MD01333)
 ✉ LI Kwok Ming Edmund • THOMAS Neil G (School of Pharmacy)# • TOMLINSON Brian • TAM Lai Shan*
- 2002-03 Endothelial Dysfunction as an Early Index of Atheromatous Disease in Systemic Lupus Erythematosus and its Association with Markers of Oxidative Stress and Inflammatory Mediators (MD02733)
- 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 (Dept of Anatomy) • LEUNG Ping Chung (Dept of Orthopaedics & Traumatology)
- 2002-03 Investigation of the Role of Mutants of Hepatitis B Virus X Protein on Pathogenesis of Hepatitis B Virus-associated Liver Cancer (MD02544)
 ✉ POON Chuen Wai • WONG Nathalie (Dept of Anatomical & Cellular Pathology) • MOK Shu Kam Tony (Dept of Clinical Oncology) • JOHNSON Philip James (Dept of Clinical Oncology)
- 2001-02 TRANSCEND - Telmisartan Randomized AssessmentNt Study in aCE iNtolerant Subjects with Cardiovascular Disease Trial (MD01729)
 ✉ SANDERSON John Elsby • YEUNG Leata Y.C.* • CHAN Kit Wan Skiva • WU Eugene Brian* •

- WONG John* • CHAN Anna* •
MA Wing Yan
- Diagnostic Radiology & Organ
Imaging) • PENNELL Dudley*
- 2001-02 ONTARGET - Ongoing Telmisartan
Alone and in Combination with Ramipril
Global Endpoint Trial (MD01796)
✉ SANDERSON John Elsby •
YEUNG Leata Y.C.* • CHAN Kit
Wan Skiva • WU Eugene Brian* •
WONG John* • CHAN Anna* •
MA Wing Yan
- 2002-03 A Study of the Potential of a
Semi-purified Extract from Chinese
Medicine *Dagencao* in Stimulating Both
Early Angiogenesis and Myogenesis in
Infarcted Heart (MD02852)
✉ SANDERSON John Elsby • LI
Ming • LEE Ka Ho Kenneth (Dept
of Anatomy)
- 2002-03 A Randomized, Double-blind, Placebo
Controlled, Parallel Group Study of the
Safety and Efficacy of SB 207266 in
Patients with Symptomatic Persistent
Atrial Fibrillation (MD02464)
✉ SANDERSON John Elsby • KUM
Chi Chiu Leo • MA Wing Yan •
CHAN Kit Wan Skiva • FUNG
Wing Hong*
- 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*
- 2002-03 A Study of Sympathetic Activity and
Cardiac Hypertrophy and Dysfunction in
Hypertensive Chronic Renal Failure
Patients (MD02348)
✉ SANDERSON John Elsby • WANG
Yee Moon Angela • METREWELI
Constantine (Dept of Diagnostic
Radiology & Organ Imaging)#
- 2000-01 A Randomised, Double-blinded,
Placebo-controlled Trial of Lamivudine
Treatment in HbeAg Negative Chronic
Hepatitis B Patients (in Asia) (MD20060)
✉ SUNG Joseph Jao Yiu • CHAN Lik
Yuen • CHAN Ka Leung Francis •
LEUNG Wai Yee Nancy • HUI Y*
- 2002-03 Left Ventricular Remodelling Post
Myocardial Infarction – The Effect of
Infarct Size, Transmural Extent and
Treatment with Spironolactone Assessed
by Contrast Enhanced MRI (MD02960)
✉ SANDERSON John Elsby • LAM
Wai Man Wynn (Dept of
- 2001-02 A Phase II Study of Lamivudine
Compared to Lamivudine Plus Adefovir
Dipivoxil for Patient with Chronic
Hepatitis B (MD00505)
✉ SUNG Joseph Jao Yiu • CHAN Lik
Yuen • CHAN Ka Leung Francis •
LEUNG Wai Yee Nancy

- 2001-02 Multicenter Open Label Expanded Access Program Of Peg-Interferon Alfa 2a (Ro-25=8310) And Combination Therapy With Ribavirin (Ro-20-9963) In Patients With Hepatitis C (MD01964)
 ✍ SUNG Joseph Jao Yiu • CHAN Lik Yuen • CHAN Ka Leung Francis • LEUNG Wai Yee Nancy • HUNG Cheung-tsui Lawrence*
- 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 (Dept of Clinical Oncology) • JOHNSON Philip James (Dept of Clinical Oncology) • TSUI Kwok Wing (Biochemistry) • WAYE Mary Miu Yee (Biochemistry) • LEUNG Kwong Sak (Dept of Computer Science and Engineering) • HENG Pheng Ann (Dept of Computer Science and Engineering) • LEE Kin Hong (Dept of Computer Science and Engineering)
- 2002-03 A Multicentre Phase III Study of Interferon-beta-1a for the Treatment of Chronic Hepatitis C in Asian Patients (MD02926)
 ✍ SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • LEUNG Wai Yee Nancy* • HUI Y* • CHAN Lik Yuen
- 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 (Dept of Surgery) • CHUNG Sheung Chee Sydney (Dept of Surgery)
- 2002-03 Intravenous Pantoloc 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
- 2001-02 Physiological Control of Peritoneal Permeability: A Study of the Interactions between Leukocytes, Mesothelial and Endothelial Cells (MD01550)
 ✍ SZETO Cheuk Chun • LI Kam Tao Philip* • WONG Yuk Hwa, Teresa*
- 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)
 ✍ SZETO Cheuk Chun • WONG Teresa Y. H.*
- 1998-99 A Multicenter, Double-Blind, Randomized, Parallel, 36-week Dose Escalating Study to Evaluate the Efficacy and Safety of Simvastatin 40 and 80 mg/day Versus Atrovastatin 20, 40 and 80 mg/day in Patients with Hypercholesterolaemia (International) (MD98121C)
 ✍ TOMLINSON Brian
- 2000-01 Molecular Biology of Hypertension: A Study Investigating Genetic Markers and Possible Underlying Pathogenic Mechanisms of Hypertension in Chinese (CU00095)
 ✍ TOMLINSON Brian • CHAN Chung Ngor Juliana • THOMAS Neil G (School of Pharmacy)#
- 2002-03 Oxidative Stress in Patients with Type 2 Diabetes: Are There Benefits from Antioxidant Supplements? (MD02339)
 ✍ TOMLINSON Brian • THOMAS Neil G (School of Pharmacy)# • BENZIE Iris F F* • LAM Wai Man Wynnie (Dept of Diagnostic Radiology & Organ Imaging) • GRIFFITH James Francis (Dept of Diagnostic Radiology & Organ Imaging) • HAINES Christopher John (Dept of Obstetrics & Gynaecology) • LAM Wai Kei Christopher (Dept of Chemical Pathology) • CHAN Chung Ngor Juliana
- 2002-03 A Prospective Observational Study of Acute Major Organ System Failure in Septic Patients (MD02422)
 ✍ TOMLINSON Brian
- 2002-03 The Participation of the Cytoskeleton in Insulin Action in Human Skeletal Muscle (CU02124)
 ✍ TONG Peter Chun Yip • COCKRAM Clive Stewart
- 2002-03 A Rapid System for Studying the Translatability of Human IGF-I and IGF-0I Binding Protein-3 Gene in Plants (MD02308)
 ✍ TONG Peter Chun Yip • SUN Sai Ming Samuel (Dept of Biology)
- 2000-01 Epidemiology of Cardiovascular Problem in Chinese Continuous Ambulatory Peritoneal Dialysis Patients: Prevalence, Severity & Risk Factors (MD20005)
 ✍ WANG Yee Moon Angela • SANDERSON John Elsby • CHAN Kam Wing (Dept of Diagnostic Radiology & Organ Imaging)# • LUI Siu Fai
- 2001-02 Genetic Factors in the Etiology of Middle Cerebral Artery Stenosis in Chinese with Diabetes and Hypertension (MD01965)
 ✍ WONG Ka Sing Lawrence • THOMAS Neil G (School of 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
- 2001-02 A Phase III, Double-blind, Placebo-controlled, Randomised Study Comparing the Efficacy, Safety, and Tolerability of Sumanitrole versus Placebo or Ropinirole, as an Adjuvant to Levodopa, in Patients with Advanced Parkinson's Disease (MD01488)
 ✍ WONG Ka Sing Lawrence • MOK Chung Tong Vincent
- 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 Wendy*
- 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
- 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 Pharmacy)# • TOMLINSON Brian • KAY Li Chi Richard
- 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*
- 2001-02 Long Term Care for the Elderly in Hong Kong - What Constitutes Quality and What Resources are Needed to Achieve (MD01402)
 ✍ WOO Jean • CHI Iris* • PHILLIPS David* • CHAN Alfred*
- 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 (Dept of Orthopaedics & Traumatology)
- 2002-03 A Pilot Study in the Application of Telemedicine in Community Care of the Elderly (MD02718)
 ✍ WOO Jean • KWOK Chi Yui Timothy • LEE Tze Fan Diana (The Nethersole School of Nursing) • ZHANG Xuejie (Dept of Community and Family Medicine)#

- 2002-03 Consultancy on Health Care Services in Home and Community Based Model (MD02827)
 ✉ WOO Jean • HUI Elsie
 Diagnostic Radiology & Organ Imaging)# • SANDERSON John Elsby • SZETO Cheuk Chun • YU Wai Yin Alex
- 1999-00 Chinese Atherosclerosis in the Aged and Young (Cathay Study) (MD96224)
 ✉ WOO Kam Sang • WOO Jean • SANDERSON John Elsby • CRITCHLEY Julian A J H# • CHENG Gregory • LAM Ching Wan (Dept of Chemical Pathology) • LAU Tak Fai Joseph (Centre For Epidemiology & Biostatistics)
- 2002-03 A Novel Homocysteine-lowering Strategy for Atherosclerosis Prevention in China: Diet, Hyperhomocysteinaemia and Atherosclerosis (MD02967)
 ✉ WOO Kam Sang
- 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*
- 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
- 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 (Dept of
- 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*
- 2002-03 Influence of H. pylori Infection on Management of Gastroesophageal Reflux Disease in Hong Kong (MD01934)

- ✉ WU Che Yuen Justin • SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • LEUNG Wai Keung
- 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
- 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)
 ✉ YU Cheuk Man • SANDERSON John Elsby
- 2002-03 Assessment of Left Ventricular Remodeling and Myocardial Viability with Echocardiography in Patients after Myocardial Infarction: A Comparative Study with Contrast-enhanced Magnetic Resonance Imaging (MD01950)
 ✉ YU Cheuk Man • SANDERSON John Elsby • LAM Wai Man Wynn (Dept of Diagnostic Radiology & Organ Imaging) • ZHANG Yan
- 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)
 ✉ YU Cheuk Man • SANDERSON John Elsby • CHAN Kin Yin • YEUNG Leata Y.C.* • WONG John* • WU Eugene Brian* • LAM Wai Man Wynn (Dept of Diagnostic Radiology & Organ Imaging)
- 2002-03 Atherosclerotic Plaque Burden Reduction in Native and Intervened Coronary Arteries as Well as in Other Major Arteries by High Dose Atorvastatin Therapy (ANIMATE) (MD02551)
 ✉ YU Cheuk Man • CHAN Wai Man Wilson • SANDERSON John Elsby
- 2002-03 MIDHeft Study (Extension II) (MD02802)
 ✉ YU Cheuk Man • SANDERSON John Elsby • FUNG Wing Hong*
- 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 • KONG Shun Ling • MA Wing Yan • YIP Wai Kwok Gabriel • WANG Zheng (Dept of Ophthalmology and Visual Sciences)# • WONG Wing Cheong (Dept of Ophthalmology and Visual Sciences) • WONG Tai Hung John • KUM Chi Chiu Leo • LAI Hong Yee Connie*

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 (Dept of Ophthalmology and
Visual Sciences) • YIP Wai Kwok
Gabriel* • TAM Lai Shan* • LAI
Hong Yee Connie* • WONG Wing
Cheung*

RESEARCH PROJECTS

Development of Oligonucleotide Probe Microarrays for Molecular Detection of Drug Resistance in *Mycobacterium Tuberculosis*

✉ CHAN Chiu Yeung Raphael • CHENG Fun Bun Augustine# • HUI Mamie

☐ 1 August 2003

❖ Research Grants Council (Earmarked Grants)

The combat against the re-emergence of tuberculosis has been complicated by the emergence of resistant strains of *Mycobacterium tuberculosis* (MTB), especially the multi-drug resistant ones (MDR-TB). Since *M.tuberculosis* is a slow-growing organism, two to four weeks are required to obtain results from routine *in vitro* susceptibility testing, resulting in inappropriate or delayed treatment. Development in molecular biology techniques has allowed mapping of mutation sites in drug-resistant genes of *rpoB*, *katG*, *inhA*, *ahpC*, *embB*, *pncA* and *gyrA* for the elucidation of resistance to rifampicin, isoniazid, ethambutol pyrazinamide and fluoroquinolones respectively, and most of these mutations have been found to have positive correlation to different levels of drug resistance. With previous support from the Research Grant Council our laboratory has been sorting out different mutations concerning drug resistance in MTB, setting up a “library” of different mutation maps for drug-resistant genes from a collection of local MTB isolates, and comparing our results with those reported in the literature. Based on the findings by our laboratory as well as by others it is theoretically possible that we can detect drug resistance by directly detecting gene mutations, however, the choice of technique is crucial since we

need to reveal the susceptibility pattern of at least the three first line drugs plus several key second-line agents, and hundreds of different mutation sites would be involved. Recent advances in biochip technology have made it possible for rapid detection of multi-mutation sites simultaneously, but the development and design of the biochip would depend on accurate information of “mutation library” obtained. Our laboratory is now ready to move one step forward in the development and setting up of a rapid method for simultaneous detection of resistance to all the anti-tuberculosis drugs, using oligonucleotide probe microarrays, and verify the new design with our local collections of isolates as well as testing prospective clinical isolates of MTB. Results obtained from this study will serve as a pioneer in our future development of a useful and flexible tool which can accommodate for the detection of known and new mutations in drug resistant genes of MTB isolates using bio-chip technology, and will provide us with a powerful weapon for future combat of this re-emerging disease in Hong Kong.

(CU03430)

Study of the Virulence of *Mycobacterium Avium* Complex (MAC) in Relations to Its Isogenic Morphological Variations

✉ CHAN Chiu Yeung Raphael • HO Iok Ieng Yolanda*

☐ 1 November 2003

❖ CUHK Research Committee Funding (Direct Grants)

Mycobacterium avium complex (MAC) is an opportunistic pathogen which causes disseminated infections in the majority of patients with AIDS and less frequently in other immuno-compromised

patients. Treatment of MAC infections is difficult because this organism can resist intracellular killing by macrophages and is innately resistant to most antimycobacterial and antibacterial drugs. Moreover, a reliable method for testing drug susceptibility against MAC is still not available owing to transient and reversible variations of colony morphology displayed by the same isolate; hence it is difficult to work out the best treatment regimen. This organism shows highly characteristic morphological variations, producing smooth-domed opaque (SmO), smooth-transparent (SmT), and rough (Rg) colony forms when cultured on solid medium. Of the smooth forms, the transparent variants are found to be more resistant to antimicrobials and considered more virulent than the other forms as supported by evidence from studies with both *in-vitro* and *in-vivo* models. Unlike the rough form which has the chemical basis and molecular mechanisms of morphology worked out in detail, the specific virulence factor(s) of the smooth variants remain uncertain, and the basis of isogenic morphotypic switch between the SmO and the SmT colony variants is not well-defined. This study therefore aims at identifying the virulence determinants of MAC in relation to its isogenic variation between the SmT and the SmO colony forms and at elucidating the factor(s) controlling this morphotypic transition.

(MD03705)

**Genetic Variation of the SARS Coronavirus:
Molecular Epidemiology and Antigenic Variation**

✉ CHAN Kay Sheung Paul • PEIRIS J S M*
☐ 1 August 2003
❖ RGC Special Grants for Severe Acute Respiratory Syndrome (SARS) Research

Severe acute respiratory syndrome (SARS) has been the first new plague of the new millennium. Its impact on the health care as well as the socio-economic systems of the affected countries has been dramatic. Transmission of this disease has had a number of unusual characteristics, the fact that relatively few individuals contribute to the bulk of transmission and the propensity to affect health care workers have been some of them. The aetiological agent is a novel coronavirus, a group of large enveloped RNA viruses. Analysis of variable regions of the viral genome, the gene of the spike protein (S gene) in particular, will allow a molecular epidemiological analysis of viral transmission patterns to complement data obtained from conventional epidemiology. In this study, we plan to carry out a molecular epidemiological study to permit a more precise understanding of how these viruses were transmitted within Hong Kong and beyond. This understanding will help better control of transmission. In addition, the spike protein is key to the immune response to the virus. The second aim of the study, understanding the genetic variability of the S gene and its impact on antigenic change, will be key to developing effective vaccines. These objectives are to be achieved through establishing a consolidated database of available clinical specimens in Hong Kong and correlating these with epidemiological and clinical data. This database, in addition to helping achieve the immediate objectives proposed, will serve as a resource for further research in the future.

(MD03894)

Development of Monoclonal Antibody Against SARS-associated Coronavirus

✉ CHAN Kay Sheung Paul • TAM Siu Lun John

□ 5 September 2003

❖ The Hong Kong University of Science and Technology

This study aims at developing monoclonal antibodies against various components of the severe acute respiratory syndrome (SARS)-associated virus (SARS-CoV). The monoclonal antibodies produced will be used for developing diagnostic assays, and for further studies relating to the pathogenesis of the virus.

(MD03842)

Oncogenic Risk Implications of Sequence Variation, Genomic Physical Status and Viral Load of Human Papillomavirus Infection on the Development of Cervical Cancer

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

□ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

Infection with high-risk types of human papillomaviruses (HPVs) is the major cause of cervical cancer, the second most common cancer in women worldwide. However, most HPV infections, even the so-called “high-risk” types, are cleared spontaneously. The question why some infected women, but not the others, progress to cervical cancer remains unanswered. We propose this study to examine the effects of various viral factors on the development of cervical cancer. This project will: (1) Improve cervical cancer screening and management of cervical lesions: This study will

provide a means to identify HPV-infected women who are at a genuine risk of developing cervical cancer. (2) Generate essential information for developing vaccines against cervical cancer: This study will generate comprehensive data on viral sequence variability and their oncogenic implications, which are essential for the design of DNA- or peptide-based vaccines. (3) Provide fundamental data for further studies on mechanism of viral oncogenesis: This study will identify viral sequence patterns associated with higher oncogenic risk, thus providing targets for future *in-vitro* studies. (4) Benefits to the Chinese population: This study will target at the most prevalent HPV types found among Chinese cervical cancer patients. Data on these HPV types are urgently needed for controlling cervical cancer among Chinese.

(CU03429)

The Acquisition of Fluoroquinolone Resistance in Relation to the Competence for Genetic Transformation in Prevalent Clones of *Streptococcus Pneumoniae* in Hong Kong

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

□ 31 December 2003

❖ Research Grants Council (Earmarked Grants)

Streptococcus pneumoniae is the leading cause of bacterial pneumonia, meningitis and otitis media and causes significant morbidity and mortality worldwide. Penicillin-nonsusceptible *Streptococcus pneumoniae* (PNSP) has become a major problem and its rate in Hong Kong has risen sharply from 10% in 1993 to 65% in 1997 and now ranks amongst countries with the highest rates in the world. PNSP is associated with cross-resistance to other B-lactam agents, and multidrug resistance to macrolides,

co-trimoxazole, chloramphenicol and tetracycline. New generations of fluoroquinolones, eg. Levofloxacin, active against pneumococci, have thus been incorporated in guidelines for empiric choice for treatment of community-acquired pneumonia.

In 2001, Hong Kong reported the highest resistance rate to levofloxacin of 13.3% in *S. pneumoniae* in the world. The emergence of the fluoroquinolone resistance is a function of the acquisitions of resistance determinants (via mutations or by genetic transformation in the presence of an existing pool of resistance genes) and their spread. An understanding of these mechanisms involved is crucial in the formulation of strategies in minimizing widespread emergence of fluoroquinolone resistance and to establish appropriate guidelines for treatment of such infections.

The objectives of the study are: (1) To determine the prevalence of fluoroquinolone resistance in currently prevalent clones of *Streptococcus pneumoniae* in Hong Kong; (2) To characterize the fluoroquinolone resistance determinants in *S. pneumoniae*; and (3) To study the frequencies for acquisitions of altered genes associated with fluoroquinolone resistance and their relations to the competence for genetic transformation in prevalent clones of *S. pneumoniae* in Hong Kong.

(CU03432)

A Stratified, Partially Randomised (Stratum B only), Double Blind, Multicentre Trial of Lamivudine and dipivoxil Treatment for Patients with Chronic Hepatitis B Who Have Shown Disease Progression by Reaching a Clinical Endpoint

✉ TAM Siu Lun John

□ 1 August 2003

❖ GlaxoSmithKline Limited

To provide service to detect serological markers for hepatitis B in the study entitled: “A stratified, partially randomized (stratum B only), double blind, multicentre trial of lamivudine and adefovir dipivoxil treatment for patients with chronic hepatitis B who have shown disease progression by reaching a clinical endpoint” over the study period.

(MD03989)

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

Edition Title/Investigators

2001-02 Association between Human Leukocyte Antigens and Progression of Oncogenic Human Papillomavirus Infection of the Cervix (MD01071)

✉ CHAN Kay Sheung Paul • CHANG Alexander Russell (Dept of Anatomical & Cellular Pathology)# • CHENG Fun Bun Augustine# • CHEUNG Tak Hong (Dept of Obstetrics & Gynaecology)

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 (Dept of Community and Family Medicine) • LYON Donald James#

- 2002-03 Molecular Characterization of Group B Streptococcus (*Streptococcus agalactiae*) in Hong Kong (MD02329)
✉ IP Margaret • LYON D J* • CHENG Fun Bun Augustine#
- 2002-03 Genetic Characterization of *Escherichia coli* Mutants Resistant to the Fluoroquinolones (MD02514)
✉ LING Mei Lun Julia
- 2000-01 Virus Isolation in Association with a Multicentre Clinical Trial on the Safety and Efficacy of Influenza Virus Vaccine, Trivalent, Types A & B, Live Cold-Adapted (CAIV-T) in Healthy Children in Asia (MD00369)
✉ TAM Siu Lun John • FOK Tai Fai (Dept of Paediatrics) • CHENG Fun Bun Augustine#

RESEARCH PROJECTS

Testing the Reliability and Validity of a Chinese Version of the Level of Expressed Emotion Scale

✉ CHIEN Wai Tong • CHAN Wai Chi Sally

☐ 1 April 2004

❖ CUHK Research Committee Funding (Direct Grants)

The expressed emotion comprises measures of criticism, hostility and emotional over-involvement, has provided an index of the emotional climate of people with schizophrenia and other mental illness within their family environment. However, there is not any measure of expressed emotion validated for use in Chinese populations. The level of Expressed Emotion scale is translated into Chinese language in this study. Its psychometric properties are examined and its potential in measuring patient's perceived family attitude and behaviour toward their illness will be tested for research and clinical purposes.

This one-year study will be conducted in two psychiatric OPDs in the New Territories. The first phase consists of translation and back-translation of the scale and a review by an expert panel. Equivalence between the Chinese and English version, content validity, and test-retest reliability will be assessed. The second phase establishes the internal consistency, reproducibility, responsiveness, and construct validity of the scale using a sample of 300 patients with schizophrenia. This preliminary testing provides evidence for the reliability and validity of the Level of expressed emotion scale (Chinese version) for clinical use.

(MD03667)

The Effect of Pre-operative Therapeutic Play on Post-operative Outcomes of Hong Kong Chinese Children Having Surgery in a Day Surgery Unit

✉ LI Ho Cheung William • LOPEZ Violeta • YEUNG Chung Kwong (Dept of Surgery)

☐ 1 January 2004

❖ CUHK Research Committee Funding (Direct Grants)

Aims:

1 : To determine whether the severity of surgical impairment would have a differential effect on the post-operative outcomes of Hong Kong Chinese children having surgery in a day surgery unit.

2 : To test whether children who receive therapeutic play intervention pre-operatively would show less upset behaviour and better coping and adjustment post-operatively.

Design: A randomized controlled trial, with two-way factorial design will be conducted. 212 children admit for day surgery with ages 7 to 12 years old will be recruited. Children having minimally invasive surgery or invasive surgery / open surgery will be randomly assigned to receive either routine pre-operative care or therapeutic play intervention pre-operative.

Procedure: On the day of assessment, State and Trait anxiety of the children will be assessed. Children's emotional behaviours, co-operation level, mean blood pressure, heart rates and pain level during the anaesthesia induction and recovery periods will be assessed. At 4 hours after operation, state anxiety, mean blood pressure, heart rates and pain level of the children will be again assessed. One week after surgery, a follow-up telephone call and a post-hospital adjustment survey will be used to assess any behavioural disturbance of the child since surgery.

Significance of the study: This study can help understand how the severity of surgical procedure would have a differential effect on children and determine the effectiveness of therapeutic play in preparing children for surgery in day surgery units.0 (MD03604)

Exploring Hong Kong Public Awareness of Coronary Heart Disease

✉ LOPEZ Violeta • CHAN Choi Wan#

□ 3 May 2004

❖ CUHK Research Committee Funding (Direct Grants)

Background: Cardiovascular disease is one of the leading health problems in modern societies with high morbidity and mortality. Coronary heart disease (CHD) constitutes one of the major diagnoses in cardiovascular disease. In Hong Kong, the prevalence of coronary heart disease is increasing as a result of the aging population and sub-optimal control of coronary risk factors. In addition, due to the more westernized lifestyle in Hong Kong, local studies also report that more than 60% of adults do not perform enough recommended exercise routine and the percentage of obesity among the younger population is rising and, an increasing number of coronary heart disease also occurs in younger adults. The increasing prevalence of heart disease in Hong Kong maybe related to the public' lack of the disease and the risk factors associated with it even though they may have been exposed to healthcare measures through different avenues such as mass media, health campaigns, educational classes, books, journals and pamphlets.

Aim: to explore the Hong Kong public's awareness of coronary heart disease (CHD).

Method: in –depth qualitative interview using an interview guideline

Sample and setting: 94 participants from the community centres in Hong Kong Island, Kowloon and the New Territories. Eight participants will be interviewed using twelve focus groups.

Significance: No information about Hong Kong people's awareness about coronary heart disease has been published, especially data about people's thoughts, feelings, attitudes, behaviors and preventive actions towards the disease. Therefore, an exploration of CHD awareness will certainly provides valuable information to fill in the gap of knowledge about people's level of awareness to CHD. In addition, HK Chinese with the disease is increasing as indicated in the statistics. A poor rate of recognizing of CHD among the public and under exploration of people's awareness in the cardiac prevention could account for the increasing prevalence of the disease.

(MD03668)

Promotion of Evidence Based Nursing Practice

✉ THOMPSON David Robert • CHAU Pak Chun Janita

□ 1 January 2004

❖ Joanna Briggs Institute (coll. project)

The Hong Kong Centre for Evidence Based Nursing was established at the Nethersole School of Nursing, Chinese University of Hong Kong in 1997. The purpose of the Hong Kong Centre as part of the Joanna Briggs Institute is to promote research activities that will improve the effectiveness of nursing practice and health care outcomes in Hong Kong. These activities will include implementing best practice based on current and available research evidence to improve the quality of patient care, and

carrying out reviews of research literature in areas of importance to nursing practice. The Hong Kong Centre makes research findings accessible to nurses working in the busy clinical areas of Hong Kong and provides opportunity for nurses to share and exchange, at international level, information on the measurement of effectiveness of research based practice.
(MD03828)

Therapeutics) • CHANG Anne Marie* • MACKENZIE Ann E*

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

Edition Title/Investigators

2001-02 Adherence to Phase II Cardiac Rehabilitation Programme & Psychosocial Outcomes of Clients with Acute Coronary Syndrome (MD01339)
✍ CHAN Dominic Shung Kit • CHANG Anne Marie# • CHAU Pak Chun Janita

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 (Dept of Clinical Oncology) • MAK So Shan*

2002-03 Psychosocial and Physical Factors Predicting Handicap (MD02482)
✍ CHAU Pak Chun Janita • WOO Jean (Dept of Medicine &

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#

2002-03 Establishing Psychometric Properties of the Childbirth Self-Efficacy Inventory among Chinese Pregnant Women (MD02670)
✍ IP Wan Yim

2002-03 Developing a Culturally Relevant Theoretical Framework of Successful Aging for Chinese Elders (CU02228)
✍ LEE Tze Fan Diana

2002-03 Translation and Validation of Two Disease-specific Instruments in Chinese Patients with Coronary Heart Disease (MD02421)
✍ LOPEZ Violeta • THOMPSON David Robert

2002-03 Establishing Reliability and Validity of the Chinese Version of the Caregiver Strain Index and the Center for Depression (MD02761)
✍ LUI How Lin • LEE Tze Fan Diana

2002-03 Preparation for Surgery in Patients Awaiting Coronary Artery Bypass Surgery (MD02865)

- ✍ THOMPSON David Robert • GILL Furze* • ROBERT Lewin* • STEVEN Griffin* • JOHN Caplin*
- 2001-02 To Assess the Effectiveness of a Nurse-led Sexual Health Promotion Project amongst Hong Kong Adolescents (ED01702)
- ✍ TWINN Sheila Frances • LEE Albert (Dept of Community and Family Medicine) • HOLROYD Eleanor Anne • CHENG YAM Fung Khing Frances (Dept of Community and Family Medicine) • SHIU Tak Ying
- 2002-03 Increasing Knowledge and Uptake of Screening for Cervical Cancer amongst Hong Kong Chinese Women over 40 Years: An Evaluation of a Community Health Promotion Campaign (MD02557)
- ✍ TWINN Sheila Frances • HOLROYD Eleanor Anne • DICKINSON James Arthur (Dept of Community and Family Medicine)# • FABRIZIO Cecilia*
- 2002-03 Beliefs of Older Hong Kong Chinese Women and Medical Practitioners about Mammography Screening: An Explanatory Model Approach (CU02229)
- ✍ TWINN Sheila Frances • HOLROYD Eleanor Anne • SHIU Tak Ying

RESEARCH PROJECTS

Hepatitis B Carriers are More Susceptible to the Development of Cervical Intra-epithelial Neoplasia and Cervical Carcinoma after Human Papilloma Virus Infection

✉ CHUNG Kwok Hung Tony • CHEUNG Tak Hong • SIU Shing Shun Nelson • CHAN Kay Sheung Paul (Dept of Microbiology) • LIN Chi Kit* • YIM So Fan

☐ 1 April 2004

❖ CUHK Research Committee Funding (Direct Grants)

HPV Infection is a prerequisite but insufficient for cervical carcinoma development. HPV infection and related cellular changes are mostly transient and those with persistent HPV infection have an increased risk of developing CIN and potentially cervical carcinoma. The clinical course of HPV infection is therefore similar to that of the Hepatitis B infection. That is vast majority of infected individuals would recover spontaneously while a sub-group of patients who fail to eradicate the virus would become carriers, suffer from chronic hepatitis and might develop hepatocellular carcinoma.

We therefore postulate that women who develop CIN or cervical carcinoma are immunologically less competent in eradicating the viral infection. This weakness in the immune system would predispose them to become hepatitis carriers if they are infected with Hepatitis B Virus.

Our study aims at demonstrating the association of CIN and cervical carcinoma, the sequelae of persistent HPV infection, with hepatitis B Carrier. This can be accomplished by finding the prevalence of HbsAg

carrier among women with cervical carcinoma, cervical intraepithelial neoplasia and normal women.

Patient Group: stored plasma from 200 and 400 patients with cervical carcinoma and CIN

Patient Group 1: 1000 first time blood donors (majority below age of 40)

Patient Group 2: 500 pregnant women (mostly below the age of 40)

Patient Group 3: 500 women seeking gynaecological services on PWH (mostly over age of 40)

For Normal Group 3, Pap smear and HPV test would also be done to find out if they have CIN or carcinoma or are HPV carrier.

(MD03701)

The Effects of Dong Quai Buxue Tong on Key Regulators of Early Events of Atherogenesis

✉ HAINES Christopher John • CHEUNG Che Kwok • PO Lai See • BRITON-JONES Christine May# • FISCUS Ronald Ray (Dept of Physiology)

☐ 1 March 2004

❖ CUHK Research Committee Funding (Direct Grants)

This research aims to elucidate the role of Dong Quai Buxue Tong (DBT) in regulating the early molecular events involved in atherogenesis. DBT is a common formula in Traditional Chinese Medicine (TCM) which has been prescribed for thousands of years to relieve women's ailments by tonifying the blood. Oestrogen has been prescribed for thousands of years to relieve women's ailments by tonifying the blood. Oestrogen has been prescribed for many years to treat menopausal symptoms, but has also been used in the belief that it would help to reduce the increase in cardiovascular risk that is associated with the menopause (Haines et al, 1996a). DBT

decoction is prescribed to tonify Qi (life essence or energy) and the observed effects are to promote the production of blood and improve circulation by increasing Qi strength (Chen and Li, 1993).

Therefore, it is aimed at correcting Qi rather than raising estrogen concentrations. Whilst estrogen with or without a progestogen has been the mainstay of treatment aimed at preventing the increased incidence of cardiovascular disease (CVD) in menopausal women, the efficacy and safety of this treatment has recently been questioned and it has been suggested that in many women, the negative effects of treatment outweigh the benefits. There is an urgent need therefore to identify safe and effective alternative therapies.

The specific aim of this project is to determine the action of DBT on various markers of vascular endothelial cell health. This will be investigated by testing the dose and exposure time-dependent effects of DBT on human vascular endothelial cells *in vitro* on biochemical and molecular markers of early atherosclerosis.

(MD03723)

Expression of Vascular Endothelial Growth Factor and Its Corresponding Receptors in the Human Oviduct: Modulation During the Menstrual Cycle

✉ LAM Po Mui • BRITON-JONES Christine May# • HAINES Christopher John • LOK Hung Ingrid • YUEN Pong Mo

☐ 25 October 2003

❖ Hong Kong Obstetrical and Gynaecological Trust Fund

In the human reproductive system, the oviduct is the site of gamete transport, fertilization and the initial stages of embryo development. Oviductal fluid is

the essential component of the oviduct to support these reproductive events. Despite of the importance of oviductal fluid, the mechanism of regulation of oviductal fluid secretion is not fully understood. Oviductal fluid is a complex mixture of plasma-derived constituents plus proteins synthesized by the oviduct epithelium. Serum transudation is one of the essential mechanisms for the formation of oviductal fluid. Therefore, modulation of vascular permeability and so serum transudation may be an important regulator of oviductal fluid secretion.

Vascular endothelial growth factor (VEGF) is a potent mitogen for vascular endothelium and it also stimulates vascular permeability. VEGF has been localized in human oviduct. The presence of VEGF, a known permeability-enhancing factor, within the oviductal epithelium suggests that VEGF may be involved in the regulation of vascular permeability within the oviduct and it may therefore be a controller of oviductal secretion. However, to date, the modulation of expression of VEGF and its receptors in the human oviduct during the menstrual cycle has not been described. The aim of this study is to investigate the expression and modulation of VEGF mRNA and protein as well as its corresponding receptors in the human oviduct during the menstrual cycle. The understanding of the role of VEGF in the regulation of tubal luminal secretions may be important in the development mechanisms of control of embryo transport and embryo growth.

(MD03975)

Vaginal Birth after Caesarean Section - Effect on Maternal Psychosocial Function

✉ LAU Tze Kin • CHUNG Kwok Hung Tony • LEE Tak Shing Dominic (Dept of Psychiatry) • LEUNG Tse Ngong

□ 1 September 2003

❖ Research Grants Council (Earmarked Grants)

The incidence of caesarean section has reached 15-20% in most developed countries. Encouraging vaginal birth after caesarean section (VBAC) has been considered a key component of a strategy to reduce the caesarean section rate. Most medical literature has focused on the efficacy of VBAC in reducing the caesarean section rate and the physical safety of successful VBAC. However, 30-40% of these women fail to achieve a vaginal delivery. Little is known about how the uncertainty of labour outcome and a failed VBAC impact on the psychosocial function of these women. What we do know is that antenatal depression and unplanned caesarean section are major risk factors for postpartum depression, which in turn is the major cause of maternal mortality in many developed countries including Hong Kong. We propose to study a cohort of women with a prior caesarean section and presenting with a subsequent pregnancy for care. After consent and recruitment, these subjects will be randomly assigned to have a repeat caesarean section or VBAC. The medical outcomes, overall satisfaction of the subjects with the care they received, and psychosocial function will be studied. (CU03423)

Evaluation of Human Chorionic Gonadotropin mRNA in Maternal Plasma as a Potential Marker for Early Diagnosis of Ectopic Pregnancy

✉ LAU Tze Kin • LO Yuk Ming Dennis (Dept of Chemical Pathology) • CHIU Wai Kwun Rossa (Dept of Chemical Pathology) • LEUNG Tse Ngong

□ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Ectopic pregnancy is a potentially fatal condition, and is one of the leading causes of maternal mortality. Because of the invasive nature of trophoblasts of the developing pregnancy, many patients with ectopic pregnancies present with rupture of the ectopic resulting in massive intra-abdominal bleeding. Ectopic pregnancy can be effectively treated by surgical excision of the affected fallopian tube. Yet, ideally, if the condition can be diagnosed early before rupture, more conservative surgical procedure or medical therapy can be administered, so that tubal function could be preserved. Thus, the essence to the prevention of mortality and morbidity of ectopic pregnancy is early diagnosis, preferably before tubal rupture. Early diagnosis of ectopic pregnancy, however, is difficult. At present, the best diagnostic strategy is the combined use of serial monitoring of maternal serum human chorionic gonadotropin (hCG) concentration, with the addition of sonography when hCG rises beyond the discriminatory zone. However, due to the large overlap in maternal hCG level between normal pregnancies, ectopic pregnancies and spontaneous abortions, early diagnosis of ectopic using this hCG-sonographic strategy is difficult because the initial hCG level at first presentation is usually below the discriminatory zone. False positive rate is also very high. Recently, we have demonstrated that some of the mRNA species detectable in maternal plasma are placental derived, and can be quantified accurately. In this study, we plan to investigate the value of using maternal plasma fetal mRNA as a potential marker for early diagnosis of ectopic pregnancy. (MD03779)

A Study of Transabdominal Pressure Effect on the Feto-maternal Haemorrhage during External Cephalic Version

✉ LEUNG Tak Yeung • SAHOTA Daljit Singh • FOK Wing Yee • CHAN Lin Wai Daniel • LAU Tze Kin

□ 25 October 2003

❖ Hong Kong Obstetrical and Gynaecological Trust Fund

We have shown that the cell-free fetal DNA content (cffDNA) increases in maternal circulation after external cephalic version (ECV), indicating some degree of feto-maternal haemorrhage. The objective of this prospective study is to measure the applied pressure on the maternal abdomen during ECV, and to correlate it with the changes of cffDNA. Patients with singleton breech presentation at or greater than 36 weeks of gestation are recruited. Standard clinical protocol for ECV is followed, including pre-ECV cardiotocogram and ultrasonographic scan to exclude any contraindications, and 10µg intravenous bolus of hexoprenaline to relax the uterus. Ten milliliters of blood is collected from the patient for pre-ECV cffDNA analysis. A Doppler study on fetal middle cerebral artery and umbilical artery is performed before and after the administration of hexoprenaline. ECV is performed by or under close supervision of experienced clinicians. The operator wears a pair of gloves with multiple pressure transducers which are connected to a computer, which measures and analyse the applied pressure during the procedure. The procedure is abandoned when it is failed after three attempts of when the patient request. Immediately after the procedure, ultrasonographic examination, cardiotocogram, and Doppler study on the fetal circulation are repeated to

ensure fetal well-being. Another 10 ml of blood is taken again for post-ECV cffDNA (MD03354)

Women's Demand for Elective Caesarean Section - A Prospective Psychosocial Epidemiological Cohort Study of Parturients

✉ LEUNG Tse Ngong • LAU Tze Kin • LEE Tak Shing Dominic (Dept of Psychiatry) • LEUNG Kwok Ling Ares*

□ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Vaginal delivery is the natural way of giving birth. Traditionally, caesarean delivery is only performed when there is obstetric complication because it carries greater health risks for both mothers and babies. However, a trend of increasing caesarean section rate has been observed worldwide in the past 1-2 decades. One of the major reasons for this increase is that caesarean section is now perceived to be safe. Furthermore, women requesting for elective caesarean delivery has become increasingly common. Some demand it even in the absence of conventional obstetric indications. Studies performed in western societies have shown that unpleasant previous obstetric experience, fear of intractable labour pain, worries about fetal well-being, fear of vaginal damage, and psychological causes such as fear of loss of self-control and lack of trust are the main reasons for this request. There has been no similar study in the past addressing this issue in Hong Kong. The investigators propose to examine the prevalence of maternal request for elective caesarean section and the factors governing their choice if women are allowed to choose the mode of delivery in Hong Kong Chinese women.

The study will be conducted in a public hospital and in the antenatal clinics of one group of private obstetricians. Participants will be interviewed at booking and at near term gestation using standardized questionnaires. Information to be collected includes: socio-demographic and obstetric history, views of caesarean section and vaginal delivery, preferred mode of delivery and the major reasons, the source of information on caesarean section, fear towards current pregnancy and delivery, the partner's view on the mode of delivery, and data on psychological variables using the State-trait Anxiety Inventory, Multidimensional Health Locus of Control Scales, and the Trust in Physician Scales.

(MD03593)

Hyperglycemia and Adverse Pregnancy Outcome Study

✍ LI Chi Yin • ROGERS Michael Scott • NG Pak Cheung (Dept of Paediatrics)

□ 5 April 2004

❖ National Institutes of Health/Northwestern University

This is a multi-centre prospective observational study on the relationship between the level of hyperglycaemia and adverse pregnancy outcome in Hong Kong Chinese pregnant subjects. It involves 15 field centres worldwide and Hong Kong is one of the centres. The study started in April, 1999 and is expected to be completed by February, 2008.

(MD03946)

Measurement of Trocar Insertion Force and Tape Tensile Force during Application of Tension-free Vaginal Tape for the Treatment of Female Stress Urinary Incontinence

✍ SAHOTA Daljit Singh • YIP Shing Kai Alexander • PANG Man Wah Selina

□ 1 April 2004

❖ CUHK Research Committee Funding (Direct Grants)

Female stress urinary incontinence (SUI) is a common and distressing problem. Its prevalence in Hong Kong is around 20%. Surgery is one form of effective treatment of SUI and tension-free vaginal tape (TVT, Gynecare, Division of Ethicon, Somerville, NJ, USA) is one of the commonest. Extensive performance of TVT has resulted in increasing awareness by the surgical community to the types and frequency of complications associated with insertion of TVT trocars, such as to the urinary bladder, blood vessels, and the bowels. With increased force of trocar entry surgeons may have less control of penetration, thus increasing the potential for serious visceral and vascular injuries. However, there is a lack of information on the measurement of TVT trocar insertion force. We therefore propose a prospective observation study on 20 women with SUI to measure the trocar insertion force during TVT operation. A comparison between the force used on each side, and the TVT tape tensile force during pulling will also be made. The results of this study would serve as a useful database for further studies on the control of trocar insertion. The results would also modify the surgical practice in TVT application, with an aim to reduce the prevalence of potential complications. The information obtained would also contribute to the design of the trocar.

(MD03703)

A Pilot Study of Thrombophilia among Chinese Women with Thromboembolism in Pregnancy

✉ TAM Wing Hung • WONG Yick Fu • CHENG Gregory (Dept of Medicine & Therapeutics) • NG Heung Ling Margaret (Dept of Anatomical & Cellular Pathology)

□ 2 December 2003

❖ CUHK Research Committee Funding (Direct Grants)

Several studies had observed an increasing trend of venous thromboembolism (VTE) in the Chinese population. VTE is currently the commonest cause of maternal death in Hong Kong. Moreover, both the incidence and maternal death from VTE during pregnancy in Chinese have increased to the same extent as in the Caucasian. Despite the incidence of VTE is similar to that in the Caucasian, the pattern of presentation in Chinese is quite different from that of the Western population. Moreover, a high prevalence of thrombophilia up to 60% had been reported in Chinese with documented history of VTE. There has been no study regarding to the prevalence thrombophilia in Chinese women with VTE occur during pregnancy.

Our objective is to determine the risk factors of VTE amongst Chinese pregnant women and the frequency of both acquired and congenital thrombophilia in a cohort of 40 patients and 40 controls. Subjects will be followed up for medical history and blood collection of various thrombophilia.

The thrombophilic screening will include Activated protein C resistance, protein C and protein S deficiency, antithrombin III deficiency, lupus anticoagulant, anticardiolipin antibodies disorders which can be performed in the laboratory of Department of Anatomical and Cellular Pathology. Factor V (G1691->A, G1628->A and A1090->G) mutation, prothrombin gene (G 20210->A) mutation and 5,10-methylenetetrahydrofolate reductase (C677->T, A1298->C) genes mutation will be

assessed by DNA extraction, amplification by polymerase chain reaction (PCR) using primers, and electrophoresis on agarose gel. Identification of women with thrombophilia will enable better counselling and improve patient management. The finding on the frequency and pattern of thrombophilia in pregnant women with VTE will also be the basis for future research on this area.

(MD03544)

Maternal Plasma Human Placental Lactogen mRNA Level in Pregnancies Complicated by Intrauterine Growth Retardation

✉ TSUI Hang Yuet Michelle • LO Yuk Ming Dennis (Dept of Chemical Pathology) • LEUNG Tse Ngong

□ 14 July 2003

❖ Hong Kong Obstetrical and Gynaecological Trust Fund

Intrauterine growth restriction remains an important cause of morbidity and mortality in modern obstetrics practice. In this project, we aim to evaluate the possibility of using placentally derived mRNAs in the assessment of growth restricted pregnancies. One of these is the human placental lactogen (hPL) mRNA, which has recently been shown to be present in maternal plasma throughout pregnancy. Human placental lactogen is one of the important and well-known hormones produced by the human placenta, and can be used as a biochemical marker for placental function. By performing this study, we hope to gain a better understanding on specific placental gene expression in both normal and growth restricted pregnancies.

The objectives of this project include: (1) to establish reference ranges for hPL mRNA in maternal plasma at different gestations in normal pregnancies, (2) to

study the difference in hPL mRNA concentrations in those with sonographically diagnosed intrauterine growth restriction (IUGR) compared to normal controls, and (3) to determine whether diminished hPL mRNA expression at an earlier gestation can help to predict IUGR in high risk pregnancies.

(MD03927)

Clinical and Metabolic Effects of Rosiglitazone on Women with Polycystic Ovarian Syndrome

✍ TSUI Hang Yuet Michelle • TAM Wing Hung • LAM Po Mui • MA Ching Wan Ronald (Dept of Medicine & Therapeutics) • CHEUNG Lai Ping • HAINES Christopher John • TONG Peter Chun Yip (Dept of Medicine & Therapeutics) • CHAN Chung Ngor Juliana (Dept of Medicine & Therapeutics) • LAM Wai Kei Christopher (Dept of Chemical Pathology)

□ 1 April 2004

❖ CUHK Research Committee Funding (Direct Grants)

Women suffering from polycystic ovarian syndrome (PCOS) often present with oligomenorrhoea, infertility, and hyperandrogenism. They also have a higher risk of developing diabetes and coronary heart disease. Insulin resistance is recognised as the major underlying pathophysiology of PCOS. The conventional treatment, however, does not address this problem of insulin resistance and hence could not reduce the associated long term health risks.

Rosiglitazone is an oral hypoglycaemic agent which enhances peripheral insulin sensitivity. Our hypothesis is that rosiglitazone can improve insulin sensitivity and revert the underlying metabolic and clinical disturbances in PCOS women. We therefore plan to perform a double-blinded, randomized, placebo-controlled study. Subjects will

have either rosiglitazone or placebo for 12 months. Our objective is to measure any metabolic changes and clinical improvement in patients with PCOS at 6 and 12 months of treatment.

PCOS is not confined to menstrual and fertility problems but also has a major metabolic impact affecting patients' long term health risk. The findings of our study would be of international interest and will have a great potential as basis for future studies on long term therapies for PCOS. This study will certainly broaden our view on the underlying metabolic disturbances in PCOS which will be of much clinical value.

(MD03985)

Inhibition of Human Papillomavirus Type 18 Essential Genes by Small Interfering RNAs in Cervical Cancer Cells

✍ WONG Yick Fu • CHUNG Kwok Hung Tony • CHEUNG Tak Hong • SOHAIL Muhammad* • SOHAIL Muhammad* • KAHN Thomas*

□ 15 December 2003

❖ CUHK Research Committee Funding (Direct Grants)

RNA interference (RNAs) is a conserved mechanism in which double-stranded, small interfering RNAs (siRNAs) trigger a sequence-specific gene-silencing process. A siRNA is evolving into a powerful tool for manipulating gene expression in mammalian cells with potentially utility for study of gene function, for high-throughput, function-based genetic screens as well as for development as a therapeutic tool. siRNA can also silence gene expression in cells with pathogenic viruses. Cervical cancer is one of the most common genital tract malignancies in women in Hong Kong. Human Papillomavirus (HPV) DNA is found in ~90% of cervical carcinomas, with HPV16

and HPV18 being the two most prevalent types. The oncogenic capabilities of high-risk HPV have been mapped to viral early (E) proteins E6 and E7. HPV DNA replication also requires functional HPV E1 and E2. However, HPV18 E2 region is more consistently deleted when the virus genome is integrated into host cell. In this study, we wish to use siRNAs to silence HPV 18 E1, E6 and E7 gene expression in cervical cancer cell line cells with positive HPV 18 infection. This study will address whether siRNA targeted to E1, E6 and E7 HPV 16 mRNA may potentially be a novel therapy to incapacitate viral oncogenesis in cervical cancers as well as other epithelial cells without harming normal cell growth mechanism.

(MD03754)

Gene Expression Profiling of Endometrioid Endometrial Carcinoma in Hong Kong Women and Correlation with Clinico-pathological Features

✉ WONG Yick Fu • BIRRER, Michael J.* • CHEUNG Tak Hong • CHUNG Kwok Hung Tony • GARDNER, Ginger J.* • YU Mei Yung (Dept of Anatomical & Cellular Pathology)

☐ 16 December 2003

❖ Research Grants Council (Earmarked Grants)

Endometrial cancer is the third most common gynecologic malignancy and the ninth most common malignancy for females overall in Hong Kong. Its documented incidence in 1999 was 9.4 per 100,000. Although endometrial cancer has a low mortality rate compared with other gynaecologic cancers, some of these malignancies can be especially aggressive. There are different histologic subtypes in endometrial cancer with different risk factors, prevalence and prognosis. Approximately 80% or more of these

cancers are endometrioid endometrial adenocarcinoma and 10% are serous adenocarcinoma. Previous molecular genetics studies have reported mutations of tumor suppressor gene TP53 in over 90% of serous endometrial cancers. In contrast, none were found in endometrioid tumors. This finding suggests that different subgroups of endometrial cancers may have different genetic profiles and different molecular pathways of carcinogenesis and metastasis. Recently, the development of large-scale gene expression analysis has proved to be a valuable tool for gene discovery and disease classification. In this proposed study, we plan to perform an integrated, genome-wide analysis of gene expression in a large set of endometrioid endometrial adenocarcinoma and compare this to normal cell using advanced techniques combining laser capture microdissection, RNA amplification and high density cDNA microarrays. From this study, genetic changes crucial to the development and progression of endometrioid endometrial cancer may become apparent. Further characterization of these genes will allow them to be exploited in diagnosis, prognosis, anticancer therapy, and molecular classification of endometrial cancer.

(CU03427)

Microsatellite Instability Profiles and Their Correlation with Clinico-pathological Features in Endometrial Cancer

✉ WONG Yick Fu • CHUNG Kwok Hung Tony • CHEUNG Tak Hong • HAMELIN Richard* • DUVAL Alex* • BUHARD Oliver*

☐ 1 January 2004

❖ France/Hong Kong Joint Research Scheme

To detect and evaluate microsatellite instability (MSI) in endometrial cancer, a proposed panel of 5 quasimonomorphic mononucleotide repeat markers will be used in a multiple polymerase chain reaction (PCR) in a cohort of 80 sporadic endometrial adenocarcinomas. A comparison to the MSI status detected in the same cancer population by using a reference panel of 5 markers originally recommended by the National Cancer Institute (USA) for colorectal cancer will be performed. Our aims are (1) to find optimal microsatellite marker set for diagnosis of MSI in endometrial cancer, and (2) to investigate the clinical significance of MSI in endometrial cancer. From this study, a method to detect MSI in endometrial cancer would be validated. Furthermore, the correlations of MSI profiles from individual tumor samples to pathologic feature and clinical outcome data hold the promise of better classification of endometrial cancer, and subsequently improved prognostic information for patient management.

(MD03434)

Gene Expression Profiling of Cardinal Ligament in Hong Kong Chinese Women with Pelvic Prolapse

✉ YIP Shing Kai Alexander • WONG Yick Fu • PANG Man Wah Selina

☐ 5 March 2004

❖ CUHK Research Committee Funding (Direct Grants)

Pelvic prolapse is a common yet distressing pelvic floor dysfunction affecting women of all ages, particularly the elderly. Preliminary data have shown that there is a relationship between pelvic prolapse, abnormal cardinal ligament collagen metabolism, and differential gene expression. There

is also evidence to show a racial difference in the cardinal ligament collagen metabolism between Chinese and Caucasian women. This is a feasibility study to examine the gene expression profiles amongst Chinese women with pelvic prolapse. We propose to study the gene expression profile of the cardinal ligament in ten Chinese women with pelvic prolapse and ten age-matched normal controls. In this study, we will combine two powerful technologies, RNA amplification and high density cDNA microarray, together as a high throughput methodology designed to determine an integrated, genome-wide picture of changing gene function in the cardinal ligament. From this study, gene changes crucial to the development and progression of pelvic prolapse can be discovered. Comparative studies on tissues recovered from the cardinal ligaments may help to elucidate the genetic changes vital to the progress of pelvic prolapse. Further characterisation of these molecular targets will allow them to be exploited in the diagnosis and prognosis, as well as treatment of this distressing condition. In addition, the correlations of molecular profiles from individual tissue samples to pathologic features and clinical outcome data hold the promise to better classification of pelvic prolapse, and subsequently improved diagnostic and prognostic information for patient management.

(MD03845)

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

Edition Title/Investigators

- 2001-02 Global Protein Profiling of Cervical Cancer Using a Novel Protein Biochip Technology: A Pilot Study (MD01480)
 ✍ CHUNG Kwok Hung Tony • WONG Yick Fu • CHEUNG Tak Hong • MOK Samuel C*
- 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 (Dept of Anatomical & Cellular Pathology)
- 2002-03 Proteomic Approach to the Serological Markers of Pre-eclampsia (MD02649)
 ✍ LEUNG Tse Ngong • POON Chuen Wai (Dept of Medicine & Therapeutics) • WANG Chi Chiu • LAU Tze Kin • ROGERS Michael Scott
- 2000-01 Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study (MD98171)
 ✍ LI Chi Yin • ROGERS Michael Scott • NG Pak Cheung (Dept of Paediatrics)
- 2002-03 Expression of Leptin and Leptin Receptor in Pathological Pregnancies (MD02301)
 ✍ LI Hang Wun • WONG Yick Fu • YU Mei Yung (Dept of Anatomical & Cellular Pathology)
- 2001-02 Evaluation of Green Tea Polyphenols in Pregnancy (MD01077)
- 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 (Dept of Paediatrics) • PANG Chi Pui Calvin (Dept of Ophthalmology and Visual Sciences) • TAM Wing Hung • WANG Chi Chiu
- 2001-02 The Effect of Interactions Between Genetic and Environmental Factors and History of Gestational Diabetes on the Incidence of Diabetes and Metabolic Syndrome in Hong Kong Chinese Women and Their Offspring (MD01482)
 ✍ TAM Wing Hung • CHAN Chung Ngor Juliana (Dept of Medicine & Therapeutics) • KO Tin Choi (Dept of Medicine & Therapeutics) • NG Chor Yin (Dept of Medicine & Therapeutics)# • TONG Peter Chun Yip (Dept of Medicine & Therapeutics) • COCKRAM Clive Stewart (Dept of Medicine & Therapeutics) • ROGERS Michael Scott
- 2002-03 The Effect of Interactions between Genetic and Environmental Factors and History of Gestational Diabetes on the

- Incidence of Diabetes and Metabolic Syndrome in Hong Kong Chinese Women (MD02964)
 ✍ TAM Wing Hung • CHAN Chung Ngor Juliana (Dept of Medicine & Therapeutics) • TONG Peter Chun Yip (Dept of Medicine & Therapeutics) • COCKRAM Clive Stewart (Dept of Medicine & Therapeutics) • ROGERS Michael Scott • KO Tin Choi Gary* • NG Chor Yin (Dept of Medicine & Therapeutics)#
- 2002-03 Molecular Neurogenesis of Down's Syndrome (MD02548)
 ✍ WANG Chi Chiu • ROGERS Michael Scott • KAZUHO Ikeo* • TAKASHI Gojobori*
- 2001-02 Gene Expression Profiles in Cervical Neoplasms in Hong Kong Chinese Women: Analysis by cDNA Array Hybridization (MD01084)
- ✍ WONG Yick Fu • CHEUNG Tak Hong • CHUNG Kwok Hung Tony • TSAO George*
- 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
- 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*

RESEARCH PROJECTS

Control of Myopic Progression in Moderate to High Myopic Chinese Children by Topical Atropine

✉ FAN Shu Ping Dorothy • LAM Shun Chiu Dennis • YU Bing On Christopher • WONG Chun Yu • YIP Wai Kuen

☐ 1 September 2003

❖ CUHK Research Committee Funding (Direct Grants)

Myopia, or short-sightedness, is the commonest eye disorder worldwide. It is especially important in Hong Kong. Over 90% of University students in Hong Kong are myopic. Among primary school students, in whom progression of myopia is most rapid, over one third (36.71%) are shortsighted. High degrees of myopia may also lead to permanent visual impairment or blindness from cataract, glaucoma, retinal detachment and macular degeneration. These myopic related disorders also tend to occur at an earlier age than other blinding disorders such as diabetic retinopathy and age-related macular degeneration. Atropine eye drops is the only treatment that has been shown to be effective in the deceleration of myopic progression in children to date. However, previous study populations have been children with mild degrees of myopia (-3.0 D). There is inadequate information in the safety and effectiveness of atropine in the prevention of myopic progression in children with moderate (>-3.0 D to -6.0 D) to severe myopia (>-6.0 D). These children have greater myopic progression compared to those with mild degrees of myopia. In our proposed study, the children will be randomized to

receive atropine ointment either twice daily or placebo for 1 year. The myopic progression between the two groups will be compared. From the proposed study, we plan to find out the safe and effective dose of atropine treatment, which will enable a reduction in myopic progression among highly myopic children in Hong Kong.

(MD03729)

A Prospective Study to Evaluate the Clinical Performance of the Bausch & Lomb Akreos FIT[®] Intraocular Lens in Patients Undergoing Routine Cataract Surgery

✉ LAM Shun Chiu Dennis • YOUNG Alvin Lerrmann

☐ 1 July 2003

❖ Bausch & Lomb Incorporated

Surgeons have several choices of Intraocular Lenses (IOL) to implant following cataract surgery. The Bausch & Lomb Akreos Fit[®] IOL has the potential advantages of lowering the incidence of posterior capsular opacification (PCO) and Lens Epithelial Cell migration (related to a square edge design and 26% water content hydrophilic material). The IOL also provides for potentially easier handling and insertion characteristics for the surgeon due to the design of the packaging. This study will allow the investigator to evaluate the clinical performance of the Bausch & Lomb Akreos Fit[®] IOL. Should these potential advantages been found out to be valid, patients will be benefit from a better choice of IOL.

The objective of this study is to assess the clinical performance of the Bausch & Lomb Akreos Fit[®] IOL. Safety will be assessed through the incidence of operative and postoperative complications (including corneal endothelial evaluation through specular microscopy). Efficacy will be assessed

through the ease of implantation, accuracy of visual correction, and the changes of PCO.

A single site in Hong Kong (DOVS) will participate in this prospective, observational analysis of the test lens. A total of 50 patients (50 eyes) will be studied. Evaluation of PCO will be done using the slit lamp grading scale as specified in the protocol.

Primary objective outcome measure will be the adverse response rate. Secondary measures will include ease of implantation and accuracy of visual acuity (postoperative) and PCO as assessed by the grading scale as specified in the protocol.

All patients would undergo modern standard pre-operative assessment, cataract extraction and post-operative medications. The 'only' variable/difference we are assessing or testing in this current study is the type of IOL. All other parameters are fairly standard for modern cataract operations. The follow-up assessment will not adversely affect the course of recovery and will only add value to clinical care and monitoring.

(MD03380)

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)

✉ 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

☐ 1 October 2003

❖ Research Grants Council (Earmarked Grants)

Acute attack of primary angle-closure glaucoma (PACG) is a common condition in Asian populations,

including Chinese. Conventional treatment to abort the acute attack includes the use of intraocular pressure (IOP) lowering medications and relieve of pupillary block by peripheral laser iridotomy (PI). Despite successful initial management, a recent Singaporean showed that 58% of patients developed a persistent rise in IOP with angle closure, known as chronic angle-closure glaucoma (CACG), in the long run. Once CACG is developed, IOP lowering surgeries are often required and the final visual outcomes are usually compromised.

It is known that the lens, particularly of those with cataract, can narrow the angle by pushing the peripheral iris anteriorly. Cataract may be a major contributing factor in angle closure as many presenting PACG patients are elderly and have concomitant cataracts. Some studies have demonstrated that cataract extraction widens the angle, which if done early after an acute attack, may prevent Peripheral Anterior Synechiae (PAS) formation. PAS consists of fibrotic tissues bridging the peripheral iris and cornea resulting in angle closure and CACG. Our pilot study confirmed such findings and the CACG rate could be reduced to as low as 10%.

This proposed prospective randomized controlled study aims to directly compare early cataract extraction with conventional observational treatment on incidence of CACG after acute PACG. No such information is available in literature.

(CU03350)

A Study on Glaucoma Patient's Understanding of Their Own Disease, and Changes in Quality of Life after Glaucoma Surgery

✉ THAM Chee Yung Clement • CHAN Wai Nang Clement • CHAN C K Vesta* • LAM Shun

Chiu Dennis • LAM Sze Wing • POON Shuet Yan

□ 1 May 2004

❖ CUHK Research Committee Funding (Direct Grants)

Glaucoma is the leading cause of permanent blindness in Hong Kong.¹ Since chronic glaucoma is an asymptomatic disease until advanced stages, glaucoma patients tend to comply poorly with medications. Better understanding of their own disease can improve drug compliance.^{2,3,4} The level of understanding of their own disease in glaucoma patients in Hong Kong has never been studied. In the first part of this questionnaire study, we aim to evaluate knowledge of their own disease in glaucoma patients listed for glaucoma surgery, and its correlation, if any, with surgical outcomes.

Several recent studies show that patients' subjective assessments of their visual function and vision-related problems can reliably reflect their visual impairment and quality of life.⁵⁻¹⁰ This quality of life assessment can be achieved by simple questionnaires with relevant questions.¹¹⁻¹³ In the second part of the study, quality of life in glaucoma patients undergoing glaucoma surgery will be assessed both pre-operatively and at 4 months after surgery, using a questionnaire that has previously been used to assess changes in quality of life after cataract extraction in local patients.¹⁴ Factors, both ophthalmic and social, that correlates with greater quality of life benefits in operated patients will be identified. Changes in quality of life after glaucoma surgery can be compared directly to that after cataract extraction in local patients.

200 consecutive glaucoma patients undergoing primary glaucoma surgery will be recruited and interviewed in a standardized manner by a trained

research assistant in Chinese (Mandarin or Cantonese) at the Prince of Wales Hospital. (MD03388)

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

Edition	Title/Investigators
2001-02	Endolaser and Internal Limiting Membrane Removal around Macular Holes Causing Retinal Detachment in High Myopes (MD01509) ✉ CHAN Wai Man • LAM Shun Chiu Dennis
2002-03	Study of <i>RPI</i> Mutations Causing Autosomal Dominant Retinitis Pigmentosa (MD02618) ✉ CHAN Wai Man • PANG Chi Pui Calvin • LAM Shun Chiu Dennis • FAN Shu Ping Dorothy
2002-03	A Randomized, Controlled Trial of Photodynamic Therapy with Verteporfin for Choroidal Neovascularization in Pathologic Myopia in Chinese (CU02140) ✉ CHAN Wai Man • FAN Shu Ping Dorothy • KWOK Kwan Ho • LAM Shun Chiu Dennis
2002-03	Effects of Preoperative Keratometry on Postoperative Refractive Outcomes and Corneal Curvature in Patient with Myopic LASIK (MD02372)

- ✎ CHENG Chak Kwan Arthur • LAW Wai Kee • LAM Shun Chiu Dennis
- 2000-01 Use of Conjunctival-limbal Autografts Versus Intraoperative Application of Mitomycin-C in Treatment of Recurrent Pterygium in Hong Kong (CU00052)
- ✎ LAM Shun Chiu Dennis • RAO Srinivas Kamalakar • YU Yau Woon Edward# • LAW Wai Kee
- 2001-02 A Prospective Randomized Comparative Study on the Safety and Efficacy of Argon Laser Peripheral Iridoplasty (ALPI) versus Systemic Intraocular Pressure Lowering Medications for the Immediate Management of Acute Attack of Primary Angle Closure Glaucoma (PACG) (MD01090)
- ✎ LAM Shun Chiu Dennis • CHUA Kien Han John • LAI Shiu Ming Jimmy • POON Shuet Yan • THAM Chee Yung Clement
- 2001-02 PIR207A - A Second Year of Treatment in a One Year Multi-center, Double-masked, Placebo-controlled, Parallel, Safety and Efficacy Study of 2% Pirenzepine (MD01995)
- ✎ LAM Shun Chiu Dennis • FAN Shu Ping Dorothy • LAM Robert Fung • CHENG Chak Kwan Arthur
- 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 • WONG Tak Hung • FAN Shu Ping Dorothy • CHAN Kar Mun Carmen
- 2002-03 Intraocular Pressure Profile, Endothelial and Nerve Fibre Analysis in Patients on Systemic Steroid (MD02783)
- ✎ LAM Shun Chiu Dennis • FOK Tai Fai (Dept of Paediatrics) • CHIK Ki Wai (Dept of Paediatrics) • LI Tsz Ha Randa
- 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 • FAN Shu Ping Dorothy • LAM Robert Fung • CHENG Chak Kwan Arthur • CHAN Kar Mun Carmen
- 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)
- ✎ 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

- 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
- 2001-02 Identification of DNA Methylation Sites in Cancer-related Genes in Retinoblastoma Genome (MD01091)
✍ PANG Chi Pui Calvin • CHOY Kwong Wai (Dept of Obstetrics & Gynaecology) • FAN Shu Ping Dorothy • LAM Shun Chiu Dennis • LO Kwok Wai (Dept of Anatomical & Cellular Pathology) • TO Ka Fai (Dept of Anatomical & Cellular Pathology) • YU Bing On Christopher
- 2002-03 Gene Expression Profiling of Glaucoma (MD02455)
✍ PANG Chi Pui Calvin • LEUNG Yuk Fai# • LAM Shun Chiu Dennis • FAN Shu Ping Dorothy

RESEARCH PROJECTS

A Study of Tendon Healing in Sports Injury : The Manipulation of Transforming Growth Factor Beta (TGF- β) on Matrix Deposition

✉ 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

☐ 1 September 2003

❖ Research Grants Council (Earmarked Grants)

Tendon injury is a common sporting injury from the epidemiological perspective. The diversity of tendon injury spans from acute traumatic tendon rupture to chronic overuse type of injuries which are very often loosely termed tendinosis. It is suggested that tendinosis also rooted from failed healing of repeated injuries. Thus a clear understanding in the study of tendon healing will be beneficial to all type of tendon injury.

TGF- β is a cytokine that mediates matrix deposition in soft tissue healing. Different isoforms of TGF- β may play distinct roles in tendon healing to ensure a proper and timely reconstitution of extracellular matrix. However, the interplay of TGF- β isoforms in the contexts of tendon healing and non-healing is not studied.

In the present study, we hypothesize that the biological activities of TGF- β isoforms were affected by the micromilieu in healing tendons, and elevated TGF- β activities in combination with the micromilieu in the healing tendons would result in healing disturbances, manifested as excessive collagen or proteoglycan deposition. *In vitro*, we

will use tendon fibroblast culture to assess if the effect of TGF- β 1, - β 2, - β 3 on gene expression of matrix proteins is altered by different extracellular matrix substrata. *In vivo*, the expression of TGF- β 1, - β 2, - β 3 in healing Achilles tendon will be measured in a well-established rat model, and injection of TGF- β 1, - β 2, - β 3 will be used to study healing disturbances with abnormal matrix deposition. The study will reveal if altered activity leads to healing disturbances and it will serve as a basis to devise strategies to treat healing disturbances in tendon as well as to promote tendon healing.

(CU03354)

Effect of Extracorporeal Shockwave Treatment on the Delayed Consolidation of Distraction Osteogenesis in Rabbit Tibial Model

✉ CHENG Chun Yiu Jack • LEUNG Kwok Sui • KWONG Shek Chuen Kevin* • GUO Xia* • CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)

☐ 1 July 2003

❖ CUHK Departmental Funding

Distraction osteogenesis is known as the process of regeneration of osseous tissue under distraction tension stress. It has been successfully applied in the treatment of clinical problem such as limb discrepancy and large bone segment loss resulting from trauma. The whole treatment course of distraction osteogenesis can be divided into three phases: osteotomy, distraction and consolidation phase. Although clinical outcome can be gratifying, the procedure is often associated with many complications, some of which are related to the prolonged application of lengthening device. The lengthening device has to be kept *in situ* until

adequate bone mineralisation, which is necessary in providing sufficient mechanical strength. In order to shortening the duration of distraction osteogenesis, several methods has been tried or applied. This includes dynamisation of fixation, bone marrow injection, cyclic compression, and low intensity pulsed ultrasound. Although they are reported to have positive effects on distraction osteogenesis, prolonged and repeated applications are often necessary.

In this proposal, we will study the effect of extracorporeal shockwave treatment on delayed consolidation of distraction osteogenesis. The aims are to study whether the duration of external fixation can be shortened and whether bony remodeling and maturation and bone strength can be enhanced with different extracorporeal shockwave treatment programme in a rabbit model. The results will help us to modify clinical treatment protocol with the hope of decreasing the complications associated with lengthening. The information obtained will also strengthen our understanding of the mineralisation, ossification and remodeling of the bony tissue in distraction osteogenesis.

(MD03814)

Are Estrogen and Vitamin D Receptor Gene Polymorphism Associate with the Occurrence and Growth Abnormality of Adolescent Idiopathic Scoliosis?

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

☐ 1 November 2003

❖ CUHK Research Committee Funding (Direct Grants)

Study Background:

Despite the many advances in the treatment of adolescent idiopathic scoliosis (AIS), the etiology still remains largely controversial. Results of our previous studies in the past 10 years have revealed the presence of generalized osteopenia with significant lower bone mineral density (BMD) in over 58% of AIS subjects. Delayed onset of puberty, taller sitting height as well as longer arm-span were also found when compared with age-, sex- and maturity-matched normal controls. Estrogen receptor (ERα) gene and vitamin D receptor (VDR) gene are well known to be related to bone mineralization, longitudinal bone growth and sexual maturation.

Aims of Study:

The aims of the study are to answer the following questions:

Are the ERα and VDR gene polymorphism associated with the presence of Adolescent Idiopathic Scoliosis? Are the generalized osteopenia, abnormal longitudinal bone growth, and delay sexual maturation in AIS associated with these genes?

Materials and Methods:

50 cases of AIS girls between age 10 to 15 years and 50 age- and sex-matched normal subjects will be recruited into this cross-sectional study for determination of 1) BMD; 2) anthropometry; 3) sexual maturity; 4) gene polymorphism of VDR and ERα.

Clinical significance:

Result of the present study may help to improve our understanding of the etiopathogenesis of AIS. It may also provide opportunity in early screening and prognostication of AIS candidates.

(MD03960)

Tissue Engineering of Mesenchymal Stem Cell-calcium Phosphate Ceramic Composite - Study on Application in Spinal Fusion

✉ CHENG Chun Yiu Jack • QIN Ling • LEE Kwong Man, Simon* • YEUNG Hiu Yan • HU Yun Yu*

□ 1 January 2004

❖ AO Research Commission

Spinal deformities and degenerative diseases require surgical stabilization and posterior spinal fusion (PSF). Solid bony fusion is the most important for the successful outcome of the treatment. Failure of fusion can result in significant morbidity. 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 blood vessels and 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. The differentiation of the MSCs can be directed to osteogenic cells. When the MSCs was seeded on the calcium phosphate ceramics and implanted subcutaneously, bone formation inside the ceramics was observed. The objectives of the project are 1) to characterize the differentiated MSCs grown on calcium phosphate ceramic; 2) to use a well established rabbit PSF model to study the osteogenic effect of tissue engineered osteogenic cell-calcium phosphate ceramic composite in fusion process; 3) to explore the possibility of undecorticated posterior

spinal fusion surgery when the tissue engineered composite is applied to the fusion site.

The outcome of this study will shed light on our understanding of engineered autologous MSCs in enhancing bone fusion of PSF and the role of decortication. This new approach would eliminate the addition surgical procedure needed to decorticate and to obtain autologous bone grafting. It would provide unlimited supply of bone substitute and reduce the associated complications at the donor site.

(MD03824)

Are VDR, Era and PTHR1 Genes Associated with the Occurrence as well as Abnormality in Bone Growth and Sexual Maturation in Adolescent Idiopathic Scoliosis?

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

□ 1 April 2004

❖ Scoliosis Research Society (SRS) Research Fund

Despite the many advances in the treatment of adolescent idiopathic scoliosis (AIS), the etiology still remains largely controversial. Results of our previous studies in the past 10 years have revealed the presence of generalized osteopenia with significant lower bone mineral density (BMD) in over 58% of AIS subjects. Delayed onset of puberty, taller sitting height as well as longer arm-span were also found when compared with age-, sex-, and maturity-matched normal controls. VDR, ER α and PTHR1 genes are well known to be related to bone mineralization, longitudinal bone growth and sexual maturation. The aims of the study are to answer the following questions: (1) Are the VDR, ER α and PTHR1 gene polymorphism associated with the

presence of Adolescent Idiopathic Scoliosis? (2) Are the generalized osteopenia, abnormal longitudinal bone growth, and delay sexual maturation in AIS associated with these genes? Result of the present study may help to improve our understanding of the etiopathogenesis of AIS. It may also provide opportunity in early screening and prognostication of AIS candidates.

(MD03862)

Tissue Reactions and Dose Response Characteristics of Electromotive Vancomycin Delivery

✉ HUNG Leung Kim • CHAN Chiu Yeung Raphael (Dept of Microbiology) • FU Sai Chuen Bruma*

□ 30 June 2004

❖ CUHK Research Committee Funding (Direct Grants)

Vancomycin is one of the most effective antibiotics against methicillin resistant staphylococcus infections. The drug requires intravenous administration. However tissue concentration is not high and complications related to intravenous administration is frequent and can be serious. Recent studies are directed towards local delivery of the drug by sustained drug release or by means of depot systems. Our previous studies have shown that an application of an electric field locally can enable the drug to penetrate directly through skin and cortical bone and be concentrated in the subjacent tissues. This mode of electromotive drug delivery, or iontophoresis, has already been studied in different fields in medicine. In the first part of this study vancomycin at different concentrations is administered transcutaneously at different current densities for different durations. This is compared to single intravenous injection of

the drug or application of the electric field without drug. In the second part of the study vancomycin is infused slowly with a subcutaneous catheter. Serum drug levels and tissue drug levels are sampled at intervals and vancomycin is assayed with FPIA technique using the TDx kits (Abbott laboratories). Histological sections of tissues deep to the drug electrode are studied to investigate the degree of tissue reactions and the extent of tissue toxicity.

(MD03471)

Aminobisphosphonates and Farnesyl Transferase Inhibitors as Adjuvants in the Treatment of Giant Cell Tumor of Bone

✉ KUMTA Shekhar Madhukar • HUANG Lin (Dept of Surgery) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • ROSIER R. N.*

□ 15 December 2003

❖ CUHK Research Committee Funding (Direct Grants)

Giant cell tumor (GCT) is the most common non-malignant primary bone tumor reported in Hong Kong, being much more prevalent in the oriental than in the Caucasian population. It usually affects young adults between the ages of 20-40. This tumor is well known for its potential to recur following treatment. An extensive surgical removal may reduce local recurrence but it implies the sacrifice of a larger segment of bone, usually adjacent to a joint and may jeopardize limb function consequently. In an attempt to reduce the magnitude of surgery surgeons have tried adjuvant local therapy and high-dose radiation, both of which have significant disadvantages. To date there is no effective adjuvant therapy for Giant Cell Tumors. Our

previous studies on GCT have shown that stromal tumor cells are the neoplastic component of this tumor. Stromal cells recruit and stimulate osteoclasts which eventually destroy the affected bone, and therefore are prime targets for possible adjuvant control. Bisphosphonates are well known non-toxic drugs used for their anti-osteoclast actions. Our pilot studies have shown that Bisphosphonates may also induce apoptotic cell death of the stromal cells at non-toxic concentrations. Farnesyl Transferase inhibitors (FTI) are yet another class of non-toxic drugs that act synergistically with Bisphosphonates and have been used in clinical studies on some cancers. FT Inhibitors also sensitize cells and make them susceptible to low doses of radiation. Our project therefore aims to study the effect of Bisphosphonates and FT Inhibitors in various combinations and with radiation on the Stromal Cell component of Giant Cell Tumors. This may eventually result in an effective adjuvant therapy that will reduce the magnitude of surgery in GCT and result in preservation of better limb function in this relatively young GCT patient population.

(MD03555)

Modification of Home Environmental Hazards for the Elderly

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

☐ 15 August 2003

❖ S.K. Yee Medical Foundation

With the support of S.K. Yee Medical Foundation in 2002 (Ref no: 202215), our team started a fall prevention program to educate elderly to prevent falls. In running the program with home visits, we have

identified many environmental risks of fall at home of the elderly. Simple modification of home environment will effectively help to reduce the fall risks. The elderly urgently need these devices and we believe that provision of assistive aids will significantly reduce the fall incidents. However, most of these elderly are unable to afford the installation of assistive aids. With this proposal, the poor elderly will be benefited by providing assistive devices, including night lights, handrails, walking aids, shower chair, bath board, and hip protectors free of charge. Together with our previous funded project, we will continue to conduct home visits and home safety will be inspected. Obstacles will be removed and whenever necessary, assistive devices will be distributed and installed accordingly with the newly available funding. Knowledge of fall prevention will also be reminded to reinforce their awareness of fall injuries.

While the community service of fall prevention will continue to many of the active elderly, the present proposal is targeting to those less active elderly whom stay in their home most of the time and modification of home environment will help them tremendously. It is hoped that the assistive devices will help to further reduce fall incidence and thus the serious consequences from the fall injuries.

(MD03868)

High Frequency, Low Magnitude Vibration Therapy for Preventing Osteoporotic Fracture

✍ LEUNG Kwok Sui • CHEUNG Wing Hoi • QIN Ling • SIU Wing Sum# • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)

☐ 1 October 2003

- ❖ CUHK Research Committee Funding (Direct Grants)

Osteoporotic fracture is one of the commonest geriatric orthopaedic problems and caused heavy social-economical burdens on government. Recent research shows that a low magnitude, high frequency (>20Hz) signal persists in bones all the time in daily activities, which are partially contributed by muscle fibre IIA contractions. These signals may be very critical to maintain the BMD. Loss of muscle fibre IIA due to aging is associated with the deterioration of BMD, causing osteoporosis. As muscle fibre IIA is also important for postural balance, loss of these fibres in elderly will lead to poor balancing ability, causing high risk of falls. Therefore, compensatory treatment for the loss of >20Hz signals may be another new approach to prevent osteoporotic fractures. The objective of this study is to testify the mechanism of vibration therapy on the restoration of muscle fibre IIA and BMD in our well-established osteoporotic goat model. This is the first study to look into the mechanism of vibration therapy. We hope that the results of this study will help to understand the mechanism of vibration treatment on the BMD via the effect on muscles.

(MD03361)

Osteoporotic Fractures in Chinese Men: Mr Os Hong Kong

- ✉ LEUNG Ping Chung • WOO Jean (Dept of Medicine & Therapeutics) • WONG Yeung Shan Samuel (Dept of Community and Family Medicine) • CUMMINGS Steve* • LANG Tom* • NEVITT Michael C* • STONE Katie* • ORWOLL Eric*

☐ 26 August 2003

- ❖ National Institutes of Health

Asian men constitute a large proportion of the population of the world and the U.S., but there have been no prospective studies of their risk of vertebral fractures. In preliminary studies, we found that Asian men have lower areal bone density than do Caucasian men. However, instead of having a higher prevalence, Asian men appear to have a lower prevalence of vertebral fractures. Understanding this paradox will elucidate the causes of vertebral fracture in men-and women.

Caucasian men are much larger than Asian men. We hypothesize that the difference in fracture rates, is due primarily to differences in bone size and body size. We propose to add two measurements: follow-up lateral spine radiographs and quantitative computed tomography (QCT) to the Hong Kong arm (consisting of 2,000 men) of the ongoing Mr. OS U.S. study (consisting of 6,000 men and funded by NIAMS and NIA). This will allow the Mr. OS study to prospectively test the hypothesis that smaller Asian men have a lower incidence of vertebral fracture than do Caucasian men. We will test the hypothesis that Asian men have higher volumetric BMD (by QCT) and that they have a higher compression strength than the larger Caucasian men. We hypothesize that these differences will be large enough to account for the lower risk of vertebral fractures in Asian men. Finally, by assessing risk factors in the same way in the US and Hong Kong studies, we will be able to test the hypothesis that differences in environmental exposures and other risk factors account for a portion of the differences in vertebral fracture rate. These hypotheses must be tested in cohorts of Caucasian and Asian men that are assessed in the same ways, as we are doing in the Mr. OS study.

This study efficiently builds on the ongoing Mr. OS study, using the same protocols and systems for data collection and management. Furthermore, the

proposed study leverages the fact that Hong Kong Jockey Club Center for Osteoporosis Care and Control will provide the staff, dual X-Ray densitometry measurements and measurements.

(MD03838)

National Institutes of Health - US-China-Japan Research Consortium on Herbal Medicine

✉ LEUNG Ping Chung • FUNG Kwok Pui (Biochemistry) • BUT Pui Hay Paul (Dept of Biology) • LEE Ming Yuen (Institute of Chinese Medicine) • FONG Yuet Shim Carmen (Institute of Chinese Medicine)

□ 25 September 2003

❖ National Center for Complementary and Alternative Medicine, NIH

This is one of the first research projects awarded grants by the National Centre for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (NIH) to support new partnerships between US and international research teams to create the infrastructure and scientific foundation for research into complementary and alternative medicine. The US-China-Japan Research Consortium on Herbal Medicine is led by the Harvard Medical School, with participation from the Institute of Chinese Medicine, the China Academy of Traditional Chinese Medicine, and Keio University of Japan. Promising herbal medicines for untreatable diseases will be identified and procured, extracted, characterized and tested for the systematical evaluation of quality, safety, efficacy and the basic scientific mechanism. Further preclinical testing and multi-site international human clinical trials are anticipated for the second phase.

(MD00555)

Low Intensity pulsed Ultrasound for Early Restoration of Fibrocartilage Zone and Proprioception in Bone-Tendon Junction Repair - A Partial Patellectomy Model in Rabbits

✉ QIN Ling • CHEN Hong Hui*

□ 1 July 2003

❖ AO Foundation

Our previous animal study supported by AO Grant (AO/ASIF 97-L15) showed that the restoration of fibrocartilage zone in bone-tendon (B-T) junction was slow and difficult. It requires longer period of immobilization for such repair and the adverse effects of immobilization on musculoskeletal tissues are well known. How to accelerate B-T repair has therefore become a focus of our joint research program.

Recent studies of others and our group demonstrated beneficial effects of the cost-effective low intensity pulsed ultrasound (LIPUS), which otherwise well documented for enhancing fracture healing, treat delayed union, non-union, and soft tissue injuries, possibly by stimulating some endogenous biological growth factors. Our primary histological findings revealed that LIPUS was able to induce earlier bone remodeling at bony end, tissue integration at B-T healing interface, and restoration of fibrocartilage zone after partial patellectomy. This suggests that LIPUS may enhance B-T repair during immobilization so that we may shorten the time required for immobilization and initiate early remobilization.

In order to substantiate observations from our pilot study, we will use our established partial patellectomy model to study LIPUS for accelerating B-T junction repair in rabbits, together with early mobilization via functional electrical stimulation (FES) on quadriceps muscles. Healing quality of

B-T repair after discontinuing active postoperative rehabilitation program will also be evaluated.

Endpoint measures include:

Restoration of B-T junction fibrocartilage zone by studying the thickness of the restored fibrocartilage zone, its matrix collagen distribution, and mRNA expression in fibrochondrocytes;

Restoration of joint proprioception by evaluating sensory nerve endings in healing tendon next to the B-T healing interface, and

Restoration of mechanical properties by determining the tensile strength of B-T healing complex.

The results to be obtained will help us to modify our clinical treatment protocols, which may lead to shortening of immobilization period and an active functional rehabilitation of the operated knee for avoiding associated complications. The potential beneficial effects from this study may also be generalized to other regions involving direct B-T repair, such as hand, foot and ankle, and shoulder.

(MD03502)

New Bone Formation and Tendon Cartilaginous Metaplasia Prevent Postoperative Articular Cartilage Deterioration and Improve Joint Tracking - A Partial Patellectomy Model in Rabbits

✉ QIN Ling • CHAN Kai Ming • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • LEUNG Kwok Sui • ZHENG Yong Ping*

□ 1 December 2003

❖ Research Grants Council (Earmarked Grants)

Our experimental studies and clinical arthroscopic examinations reveal postoperative enlargement of the remaining patella via new bone outgrowth and patellar outgrowth and patellar tendon cartilaginous

metaplasia next to the healing interface with healing over time. This adaptation can increase patellofemoral joint (PFJ) contact area and is beneficial for restoration of PFJ tracking.

In this study, we will use the established partial patellectomy model in rabbits to conduct an interventional experimental study and investigate association between the extent of patellar enlargement and different PFJ compression loading conditions. Findings of our experimental study will provide scientific evidences to establish and / or modify our orthopaedic rehabilitation programs for patients who have undergone partial patellectomy for facilitating earlier restoration of PFJ anatomy and function and for avoiding or minimizing PFJ degeneration of the operated knee.

(CU03342)

Vibration Therapy for Preventing Osteoporotic Fracture in Post-menopausal Women

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

□ 1 April 2004

❖ CUHK Research Committee Funding (Direct Grants)

Osteoporotic fractures are caused by low bone mineral density (BMD) and falls due to poor balancing power in elderly. The best strategy to prevent osteoporotic fractures, therefore, is to train up the balancing ability and increase the BMD simultaneously.

Loss of muscle fibre IIA in advancing age has been reported to cause the poor balancing ability and the deterioration of BMD, i.e. osteoporosis (Huang *et al.*, 1999). Recent research also shows that a low magnitude, high frequency (>20Hz) signal persists in

bones all the time in daily activities, which are partially contributed by muscle fibre IIA contractions. These signals may be very critical to maintain the BMD. Therefore, compensatory treatment for the loss of >20Hz signals may be an approach to prevent osteoporotic fractures.

Low magnitude (<10 microstrain), high frequency (30Hz) vibration mechanical signals was recently reported to be anabolic to bone tissue by increasing the BMD by 34.2% in normal sheep. This study, however, focused on investigating the effect of vibration therapy on normal animals only. The effect on osteoporotic bones in human is still unknown yet. Therefore, it is of great clinical significance to have a clinical study on investigating the effect of vibration therapy on osteoporosis. As vibration platform generates the required essential signals (30Hz), which may help to regulate fine posture control by contraction at the firing frequency originally contributed by muscle fibre IIA, we will use it in this study to treat post-menopausal women. The study will prove the effect of the vibration therapy in treating osteoporosis in human.

(MD03559)

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

✉ YUNG Shu Hang Patrick • TONG Wai Chung Christopher • CHAN Kai Ming • CHAN Tan Jessica

☐ 1 March 2004

❖ Pfizer Corporation

Conventional NSAIDs are widely used for pain relief and for the treatment of a variety of inflammatory diseases including osteoarthritis and rheumatoid arthritis. While NSAIDs are effective therapeutic agents, their use is associated with a significant incidence of side effects including gastrointestinal bleeding, ulceration and alteration of platelet function.

The investigational drug, Valdecoxib, is a highly selective COX-2 inhibitor and is expected to exhibit anti-inflammatory and/or analgesic activity without the concurrent adverse effects associated with the inhibition of COX-1. The pain-relieving efficacy of the investigational drug, valdecoxib, will be investigated and compared to those seen with diclofenac sodium. This study will be performed in patients undergoing anterior cruciate ligament reconstruction (ACL); a procedure that results in significant post-operative pain in most individuals.

This study will be a multicentre, double-blind, double-dummy, randomised trial comparing valdecoxib 20mg twice daily (with an initial loading dose of 40mg followed by a second dose of 20mg only on the first day) vs. diclofenac sodium delayed release 75mg twice daily for the treatment of pain in patients undergoing knee arthroscopy procedure for anterior cruciate ligament reconstruction, when administered for 6 (\pm 1) days.

A total of 3 visits is required including a screening, a baseline and a final visit. The patient's assessment of pain (Pain VAS) at Day 6 / Final visit will be recorded for this study. The patients will also have to fill out a Global Evaluation of Study Medication throughout the treatment period, and report the daily consumption of rescue medication and drug-related adverse events. Health outcome endpoints including the Modified Brief Pain Inventory will also be assessed.

(MD03917)

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 (Dept of Sports Science & Physical Education)# • HONG Youlian (Dept of Sports Science & Physical Education) • LAU Edith Ming Chu (Dept of Community and Family Medicine)# • WOO Jean (Dept of Medicine & Therapeutics)

2002-03 A Study of Tendon Healing in Sports Injury: The Manipulation of Transforming Growth Factor beta (TGF- β) on Matrix Deposition (MD02851)

✉ CHAN Kai Ming • WONG Wan Nar Margaret • FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)

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 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

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
- 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
- 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*
- 2000-01 Virtual Reality (VR) Based Systems for Training on Endoscopic Surgery and Diagnostic Ultrasound Procedures (EE20028)
- ✍ CHENG Chun Yiu Jack • HENG Pheng Ann (Dept of Computer Science and Engineering) • CHAN Kai Ming • CHUNG Chi Kit Ronald (Dept of Auto. & Computer-Aided Engin.) • CHUNG Sheung Chee Sydney (Dept of Surgery) • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Kwong Sak (Dept of Computer Science and Engineering) • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • TSUI Hung Tat (Dept of Electronic Engineering) •
- WONG Tien Tsin (Dept of Computer Science and Engineering) • XU Yangsheng (Dept of Auto. & Computer-Aided Engin.) • YIM Ping Chuen Anthony (Dept of Surgery) • SHI Peng Cheng* • TSO Shiu Kit*
- 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
- 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
- 2001-02 Promoting a safer Household Environment: A Volunteer-based Home Visit Programme (MD01665)
- ✍ CHENG Chun Yiu Jack • CIPRA members*
- 2001-02 Relationship between Postural Balance, Somatosensory Evoked Potential and the Progression of Scoliotic Deformity in Adolescent Idiopathic Scoliosis - A Longitudinal Study (MD01864)
- ✍ CHENG Chun Yiu Jack • HUI Chan W Y Christina* • GUO Xia*
- 2002-03 The Effect of Weight of School Bag on Subjects with Adolescent Idiopathic

	Scoliosis: A Biomechanical and Physiological Study (MD01907)		✍ HUNG Leung Kim • WONG Man Wah • HO Pak Cheong • AU Kin Ming* • CHAN Ping Tak*
	✍ CHENG Chun Yiu Jack • CHOW Hung Kay, Daniel* • YAO Y D Fiona* • WONG Man Sang*	2001-02	Promotion of Experience Sharing and Sharing of Good Teaching and Learning Practices in CUHK 2001 - Teacher Focused Workshops to Enable the Development of Interactive Web-based Strategies Designed to Foster Critical Thinking in Students (ED01533)
2002-03	Combination of Extra-corporeal Shock Wave Therapy and Low Intensity Ultrasound for Inducing Non-Union Healing in a Rabbit Model (MD01503)		✍ KUMTA Shekhar Madhukar • CHENG Chun Yiu Jack • HUNG Leung Kim
	✍ CHENG Chun Yiu Jack • GUO Xia* • KWONG S C*	2002-03	The Learning Objects Initiative (ED02513)
2002-03	Formative Assessment Case Studies (FACS): Establishing Life-Long Learning Skills in Health Science Students (ED01398)		✍ KUMTA Shekhar Madhukar • HART Ian* • CHAN Rita* • Blurton, Craig*
	✍ CHENG Chun Yiu Jack • KUMTA Shekhar Madhukar	2000-01	Monteggia Fracture in Children - A Review of 30 Cases (MD00535)
2002-03	The Biology and Efficacy of Low-intensity Pulsed Ultrasound Treatment on Posterior Spinal Fusion – A Study in Rabbit Model (MD02873)		✍ LAM Tsz Ping • MA RF* • NG Kin Wah Bobby • CHENG Chun Yiu Jack
	✍ CHENG Chun Yiu Jack • QIN Ling • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • HU Yun Yu*	2000-01	Anterior Spinal Fusion with Halm-Zielke Instrumentation System in Adolescent Idiopathic Scoliosis (MD00788)
2001-02	Electromotive Antibiotic Delivery to Bone by Iontophoresis (MD01360)		✍ LAM Tsz Ping • NG Kin Wah Bobby • CHENG Chun Yiu Jack • MA RF*
	✍ HUNG Leung Kim • CHAN Chiu Yeung Raphael (Dept of Microbiology) • WU Hay Tong#	2000-01	Calcium Intakes in Patients with Adolescent Idiopathic Scoliosis (AIS) (MD00838)
2002-03	A Prospective Randomized Study on Two Methods of Mobilization After Flexor Tendon Repair (MD02742)		✍ LEE Tak Keung Warren • CHEUNG Siu King • LAM See Way Sylvia

- (School of Public Health) • LEE Ching Shun Christine* • CHAU Wai Wang • CHENG Chun Yiu Jack
- 2000-01 Reconstruction of Damaged Physis 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 Fall and Fractures Prevention Program for the Elderly (MD02439)
✍ LEUNG Kwok Sui • CHEUNG Wing Hoi • CHAN Tan Jessica • WONG Josephine* • LAU Herman*
- 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 • SIU Wing Sum#
- 2002-03 The Effectiveness of a Fall Prevention Program for the Elderly Living in the Community (MD02347)
✍ LEUNG Kwok Sui • CHEUNG Wing Hoi • CHAN Tan Jessica
- 2002-03 The Provision of 850 nos. of Hip Protector and Production of Fall Prevention Handbook and VCD to Promote the Awareness of Fall Prevention in Nursing Home (MD02578)
✍ LEUNG Kwok Sui • CHEUNG Wing Hoi • SZE Pan Ching • LAM Pui Sze • CHAN Tan Jessica
- 2000-01 Development and Clinical Trials of Compound Yun Zhi (Jiang Su) and Danshen (He Nan) Products (MD20043)
✍ LEUNG Ping Chung • FUNG Kwok Pui (Biochemistry) • LAM Wai Kei Christopher (Dept of Chemical Pathology)
- 2001-02 Chinese Medicine Research and Further Development (MD01714)
✍ LEUNG Ping Chung • FUNG Kwok Pui (Biochemistry) • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • HAINES Christopher John (Dept of Obstetrics & Gynaecology) • SUNG Yn Tz Rita (Dept of Paediatrics) • WOO Kam Sang (Dept of Medicine & Therapeutics) • CHE Chun Tao (School of Chinese Medicine) • CHAU F T* • TSIM Karl W K* • FONG W F*
- 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*

- 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 (Dept of Medicine & Therapeutics) • CHOY Tak Kee Dicky (HK JCC for Osteoporosis Care and Control) • WONG Yeung Shan Samuel (Dept of Community and Family Medicine)
- 2002-03 The Prevalence of Vertebral Deformity in Asian Men and Women (MD02449)
 ✍ LEUNG Ping Chung • WONG Yeung Shan Samuel (Dept of Community and Family Medicine)
- 2002-03 Comparison of Teriparatide and Calcitonin in the Treatment of Postmenopausal Women with Osteoporosis (MD02656)
 ✍ LEUNG Ping Chung • CHOY Tak Kee Dicky (HK JCC for Osteoporosis Care and Control)
- 2000-01 Associated Osteoporosis of the Host Bone in Tibial Lengthening (MD00633)
 ✍ NG Kin Wah Bobby • HUNG Wing Yin Vivian • CHENG Chun Yiu Jack
- 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 Development and Biomechanical Characterization of Tissue Engineering Scaffolds for Articular Cartilage Regeneration (BL00359)
 ✍ QIN Ling • MAK F T Arthur* • VUNJAK-Nova Kovic G* • YAO K D*
- 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*
- 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
- 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)
- 2000-01 Culture of Rabbit Chondrocytes Released from Rib Cage on Calcium Phosphate Ceramic and Collagen Sponge (MD98751)
✍ YEUNG Hiu Yan • LEE Kwong Man, Simon* • CHEUNG Wing Hoi • LAW Lai Pang (Institute of Chinese Medicine)# • TABATA Yasuhiko* • CHENG Chun Yiu Jack

RESEARCH PROJECTS

***In vitro* Study of the Mechanism of Angelica Polysaccharide on Platelet Production in Human Haematopoietic Stem Cells**

✉ CHIK Ki Wai • YANG Mo • SUNG Yn Tz Rita
• LI Kwai Har Karen • FOK Tai Fai

☐ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Thrombocytopenia is a common cause of bleeding tendency. Platelet transfusion from voluntary donors remains as the standard supportive therapy despite the understanding of thrombopoietin (TPO) as a key growth factor for platelet production. Danggui (當歸) has been used as a remedy for “regulating and enriching blood” for more than 2000 years in Chinese Medicine. It is known that the effect of Danggui on platelet production is related to its polysaccharides component. Our preliminary studies have shown that angelica polysaccharide (APS) significantly enhanced *in vitro* TPO-induced megakaryocytopoiesis and *in vivo* platelet production in mice. In this project, we will further investigate the effect and the mechanism of purified APS on human megakaryocytopoiesis. We hypothesize that the mechanism of APS on platelet production may include: (1) direct action on megakaryocytes through modulation of TPO activities; (2) indirect action on the megakaryocytes via promoting the production of TPO and other hematopoietic growth factors from bone marrow stromal cells. Our objectives include: (i) to investigate the mitogenic effect of APS on the *in vitro* expansion of human CD34+ cells, human CFU-MK formation and human megakaryocytic cell

lines; and (ii) to investigate the TPO expression in human bone marrow stromal cells. We believe further characterization of the APS as a treatment modality could benefit patients with thrombocytopenia due to various conditions.

(MD03602)

Mobilization of Endogenous Stem and Progenitor Cells from Bone Marrow for the Repair of Neonatal Hypoxic-ischemic Brain Damage

✉ FOK Tai Fai • YANG Mo • LI Kwai Har Karen
• CHIK Ki Wai

☐ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

The transplantation of bone marrow cells into the damaged brain has been proposed as a new treatment for brain injury. Alternatively, we hypothesize that (a) mobilization of endogenous bone marrow stem/progenitor cells into the circulation by growth factors might repair brain damage; and (b) neural protection factors: thrombopoietin (TPO), erythropoietin (EPO) and serotonin (5-HT) are effective agents for mobilizing bone marrow stem/progenitor cells for neural regeneration. In this study, our objectives are (1) To establish the mobilization method for endogenous stem/progenitor cells in a neonatal rat model with hypoxic-ischemic brain damage; (2) To confirm the hypothesis that neural protection factors: TPO, EPO and 5-HT, like granulocyte-colony stimulating factor (G-CSF), may have a mobilizing effect on bone marrow stem/progenitor cells for neural repair in this neonatal rat model; and (3) To evaluate the optimal combination of these hematopoietic growth factors (G-CSF, EPO and TPO) and neurotransmitter 5-HT on stem cell mobilization and neural regeneration.

The effective mobilization of autologous stem cells for neural repair is new concept, if proven, could be developed for the treatment of hypoxic-ischemic brain damage, other neural damages and degenerative diseases.

(MD03469)

Prospective, Hospital-based, Multi-center Study to Assess the Incidence of Intussusception in Children <2 Years of Age in Hong Kong

✉ LAU Chun Yuen David • YEUNG Chung Kwong (Dept of Surgery) • Paul TAM* • KWOK Wing Kin*

□ 1 April 2004

❖ GlaxoSmithKline Biological S. A.

All intussusception cases (definite, probable, possible, suspected intussusception) will be enrolled prospectively from children who receive care at participating hospital and listed on a Screening Sheet. Subjects will be enrolled during a period of at least two years beginning at study start. Once a subject has been enrolled into the study, the participation in the study will consist of interview of the subject's parents and review of medical chart. For the purpose of the analysis, case-subjects will be those with definite intussusception.

(MD03530)

Innate Immunity and Asthma in Chinese Children

✉ LEUNG Ting Fan • TANG Leung Sang Nelson (Dept of Chemical Pathology) • WONG Wing Kin Gary • WONG Chun Kwok (Dept of Chemical Pathology) • LAM Wai Kei Christopher (Dept of Chemical Pathology)

□ 1 November 2003

❖ CUHK Research Committee Funding (Direct Grants)

Asthma is a major healthcare burden in Hong Kong schoolchildren. The pathogenesis of asthma involves a complex interaction between exposure to environmental allergens and respiratory irritants as well as genetic predisposition of the patients. A number of major susceptibility loci for asthma and atopy have been described in the Caucasian populations. These genes are responsible not only for causing asthma or atopy but also involved in the regulation of the severity of asthma. On the other hand, high environmental endotoxin exposure is recently reported to confer protection against the development of atopic disorders in Caucasian children. Innate immune system plays a major role in modulating the human defense against microbes. Significant deficiency of this system leads to recurrent infections and the development of autoimmune diseases. As asthma is an immune dysregulatory disease, it is likely that innate immunity genotypes will also exert influences on its susceptibility and disease severity. In fact, recent reports suggest that several genotypes of CD 14, the endotoxin receptor, are associated with childhood asthma and atopy in Caucasians. However, the relevant data in the Chinese population is lacking. This study will delineate the interaction between innate immunity genes and environmental endotoxin exposure in regulating atopic disorders in Hong Kong Chinese children.

(MD03742)

Mechanism of a Novel Mannose-binding Lectin as a Preservation Factor for Human Hematopoietic Stem and Progenitor Cells

✉ LI Kwai Har Karen • OOI Vincent Eng Choon
(Dept of Biology)

□ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

A new mannose-binding lectin (MBL) was isolated from leaves of the Chinese daffodil *Narcissus tazetta* and characterized as an unglycosylated homodimer with a molecular mass of 26 kDa. This protein upregulates immunomodulatory cytokines such as interferon- γ , interleukin- β and tumor necrotic factor- α in mice *in vivo*. Our preliminary data demonstrated that this MBL possesses a unique function in preserving human hematopoietic stem and progenitor cells. Our hypothesis is that this MBL functions as a preservation factor for hematopoietic stem and progenitor cells by inducing specific survival signals. In this study, we shall (1) establish the function of MBL in and *in vivo* transplant model of human stem cells in the non-obese diabetic (NOD)/ severe-combined immunodeficient (SCID) mouse model and (2) investigate the signal pathway of MBL by molecular and protein technology: microarray, real-time PCR and Western blot analysis. Uncoding the mechanism of this pathway might lead to better management of hematopoietic stem cell transplantation and *ex vivo* expansion.

(MD03711)

Assessment of Cough Frequency in Children with Stable Asthma: Comparison with Lung Function and Other Non-invasive Markers of Airway Inflammation

✉ LI Man Chim Albert Martin • LEUNG Ting Fan
• CHAN Fung Ying • SUNG Yn Tz Rita • FOK
Tai Fai

□ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Cough is an important symptom of respiratory disease, particularly asthma. In childhood asthma cough may be the most frequent symptom, or its only symptom, yet it remains difficult to assess. Cough assessment in patients with lung disease relies on subjective recording and therefore can be variable. In fact, one of the major difficulties in cough research has been our inability to accurately quantify clinically relevant cough. Reporting of nocturnal cough with asthma diaries has repeatedly been found to show poor agreement with recorded cough. Previous investigators have used conventional tape recorders to quantify cough objectively but their bulk and lack of portability preclude their use in daytime cough assessments during normal activity. Furthermore, they rely exclusively on an audio signal. Recently the use of an ambulatory cough monitoring device has been validated and was found to be highly acceptable to children and no adverse effects during recording were reported. Such objective data on cough outside the laboratory setting are unique and will definitely help in the diagnosis and assessment of many respiratory diseases and especially asthma.

Our aim for this study is twofold: (1) to measure cough frequency in stable asthmatic children and (2) to assess correlation between cough frequency of asthmatic children and the following parameters: [a] spirometric lung function, [b] exhaled nitric oxide and [c] inflammatory markers in breath condensate. Our hypothesis is that increased cough frequency is more sensitive to airway inflammation than is spirometry. In other words, a child may have an inflamed airway with an abnormal cough frequency and yet his lung function is normal.

The outcome of the proposed study may shed light on the pathophysiology of cough in asthmatics. This may lead to the discovery that cough is a better indicator of disease control and lay the foundation for establishing a more evidence-based approach to the better management of this common symptom.

(MD03685)

Case Note Audit of Childhood Intussusception in Hong Kong

✉ NELSON Edmund Anthony Severn • TAM Siu Lun John (Dept of Microbiology) • IP K S* • NG C H* • POON K H* • LAU Y L* • CHIU S S* • LAU D* • NG Daniel*

□ 1 July 2003

❖ GlaxoSmithKline Biologicals

The incidence of hospitalisation for intussusception in Hong Kong infants has been estimated to be 78-100/100,000 for the period July 1997 to June 1999 using the Clinical Management System (CMS) discharge database for all Hospital Authority hospitals. This rate was greater than that found in similar studies in the US and Europe. This study will review the case notes of all children under the age of 5 years who had a CMS discharge diagnosis indicating intussusception or a procedure indicating reduction of intussusception during the six-year period 1 July 1997 to 30 June 2003.

(MD03416)

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

✉ NELSON Edmund Anthony Severn • TAM Siu Lun John (Dept of Microbiology)

□ 1 May 2004

❖ GlaxoSmithKline Limited

This is a double-blind, placebo-controlled, randomised study to evaluate the safety and efficacy of the GSK Biologicals' Human Rotavirus Vaccine (HRV) in healthy infants. Infants will be recruited at approximately 2 months of age. Each subject will have a maximum of 6 study visits: Visit 1 (Day 0), Visit 2 (1 to 2 months later), Visit 3 (2 to 4 months later), Visit 4 (9 to 10 months later), Visit 4A (at 18 months) and Visit 5 (when the child is approximately 2 years old). The HRV or the placebo will be given to the participants at the same time as their routine childhood immunisation.

(MD03539)

The Use of Proinflammatory and Anti-inflammatory Cytokines for Early Diagnosis of Systemic Infection in Preterm Infants

✉ NG Pak Cheung • LI Kwai Har Karen • WONG Pui On Raymond (Lee Hysan Clinical Research Laboratories) • FOK Tai Fai

□ 1 October 2003

❖ 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 proinflammatory and anti-inflammatory cytokines: interleukin- (IL)- 1 β , IL-6, IL-8, IL-10, IL-12p75 and TNF α for early diagnosis of late-onset (>72 hours of

age) neonatal infection in preterm, very low birth weight infants.

Late-onset nosocomial bacterial infection is an important cause of morbidity and mortality in infants requiring intensive care. Preterm, very low birth weight (VLBW) infants are particularly vulnerable because of immune immaturity, severe underlying conditions, and frequent requirement of invasive procedures such as umbilical and indwelling long lines. Despite the development of new broad-spectrum antibiotics and advanced life support treatment, a significant proportion of infected infants still follows a rapid downhill course leading to septicemic shock, disseminated intravascular coagulation, and death within hours of deterioration. Thus, a reliable set of infection markers are required to promptly and accurately identify the infected cases so that treatment can be started without delay. Equally difficult is the exclusion of infection in infants with suspected sepsis, as continuation of broad-spectrum antibiotics for presumptive bacterial infection frequently leads to unnecessary treatment and emergence of resistant organism. Hence, this study attempts to define the optimal cut off value for each infection marker and to determine the best marker or combination of markers for the early detection of late-onset sepsis.

(MD03519)

Generation of Cardiomyocytes from Bone Marrow Cells and Their Capacity in Engrafting and Repairing the Infarcted Heart

✉ SUNG Yn Tz Rita • SANDERSON John Elsby (Dept of Medicine & Therapeutics) • LI Kwai Har Karen • YANG Mo • LI Ming (Dept of Medicine & Therapeutics) • YI Qi Jian*

□ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Myocardial infarction is a highly fatal disease caused by the irreversible damage of tissues and the subsequent impairment of cardiac function. As the remaining myocytes are unable to reconstitute the necrotic tissue, the post-infarction heart function deteriorates with time. Recent *in vivo* studies have suggested that bone marrow cells possess the capacity to differentiate into cardiomyocytes, which potentially could repair damaged cardiac muscles. In this study, we aim to optimize this potentially applicable technology by two approaches: (1) an *in vitro* culture system that generates functional cardiomyocytes from murine bone marrow stromal cells; and (2) induction of autologous repair of the infarcted heart by mobilization of bone marrow progenitor cells. We shall also establish the optimized conditions of bone marrow progenitor cell mobilization with various combinations of growth factors including granulocyte macrophage-colony stimulating factor (GM-CSF), stem cell factor (SCF), flt-3 ligand (FL), platelet-derived growth factor (PDGF) and granulocyte-colony-stimulating factor (G-CSF). The capacity of progenitors synthesized by these methods on regenerating the infarcted heart will be assessed by echocardiography, hemodynamics, morphology and survival. The generation of myocardial progenitors from bone marrow cells would be potentially applicable to the treatment of myocardial infarction and degenerative diseases of the heart.

(MD03987)

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

✉ WONG Wing Kin Gary • LEUNG Ting Fan

□ 8 September 2003

❖ Merck Sharp & Dohme (Asia) Ltd

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

Childhood wheezing disorder is a common condition. The role of montelukast as an anti-inflammatory agent in the treatment of bronchiolitis, a common wheezing problem, is not clear. This is a randomized trial to assess the efficacy of montelukast in the treatment of bronchiolitis in young children.

(MD03878)

2002-03 Identification of Predisposition Genes for Atopic Dermatitis in Chinese Children (MD02691)

✉ HON Kam Lun • LEUNG Ting Fan • TANG Leung Sang Nelson (Dept of Chemical Pathology) • MA Kwok Chiu* • LAM Wai Kei Christopher (Dept of Chemical Pathology)

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

Edition Title/Investigators

2002-03 Application of Hematopoietic Growth Factors in the Protection and Repair of the Central Nervous System: An Experimental Study in Neonatal Rats with hypoxic-ischemic Brain Damage (MD02440)

✉ CHIK Ki Wai • YANG Mo • FOK Tai Fai • LI Kwai Har Karen

2001-02 Effects of Oxygen-induced Lung Damage on Megakaryocytopoiesis in Neonates Receiving Mechanical Ventilation (MD01554)

✉ FOK Tai Fai • LI Kwai Har Karen • YANG Mo

2002-03 A Pilot Study of Exhaled Chemokines as Novel Non-invasive Inflammatory Markers for Childhood Asthma (MD02947)

✉ LEUNG Ting Fan • WONG Wing Kin Gary • WONG Chun Kwok (Dept of Chemical Pathology) • LAM Wai Kei Christopher (Dept of Chemical Pathology)

2002-03 *In vitro* Induction of Human Embryonic Stem Cells into Functional, Multi-potent Hematopoietic Stem Cells (MD02937)

✉ LI Kwai Har Karen • TSANG Kam Sze Kent (Dept of Anatomical & Cellular Pathology)

2002-03 The Role and Mechanism of Stem Cells in Regenerative Medicine (MD02328)

✉ LI Kwai Har Karen • NG Ho Keung (Dept of Anatomical & Cellular Pathology) • CHAN Chung Ngor

- Juliana (Dept of Medicine & Therapeutics) • CHAN Hsiao Chang (Dept of Physiology) • SUNG Yn Tz Rita • FOK Tai Fai
- 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 (Dept of Surgery) • LAU Tak Fai Joseph (Centre For Epidemiology & Biostatistics) • WING Yun Kwok (Dept of Psychiatry)
- 1998-99 WHO/GSTF Maternity Advice Study (MD98123)
 ✍ NELSON Edmund Anthony Severn • COWAN S* • MANGIATERRA V* • CAFFERATA M.*
- 2002-03 Assessment of Daily Glycaemic: A Pilot Study (MD02429)
 ✍ NELSON Edmund Anthony Severn • SUNG Yn Tz Rita • WONG Wing Kin Gary
- 2000-01 The Effect of Continuous versus Pulsed Maternal Corticosteroid Treatment on Neonatal Pituitary-adrenal Function (MD00593)
 ✍ NG Pak Cheung • LAM Wai Kei Christopher (Dept of Chemical Pathology) • FOK Tai Fai
- 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 (Dept of 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 (Dept of Microbiology)# • CHOW C B* • FOK Tai Fai
- 2002-03 Generation of Cardiomyocytes from Bone Marrow Stromal Cells: The Effect of Serotonin (MD02591)
 ✍ SUNG Yn Tz Rita • YANG Mo • LI Kwai Har Karen • YI Qi Jian*
- 2002-03 A Randomised Trial on the Effects of Rope Skipping in Normal Weight and Overweight Children (MD02719)
 ✍ SUNG Yn Tz Rita • WOO Kam Sang (Dept of Medicine & Therapeutics) • LAU Wing Chung Patrick*
- 2001-02 Thyroid Volumes in Chinese Children (MD01520)
 ✍ WONG Wing Kin Gary • LAM Wai Kei Christopher (Dept of Chemical Pathology) • AHUJA Anil Tejbhan (Dept of Diagnostic Radiology & Organ Imaging)

- 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 24-Week Randomized, Double-Blind, Active-controlled, Multicenter Study to Evaluate the Safety and Efficacy of Rosiglitazone when Administered to Pediatric Patients with Type 2 Diabetes Mellitus (MD02480)
✍ WONG Wing Kin Gary • FOK Tai Fai
- 2002-03 A 12-week, Randomized, Double-blind, Parallel-group, Multicentre, Phase-III Study to Compare the Efficacy and Safety of Symbicort pMDI (budesonide/formoterol 80/4.5 mcg 2 actuations bid, delivered dose) with that of Pulmicort pMDI (budesonide 100 mcg 2 actuations bid, metered dose) and Symbicort Turbuhaler (budesonide/formoterol 80/4.5 mcg 2 inhalations bid, delivered dose) in Children with Asthma (MD02815)
✍ WONG Wing Kin Gary • LEUNG Ting Fan • FOK Tai Fai
- 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
- 2000-01 Effects of Oxygen Toxicity on Megakaryocytopoiesis and Thrombopoitin Production in Neonates - A Rat Model (CU00137)
✍ YUEN Man Pan Patrick • FOK Tai Fai • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • LI Kwai Har Karen • YANG Mo

RESEARCH PROJECTS

Role of Somatostatin in Joint Inflammation

✉ LAM Fu Yuen

☐ 1 June 2004

❖ CUHK Research Committee Funding (Direct Grants)

Somatostatin is considered as an anti-inflammatory neuropeptide. The release of this peptide from peripheral nerve terminals is thought to provide a balance on the actions of pro-inflammatory peptides such as substance P (a tachykinin) to maintain homeostasis in the innervated tissue. Accumulated evidence indicates that somatostatin acts as a negative feedback messenger on presynaptic nerve terminals to inhibit the release of pro-inflammatory neuropeptides, whence reduces the subsequent inflammatory reaction. Another mechanism that could account for the anti-inflammatory effect of somatostatin is inhibition of postsynaptic tachykinin receptors. This has been reported for a somatostatin analogue, vapreotide, but it has yet to be confirmed for somatostatin.

Recently, the investigator has demonstrated that somatostatin could increase the leakage and caliber of blood vessels in rat knee joints. These are cardinal signs of acute inflammation. Therefore, somatostatin is suspected to play a part in both pro-inflammatory and anti-inflammatory processes. The proposed study will elucidate the mechanisms and significance of the anti-inflammatory and pro-inflammatory actions of somatostatin. This should yield important information that could be used to evaluate the deployment of somatostatin or its analogues as anti-arthritis and analgesic agents.

(MD03387)

Interaction between Nitric Oxide and Human Mast Cells

✉ LAU Hang Yung Alaster • HUANG Yu (Dept of Physiology) • WONG Chun Kwok (Dept of Chemical Pathology)

☐ 1 November 2003

❖ Research Grants Council (Earmarked Grants)

Mast cells are well known for their pivotal roles in the pathogenesis of inflammatory reactions by releasing a whole spectrum of preformed and newly synthesized mediators and cytokines. Studies on rodent mast cells have demonstrated that these cells are also capable of synthesizing the gaseous messenger nitric oxide (NO). The exact role of NO in inflammation is not well-defined but it has been shown to suppress activation of inflammatory cells including mast cells. However, the evidence for a regulatory role of NO on mast cells again came only from studies in the rodent. Since mast cells from different species or anatomical locations are known to be different, this project will investigate if similar interaction between mast cells and NO also exists in human. Large number of human mast cells will be cultured from progenitor cells in buffy coat. We will investigate (1) if the human mast cell is a source of NO; (2) the expression of nitric oxide synthase (NOS) isoforms in unstimulated human mast cells or in cells treated with mast cell activators or different cytokines; (3) the effects of NO on mediator release from mast cells; (4) the effects of NO on signaling pathways in human mast cells; (5) the effects of anti-allergic compounds on the expression of NOS isoforms and the production of nitric oxide from human mast cells; and (6) the effects of NO on the mast cell stabilization actions of anti-asthmatic

compounds. Results from the proposed study will certainly facilitate our better understanding of the roles of NO and mast cell in various allergic and inflammatory diseases such as asthma.

(CU03337)

Study of Hepatotoxic Pyrrolizidine Alkaloid-containing Chinese Medicinal Herbs

✉ LIN Ge

□ 1 January 2004

❖ 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.

(MD03797)

Investigation of a Taisho Pharmaceutical Co. Ltd. Research Compound to Inhibit Cisplatin-Induced Emesis in the Ferret

✉ RUDD John Anthony

□ 26 July 2003

❖ Taisho Pharmaceutical Co. Ltd.

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 a novel compound supplied by Taisho Pharmaceutical Co. Ltd., Japan, to antagonize cisplatin-induced acute and delayed emesis in a ferret model.

(MD03483)

Effect of a Novel Neuropeptide on Emesis Induced by Cisplatin in the Ferret

✉ RUDD John Anthony • SANGER Gareth J*

☐ 1 November 2003

❖ GlaxoSmithKline Research & Development 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 peptide supplied by GlaxoSmithKline Research and Development Limited, United Kingdom, to antagonize cisplatin-induced emesis in a ferret model. (MD03630)

Evaluation of the Pungency and Anti-nociceptive Action of Selected Vanilloids in *Suncus Murinus*

✉ RUDD John Anthony • YEUNG Hok Keung John

☐ 1 May 2004

❖ CUHK Research Committee Funding (Direct Grants)

The recent discovery of the broad-spectrum anti-emetic potential of the tachykinin NK₁ receptor antagonists provides insight into the importance of substance P in the emetic reflex. However, no drug is completely effective in preventing chemotherapy-induced acute and delayed emesis and other causes of emesis are also resistant to conventional anti-emetic drugs. Vanilloids are capable of modulating substance P and other

transmitter function via TRPV1 receptors and may afford superiority over other anti-emetic drugs that are only targeted to single transmitter systems. However, only pungent (irritant) vanilloids have been investigated in animals and they may initially induce transient emesis before conferring a long lasting broad-spectrum anti-emetic protection. Conversely, both pungent and non-pungent vanilloids also have a useful analgesic action. The proposed project will evaluate the pungency of several vanilloids in *Suncus murinus* necessary to determine if irritancy (i.e. pungency, which may be related to the mechanism of emesis) is dissociated from the useful anti-nociceptive and potential anti-emetic action. This information is necessary for the development of vanilloids as novel anti-emetic drugs.

(EE03429)

Evaluation of the Anti-Emetic Activity of AMX174 in the Cisplatin-Induced Emesis Model in Male Ferrets Following Oral Administration

✉ RUDD John Anthony • WARNECK Julie*

☐ 30 May 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 compound supplied by Amedis Pharmaceuticals

Limited, United Kingdom, to antagonize cisplatin-induced emesis in a ferret model. (MD04389)

2001-02 Investigation of the Mechanisms and Significance of Altered Neurogenic Responses in Arthritic Rat Knee Joints (MD01988)

✉ LAM Fu Yuen

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

2002-03 Neural Mediation of Inflammatory Joint Disease (MD02658)

✉ LAM Fu Yuen

Edition Title/Investigators

2000-01 Mapping Signal Transduction Networks by Multidisciplinary Approach (BL99452)

✉ JONES Robert Leslie • WISE Helen • HUANG Yu (Dept of Physiology) • IP Y Nancy* • WONG Yung-hou* • TSIM Karl W K* • BARNARD Eric A* • POON Y C Randy* • SUCHER Nikolaus*

2000-01 The Roles of Mast Cells in the Pathogenesis of Aspirin Sensitive Asthma (CU00064)

✉ LAU Hang Yung Alaster • LEUNG Po Sing (Dept of Physiology) • NAGAKURA Toshikazu* • OBATA Toru* • SAITO Hirohisa* • WU Young Yuen Adrian*

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*

2002-03 Pharmacological Characterisation of Cyclic Nucleotide Phosphodiesterases in Rat Peritoneal Mast Cells (MD02396)

✉ LAU Hang Yung Alaster

2002-03 The Role of Nitric Oxide and Mitogen-Activated Protein Kinase in Mediating the Inhibition by b3-Adrenoceptor Activation of Voltage-Dependent L-type Calcium Channels of Guinea-pig Single Ventr (CU02166)

✉ KWAN Yiu Wa • LIU Wing Keung Ken (Dept of Anatomy) • TSUI Kwok Wing (Biochemistry)

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* • SEMPLE Hugh A* • LI Xing Fang* • DAMARAJU Vijayalakshmi*

2002-03 Investigation of Chuanxiong Herbal Materials with GAP Standard (MD02951)

✉ LIN Ge • LI Songlin# • CHUNG Hoi Sing

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|---------|---|---------|---|
| 2002-03 | Development of a Model of Cisplatin-induced Acute and Delayed Kaolin Consumption in <i>Suncus murinus</i> (MD02667) | 1998-99 | Metabolic Studies of a Series of Drugs in Horses (MD98082) |
| | ✉ RUDD John Anthony • TAKEDA Noriaki* • YAMATODANI Atsushi* | | ✉ YEUNG Hok Keung John • WONG Nai Ching Henry (Dept of Chemistry) |
| 2002-03 | Growth Hormone Secretagogue Receptors: Cell Signalling and Receptor Oligomerization (CU02267) | 2002-03 | A Study to Investigate the Mechanisms of the Drug Interaction between Warfarin and Danshen (<i>Salvia Miltiorrhiza</i>): Effects on Specific Human Cytochrome P450 Isoforms (MD02444) |
| | ✉ WISE Helen • CHENG Hon Ki Christopher (Biochemistry) | | ✉ YEUNG Hok Keung John |

RESEARCH PROJECTS

Statin Utilization for Secondary Prevention in Patients with Acute Myocardial Infraction in Hong Kong

✉ LEE Kwing Chin Kenneth • LEE Wing Yan Vivian • TOMLINSON Brian (Dept of Medicine & Therapeutics) • CHAN Wai Kwong*

□ 1 March 2004

❖ Merck Sharp & Dohme (Asia) Ltd

Coronary heart disease (CHD) is the second leading cause of death in Hong Kong. Atherosclerosis is one of the many etiologies of CHD. Efforts to prevent clinical manifestation of atherosclerosis have been emphasized resulting in impressive clinical outcomes in the past 3 decades. The secondary prevention of CHD has become the emphasis of healthcare teams dealing with cardiovascular medicine.

Retrospective case notes will be reviewed in approximately 100 to 150 randomly selected patients at each hospital aforementioned. The list of cost items to be studied is as follows: patient demographics; medical history; drug history; hospitalization history; reasons for statin therapy; initial date for statin therapy; dose of statin therapy; laboratory results on lipid panels, liver function tests, renal function tests, etc.; actions taken when low density lipoprotein (LDL) therapeutic goal was not reached and the 10-year risk of CHD using the Framingham Risk Equations. The unit cost of drugs will be based on the Hospital Authority Drug Acquisition Cost 2001. The purpose of this study is to compare the treatment outcomes of patients with lipid-lowering medications and have reached the cholesterol therapeutic goals with those who have not.

The current study will provide baseline information of the current prescribing pattern of statins at local public hospitals in Hong Kong. This information will address whether there is further room for improvement of using statins for secondary prevention to decrease mortality and morbidity. The results obtained by prediction will provide decision-makers with information of how the current resources could be more appropriately utilized.

(MD03424)

Clinical Impact of CYP 2C19 Genetic Polymorphisms on Proton Pump Inhibitors Metabolism

✉ LEE Wing Yan Vivian • LEE Kwing Chin Kenneth • WAYE Mary Miu Yee (Biochemistry) • CHAN Ka Leung Francis (Dept of Medicine & Therapeutics)

□ 1 January 2004

❖ CUHK Research Committee Funding (Direct Grants)

Proton pump inhibitors (PPIs) have an important role and been widely used in the management of *Helicobacter pylori* (*H. pylori*) eradication. Currently, there are five PPIs available in Hong Kong including omeprazole, esomeprazole, pantoprazole, lansoprazole, and rabeprazole. They are all prodrugs and undergo extensive metabolism in the liver involving the cytochrome P450 enzyme especially with CYP 2C19 and 3A4. Genetic polymorphism of the CYP 2C19 has been documented to have an impact on the metabolism of PPIs. There are currently more than 10 allelic variants of CYP2C19. However, out of the five PPIs, only omeprazole has been involved in most genetic polymorphism studies. Majority of the studies is carried out in Caucasians, Japanese and

Korean. There is no pharmacogenetic information available in Hong Kong Chinese patients using PPI for *H. pylori* eradication therapy.

Chinese men or women aged 18 or above with a documented positive endoscopic findings of *H. pylori* and non-ulcer dyspepsia (NUD) and are started with one-week triple therapy for *H. pylori* eradication at the endoscopy center of Prince of Wales Hospital will be recruited. Written informed consents and peripheral blood samples will be obtained from patients for genotyping analysis. The primary clinical outcome measurement is the success/failure rate of *H. pylori* eradication. Other clinical information will also be recorded such as patient demographics, past medical history and concurrent medications.

The findings of this study will identify the clinical significance of CYP 2C19 polymorphism in Chinese *H. pylori* positive NUD patients.

(MD03475)

Development of a “High-throughput” *in vitro* Method for Predicting Herb-drug Interactions: an Initial Evaluation with *Ginkgo biloba*

✉ YIN Qiping • CHOW Sing Sum Moses • LAI Bo San Paul (Dept of Surgery)

☐ 1 July 2003

❖ CUHK Research Committee Funding (Direct Grants)

Despite the wide use of herbal products, only sparse data exist on herb-drug interactions. The low number and poor quality of majority of the reported herb-drug interactions is due in part to a lack of a mechanism-based simple high-throughput method for screening or detection of such interactions. The purpose of this project is to develop a simple “high-throughput” *in vitro* method for predicting

herb-drug interactions involving oxidative drug metabolism as the mechanism.

A “high-throughput” *in vitro* method for assessment of CYP inhibition will be developed by using human liver microsomes. An *in vitro* “cocktail” of 6 probe drugs will be utilized to measure multiple CYP isozyme activities (represent more than 90% of drug oxidative metabolism). These include caffeine (1A2), diclofenac (2C9), mephenytoin (2C19), debrisoquine (2D6), chlorzoxazone (2E1) and midazolam (3A4). The ability of the cocktail for rapid screening of CYP inhibition will be assessed by using specific CYP isozyme inhibitors as well as extract of *Ginkgo biloba* as the prototype herb. Formation of the marker metabolites in microsomal incubations with or without the inhibitors will be quantified by a fast gradient LC-MS-MS method. The *in vitro* results will be compared to our *in vivo* data already in existence for validation of the applicability of the *in vitro* method.

The successful development of the *in vitro* method will: (1) provide a useful screening tool for product development by pharmaceutical/health food industry regarding herb-drug interactions involving drug metabolism; (2) provide a practical and cost-effectiveness approach for detecting such interactions between herbal products commonly used and other conventional drugs, and thus leading to better and safer combined herb-drug therapy in patients.

(MD03577)

Development of an *in vitro* Screening Method for Herb-drug Interaction Involving Glucuronidation - A Preliminary Feasibility Study

✉ YIN Qiping • CHOW Sing Sum Moses • TOMLINSON Brian (Dept of Medicine &

Therapeutics) • ZHONG Ming Kang* • SHI Xiao Jin*

□ 1 June 2004

❖ CUHK Research Committee Funding (Direct Grants)

Many drugs (both western drug and TCM) undergo Phase II metabolic reactions (glucuronidations, sulfation and acetylation) in our body. Thus, herb-drug interactions involving Phase II metabolism are likely to occur, but very little is known about such interactions due to lack of a suitable method. The purpose of this project is to develop an *in vitro* method for the prediction of herb-drug interaction involving glucuronidation, a common reaction for a number of drugs and TCM (flavonoids, polyphenols). Our preliminary *in vitro* study has already shown inhibition of paracetamol glucuronidation by *Ginkgo biloba*. Thus, in this project, we intend to investigate the feasibility of using better or specific markers of glucuronidation, i.e. imipramine, 4-nitrophenol, propofol and 3'-azido-3'-deoxythymidine (AZT) for detecting specific UGT1A4, 1A6, 1A9 and 2B7 activity and study the effect of *Ginkgo biloba* on these activities. All *in vitro* enzyme reactions will be conducted under physiologic conditions and glucuronide metabolites of the markers quantified by HPLC methods. The *in vitro* effects will be subsequently verified by *in vivo* pharmacokinetics studies in healthy human subjects. The development of this *in vitro* method (1) will allow screening of potential herb-drug, drug-drug and herb-herb interactions involving glucuronidation and (2) provide the basis for further development of screening methods for other phase II interactions.

(MD03746)

Influence of CYP 2C9 genetic Polymorphisms on Warfarin Metabolic Clearance in Chinese Patients

✉ YOU Hoi Sze Joyce • ZUO Zhong • WAYE Mary Miu Yee (Biochemistry) • CHENG Gregory (Dept of Medicine & Therapeutics)

□ 1 June 2004

❖ CUHK Research Committee Funding (Direct Grants)

Background: Genetic polymorphisms of CYP2C9, with different metabolic activities, have a major effect on the clearance of the S-enantiomer of warfarin.

Objective: To determine the influence of CYP2C9 genetic polymorphisms on warfarin metabolic clearance and dose requirement in Chinese patients.

Methods: In this observational cohort study, approximately 90 patients receiving stable maintenance dose of warfarin will be recruited at the anticoagulation clinic of the Prince of Wales Hospital and divided into 3 groups according to the averaged daily warfarin dose: (1) low dose (<2mg/day); (2) median dose (2-5mg/day); (3) high dose (>5mg/day). Steady state plasma concentration of S-warfarin and urinary concentration of S-7-hydroxywarfarin will be measured. Allelic variants of CYP2C9*2 and CYP2C9*3 will be identified by polymerase chain reaction and restriction enzyme analysis.

Significance: The findings of this study will identify the clinical significance of CYP2C9 polymorphism in metabolic clearance and dose requirement of warfarin therapy for 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.

(MD03313)

Evaluation of Transportation and First-pass Metabolism of Flavonoids in Small Intestine

- ✍ ZUO Zhong • LIN Ge (Dept of Pharmacology)
 ☐ 1 June 2004
 ❖ 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 a series of structurally related flavonoids belonging to the flavones and flavonols subgroup, namely Chrysin, Apigenin, Baicalein, Luteolin, Galangin, Kaempferol, Quercetin, and Gossypetin. 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 possible first-pass metabolites formed, their formation rates and the enzyme responsible for the biotransformation will be delineated. Combined 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. (MD03386)

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

Edition Title/Investigators

- 2000-01 Establishment of a University Based Drug Development Centre for Anticancer and Cerebro/Cardio-vascular Drugs (MD20024)
 ✍ CHOW Sing Sum Moses • HO Walter K. K. (Biochemistry) • JONES Robert Leslie (Dept of Pharmacology) • HO Yee Ping • LAU Bik San Clara • LIN Ge (Dept of Pharmacology) • JAMES Anthony Edward (Laboratory Animal Services Centre) • CHOW Hee Lum Albert
- 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 (Dept of Surgery) • YIN Qiping • TOMLINSON Brian (Dept of 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 (Dept of 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 (Dept of 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 (Dept of Pharmacology) • JAMES Anthony Edward (Laboratory Animal Services Centre) • SHAW Pang Chui (Biochemistry) • BUSWELL John Anthony (College Office, SC) • LIEBERMAN Ron*
- 2001-02 Absorption of Active Components from Hawthorn and Green Tea - *In vitro* and *In vivo* Relationship (MD01122)
 ✍ ZUO Zhong • CHOW Sing Sum Moses
- 2000-01 The Effect of Orlistat and Rosiglitazone on Insulin Action in a Group of Chinese Patients Affected by the Metabolic Syndrome - A Randomized, Single-blinded and Placebo-controlled Study (CU00069)
 ✍ LEE Kwing Chin Kenneth • CHAN Chung Ngor Juliana (Dept of Medicine & Therapeutics) • TOMLINSON Brian (Dept of Medicine & Therapeutics) • YOU Hoi Sze Joyce
- 2002-03 *In-vitro* Evaluation of Glucuronidation of Selected Flavonoids in Gut and Liver (MD02576)
 ✍ ZUO Zhong • LIN Ge (Dept of Pharmacology)
- 2002-03 Clinical Impact of Genetic Polymorphism in the Cytochrome P450 CYP2C9 on the Management of Warfarin in Chinese Patients (MD02882)
- 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 (Dept of Medicine & Therapeutics) • CHAN Yan Keung Thomas (Dept of Medicine & Therapeutics)
- ✍ LEE Wing Yan Vivian • YOU Hoi Sze Joyce • LEE Kwing Chin Kenneth • WAYE Mary Miu Yee (Biochemistry) • CHENG Gregory (Dept of Medicine & Therapeutics)

RESEARCH PROJECTS

Investigation of the Role of a Novel Epididymis-specific Gene, Bin-1b, in Sperm Maturation

✉ CHAN Hsiao Chang • ZHANG Yong Lian*

☐ 1 August 2003

❖ Research Grants Council (Earmarked Grants)

We have recently discovered a novel epididymis-specific gene, Bin1b, in the rat and demonstrated its antimicrobial activity and its role in host defense (*Science* 291:1783-1785, 2001). The unique expression of Bin1b in the caput epididymidis has led us to the hypothesis that this caput-specific novel gene may play a role in influencing sperm maturation in addition to its host defense role in the male reproductive tract. The present project will test this hypothesis using a rat epididymal epithelial cell and sperm co-culture system and a stably transfected Bin1b expressing epithelial cell line in conjunction with antibodies against Bin1b to examine the effect of Bin1b on sperm motility. Possible underlying mechanism by which Bin1b affects sperm maturation will also be investigated. The results of the proposed study will provide better understanding of the molecular mechanism underlying sperm maturation and may provide grounds for the development of new epididymis-specific contraceptives.

(CU03365)

The Role of Epididymis-specific Defensin, Bin 1b, in Sperm Maturation

✉ CHAN Hsiao Chang • ZHOU CHENXI

☐ 1 April 2004

❖ Lalor Foundation - Postdoctoral Program

We have recently discovered a novel epididymis-specific gene, Bin1b, and demonstrated its antimicrobial activity (*Science* 291:1783-1785, 2001). However, the region-specific expression pattern of Bin1b in the epididymis, exclusively in the caput (head), has led us to the hypothesis that it may influence sperm maturation and thus male fertility in addition to its role in host defense against bacterial infections in the male reproductive tract since region-specific epididymal secretions are thought to provide a unique fluid environment responsible for sperm maturation and storage.

The present project will test this hypothesis with the aim: using an epididymal epithelial cell and sperm co-culture system in conjunction with antibodies against Bin1b to examine the effect of Bin1b-expressing.

(MD03885)

Long-term Effect of Ovariectomy and Raloxifene (SERM) Replacement Therapy on Endothelial Function and on Regulation of Smooth Muscle Ion Channels

✉ HUANG Yu • LAHER Ismail* • YAO Xiaoqiang

☐ 15 December 2003

❖ Research Grants Council (Earmarked Grants)

Despite the epidemiological evidence that postmenopausal estrogen therapy is cardioprotective, estrogens are thought to induce breast and uterine cancer, as well as resumption of menses, mastodynia, and weight gain. In the search for more selective agents, selective estrogen receptor modulators (SERMs) have been developed, which act as estrogen

receptor antagonists in the breast and uterus, devoid of the harmful effects of estrogens but preserving the beneficial effects of estrogen on bone, lipids, and the cardiovascular system. Raloxifene, one of SERMs, has recently been approved for the treatment of postmenopausal osteoporosis. The beneficial effects of SERMs on vascular cells could potentially lead to novel therapeutic strategies for the treatment of hypertension, stroke, and atherosclerosis. The cellular and molecular mechanisms by which raloxifene exerts cardiovascular effects, however, are basically unclear, particularly in the cerebral resistance arteries, changes of which diameter regulate blood flow to the brain. Our hypotheses propose that (1) raloxifene treatment prevents or inhibits impaired endothelial function by restoring normal production of endothelium-derived beneficial factors such as nitric oxide; (2) raloxifene prevents or inhibits endothelium cell death (apoptosis). The primary objective of this proposal is to investigate these hypotheses, presenting the cellular and ionic mechanisms linking raloxifene-induced action on the endothelium and arterial smooth muscle to restoration of vascular function following ovariectomy (declining of circulating estrogen levels, a natural state of estrogen deficiency after menopause). The proposed studies should be the first of their kind and should provide new insight into the mechanisms involved in the potential cardiovascular protective action of raloxifene against cerebrovascular disease such as stroke.

(CU03366)

Effect of *Scutellariae Radix* (Huangqin) and Its Major Flavonoids on Experimental Ulcerative Colitis in Rats

✉ KO Wing Hung

□ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Scutellariae Radix (Huangqin), the root of *Scutellaria baicalensis* Georgi, has been frequently used in combination with other herbs in Kampo medicines or Traditional Chinese medicines (TCM) for centuries. It has been used to treat inflammatory - related disorders such as gastroenteritis in China and Japan for many years. Many biological activities of *Scutellariae Radix* are related to the flavonoids in the herb. Examples are baicalein, baicalin, and wogonin.

Inflammatory bowel disease (IBD) includes both ulcerative colitis and Crohn's disease, which are major chronic inflammatory diseases of the gastrointestinal tract in human. Conventional therapies used in IBD are not totally successful and their side effects remain a major clinical problem. Therefore, there is an increasing interest in using TCM as an alternative or adjunct therapy. Recent studies suggest that *Scutellariae Radix* has the strongest pharmacological effect against murine colitis and baicalein is the most active ingredient. However, the physiological basis and the precise mechanism of action of *Scutellariae Radix* or its individual constituents are still unclear. The purpose of the present proposal is to investigate whether the total extract and the major flavonoids derived from *Scutellariae Radix* have beneficial effect in treating experimental ulcerative colitis in rats. Experiments will be conducted using morphological, histological, biochemical and electrophysiological approaches. The information obtained from this study will give us a better understanding of the therapeutic potential of *Scutellariae Radix* with respect to their specific effect(s) on mucosal changes in rat colonic epithelia.

(MD03511)

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

✍ LEUNG Po Sing

□ 1 January 2004

❖ CUHK Research Committee Funding (Direct Grants)

A local pancreatic rennin-angiotensin system (RAS) has been established, which exhibits potential endocrine and exocrine roles in the pancreas as reviewed recently. Indications for a role of such a local RAS in the endocrine pancreas were provided with the perfusion of whole rat pancreata, where the first phase of glucose-stimulated insulin release was impaired by the infusion of angiotensin II (Ang II). Interestingly, some large clinical trials, such as CAPPP, LIFE, and NAVIGATOR, suggest that inhibition of the RAS by virtue of using ACE inhibitors such as ramipril and captopril, and Ang II type I receptor (AT₁-R) antagonists such as losartan and valsartan can decrease the incidence of type-2 diabetes mellitus (T2DM). The potential mechanism for the protection by these specific RAS blockers against diabetic patients is unknown, but drugs in this class have been shown in some studies to improve the secretion and action of insulin. In this regard, our recent data have shown the existence of an islet RAS that Ang II can induce a marked dose-dependent inhibition of glucose-stimulated insulin release and reduce pro-insulin biosynthesis in isolated pancreatic islets. This inhibitory action was fully preventable by pretreatment of the islets with the AT₁-R antagonist losartan. These results

indicate that an islet RAS may have an importance in the physiological regulation of glucose-stimulated insulin release from the endocrine pancreas. Notwithstanding this evidence for the involvement of the islet RAS in islet function, there has been a lack of basic science for the potential role of islet RAS and changes of expression and function in T2DM, thus its implication for a novel regulatory pathway in islet insulin secretion. The present pilot study is, therefore, designed to study and compare the changes of expression insulin secretion for islet RAS in animal models of T2DM. In order to achieve these aims, three animal models of T2DM with obesity and without obesity are employed in this study. (1) Neonatal streptozotocin (STZ)-induced rats; (2) Adult STZ plus nicotinamide-induced rats; and (3) Obese db/db mice. The former two experimental models are well recognized as T2DM without associated obesity while the third one is associated with a genetically obese T2DM. The results of this pilot study should provide important data on the changes of islet RAS and islet insulin function in T2DM and the involvement of islet RAS in regulating endocrine function, thus casting new insights into the potential mechanism of RAS inhibition for the protection of T2DM.

(MD03430)

Basal Cells as Regulators of Epididymal Principal Cell Functions

✍ WONG Patrick Yee Ding

□ 1 August 2003

❖ Research Grants Council (Earmarked Grants)

The epithelia lining the epididymides of many species including the human are known to consist of several cell types. Among them, the principal cells are the most abundant and their functions most

extensively studied. There are other cell types such as the narrow cells, clear cells, halo cells, basal cells which are scattered along the duct in lesser number. Although these minority cell types have not been studied to the same extent as the principal cells, it is conceivable that their presence are essential to the integrated functions of the epididymis. Recently our attention has been focused on the basal cells. In the intact epididymis, these cells can be seen adhering to the basement membrane forming close contact with the principal cells above them. Previous work in our laboratory has provided evidence that basal cells regulate electrolyte and water transport by the principal cells through the release of paracrine factors. In this project, I propose to substantiate the role of the basal cells as humoral regulators of the principal cells. I plan to isolate basal cells from the rat epididymis and carry out physiological experiments on them. Attention will be focused on the role of the transient receptor potential (Trp) proteins. It is hoped that these studies will increase our knowledge of the basal cells, and in a broader sense, their roles in sperm maturation and storage in the epididymis.

(CU03371)

Functional Role of VRL-2 Channels in Kidney Proximal and Cortical Collecting Duct Cells

✉ YAO Xiaoqiang • HUANG Yu

☐ 1 December 2003

❖ CUHK Research Committee Funding (Direct Grants)

In response to osmotic challenge, mammalian cells are able to regulate their cell volume in order to avoid excessive alterations of cell volume that may jeopardize structural integrity and cellular function. One of the earliest cellular signals after exposure of cells to hypotonic condition is Ca^{2+} influx. The rise

of cytosolic Ca^{2+} may then serve as a second messenger to activate other volume regulatory mechanisms. In kidney epithelial cells, volume regulation has an additional important function of coordinating the transepithelial Na^+ transport. For these cells, volume regulatory mechanism may serve to maintain the continued substance transport across renal epithelia cells. Recently, a volume-sensitive Ca^{2+} -permeable channel VRL-2 is cloned in mammals. There are compelling reason to believe that this channel may represent the molecular identity of volume-sensitive Ca^{2+} influx channel that are crucial for volume regulation and renal epithelial transport. We have extensively studied the expression of VRL-2 in many different human tissues. We found that the channel is abundantly expressed in kidney, gastric gland, pancreas and vascular endothelial cells. In this study, we propose to study the functional role of VRL-2 in the kidney epithelial cells. We will test the hypothesis that VRL-2 is indeed a crucial channel in controlling volume regulation and influencing epithelial transport in these cells. Our study may expand our knowledge on the regulation of swelling-activated Ca^{2+} influx and on the renal substance reabsorption as a whole.

(MD03786)

The Neurotrophic Action of Secretin in the Developing Cerebellum

✉ YUNG Wing Ho • CHAN Ying Shing* • CHOW K C Billy* • WANG Jian Jun*

☐ 1 January 2004

❖ NSFC/RGC Joint Research Scheme

There is emerging evidence that the hormone secretin is neuroactive in the mammalian central nervous system. We hypothesize that this peptide is neurotrophic to the cerebellum and is therefore

critical for its normal development. This idea is scrutinized in the present proposal using the rat as an experimental model. The first specific aim is to determine the presence of secretin and its receptors, and also their spatial and temporal expression patterns, in the prenatal and early postnatal rat cerebellum by means of *in situ* hybridization and immunohistochemical techniques. Based on these results our second specific aim is to demonstrate the neurotrophic action of secretin in the proliferation and maturation of cerebellar neurons *in vivo* and in the *in vitro* culture. Our final specific aim is to complement and extend the above approaches by examining the effects of secretin in the functional maturation of the cerebellar neurons and their synaptic connectivity. Parameters indicating the maturation of the cerebellum at the single neuron and circuit levels will be assessed by electrophysiological techniques. Since secretin has been implied in the etiology of the neurodevelopmental disorder autism, confirmation of a neurotropic role of secretin in the cerebellum is interesting not only scientifically but also has a significant impact on the understanding and treatment of autism.
(MD03619)

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

Edition	Title/Investigators
1998-99	Research in Epithelial Cell Biology (MD98084) ✉ CHAN Hsiao Chang • CHEW CHENG Siew Boon • FISCUS Ronald Ray • LEUNG Po Sing •

	WONG Patrick Yee Ding • YAO Xiaoqiang
2001-02	Epithelial Cell Biology and Functional Genomics (MD01001) ✉ CHAN Hsiao Chang • CHEW CHENG Siew Boon • CHOW Pak Ham Patricia (Dept of Anatomy) • FISCUS Ronald Ray • LEUNG Po Sing • WONG Patrick Yee Ding
2002-03	Development of Globally Marketable Proprietary Natural Products for Treating Insomnia (MD02645) ✉ CHAN Hsiao Chang • ZHANG Zhi Yan*
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)
2000-01	Investigation into Mechanisms of Vascular Action of Purified Neferine from <i>Nelumbo nucifera</i> Gaertn in Rat and Mouse Arteries (MD20025) ✉ HUANG Yu • CHAN Wood Yee (Dept of Anatomy) • CHEN Zhenyu (Biochemistry) • KO Wing Hung • YAO Xiaoqiang • YEW Tai Wai David (Dept of Anatomy) • TSANG Suk Ying
2002-03	Mechanisms of Vasorelaxation Induced by the Novel Ca ²⁺ Channel Blocker

	Cilnidipine and Metabolites of Cytochrome P450 in Coronary Vasculature (CU02170)		✉ LEUNG Po Sing • IP Siu Po (School of Chinese Medicine) • WONG Tung Po • SCHUPPAN Detlef*
	✉ HUANG Yu • GOLLASCH Maik* • YAO Xiaoqiang	2002-03	Angiotensin-converting Enzyme Genotype in High-altitude Populations of Yunnan, China (MD02436)
2002-03	Stimulatory Effect of Scutellariae Radix (Huangqin) and Its Major Flavonoids on Electrolyte Transport in Rat and Human Colonic Epithelia (CU02171)		✉ LEUNG Po Sing • TAM Michael S C • ZHENG Yong Tang* • HUGH Montgomery*
	✉ KO Wing Hung • HUANG Yu	2002-03	Functional Genomics on the Sexual Differentiation of the Rat Brain (MD02363)
2000-01	Regulated Expression and Function of Pancreatic Renin-angiotensin System: Its Significance in Transplanted Pancreatic Islets (MD20057)		✉ WONG Chun Cheung
	✉ LEUNG Po Sing • CARLSSON Per-Ola*	2002-03	The Role of Organic Anion Transporters (OAT) in the Accumulation of Antifertility Drugs by the Rat Epididymis (CU02268)
2001-02	Activation of Pancreatic Renin-angiotensin System: Its Role in the Regulation of Reactive Oxygen Species and Apoptosis in Pancreas (MD01116)		✉ WONG Patrick Yee Ding
	✉ LEUNG Po Sing • IP Siu Po (School of Chinese Medicine)	2000-01	Nucleotide Modulation of Non-selective Cation Channels in Vascular Endothelial Cells (MD00479)
2002-03	Angiotensin IV Receptors AT ₄ : Its Expression, Regulation and Potential Role in Chronically Hypoxic Carotid Body (MD02805)		✉ YAO Xiaoqiang • GARLAND Christopher*
	✉ LEUNG Po Sing	2000-01	Protein Kinase G-sensitive Ca ²⁺ Influx in Endothelial Cells and Its Role in Vasoregulation (CU00079)
2002-03	The Role of Angiotensin and Endothelin in the Regulation of Fibrogenic/Anti-fibrogenic Factors in Hepatic Kupffer Cells: Its Clinical Implications for Hepatic Fibrosis (MD02871)		✉ YAO Xiaoqiang • HUANG Yu • YE W Tai Wai David (Dept of Anatomy)
		2001-02	Role of Vesicle Fusion and Protein Kinase G in Regulating Store-operated Calcium Influx (MD01340)
			✉ YAO Xiaoqiang • VILLAZ Michel*

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| 2002-03 | Functional Roles of Trp (Transient Receptor Potential) Channels in Vascular Endothelial Cells (CU02174)
✉ YAO Xiaoqiang | 2002-03 | Subunit Composition, Spatial Distribution and Pharmacological Profiles of GABA-A Receptors in Globus Pallidus Neurons : Correlation with Different Synaptic Inputs (CU02175)
✉ YUNG Wing Ho • YUNG Kin Lam Ken* |
| 2000-01 | Analysis of GABAergic Neurotransmission in Rat Globus Pallidus: Correlation of Electrophysiology with Ultrastructural Immunocytochemistry (CU00080)
✉ YUNG Wing Ho • BOLAM John Paul* • YUNG Kin Lam Ken* | | |

RESEARCH PROJECTS

Suicide in Non-elder Population in Hong Kong: A Psychological Autopsy Study

✉ CHAN Sau Man Sandra • CHIU Fung Kum Helen

☐ 1 November 2003

❖ Research Grants Council (Earmarked Grants)

Suicide is one of the leading causes of death in economically active population in Hong Kong. The design of effective suicide prevention strategies will hinge on the identification of specific risk factors. The principal objective of this proposal is to examine whether the specific factors that have been shown in the literature in the West are present significantly more often in suicide victims than in controls matched for age and gender, using a case-control design. Our specific aims are to determine whether suicide victims are distinguished by specific variables in each of the four domains: 1) Psychiatric diagnosis & phenomenology; 2) Personality traits; 3) Physical health; 4) Stressful life-events and social support. Using the psychological autopsy method, we will conduct interviews with knowledgeable informants concerning suicide victims. The secondary objective of the study is to investigate reliability of information obtained from victims' informants, the core and only available method to ascertain the psychological and social circumstances in suicide victims in psychological autopsy study. This area will be investigated by doing a parallel case-control survey on suicide attempters using the same assessment measures and interviewing procedure as in the psychological autopsy. In this survey both the attempters and knowledgeable informants will be

interviewed independently and the Kappa values will be worked out for different domains of assessment yielded from two information sources.

(CU03373)

Association of Pro-inflammatory Genotypes and Progress of Cognitive Decline in Prodromal Alzheimer's Disease

✉ LAM Chiu Wa • TANG Leung Sang Nelson (Dept of Chemical Pathology) • CHIU Fung Kum Helen

☐ 1 December 2003

❖ CUHK Research Committee Funding (Direct Grants)

With rapid increase in aging population, Alzheimer's disease (AD) has become one of the most disabling degenerative disorders. The progressive intellectual failure not only affects the sufferers, but also causes tremendous impact to the caregivers. Moreover, dementia care poses significant financial burden to the society. Recent advances have brought insight into the molecular genetics of AD. Pharmaceutical companies have been very active in the search for an agent that would halt, or even reverse, the progress of the disorder. A composite of genetic, physical and lifestyle factors are found to be associated with AD. As multiple factors are involved, the identification of specific high risk groups for early intervention will be of immense clinical value.

This project aims to study the progress of cognitive functions in subjects in the prodromal phase of AD with special reference to potentially remediable genetic risk factors. A group of cognitively high risk individuals, subjects with mild cognitive impairment (MCI) with high likelihood of prodromal AD, will be identified. Their cognitive function will be monitored periodically for 9 months. For the

specific genetic risk factor, the investigator team has recently identified significant association between AD and a genetic factor that has propensity for increase inflammatory response (Tumor Necrosis Factor-alpha) (TNF- α). Thus, the subjects will be classified according to their genetic makeup for TNF- α . The rates of cognitive decline in different groups will be compared. If a faster rate of cognitive decline or conversion to AD is found with subjects having pro-inflammatory genotypes, the “Inflammatory hypothesis of AD” can be clinically substantiated. These will provide a rational basis for the use of anti-inflammatory agents in genetically and cognitively at-risk individuals for early intervention of AD.

(MD03506)

Economic Reform and People's Well-Being in China: An Inter-Disciplinary Study

✉ LEE Tak Shing Dominic • HSIAO William* • KLEINMAN Arthur* • YIP Winnie*

☐ 1 August 2003

❖ Harvard University Asia Center

Economic growth has been advocated as a main goal of most modern states because of the belief that an increase in income leads to an increase in welfare. Economists generally assume that having more goods lead directly to greater overall welfare, but recent empirical work has raised doubts about this simple assumption. In particular, Easterline’s seminal work on income growth and happiness show that in time series data, people’s subjective well-being (SWB, or commonly known as happiness) does not grow linearly with increase in GDP (Easterline, 1974). Similar pattern was found in many other studies that follow (Frey and Stutzer, 2002).

Economic reform in China in the past two decades has brought about unprecedented income growth. Nominal GDP per capita has been growing near double-digit, averaging 8.9% between 1980-2000 (World Bank Group, www.worldbank.org). Real average income has risen by 212 percent between 1979 and 1997 (The National Bureau of Statistics, 1998). During 1980-1995, the number of residents living in absolute poverty has declined by 210 million. Behind these favorable statistics, are people happier? Are people more satisfied with their lives? Anecdotal evidence and casual observation may suggest skepticism.

This research proposal complements the *Seminar Series on Economic Development, Culture, Social Changes, Individual Preferences and Health*, that we have received funding for from the Asia Center. The seminar series intends to bring together faculty and students on a regular basis to discuss the intellectual issues related to the dynamic relationships between economic development and well-being/health. This proposal will initiate a small study for actual interdisciplinary collaboration and to provide the seminar series with discussion topics and material. The preliminary findings will also inform the discussions.

(MD03928)

Paternal Postpartum Depression in Hong Kong Chinese

✉ LEE Tak Shing Dominic • YIP Shing Kai Alexander (Dept of Obstetrics & Gynaecology)

☐ 1 October 2003

❖ CUHK Research Committee Funding (Direct Grants)

Postpartum depression is a common and serious mental disorder. It causes tremendous distress and

sufferings at a time of anticipated joy. Current research and clinical services have largely conceptualized postpartum depression as a maternal health problem. This incomplete model fails to take into account that the fathers can also be overwhelmed by the profound biopsychosocial changes - such as sleep deprivation and role conflicts - of early parenthood. There is now growing evidence that psychosocial risk factors of maternal postpartum depression can also put the fathers at risk of depressive illness in the postpartum period. Besides, maternal and paternal postpartum depressions are closely connected. When maternal postpartum depression lingers on, paternal postpartum depression may eventually set in. The exact pathway among the risk factors, maternal depression, and paternal depression, however, remains to be ascertained. More research is needed to understand how fathers adjust to childbirth and childbearing, and how paternal psychological morbidity and maternal psychological morbidity influence each other in the postpartum period.

We propose to study prospectively the rates and risk factors of maternal and paternal postpartum depression among Hong Kong Chinese couples. A total of 100 consecutive couples will be recruited among those who delivered their baby at a University affiliated general hospital. With informed consent, the fathers and mothers will be interviewed semi-structurally for sociodemographics and risk factor status within a few days of delivery. They will also complete a depression rating scale. Three months postpartum, the fathers and mothers will repeat the depression rating scales and receive a fully structured psychiatric diagnostic interview.

This study will determine the rates of postpartum depression and other psychiatric morbidity among local fathers and mother. The link between paternal and maternal postpartum depression will be clarified.

The study will also ascertain how various psychosocial and cultural factors differentially lead to paternal and maternal postpartum depression.

This will be the first large-scale epidemiological study that examines paternal and maternal postpartum depression simultaneously. The findings will remake an etiological model of postpartum depression that encompasses both men and women. A more comprehensive and holistic model will ultimately help researchers, service providers and policy makers to rethink if the father should be routinely involved in future postpartum depression research and clinical care.

(MD03600)

A Supplementary Drug Abuse Monitoring System

✉ LEE Tak Shing Dominic

☐ 1 January 2004

❖ Beat Drugs Fund Association

Background

Effective surveillance of drug abuse trends and pattern commonly employs several monitoring system of different properties. Although the Central Registry of Drug Abuse (CRDA) in Hong Kong has proved to be useful in monitoring the trends of drug abuse, addition of other drug abuse monitoring systems can broaden the scope and sensitivity of drug abuse surveillance.

Objective

To establish a monitoring system that complements the CRDA in monitoring the trend and pattern of drug abuse among local population.

Design and Method

The research will establish a supplementary system that consists of three components. The first module will draw together drug related statistics that are currently compiled by independent departments and

agencies in Hong Kong. The second module will go beyond case/event counting to collect qualitative data pertaining to the pattern, characteristics, and consequences of drug abuse. The third component of the monitoring system will examine the CRDA reports that fall short of the minimal data set requirement. An expert panel will be formed to guide data analysis.

Expected Deliverables and Outcomes

Upon completion of the study, the supplementary system will be transferred to the government for continual operation.

Potential Impact

The supplementary system will broaden the scope of drug abuse surveillance in Hong Kong. This will be of profound use to policy makers, front line drug workers, and researchers.

(MD03512)

Depressive Disorders and Alcohol Related Disorders among Patients with Pneumoconiosis in Hong Kong

✉ TANG Wai Kwong • UNGVARI Gabor Sandor
 • LUM Chor Ming Christopher (Dept of Medicine & Therapeutics)

☐ 1 August 2003

❖ Pneumoconiosis Compensation Fund Board

Pneumoconiosis is common industrial chronic lung disease among construction site workers in Hong Kong. The commonest cause of pneumoconiosis in Hong Kong is silicosis, which is a tissue reaction within the lung to the silica dust. Limited literature reveals that depression and alcohol-related disorders (alcohol abuse or dependence) may be common among these patients, although on large-scale systematic investigation has been carried out so far. These psychiatric morbidities are frequently

unrecognized and untreated, even though they adversely affect patients' quality of life and are amenable to psychological and physical treatment. The aim of this project is to examine the prevalence, performance of screening instruments, risk factors of depressive disorders and alcohol related disorders in patients with Pneumoconiosis. 300 and 100 Pneumoconiosis and healthy control subjects will be recruited from the case register of the Pneumoconiosis Compensation Fund Board and social centers for the elderly. Demographic and clinical data, reflecting the severity of patients' Pneumoconiosis diseases, will be collected. Screening instruments for psychiatric problems will be administered. In addition, a psychiatrist will conduct a structured clinical interview (SCID-DSMIV) to diagnose psychiatric diseases, according to DSMIV criteria. Subjects' quality of life, functioning, psychosocial risk factors and severity of depression will be measured.

(MD03827)

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

Edition	Title/Investigators
2001-02	"Life Clinic", 3-Tier Coordinated Service Model, Joint Project on Prevention of Elderly Suicide (MD01324) ✉ CHIU Fung Kum Helen • LAM Chiu Wa
2000-01	Attitudes toward and Cultural Meanings of Suicide in Contemporary Chinese Society (CU00380)

- ✍ LEE Sing • Arthur KLEINMAN* • Michael PHILLIPS* Keung* • CHAN Ronald* • LAM Ming
- 2002-03 A Telephone Survey on Perception of the Public on SARS-related Issues (SS02373) 2002-03 Poststroke Depression in Hong Kong Chinese Patients (MD02628)
✍ LEE Sing • CHAN Yu Yee (Hong Kong Mood Disorders Centre)# • MAK Ka Hi# • TONG Bianca* ✍ TANG Wai Kwong • UNGVARI Gabor Sandor • SZE K H Frank* • WOO Jean (Dept of Medicine & Therapeutics) • KAY Li Chi Richard (Dept of Medicine & Therapeutics) • CHIU Fung Kum Helen • AHUJA Anil Tejbhan (Dept of Diagnostic Radiology & Organ Imaging)
- 2001-02 A Database on Traditional Chinese Medicine Treatment for Drug Addiction (MD01884) 2002-03 A Family and Genetic Study of Narcolepsy in Chinese (MD02428)
✍ LEE Tak Shing Dominic • LEUNG Ping Chung (Dept of Orthopaedics & Traumatology) • XU Min* ✍ WING Yun Kwok
- 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

RESEARCH PROJECTS

Natural History of the Elimination Syndrome of Childhood

✍ BOWER Wendy Fiona • YIP Shing Kai Alexander (Dept of Obstetrics & Gynaecology) • YEUNG Chung Kwong

☐ 16 March 2004

❖ CUHK Research Committee Funding (Direct Grants)

Children with Elimination Syndrome present with urinary incontinence, non-monosymptomatic nocturnal enuresis, recurrent urinary tract infections, imperative urgency to void, exceptional urinary frequency, bowel dysfunction and encopresis. On investigation they are noted to have poor voiding efficiency, vesicoureteric reflux, constipation, infrequent toileting and no regular bowel routine. This disturbance of the elimination processes is most commonly associated with inappropriate recruitment of either the muscles of the pelvic floor or voluntary fibres of the external urinary or anal sphincter during attempted emptying.

This initial functional obstruction to emptying has serious ramifications for the urinary system, resulting in bladder hypertrophy and overactivity, and damage to the vesicoureteric junctions. These changes further evolve into detrusor fatigue, bladder over-distension and eventual detrusor de-compensation. At the same time bowel emptying is incomplete, infrequent and poorly executed and progresses until the child develops distension of the rectum and descending colon, becomes poorly sensate, and evidences faecal soiling and constipation.

The natural history of the Elimination Syndrome beyond childhood remains unclear. At the present time very little is also known about the elimination status of adult Hong Kong Chinese women. This study therefore aims to evaluate the history of childhood symptoms of the Elimination Syndrome in adult women with and without known bladder dysfunction and to identify aspects of the disorder that do not remit alongside those symptoms which resolve spontaneously. A further aim is to evaluate the relative risk of elimination dysfunction in Asian women as compared to Caucasian women. (MD03818)

A Study of Paracrine Factors Involved in Keratinocyte-melanocyte Interaction in a Laser Induced Model

✍ BURD David Andrew Ross • POON Kwok Man

☐ 1 December 2003

❖ CUHK Research Committee Funding (Direct Grants)

Clinical laser practice relies heavily on selective photothermolysis where specific wavelengths are chosen to target and destroy selected chromophores. The potential for harnessing electromagnetic radiation (emr) to modify cell-cell and cell-matrix events by manipulating processes at the molecular level without targeting specific chromophores is both unexploited and poorly understood. Our interest in this field has evolved from an initial experience using a 532nm laser to target melanin in cells. Using sub-lethal irradiation, the melanin was destroyed and the melanoma cell survived but its behaviour changed. Amelanotic cells used as controls also exhibited changes at the molecular level. 532nm is of particular interest as this seems to be least absorbed by cellular components such as mitochondria, golgi

apparatus and cell nuclei. Further experiments on dermal fibroblasts demonstrated upregulation of basic fibroblast growth factor, although in co-culture conditions laser induced fibroblasts had no effect on melanocytes. Following these initial studies we have now focused on the interaction between keratinocytes subject to sub-lethal irradiation and melanocytes. We have established a bank of keratinocytes from adult and paediatric tissues. We have established the LD₅₀ and are detailing the general response of keratinocytes to low level laser energy. In this project we propose to investigate the specific paracrine effects of laser induction of keratinocytes on melanocytes using co-culture and tissue composite models. Through this study we hope to further the understanding of the fundamental biology of cutaneous pigmentation in particular hyperpigmentation, which is a major problem in Chinese skin.

(MD03529)

The Design and Development of a Novel Bio-interactive Electro-chemical Wound Dressing Incorporating the Physical Vapour Deposition of Nanoscale Silver Ions

✉ BURD David Andrew Ross • IP Margaret (Dept of Microbiology) • LAM Wai Kei Christopher (Dept of Chemical Pathology) • POON Kwok Man

□ 1 May 2004

❖ Funding from Industrial Sponsors • Innovation and Technology Support Programme, ITF, Innovation & Technology Commission

Wound dressing products represent a considerable proportion of Health Care expenditure world wide. Dressings have to serve a number of functions depending upon the nature of the wound which may

be acute or chronic, clean or infected. In this proposal we are developing a new dressing construct that can serve multiple functions. We are combining a nanogel technology with a nanoscale silver deposition to produce a dressing that has absorptive and antimicrobial effects. We are then going to enhance the antimicrobial effect using electrical field stimulation. This will also enhance wound healing. Each stage of development will be monitored for safety and efficacy using bacteriological, cell, tissue and animal studies. The final product will be a multifunctional bio-interactive electro-chemical dressing that will take a unique place in a highly competitive market. With appropriate pricing, marketing and distribution such a product will have a global impact on health care and define new approaches to product development.

(MD03739)

4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), a Tobacco-specific Carcinogen, Regulates Apoptotic Molecules Via a Nuclear Factor kappa B-dependent Pathway

✉ CHEN Gong George • YIM Ping Chuen Anthony • MOK Shu Kam Tony (Dept of Clinical Oncology) • WARNER Timothy D.*

□ 31 December 2003

❖ Research Grants Council (Earmarked Grants)

The biological effects of cigarette smoking can be attributed to the thousands of chemicals present in tobacco. Among these carcinogens, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), is the most potent and is known to transform normal lung cells to carcinoma. NNK increases the level of reactive oxygen species and initiates DNA oxidation and micronucleus formation. However, how NNK promotes the tumor formation is still not

completely understood. It is well known that reactive oxygen species are able to activate nuclear factor kappa B (NF- κ B). We and others have demonstrated that the level of NF- κ B is increased in tumor tissues of lung cancer than non-tumor lung tissues. Inhibition of NF- κ B arrests the growth of lung cancer cells and increases the chemosensitivity of lung cancer via an apoptotic pathway. NF- κ B is known to control or regulate the expression of several genes including inducible nitric oxide (iNOS), cyclooxygenase-2 (COX-2), c-JUN N-terminal kinase (JNK) and inhibitor of apoptosis protein (IAP). We hypothesize that a high level of NF- κ B induced by NNK promotes the expression of COX-2 and iNOS, which stimulates the production of IAP and subsequently changes the balance between pro-apoptosis and anti-apoptosis in favor of the later. It is also possible that there is a defect in the negative regulation of JNK by NF- κ B, which results in over-expression of JNK. JNK is known to stimulate the production of COX-2 and iNOS. The proposed study is to test this hypothesis using *in vitro* lung cell culture system and lung cancer animal model.

(CU03390)

Cytotoxic Effect of *Pteris semipinnata* L on Human Colorectal

✉ CHEN Gong George • LEE Fung Yee Janet • LIAN Nianci*

☐ 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.

(MD03565)

Function of Potassium Channels in the Coronary / Pulmonary Arteries during Heart / Lung Surgery

✉ HE Guo Wei • HUANG Yu (Dept of Physiology) • YAO Xiaoqiang (Dept of Physiology)

☐ 31 December 2003

❖ Research Grants Council (Earmarked Grants)

Potassium channels (PC) in the coronary/pulmonary artery play important roles in the function of heart and lung. There are many subtypes of PC including calcium-activated PC (KCa) and ATP-sensitive PC (KATP). KCa is mainly related to the endothelium-dependent and KATP, the endothelium-independent hyperpolarization and relaxation. The endothelium-dependent

hyperpolarization may be related to nitric oxide (NO) and a chemically unidentified endothelium-derived hyperpolarizing factor [EDHF]. In the coronary circulation, both KATP and KCa play a role in maintaining the coronary tone. Kca regulates coronary endothelium-smooth muscle function through endothelium-derived relaxing factors (EDRFs), particularly NO and EDHF, to maintain the normal function of the coronary circulation.

During open heart surgery/heart (lung) transplantation, the heart/lung are subject to ischemia-reperfusion injury, causing subsequent heart/lung dysfunction. Our previous work demonstrated that hyperkalemic cardioplegia/organ preservation solutions reduce the EDHF-mediated relaxation and membrane hyperpolarization in coronary arteries and that this function may be restored by hyperpolarizing cardioplegia using potassium channel openers. However, the mechanism has not been understood at the level of single ion channels. Further, little is known about 1) the effect of important ions (K⁺, Mg²⁺, exc.) and other components in cardioplegia/organ preservation solutions on PC; 2) the effect of ischemia-reperfusion on PC; 3) the possibility that the changed activities of PC may be restored by pharmacological agents (PC openers and Mg²⁺ cardioplegia). We propose this study to answer the above questions at the level of both vessel and cellular (single ion channel) levels. The single PC studies will be carried out by patch-clamp technique. Coronary/pulmonary arteries from pig hearts/lungs will be examined. The study will be also conducted in isolated coronary/pulmonary arteries in organ chambers/myographs. Direct measurement of the membrane potential in a single cell will be performed. The results will provide important knowledge to further understand the molecular mechanism of cardiopulmonary function during heart/lung surgery

in order to develop new methods to prevent and treat perioperative cardiovascular complications in heart/lung surgery/transplantation.

(CU03383)

Surveillance of Bleeding Peptic Ulcers Using Wireless Capsule Endoscopy

✉ NG Enders Kwok-wai • CHAN Ka Leung Francis (Dept of Medicine & Therapeutics) • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • WONG Kin Hung Simon

☐ 1 September 2003

❖ Research Grants Council (Earmarked Grants)

This proposal studies the feasibility of using wireless endoscopy in patients who has had endoscopic therapy for bleeding peptic ulcers to detect rebleeding.

Acute gastrointestinal bleeding from peptic ulcers is a common medical problem. Endoscopic therapy is now the first line treatment. In experienced hands it is highly successful in stopping acute bleeding. In 10-15% of cases rebleeding occurs, and rebleeding under these circumstances is dangerous and carries significant morbidity and mortality.

If rebleeding can be identified early treatment can be instituted to stem the haemorrhage before the patient suffers the harmful effects of blood loss. Unfortunately clinical features of rebleeding appear late and prediction of rebleeding from clinical and endoscopic features are not sensitive enough to direct therapy. Daily repeated endoscopy for patients at high risk of rebleeding is practiced in some European centers. This policy, subjects many patients to unnecessary endoscopy and cannot detect rebleeding occurring in the interim.

A pill sized capsule that can transmit endoscopic images from within the intestinal tract is available.

At present its main indication is for the investigation of small bowel pathology. We propose to adapt this capsule and attach it adjacent to bleeding ulcers to achieve continuous visual monitoring for rebleeding. (CU03382)

A CT Decision-making Tool for Mild Head Injury

✉ POON Wai Sang • CHAN Yu Leung (Dept of 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

□ 1 November 2003

❖ Research Grants Council (Earmarked Grants)

Mild head injury (MHI) is a common reason for hospital admission (1-300/100,000 population per annum). Liberal and early Computed Tomography (CT) of the brain has significantly reduced morbidity and mortality in this group of patients. Routine CT scanning of every patient with MHI is costly, but a successful selective approach is dependent on a set of effective guidelines, these being a source of continued controversy. To address this clinical problem, two recent studies have prospectively derived clinical decision rules for the use of CT in patients with MHI (Haydel et al., 2000; Stiell et al., 2001). However, they have either omitted some important predictor variables in the clinical assessment of the MHI, or have failed to follow up all patients with head trauma. Therefore, questions have been raised on the reliability and predictive power of the decision rules derived. Their validity and general application require further verification with other culturally distinct sample populations as well as tighter methodologies.

This research will attempt to meet these requirements by evaluating all potential risk factors associated with adverse CT outcomes in a sufficiently large patient group (n=2900), employing a 100% CT rate and clinical outcome follow up in all patients admitted with MHI in the Hong Kong Chinese population. A multi-centre clinical observational design will be employed to develop and validate a CT decision-making tool for MHI. This study will provide frontline clinicians with a clear set of guidelines in identifying high-risk MHI patients for early CT. The expected outcomes of the study will have management and resource implications, such as a reduction in the number of CT scans performed and avoidance of unnecessary hospital in-patient admissions. (CU03386)

Estradiol Inhibits Apoptosis by Promoting the Expression of Metallothionein II and NF-kappaB in Human Thyroid Cancer Cells

✉ VAN HASSELT Charles Andrew • VLANTIS Alexander Chris • CHEN Gong George • CHERIAN M. George* • LEUNG Chi Hang Bertrand

□ 1 December 2003

❖ Research Grants Council (Earmarked Grants)

Although there are a number of predisposing factors to the development of thyroid carcinoma, the underlying pathogenesis remains unknown. A striking feature of this cancer is its predilection for females of reproductive age relative to males. Our recent experiments showed that 17β-estradiol increased the expression of metallothioneinII (MTII) RNA in a dose-dependent manner in thyroid cancer cells. Apoptosis induced by 1 μM of staurosporine (STS) was significantly lower in thyroid cancer cells

treated with 17 β -estradiol than those treated with the vehicle control. The time course study revealed that the increase of MTII preceded the occurrence of apoptosis. MTII is known to be required for cell survival in several types of cells. Therefore, our study suggests that 17 β -estradiol protects human thyroid follicular carcinoma cells from apoptosis via a pathway related to MT II. This study will further determine in detail how 17 β -estradiol and MTII affects apoptosis. Particular attention will be paid to NF-kappaB whose level can be regulated by MT and which is an important survival signal in cancer cells. (CU03387)

NF kappaB is Involved in Resistance to Apoptosis in Squamous Epithelial Cells Infected with HPV 16

✉ VLANTIS Alexander Chris • CHEN Gong George • VAN HASSELT Charles Andrew

□ 1 February 2004

❖ CUHK Research Committee Funding (Direct Grants)

People infected with Human papillomavirus (HPV) 16 are at an increased risk of developing carcinoma. E6 and E7 are known to be the main viral oncoproteins of HPV 16 that cause the uncontrolled growth of infected cells. A variety of cell proliferation and growth molecules are altered by E6 and E7. One of the common features of these molecules is that they are governed by the transcription factor NF kappaB (NF-kB). A recent study of ours indicated that in laryngeal cancer tissues, a positive correlation exists between E7 and a subunit of NF-Kb, p65. The study also suggested that NF-kB is constitutively activated in laryngeal cells infected with HPV 16. This finding is in line with studies performed on cervical cancer cells that

were positive for HPV 16. Those results prompted us to examine further the role that NF-kB plays in the resistance to apoptosis of squamous epithelial cells infected with HPV 16. This study will analyze several downstream molecules in the NF-kB-related apoptotic pathway in laryngeal squamous epithelial cells infected with HPV 16.

(MD03419)

Efficacy of Acupuncture Versus Standard Therapy for Children with Primary Nocturnal Enuresis and the Implications of Brainstem and Bladder Functional Changes

✉ YEUNG Chung Kwong • LEUNG Ping Chung (Dept of Orthopaedics & Traumatology) • BOWER Wendy Fiona

□ 1 July 2003

❖ Research Grants Council (Earmarked Grants)

Primary nocturnal enuresis (PNE), or bedwetting, is the most common form of urinary incontinence in childhood. It is associated with bladder instability, arousal disturbance and a derangement of antidiuretic hormone (ADH) secretion resulting in a deficiency of nocturnal urine concentration. Recent studies have also noted two important changes in brainstem function among enuretic patients: 1) an elevated arousal threshold and 2) a deficient response to startle sounds, or prepulse inhibition (PPI).

Few studies have considered the relationship between this indication of brainstem dysfunction and bladder activity. Our previous study showed EEG arousal episodes to be positively correlated to unstable contractions of the bladder. Treatment results suggest that arousability may normalize when bladder activity becomes more stable. We hypothesize that there are two types of brainstem dysfunction in enuretic patients; firstly, brainstem dysfunction that is

a cause of enuresis in patients with normal bladder functions. Patients with this primary brainstem dysfunction are not expected to improve the PPI of startle, arousal threshold and brainstem evoke potential (BAEP) after enuresis management. Secondly, brainstem dysfunction that is a direct effect of bladder dysfunction, in which the PPI of startle, arousal threshold and BAEP would be expected to improve after successful management of nocturnal enuresis.

The aim of this study is to evaluate the relationship between brainstem function and nocturnal enuresis and to quantify the efficacy of acupuncture as a treatment for nocturnal enuresis. Baseline and post-treatment measures will include: frequency and volume of bedwetting episodes. PPI of startle, arousal threshold and BAEP.

(CU03389)

A Longitudinal Study on Primary Nocturnal Enuresis in Hong Kong Children

✉ YEUNG Chung Kwong • CHAN Wai Fung Anita • SIHOE Dart Yin Jennifer* • SHIT Kam Yee Frances* • MAK Kwok Hang*

□ 15 June 2004

❖ CUHK Research Committee Funding (Direct Grants)

Traditionally, urinary incontinence has been regarded as normal for young children in most Chinese families, and bedwetting had hardly received any attention from parents and even medial practitioners as a condition that warranted any investigations or treatment. A large epidemiological survey was carried out in 2000 to reevaluate the prevalence of PNE in Hong Kong school children. The results of monosymptomatic PNE was found to be 2.46% amongst Hong Kong school children. From this

study, we also noted that there was a marked reduction in overall prevalence of PNE with advancing age. At age 5, 16.2% children had PNE whereas at age 10 and 19, 2.8% and 1.5% children had PNE respectively. However, this reduction was significantly more apparent among those with mild enuretic symptoms (wets less than 3 nights per week), as compared with those with more frequent bedwetting. At age 5, 14% of enuretic children had wetting 7 nights per week, as compared to 37% at age 19($p<0.05$). The aim of this study is to find out the evidences to support the need to address the PNE issue. Therefore to establish a referral system to monitor and assist the children who have PNE problem, in order to have early and proper treatment for the patient.

(MD03452)

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

Edition	Title/Investigators
2002-03	Switching from Sildenafil Citrate to Tadalafil in Treatment of Erectile Dysfunction: Multinational Assessment of Treatment Preference (MD02735) ✉ CHAN Lung Wai • CHAN Shu Yin Eddie*
2001-02	Apoptosis in Infiltrating Mononuclear Cells of Colorectal Cancer is a Novel Mechanism for Tumor Escape (MD01624) ✉ CHEN Gong George • LEE Fung Yee Janet

- 2002-03 Development of Bid Recombinant Adenovirus and Its Application in Induction of Apoptosis in Hepatocellular Carcinoma Cells (MD02472)
 ✉ CHEN Gong George • MIAO Ji
- 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 (Dept of Diagnostic Radiology & Organ Imaging) • KWOK Po Yin Samuel • LEONG Heng Tat • LEUNG Sing Fai (Dept of Clinical Oncology) • ONG Lina Lilian • LI Ka Wah Michael
- 2000-01 A Randomized Trial on the Need for Cholecystectomy in Elderly Patients after Endoscopic Sphincterotomy for Bile Duct Stones (MD00455)
 ✉ CHUNG Sheung Chee Sydney • LAU Yun Wong James • CHAN Chi Wai Angus • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • LAU Wan Yee Joseph • NG Enders Kwok-wai
- 2001-02 The Interaction between Endothelium and Smooth Muscle/Cardiac Myocytes During Heart Surgery and Clinical Significance (MD01127)
 ✉ HE Guo Wei
- 2002-03 Function of Potassium Channels in the Coronary/Pulmonary Arteries and Myocardium during Heart/Lung Surgery: Clinical Implications (MD02451)
 ✉ HE Guo Wei
- 1997-98 Prospective Study on the Relationship of Central Venous Pressure and Blood Loss During Hepatectomy (MD96217)
 ✉ LAI Bo San Paul • CHUI Po Tong (Dept of Anaesthesia & Intensive Care) • LEOW Chon Kar# • LAU Wan Yee Joseph
- 2001-02 Expression of Double-stranded RNA-activated Protein Kinase in Hepacellular Carcinoma with Hepatitis B Virus Infection (MD01468)
 ✉ LAU Wan Yee Joseph • CHEN Gong George
- 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 (Dept of Microbiology) • CHENG Fun Bun Augustine (Dept of Microbiology)# • LEUNG Wai Keung (Dept of Medicine & Therapeutics) • LING Kin Wah Thomas (Dept of Microbiology) • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics)
- 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 (Dept of Anaesthesia & Intensive Care) • LAM Ming Kuen Joseph • BOET Ronald
- 2002-03 Glioblastoma Cell-targeting Vaccination Generated by Tumour Lysate-pulsed Macrophages Engineered to Produce Tumour Necrosis Factor Alpha (TNF α) and Interferon Gamma (IFN γ) (MD02710)
 ✍ POON Wai Sang • CHEN Gong George • NG Ho Keung (Dept of Anatomical & Cellular Pathology)
- 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 (Dept of Decision Sciences and Managerial Economics) • REVICKI Dennis*
- 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
- 2001-02 Children's Continence Care Centre (MD01896)
- ✍ YEUNG Chung Kwong • BOWER Wendy Fiona • SIT K Y Frances* • YEW Siu Yin*
- 2002-03 Open Label Extension and Long Term Safety Study of Tolterodine PR Capsules in Children 5 to 11 Years of Age with Symptoms of Urge Urinary Incontinence Suggestive of Detrusor Instability (MD02921)
 ✍ YEUNG Chung Kwong • SIHOE Dart Yin Jennifer* • SHIT Kam Yee Frances*
- 2002-03 Effects of Insufflation of the Bladder with Carbon Dioxide (Pneumovesicum) on Renal and Cardio-respiratory Physiology in an Animal Model (MD02818)
 ✍ YEUNG Chung Kwong • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging)# • AUN Sui Tee Cindy (Dept of Anaesthesia & Intensive Care) • KARMAKAR Manoj Kumar (Dept of Anaesthesia & Intensive Care)
- 1995-96 Video Assisted Thoracic Surgery (MD92192)
 ✍ YIM Ping Chuen Anthony
- 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)

✍ YIM Ping Chuen Anthony • ARIFI
Ahmed A* • HE Guo Wei •
JEREMY Jamie* • NEWBY
Andrew C* • WAN Song

Porcine Vein Graft Thickening
(MD02883)

✍ YIM Ping Chuen Anthony • WAN
Song • JEREMY Jamie* • BAKER
Andrew* • ARIFI Ahmed A*

2002-03 Role of Angiogenesis in Mediating the
Inhibitory Effect of the External Stent on

RESEARCH PROJECTS

Investigation into Circulating Nucleic Acids in Patients with Stroke

✉ RAINER Timothy Hudson • LAM Wai Man Wynnie (Dept of Diagnostic Radiology & Organ Imaging) • LO Yuk Ming Dennis (Dept of Chemical Pathology) • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging)# • WONG Ka Sing Lawrence (Dept of Medicine & Therapeutics)

☐ 1 September 2003

❖ Research Grants Council (Earmarked Grants)

Stroke is an acute brain syndrome which results either from an acute bleeding episode or because a blood vessel is blocked. It is the second leading cause of death worldwide and accounted for 10% of all deaths in Hong Kong. Unlike in patients with heart syndromes such as angina or heart attacks where there are a number of blood markers which may be used to detect the condition and to predict whether the patient will recover well or not, no similar tests exist for patients with stroke. If a simple and easy to use blood marker could be identified, then this may improve our ability to detect stroke and predict patient's recovery. As patients with stroke have both cell death and a compromised blood brain barrier, it is likely that cell proteins and nucleic acids will be liberated into plasma. These substances may be detected by simple blood sampling, and analysis using the polymerase chain reaction.

In this project we propose to establish whether circulating nucleic acid levels improve diagnosis and risk-stratification in patients with stroke over and

above existing predictive strategies. We aim firstly to investigate the predictive value of β -globin DNA, S100 protein and S100 RNA in patients with stroke and other acute brain syndromes. Secondly, we shall investigate whether levels of these proteins and nucleic acids in plasma vary dramatically with time after the beginning of stroke.

(CU03402)

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

Edition	Title/Investigators
2001-02	Role of Plasma DNA and Other Markers in the Prediction and Development of Post-traumatic Complications 1224/1202 (MD01839) ✉ RAINER Timothy Hudson • LO Yuk Ming Dennis (Dept of Chemical Pathology) • JOYNT Gavin Matthew (Dept of Anaesthesia & Intensive Care)
2002-03	Plasma Nucleic Acids as a Non-invasive Marker of Severity in Acute Coronary Syndrome (MD02581) ✉ RAINER Timothy Hudson • LO Yuk Ming Dennis (Dept of Chemical Pathology) • WOO Kam Sang (Dept of Medicine & Therapeutics) • CAMERON Peter Alistair#

RESEARCH PROJECTS

Clinical Data Management and Medical Statistics Functions for CK Life Sciences Development Inc.

✍ LAU Tak Fai Joseph

☐ 1 August 2003

❖ CK Life Sciences Development Inc.

Contracted services to manage data and perform analysis for a project of the CK Life Sciences Development Inc.

(MD03532)

Prospective Randomized Study on the Therapeutic Gain for the Nasopharyngeal Carcinoma Patients

✍ LAU Tak Fai Joseph • XU Liying (School of Public Health)

☐ 1 August 2003

❖ The Hong Kong Nasopharyngeal Cancer Study Group

This is a contracted service, commissioned by the Hong Kong Cancer Fund. Data management services will be provided to support a multi-centre clinical trial study (nasopharyngeal carcinoma)

(MD03576)

The Impact of Calcium Intake on Blood Pressure and Prevalence of Hypertension: A Pilot Cross-sectional Study of Older Chinese Subjects in Hong Kong

✍ LAU Tak Fai Joseph • CHAN Yan Keung Thomas (Dept of Medicine & Therapeutics) •

KWOK Chi Yui Timothy (Dept of Medicine & Therapeutics) • WOO Jean (Dept of Medicine & Therapeutics)

☐ 15 September 2003

❖ CUHK Research Committee Funding (Direct Grants)

Hypertension, defined as a blood pressure (BP) >140/90 mmHg, is the major modifiable risk factor for cardiovascular morbidity and mortality, especially in the elderly. The prevalence of hypertension increases with age. Calcium intake is much lower in Asian communities, especially among the elderly. It has been suggested that the high sodium diet combined with low potassium and calcium intakes that are seen in many elderly subjects may be in part responsible for the prevalence of hypertension and related complications such as stroke and congestive heart failure. In this pilot cross-sectional study of 100 older subjects in Hong Kong, we shall determine: (1) the independent association between habitual calcium intake, BP, and the prevalence of hypertension; (2) whether higher calcium intake has a protective effect on the risk of high sodium/potassium ratios on hypertension; (3) the sources of calcium in subjects with low or high intakes and factors determining the levels of intake; (4) the general knowledge of hypertension among normotensive and hypertensive subjects. We shall determine if the common occurrence of hypertension among older subjects in Hong Kong is in part related to their habitually low calcium intake. The pilot study will form a basis for further studies.

(MD03385)

Data Analysis for the Valsartan Study (DIO-HK-02)

✉ LAU Tak Fai Joseph • WONG Ming Chung
(School of Public Health)

☐ 1 October 2003

❖ Novartis Pharmaceuticals (HK) Ltd

Contracted services to perform analysis for a project for Novartis Pharmaceutical (HK) Ltd.
(MD03634)

The Production of CD-Rom of Hong Kong Student Information Form Under the Understanding Adolescent Project in Primary Schools

✉ LAU Tak Fai Joseph • LAU Man Chun Mason

☐ 1 December 2003

❖ Education & Manpower Bureau, HKSAR Government

The Education and Manpower Bureau commissioned the Centre of Epidemiology and Biostatistics of the Chinese University of Hong Kong to develop a CD-ROM of the Hong Kong Student Information Form (HKSIF) for the screening of at-risk students under the Understanding of Adolescent Project (Primary) in 2004/05 school year. With some training and help desk service, individual school will be able to conduct the screening process at their own schedule. Around 400 primary schools will use this CD-ROM to conduct the screening process.

The tasks are to develop a master CD-ROM of HKSIF with built-in self-generating results for student classification of their HKSIF status which can be used both on the window based environment and intranet-based environment; to duplicate 450 CD-ROM with design in at least 2 colours for the plastic package and the surface of the disc; to design and produce 450 copies of users' manual of the CD-ROM; to conduct a maximum of 30 identical

2-hour training sessions for primary school personnel on the operation of the CD-ROM; to provide telephone help desk service or on-site technical supports to 400 UAP schools from 1 September 2004 to 31 December 2004 and to produce a statistical report on the screening results in 400 schools joining the UAP (Primary).

(ED03821)

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

✉ LAU Tak Fai Joseph • KIM Jean Hee • TSUI Hi Yi

☐ 16 November 2004

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

Hong Kong Chinese male cross-border truck drivers have been found to have frequently engaged in HIV-related risk behaviors in mainland China. They are not only at risk of contracting HIV themselves, but also act as a potential 'bridging' population for transmitting HIV to their other sex partners. Hence, they are an important at-risk group for HIV prevention effort. The present study aims to evaluate the relative efficacy of using the Voluntary Counseling and Testing (VCT) approach and the Information Distribution approach in reducing HIV-related risk behaviors among this HIV vulnerable population. Results of the study provide valuable evidence-based information for the design/implementation of effective cross-border HIV prevention programs.

Male cross-border truck drivers who self-reported having engaged in sexual intercourse with female sex workers or non-regular female sex partners in mainland China in the last 6 months will be invited to participate in the study at the Kwai Chung Container Terminals or Man Kam To checkpoint. With informed consent, they will be randomized into either of the 2 intervention groups (the VCT group or the information group). Assessments, using an anonymous structured questionnaire and a locally validated computer-assisted data collection method, will be made at the beginning of the study (baseline measurement), and 1 month and 2 months respectively after the intervention takes place. The VCT group will also complete a post-test questionnaire. The target sample size is about 200 per group.

The study is in collaboration with AIDS Concern, a HIV/AIDS-specific non-governmental organization. (MD03908)

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

Edition Title/Investigators

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 (Dept of Psychiatry) • LAU Man Chun Mason

2002-03 Statistical Evaluation for the COPD Audit Program (MD02417)

✉ LAU Tak Fai Joseph • XU Liying (School of Public Health)

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

RESEARCH PROJECTS

Investigation of *BRE* as a Gene Affecting Tumor Growth and Metastasis

✍ CHUI Yiu Loon • CHING Kar Keung

☐ 1 March 2004

❖ CUHK Research Committee Funding (Direct Grants)

Our recent study of a novel human gene, *BRE*, has revealed its anti-apoptotic characteristic *in vitro* and ability to enhance mouse tumor growth *in vivo*, upon over-expression. In a screen of 241 pairs of tumor and normal tissues of a variety of human cancers, a remarkable association was found between the change in *BRE* expression and the primary tumors of the kidney. Our preliminary data suggest that down-regulation of *BRE* expression may be associated with non-metastatic tumors, whereas the up-regulation may be related to metastasis. Our proposed research here includes: 1) to expand the screening of human cancers for change in *BRE* expression to establish the extent and mode of involvement of this gene in human carcinoma in general, and in renal carcinoma in particular; and 2) to knock down the expression of *BRE* in cell lines and mouse tumor models to gain understanding of the mechanism underlying the probable association between down-regulation of *BRE* expression and non-metastatic tumors. The proposed research will better our understanding of the function of a novel human gene, which is involved not only in the life and death of cells, but also in cancer development. The new insights gained may open more ways for developing cancer therapy. In addition, identification of a new gene taking part in controlling

apoptosis in response to TNF- α and Fas may impact on the treatment of autoimmunity and hypersensitivity.

(MD03382)

Development of Specific Immunotherapeutics and Rapid Immunodiagnostics for Severe Acute Respiratory Syndrome

✍ LIM Pak Leong • CHAN Kay Sheung Paul (Dept of Microbiology) • LEUNG Tze Ming • TAM Siu Lun John (Dept of Microbiology)

☐ 30 September 2003

❖ RGC Special Grants for Severe Acute Respiratory Syndrome (SARS) Research

We plan to develop immunological compounds that can be used to protect people from getting SARS (as vaccines) or to manage the disease in SARS patients (as therapeutics). These same compounds will also be used to establish quick and efficient tests to diagnose SARS. The compounds are of 3 types: (1) ANTIGENS, components of the virus which will be produced from the virus grown in culture, or by genetic engineering of the individual viral genes in bacterial or human cells; (2) ANTIBODIES, produced normally in a person or an animal to fight an infection, will be made to various parts of the SARS virus in mice or produced in cultures as mouse monoclonal antibodies, and (3) PEPTIDES, which are like antigens but are much smaller in size and are chemically synthesized, will be made as a variety. The effectiveness of these compounds to prevent infection of human cell cultures by the SARS virus will be examined. Ones which are inhibitory will be investigated further for their therapeutic potential. The potential of the antigens as vaccines will only be assessed at this stage by their ability to induce

production of the neutralising (inhibitory) antibodies in mice.
(CU03527)

✉ CHUI Yiu Loon • CHAN Yeuk Hon
John* • CHING Kar Keung • LEE
Ka Ho Kenneth (Dept of Anatomy)

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

2002-03

Crystallisation of a Carrier-specific Antibody and Its Reconstruction as a Bona Fide Antibody Fragment (CU02092)

✉ LIM Pak Leong • SUTTON Brian*

Edition Title/Investigators

2002-03 Functional Studies of a Putative Peroxisomal Regulating Gene, BRE - Its Roles in Cellular Survival, Immune System and Tumorigenicity (CU02090)