Faculty of Medicine

RESEARCH PROJECTS

Context Sensitive Half-time of Remifentanil After Long Neurosurgical Procedure

- □ 1 December 1998
- CUHK Departmental Funding

The context-sensitive half time (CSHT) is the time to halving the blood concentration after termination of drug administration by an infusion targeted to maintain a constant concentration. This concept allows better prediction of recovery from intravenous infusion at the termination of surgery. Previously CSHT was only estimated using computer simulation. It is not certain whether the predicted CSHT is accurate after prolonged remifentanil infusion in long neurosurgical procedure. This study aims to determine the *in vivo* CSHT after long neurosurgical procedures. (MD98163)

Dose Response of Cisatracurium Besilate in Children During Intravenous Anaesthesia

- CHAN Matthew Tak Vai CHEE Yee Eot AUN Sui Tee Cindy
- ☐ 31 December 1998
- CUHK Departmental Funding

Children require a greater dose of non-depolarising neuromuscular blockers. This age-dependency phenomenon has been documented. Changes in the sensitivity of neuromucular junction and the volume of distribution may explain the change in dose requirements. Cisatracurium besylate is a purified form of one of the ten stereoisomers, R-cis, R'-cis isomer. Recent data showed that time of recovery from cisatracurium block in children was not different from adult, suggesting the potency of cisatracurium between the two groups were similar. There are no 'direct data' regarding the dose-response relation of cisatracurium in paediatric patients from newborns to adolescents. This study construct the dose response curves of cisatracurium in children. (MD98162)

The Electroencephalographic Effects of Regional Anaesthesia and Their application During Combined Regional and General Anaesthesia

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 CHUNG David Chi Wai MORLEY Andrew
 Peter# CHAN Matthew Tak Vai
- ☐ 1 August 1998
- * Research Grants Council

Combined regional and general anaesthesia (CRGA) is a common anaesthetic technique for major surgery. Advantages over general anaesthesia alone include an apparent reduction in general anaesthetic requirements, though the extent of this reduction is unclear. Electroencephalograph (EEG) variables have been proposed as measures of anaesthetic depth. This project aims to establish the EEG changes accompanying regional anaesthesia, both alone and in combination with general anaesthesia. EEG variables will then be used to determine the extent to which general anaesthetic requirements are reduced by the combined technique.

EEG variables differ between patients receiving CRGA and those receiving general anaesthesia alone. In the part one of the project we intend to investigate these differences. As they may be partly explained by independent EEG changes accompanying regional anaesthesia, we will determine, in part two, the effects of regional anaesthesia alone on the EEG.

In part three, general anaesthesia will be administered to patients with (i.e. CRGA) and without regional anaesthesia, using closed loop feedback control on the EEG. In this way the same depth of anaesthesia will be maintained in each group. The anaesthetic requirements, intraoperative physiological data and recovery characteristics of the two groups will be compared.

(CU98044)

Plasma Lignocaine Level Following Topical Anesthesia of the Airway by the Aspiration

- ∠ CHUNG David Chi Wai HO Ming Hei Anthony WOODWARD David Keith
- ☐ 26 April 1999
- CUHK Departmental Funding

To check blood level of lignocaine following airway anaesthesia by aspiration of lignocaine a technique developed at the Prince of Wales Hospital. (MD98160)

The Use of Dihydroergotamine in Spinal Anaesthesia

- ☐ 1 June 1999
- CUHK Departmental Funding

Dihydroergotamine is an agent that raises blood pressure. Its use in anaesthesia and particularly Hong Kong is limited. This study investigates the dosage required to treat episodes of hypotension, low blood pressure, during spinal anaesthesia in elderly patients. (MD98158)

Intraocular Pressure Changes in Patients with Intracranial Hypertension

- ☐ 1 June 1999
- CUHK Departmental Funding

There is significant anatomic and physiologic basis for intraocular pressure to be affected by intracranial pressure. To delineate the correlation between the two pressures could allow non-invasive assessment of cranial pressure in patients with intracranial space occupying lesions, fluids or oedema. (MD98154)

Arteriovenous Plasma Concentration of Ropivacaine Following Epidural Administration

- KARMAKAR Manoj Kumar
 CHUNG David Chi Wai
 KWOK Wing Hong
 CHEE Yee Eot
- □ 12 November 1998
- CUHK Departmental Funding

Ropivacaine is long acting aminoamide local anaesthetic agent, which has recently been introduced into clinical practice. Ropivacaine has a chemical structure similar to Bupivacaine, the butyl group being replaced by a propyl group on the piperidine nitrogen atom. While Bupivacaine is available as a mixture containing equal proportions of the "R(-)" and "S(-)" isomer. Ropivacaine is the first local anaesthetic agent to be available as a pure "S(-)" isomer with an enantiomeric purity of 99.5%. This isomeric difference is believed to confer advantages in the toxicity profile of Ropivacaine over Bupivacaine. Recent pharmacokinetic data from adult volunteers following epidural administration of Ropivacaine has demonstrated a significant peripheral arteriovenous concentration difference (up to 50%) for as long as sixty minutes following epidural injection. This difference in plasma concentration of Ropivacaine appears to be greater and persists for longer than that seen with the use of Bupivacaine. Therefore peripheral venous plasma concentration of Ropivacaine may be a very unreliable measure of vital organ concentration (heart/brain) for assessing toxicity during systemic absorption and will necessitate arterial blood sampling in future pharmacokinetic studies.

Our review of the literature to date shows that there are no pharmacokinetic data in clinical practice comparing the simultaneous arteriovenous (central venous. arterial and peripheral venous) concentrations of Ropivacaine following epidural administration. An understanding of the plasma concentration profile at these various sites during systemic absorption mav have significant implications in the interpretation of plasma concentrations of Ropivacaine. (MD98156)

Comparative Systemic Absorption of Ropivacaine and Bupivacvaine Following Caudal Epidural Administration in Children

- **□** 8 December 1998
- CUHK Departmental Funding

Bupivacaine is the local anaesthetic agent most commonly used in children. Used for prolonged infusion it has been associated with significant systemic accumulation and clinical reports of toxicity. Ropivacaine is a local anaesthetic agent very similar in chemical structure to bupivacaine. While bupivacaine is available as a raecemic mixture Ropivacaine is the only local anesthetic agent available as a pure isomer "S". This isomeric difference is believed to confer advantage in toxicity profile of Ropivacaine.

Ropivacaine has been safely used in children for epidural administration. However there is no pharmacokinetic data to date comparing the systemic absorption of Ropivacaine and Bupivacaine. This prospective randomised double blind study aims to compare the systemic absorption of either of these two drugs during systemic absorption following caudal epidural administration. (MD98155)

Spinal Anaesthesia for Caesarean Section Using Ropivacaine

- ☐ 11 September 1998
- CUHK Departmental Funding

Ropivacaine is a new local anaesthetic with a better toxicity safety profile. While epidural of ropivacaine use has been extensively investigated there has been very little data on spinal administration. There is not publications or report so far on the use of spinal ropivacaine for caesarean section. Therefore this research is conducted to investigate the dose response of this drug when used for caesarean section. (MD98159)

Ropivacaine as an Intrathecal Agent: Part I – A Dose Response Study

- □ 3 April 1999
- CUHK Departmental Funding

Ropivacaine is a new local anaesthetic with a better toxicity safety profile. While epidural of ropivacaine use has been extensively investigated there has been very little data on spinal administration. There is very few publications or report so far on the use of spinal ropivacaine. Therefore this research is conducted to investigate the dose response of this drug when used for spinal anaesthesia. (MD98153)

Randomised Double-blind Comparison of Ephedrine and Metaraminol for the Treatment of Hypotension During Spinal Anaesthesia for Caesarean Section

- ✓ NGAN KEE Warwick Dean KHAW Kim Sun
 LEE Bee Beng LAU Tze Kin (Obstetrics & Gynaecology)
- □ 1 October 1998
- CUHK Departmental Funding

Spinal anaesthesia is a popular method of anaesthesia for Caesarean section, but has the potential to cause hypotension which can be detrimental to mother and Hypotension is traditionally treated with intravenous fluid and a vasopressor, of which historically ephedrine has been the most commonly used. Recently, there has been a reappraisal of vasopressors in obstetrics. Several human studies have shown that the direct alpha agonists may be as effective or more effective than ephedrine. In Hong Kong the main alpha agonist in use is metaraminol. Previous work from our department showed that metaraminol was more effective than ephedrine in preventing hypotension during spinal anaesthesia in non-obstetric patients. However, few data are available on the use of metaraminol in human obstetric patients. Therefore the aim of this randomised double-blind study is to evaluate metaraminol for management of hypotension during spinal anaesthesia for Caesarean section by comparing it with ephedrine. Effects on maternal haemodynamics and fetal outcome will be compared. In addition, the potential effects of metaraminol on the uterine vasculature will be assessed using Doppler ultrasound. (MD98150)

Randomized Double-Blind Evaluation of Ropivacaine-Adrenaline as an Epidural Test Dose

- MGAN KEE Warwick Dean KHAW Kim SunLEE Bee Beng
- ☐ 1 October 1998
- CUHK Departmental Funding

Ropivacaine, a new local anaesthetic agent, ropivacaine has been recently approved for use in Hong Kong. Ropivacaine has a similar

pharmacological profile to bupivacaine but has advantages of lower toxicity and a lower ratio of motor: sensory block. These properties make ropivacaine useful for obstetric anaesthesia and analgesia. However, to date, there is little information available on the use of ropivacaine as a test dose, which is an important aid to preventing adverse outcomes associated with incorrect placement of epidural catheters. Because of its lower toxicity compared with other local anaesthetics, ropivacaine is particularly suitable as an agent to detect intravenous injection. In addition, as it is likely that the use of ropivacaine will increase worldwide, it is important that the effects of intrathecally injected ropivacaine be determined. This randomised double-blind study investigates the use of an epidural test dose using ropivacaine in combination with low dose adrenaline. (MD98151)

Dose-Response Investigation of Ephedrine by Intravenous Bolus for the Prevention of Hypotension During Spinal Anaesthesia for Caesarean Section

- ✓ NGAN KEE Warwick Dean KHAW Kim Sun
 LEE Bee Beng LAU Tze Kin (Obstetrics & Gynaecology)
- ☐ 1 October 1998
- CUHK Departmental Funding

Spinal anaesthesia is popular for Caesarean section but has the disadvantage of the potential to cause hypotension from rapid onset of sympathetic block This can have and peripheral vasodilatation. detrimental effects on both mother and fetus. Therefore, there has been much interest in methods of prevention and treatment of this side effect. In general, these have focused on the use of intravenous fluid preload and vasopressors. Of the available vasopressors, historically ephedrine has been the most commonly used. However, despite the widespread acceptance of ephedrine as a standard drug in obstetric spinal anaesthesia, the optimum dose regimen for ephedrine is undetermined. Therefore the aim of this randomized, double blind study is to evaluate different doses of ephedrine (0-30mg) given as intravenous boluses for prevention of hypotension during spinal anaesthesia for Caesarean section. The primary outcome to be compared will be maternal haemodynamics. In addition, any differences in fetal outcome will be compared. (MD98152)

Determination of the Influence of Inspired Oxygen Concentration on Maternal and Neonatal Outcome During General Anaesthesia for Caesarean Section

- MGAN KEE Warwick Dean KHAW Kim Sun
 MA Kwok Chiu (Paediatrics) LEE Bee Beng
- ☐ 1 June 1999
- CUHK Research Committee Funding

The optimum concentration of inspired oxygen that should be used during general anaesthesia for Caesarean section is unknown and current practice of anaesthetists is based on questionable historical information. The aim of this prospective, randomized, double-blind controlled study is to investigate the influence of inspired concentrations of oxygen ranging from 30-100% on maternal and neonatal outcome. General anaesthesia will be maintained using a new volatile anaesthetic agent: sevoflurane. Sevoflurane has a very low blood gas partition coefficient and thus a very rapid onset of action; this will eliminate light anaesthesia and high circulating maternal catecholamine concentrations as a potential confounding factor. The primary outcome compared will be neonatal condition which will be assessed by biochemical analysis of umbilical cord blood and clinical and neurobehavioural assessment. In addition to standard blood gas analysis of umbilical cord blood, we will directly measure the actual oxygen content of samples using a technique known as co-oximetry. This has advantages over simple measurement of oxygen tension, because fetal haemoglobin has different affinity for oxygen compared with adult haemoglobin making it difficult to interpret blood gas results, especially in the face of simultaneous changes in PCO2 and pH which frequently occur at birth. Clinical neonatal assessment will include conventional Apgar scoring, plus neurobehavioural scoring which is a sensitive measurement of drug effects on the neonate. Maternal assessment will be a secondary outcome and will include measurement of intraoperative haemodynamics and plasma concentrations of adrenaline and noradrenaline at delivery, measured using high performance liquid chromatography. (MD98092)

Investigation of the Use of Ropivacaine 1% as the Sole Aaesthetic Agent for Peribulbar Anaesthesia

- □ 4 June 1999
- CUHK Departmental Funding

Peribulbar anaesthesia for eye surgery has gained favour over the retrobulbar technique because of an improved safety record with respect to sight- and life-threatening complications. A variety of local anaesthetic agents have been used, the most frequent being a mixture of bupivacaine 0.5% and lignocaine

2%, with or without hyaluronidase and adrenaline, in volumes of up to 12 mls. A recent study demonstrated that adding a large dose of hyaluronidase (300 iu/ml) to a bupivacaine / lignocaine mixture improved the quality and speed of the block.

Ropivacaine (Astra Pharmaceuticals) is a relatively new local anaesthetic recently approved for use in Hong Kong, with the advantage of improved cardiovascular and neurological toxicity profiles compared to bupivacaine. Although ropivacaine has been shown to have a 'motor sparing' effect at low concentrations, a recent report on intraorbital ropivacaine demonstrated improved ocular akinesia with a ropivacaine / lignocaine / hyaluronidase mixture when compared with a bupivacaine / lignocaine / hyaluronidase mixture. This suggests that ropivacaine may be a suitable local anaesthetic agent for peribulbar anaesthesia.

We piloted peribulbar ropivacaine 1% plus hyaluronidase 300 iu/ml in 13 patients, and found that this mixture provided satisfactory conditions for surgery in all the patients; however the rate of onset, and degree of akinesia were possibly inferior to an anaesthetic combination incorporating lignocaine.

We set out to determine whether ropivacaine alone is a suitable agent for peribulbar block, in terms of speed of onset and the quality of anaesthesia produced, when combined with 300 iu/ml hyaluronidase.

(MD98157)

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

<u>Edition</u>	<u>Title/Investigators</u>
1997-98	Comparison of Two Methods of Cardiac Output Measurements and the Effect of Lung Fluid on Their Relationship (MD97186) « CRITCHLEY Lester Augustus Hall
1997-98	Hypotension During Spinal Anaesthesia: How Should the Vasopressor be Given? (MD97185)
1996-97	Effect of Pregnancy on the Concentrations of Propofol Required for Hypnosis and Anaesthesia (MD96107) JOYNT Gavin Matthew • MORLEY Andrew Peter#
1997-98	Thoracic Paravertebral Infusion of Bupivacaine for Post-thoracotomy

Analgesia. What is the Most Effective

Concentration? (MD97184)

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see also <P981803>, <P982505>, <P982522>, <P982919>, <P990001>, <P991205>, <P992052>

RESEARCH PROJECTS

Detection of Helicobacter Pylori DNA in Serum and Plasma by Real-time Polymerase Chain Reaction

- ∠ CHAN Wing Yee LO Yuk Ming Dennis
 (Chemical Pathology) NG Enders Kwok-wai
 (Surgery)
- □ 1 December 1998
- CUHK Research Committee Funding

Helicobacter pylori (HP) infection is prevalent in Hong Kong. HP can be found in 57% endoscopic gastric biopsies. HP has been linked to chronic gastritis, peptic ulcer, gastric carcinoma and MALT type lymphomas. HP has been classified as a Class II carcinogenic agent by the World Health Organization. Eradication of HP has been shown to be a successful method for treatment of peptic ulcers. researchers are predicting a future fall in gastric cancer with control of HP infection in endemic regions. The most sensitive methods for diagnosing HP infection involve invasive procedures: biopsy and CLO (rapid urease) test and polymerase chain reaction (PCR) on gastric mucus/ tissue. Urea breath test and bacterial culture are less sensitive. They have limited value for detecting low bacterial density e.g. incomplete response to or early relapse after treatment. Serological IgG antibody titres cannot distinguish between on-going and past infections.

Recently, fetal and tumour DNA have been detected in serum and plasma, of pregnant women and cancer patients respectively. This suggests that human plasma may act as a reservoir for accumulation of foreign DNA. Using primers targeting HP specific ribosomal RNA gene sequence and fluorescence labeled nucleotides, PCR is performed in a newly available, highly sensitive thermocycler with real time display of the fluorescence labeled PCR amplified products. We aim to detect and quantify even minute amount of HP DNA in the serum or plasma.

Anticipated significance: To establish a new rapid, non-invasive method for diagnosing HP infection. (MD98022)

Molecular Characterization of Differentially Expressed Genes in Nasopharyngeal Carcinoma

- ∠ HUANG POON Wai Sin Dolly CHUI Yiu Loon (Clinical Immunology Unit) TSAO George* VAN HASSELT Charles Andrew (Surgery) TO Ka Fai PANG Chung Sean Jesse LO Kwok Wai
- ☐ 1 September 1998
- * Research Grants Council

Nasopharyngeal carcinoma (NPC) is a common cancer seen in southern Chinese. The long-term goal of our research is to find better approaches, new or improvement over existing ones, to detect, treat and prevent this malignant disease.

NPC, like other cancers, arises from accumulation of genetic changes within a clonal cell population. Using deletion mapping we have identified several specific regions on the chromosomes that are consistently deleted in the NPC cells. These are regions where putative tumor suppressor genes may reside. We further demonstrated that one of the tumor suppressor genes, p16/MTS1, localized to the deleted region on chromosome 9 at 9p21, was inactivated resulting in loss of gene expression. Currently, we are employing an expression genetic approach to look for cancer-related genes. With a subtractive hybridization technique, we have obtained several novel genes that are differentially expressed in normal nasopharyngeal epithelial cells compared with their cancerous counterparts. We are proposing to have these novel genes characterized and to examine their roles in the development of NPC. Furthermore, we propose to screen several hundred known cellular genes from commercially available cDNA expression arrays for their differential expression profiles in this cancer.

The identification and characterization of the aberrantly expressed cancer-related genes in NPC will contribute to our understanding of the molecular pathogenesis of this disease and to provide a key step toward advances in cancer prevention, early detection, diagnosis and treatment. (CU98284)

Antigen Processing in an Epstein-Barr Virus Positive Nasopharyngeal Carcinoma Cell Line (C666-1)

- ∠ HUANG POON Wai Sin Dolly

 ◆ CHEUNG Siu
 Tim#
- ☐ 1 September 1998
- CUHK Research Committee Funding

Epstein-Barr virus (EBV) is known to be present in almost 100% of undifferentiated nasopharyngeal carcinoma (NPC), a cancer highly prevalent in Southeast Asia and Hong Kong (20-50/100,000). Within the NPC cells, EBV expresses only EBNA 1, LMP 1 and LMP 2. Previous studies demonstrated that LMP 2 is a subdominant target antigen for HLA class I-restricted cytotoxic T lymphocytes (CTLs) with several target epitopes defined in this protein. The presence of such known CTL target antigen within NPC offers the possibility of a CTL-based therapy for this cancer. However, it remains to be determined why the patient's own immune response has failed to clear the tumor. One possibility is that LMP 2-specific CTLs are present at very low frequency in NPC patients, in which case boosting or eliciting such a response may prove to be an effective One way to address this issue is by therapy. analyzing EBV-specific CTL responses in NPC patients. A second possibility is that NPC cells are defective in the class I processing pathway and are therefore incapable of presenting viral antigens to CTLs. Such defects have already been described for several human malignancies, including the EBVassociated tumor Burkitt's lymphoma (which is defective in expression of the transporters associated with antigen processing, TAPs). The aim of this project is therefore to study the antigen processing function of NPC cells using a cell line C666-1, recently cloned and established in our laboratory from a NPC xenograft. (MD98023)

PCR-Based Microsatellite Polymorphism in Chromosomes 3, 5, 8, 10, 16,17 and 18 in Prostatic Carcinoma and Prostatic Intraepithelial Neoplasia

- MAC-MOUNE LAI Fernand ◆ LIEW Choong Tsek ◆ TO Ka Fai ◆ CHAN Siu Foon Peter (Surgery)
- ☐ 1 September 1998
- * Research Grants Council

Prostatic carcinoma is the second most common cause of cancer death in Western societies, and despite a ten-fold lower incidence in Asia, both the incidence and mortality of such cancer are slowly rising in Hong Kong. Such great disparity in incidence and mortality among different ethnic groups and geographic areas, have long indicated the importance of genetic and environmental factors in both the carcinogenesis and biologic behavior of such cancer. Recently developed PCR-based microsatellite assay has provided a new means in genomic DNA analysis, and early results in prostatic cancer suggest that new allelic mutations and tumor suppressor genes are operative. This project proposes to study the DNA polymorphism of prostatic carcinoma in Hong Kong Chinese, and of its associated Prostatic Intraepithelial Neoplasia (PIN) using a high-resolution PCR-based microsatellite analysis, currently representing one of the most sensitive methods to detect genetic mutations. The study will focus on chromosomes 3, 5, 8, 10, 16, 17, and 18, which have previously demonstrated some evidence of allelic mutation. The objective aim at determining a possible role of allelic losses in the disparity of cancer incidence and mortality rate, and also in the genetic events implicated in the initiation and progression of this cancer. Microsatellite analysis of PIN lesions may help to determine whether or not they are precursors to carcinoma. This study will also assess the prognostic value of potential microsatellite markers in correlation with tumor grade, tumor stage and patient survival.

(CU98259)

Biological Studies of the Endothelial Cells in Glioblastoma Multiforme

- NG Ho Keung

 TO S.S.Tony*
- ☐ 1 November 1998
- CUHK Research Committee Funding

Glioblastoma multiforme (GBM) is the commonest primary tumorin human central nervous system. In spite of advances in neurosurgical imaging and techniques, the tumor invariably kills by extensive infiltration of adjacent neural tissues. One of the mechanisms for invasion is through active proliferation of vascular endothelial cells and new vessel formation. Degrading enzymes from both endothelial and glioma cells facilitate tumor invasion. This may involve interaction or "communication" between glioma cells and endothelium cells, through regulation of adhesion molecules and extracellular matrix protein receptors. The role of the endothelium in such cell-to-cell interaction is not clear. As a first step in understanding the interaction between glioma and endothelial cells, we propose to isolate the endothelial cells from clinical samples of GBM. These cells will be examined for expression of different cell adhesion molecules and growth characteristics. The results will lead to more intensive studies on glioma and endothelial cell interaction. (MD98024)

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

Edition <u>Title/Investigators</u>

1997-98 Gastric Cancers and Helicobacter Pylori A Combined Study by Interphase
Cytogenetics, Comparative Genomic
Hybridization and Molecular Genetic
Analysis (Including Microsatellite
Analysis) (CU97624)

∠ CHAN Wing Yee • LO Kwok Wai •
 LEE Chuen Kwun Joseph (School of Chinese Medicine) • WONG
 Nathalie (Clinical Oncology)

1997-98 Isolation and Characterization of Tumor-Infiltrating Lymphocytes in Gastric Adenocarcinoma: A Comparative Study on Tumors with and without Helicobacter Association (MD97027)

∠ CHAN Wing Yee

◆ WHITNEY
Bruce Montfort

- 1993-94 The Investigation of Tumour Marker Expression in Cytology Specimens (MD94033)
 - ∠ CHANG Alexander Russell
- 1996-97 Application of Comparative Genomic Hybridization to the Detection of DNA Imbalances in Sinonasal T-cell Lymphoma (MD96010)
 - CHOW John Hei Sing WONG
 Nathalie (Clinical Oncology) •
 WOO Kong Sang John (Surgery)
- 1996-97 Correlation of the Expression of c-myc and bc1-2 Oncoproteins with the Expression of Epstein-Barr Encoded EBER mRNA, LMP-1 and bc1-2 Homologue, BHRF1 in Primary Gastric Lymphoma (MD96029)
 - CHOW John Hei Sing CHAN Wing Yee
- 1997-98 Determination of the Presence and Type of EBV in Colorectal Carcinoma and Lymphoma by *in situ* Hybridization for EBER and Characterization of LMP1 by PCR-RFLP and PCR-SSCP (MD97029)
- 1995-96 Epstein-Barr Virus (EBV) specific Latent
 Membrane Protein (LMP1) Gene and Its
 Variants in the Hong Kong Chinese
 Population: Molecular Epidemiology and
 Pathogenetic Significance in
 Nasopharyngeal Carcinoma (NPC)
 (CU95617)
 - **HUANG POON Wai Sin Dolly •
 TAM Siu Lun John (Microbiology) •
 NG Ho Keung LEUNG Sing Fai
 (Clinical Oncology) FOK Tai Fai
 (Paediatrics) VAN HASSELT
 Charles Andrew (Surgery) LEE
 Chuen Kwun Joseph (School of
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 - ∠ HUANG POON Wai Sin Dolly LO
 Kwok Wai

- 1995-96 The Investigation of Genomic Instability by Polymerase Chain Reaction to Detect Microsatellite Polymorphisms on Chromosomes 1, 2, 3, 4, 6, 7, 11, 16, 17 and 18 in Hepatocellular Carcinoma (CU95661)
 - ∠ LIEW Choong Tsek LEE Chuen Kwun Joseph (School of Chinese Medicine) LAU Wan Yee Joseph (Surgery)
- 1997-98 A Comparative Investigation of Telomerase Activity in Human Liver with Hepatocellular Carcinoma, Chronic Viral B Hepatitis, Cirrhosis, and Nomal Liver (CU97677)
 - ∠ LIEW Choong Tsek LAU Wan Yee Joseph (Surgery) • LEE Chuen Kwun Joseph (School of Chinese Medicine)
- 1995-96 Studies on the Genetic Alterations of CNS Tumours (CU95614)
 - ✓ NG Ho Keung HUANG POON
 Wai Sin Dolly POON Wai Sang
 (Surgery) WONG Nathalie
 (Clinical Oncology)
- 1995-96 Molecular Genetics of CNS Diseases in Chinese (MD96001)
 - ✓ NG Ho Keung CHEW Eng Ching (Anatomy) HUANG POON Wai Sin Dolly LEE Chuen Kwun Joseph (School of Chinese Medicine)
 LO Kwok Wai PANG Chi Pui Calvin (Ophthalmology and Visual Sciences) POON Wai Sang (Surgery) TO Ka Fai
- 1997-98 Studies on the Molecular Genetics of CNS Tumors (CU97671)
 - ∠ NG Ho Keung HUANG POON Wai Sin Dolly LAM Yeng Po Paula# LO Kwok Wai PANG Chung Sean Jesse POON Wai Sang (Surgery)
- 1997-98 Preliminary Evaluation of Antisense Epidermal Growth Factor Receptor (EGFR) RNA in the Treatment of Malignant Gliomas (MD97110)
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1997-98 "Telomerase Activity in Urinary Bladder Cancer" Does It Correlate with the Biological Behavior? (MD97030) ∠ TO Ka Fai • LO Kwok Wai

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RESEARCH PROJECTS

A Study of Gene Expression of Gonadotropin-Releasing Hormone and its Receptor in Normal and Neoplastic Rat Prostates

- CHAN Leung Franky
- ☐ 1 June 1999
- CUHK Research Committee Funding

The normal development and functioning of prostate gland, as well as its abnormal growth, is dependent on androgens. Based on this concept, it forms the basis for the endocrine therapy of prostate cancers by androgen ablation. Besides steroid hormones, other regulatory factors such as growth factors also play roles in prostate growth. In this proposal, we propose to study the mRNA expression of gonadotropinreleasing hormone (GnRH) and its receptor in normal and neoplastic rat prostates, as well as in human prostate cancer cell lines. The hypothalamic GnRH is a key hormone in the regulation of male reproductive system through its stimulation of the secretion of pituitary gonadotropins (luteinizing hormone and follicle stimulating hormone), which in turn stimulate the synthesis of androgens by testis. This decapeptide hormone (GnRH) has been traditionally thought to be functioning mainly in the pituitary gland through its specific cell-surface receptors on the gonadotrophs. Based on this hormonal relationship, GnRH analogs are developed and used to treat prostate cancers by inhibiting the However, recent studies, pituitary-testis axis. including our preliminary results, have indicated that GnRH and its receptor are expressed in a number of tumors derived from reproductive organs including prostate tumors, suggesting that GnRH may be synthesized at the level of prostate and also GnRH analogs may exert a direct effect on tumors in addition to its inhibitory effect on the pituitary-testis axis. However, the precise roles of GnRH and its receptor in male reproductive system and perhaps in prostate cancer are still unknown. Therefore, we propose in this study to examine the gene expression of GnRH and its receptor in normal and neoplastic rat prostates by using molecular biology approaches. The androgen regulation of gene expression of GnRH and its receptor in prostates will also be studied. This examination of the gene expression of GnRH and its receptor in prostates is important as it provides a precise cellular and molecular basis for the use of GnRH analogs and endocrine regimens in the endocrine therapy of prostate cancers. (MD98093)

Migration of Secondary Neural Crest Cells to the Bowel: A Study of Normal and Congenitally Aganglionic Mutant Mice

- CHAN Wood Yee
- ☐ 1 March 1999
- CUHK Research Committee Funding

Aganglionic megacolon, or Hirschsprung's disease is a congenital disease (1 in 2,000 to 10,000 live births) primarily due to a regional absence or reduction of enteric parasympathetic ganglia in the distal colon. Animal studies have already shown that all the enteric ganglia are derived from a special group of embryonic cells arising from the neural crest of the developing central nervous system (neural tube). However, the migration pathways and the contribution of the secondary neural crest cells (caudal neural crest) to the enteric ganglia of the distal colon in mammals are still unknown. It is proposed in the present study to (1) map out the migration pathways of the secondary neural crest cells in normal mouse embryos; (2) find out the relationship between defective development of the enteric ganglia and the migration of the neural crest cells in congenitally aganglionic mutant mouse embryos; and (3) restore the normal number of enteric ganglia by transplantation of neural crest cells. The results will provide new information on neural crest cell migration in normal and mutant mouse embryos and will also evaluate the feasibility of restoring normal ganglionic development by microsurgical transplantation. (MD98025)

Effect of Drug on the Nuclear Matrix of Hepatocellular Carcinoma Cells in vitro

- ∠ CHEW Eng Ching
- ☐ 1 October 1998
- * CUHK Research Committee Funding

The nuclear matrix is the non-chromatin skeleton of the nucleus. This structure contributes to the shape of the nucleus and regulates various nuclear functions. In addition, nuclear matrix has been established as playing an important role in various nuclear activities as well as carcinogenic processes. Dexamethasone inhibites the growth of cervical carcinoma cells with concurrent induction of epithelial cell differentiation. We have recently reported that the HPV E7 oncoprotein in total cellular protein as well as in nuclear matrix fractions was reduced in response to dexamethasone-treatment. In this study, the effect of dexamethasone on hepatocelluar carcinoma cells *in vitro* will be investigated. (MD98026)

Induction of Retinal Ganglion Cell Regeneration by the Eqineurium of a Peripheral Nerve

- CHO Yu Pang Eric
- □ 1 December 1998

CUHK Research Committee Funding

The inability of injured neurons of the adult mammalian central nervous system (CNS) to regenerate can be partially overcome by stimulating them with a peripheral nerve (PN) environment. Whereas a lot of evidence point to Schwann cells as the active component involved, other cellular elements in the PN remain undefined in their role. In this study, researchers explore the putative role played by one compartment of the connective tissue, the epineurium, in promoting CNS regeneration by an intravitreal transplantation paradigm. This paradigm has been used previously to demonstrate that Schwann cells in the PN act as a source of stimulus for retinal ganglion cells (RGCs) to undergo regenerative sprouting. Their preliminary evidence suggests that in the absence of Schwann cells, the isolated epineurium can stimulate RGC sprouting when transplanted intravitreally. This study will examine the characteristics of sprouting as induced by the epineurium and to elucidate some of the possible mechanisms associated with the stimulus. (MD98027)

The Influence of Mature Astrocytes on the Survival and Regeneration of Adult Retinal Ganglion Cells

- ∠ CHO Yu Pang Eric
- ☐ 1 January 1999
- * Research Grants Council

It is now known that an important factor to account for the failure of axons in the adult central nervous system to regenerate is the glial environment. Of the 3 major types of glial cells found in the central nervous system, oligodendrocytes and microglia have both been implicated to have an inhibitory effect on regeneration. The status of mature astrocytes, however, is still unclear since both inhibitory and supportive activities have been reported for this glial cell. We sought to clarify this issue by establishing a model to look at the interactions of adult astrocytes isolated from the optic nerve, with retinal ganglion cells whose axons normally run in the optic nerve and are damaged by lesions of it. We found that when optic nerve astrocytes are co-cultured with the adult retina, extensive regeneration of retinal ganglion cell axons occurs. This suggests that adult astrocytes are supportive of axonal regeneration. In this proposed study, we would like to characterise the factors which are involved in the promotion of regeneration by astrocytes, and to see if similar benefits could be obtained when the astrocytes are re-introduced back into the damaged central nervous system. (CU98265)

Male Accessory Sex Glands and Abnormalities in Embryo Development: The Role of Growth Arrest Specific 6 (Gas6) Gene

- ☐ 15 September 1998
- CUHK Research Committee Funding

In most male mammals, the accessory sex glands (ASG) comprise the paired seminal vesicle, coagulating gland, dorsolateral prostate, ampullary gland (AG) and the ventral prostate (VP). Even though secretions from these glands have been reported to have effects on sperm motility and suppression of immunogenicity of the ejaculate in the female genital tract, our studies in the golden hamster model has established that these glands, in particular, the ampullary gland and ventral prostate, are essential for preservation of reproductive efficiency by exerting an effect "after fertilization", thus ensuring proper development of embryos. Up to this point, researchers data suggest that retardation in embryonic development may be seen as early as 48h post coitus (p.c.). Recently, they observed delayed entry into the S-phase of the first cell cycle and failure of some blastomeres to express proliferating cell nuclear antigen (PCNA) leading to structural malformation of implanting embryos. Researchers hypothesize that growth of some of the bastomeres is arrested. As part of their effort to elucidate the underlying cause of this abnormality, they propose to examine the expression pattern of growth arrest specific 6 (gas) gene and its Axl receptor in the experimental embryos. (MD98029)

Ampullary Gland, Ventral prostate and Embryo Implantation

- ∠ CHOW Pak Ham Patricia O Wai Sum*
- ☐ 1 October 1998
- * Research Grants Council

Beyond the epididymis, mammalian spermatozoa are exposed to products from male accessory sex glands (ASG) in the form of seminal plasma. Research on the function of each of these glands has been hampered by the extreme complexity of their biochemistry and interactions between individual components. Functional studies performed on whole animals have shown that in all common laboratory rodents, the presence of one or more of the ASG is essential for preservation of reproductive efficiency under natural mating conditions. In the hamster model, we have demonstrated that this is achieved, not through interference with fertilizing ability of sperm, but by ensuring proper embryonic development after fertilization. While we believe that the active agent(s) is (are) imparted onto the ovum at the time of gamete fusion via the sperm, an

understanding of how embryonic development is disrupted will give us a clue as to how the effect is brought about. We hypothesize that death of embryonic cells by apoptosis is involved and that this will ultimately lead to retardation of development and asynchrony with the maternal environment. We propose to verify this hypothesis by exploring the possible occurrence of apoptosis as well as examining events such as angiogenesis and invasion of endometrial tissues at implantation. The outcome of this study may be useful in improving success rates of assisted reproductive technology in clinical, agricultural and veterinary practice. (CU98030)

Role of Fibroblast Growth Factor Isoforms in the Development of the Mammalian Limb Musculature

- ∠ LEE Ka Ho Kenneth PAULIN Denise*
- ☐ 1 January 1999
- * Research Grants Council

In this proposed study, we will examine the development of the skeletal musculature in the limbs of developing mouse embryos. Specifically, we will investigate the role cell migration plays in muscle development. This will be achieved by implanting transgenically labelled muscle cells into the forelimbs of 11.5 day mouse embryos, exo uterolly. We will also construct a fate map of the 11.5 day limb by specifically labelling predetermined sites in the limb with a fluorescent marker. In both experiments, the operated embryos will be allowed to develop in the uterus for 1-3 days before examination under a confocal microscope. The fate map will allow us to comprehend how the limb musculature is formed at the cellular level and how also other tissues, such as cartilage and tendons, are established. Once it has been established that muscle cell migration is involved in skeletal muscle development, we will proceed to examine whether the apical ectodermal ridge (AER, a highly specialized thickening of the ectoderm found at the distal tip of the limb bud) play a role in regulating this migration process. We will again transplant transgenic muscle cells into the mouse limb but will also remove the AER. If the AER is important for maintaining muscle cell migration, we would expect this migration to be inhibited. In addition, we will determine whether the interaction between the AER and myoblast is mediated by Fibroblasts growth factor isoforms (Fgf-2, Fgf-4 and Fgf-8). (CU98273)

Regulation of Apoptosis and Differentiation by a Novel Gene BRE that Modulates TNF-a Action

∠ LEE Ka Ho Kenneth • CHAN Yeuk Hon John (Clinical Oncology) • YEW Tai Wai David

- ☐ 1 June 1999
- CUHK Research Committee Funding

This research is aimed at elucidating the function of a novel gene BRE which we have recently found to induce apoptosis or cellular differentiation. Enhanced expression of BRE was also found in embryonic cells of the mouse, that were about to undergo apoptosis. BRE binds to the p55-tumor necrosis factor- α receptor-1 (TNFR1), and inhibits the activation of the transcriptional factor NF- κ B. By blocking the survival pathway induced by NF- κ B and facilitating cell death, BRE may play a very important role in regulating specific actions of cytokines in various pathological and physiological conditions. We propose the followings:

- (1) to further analyze if the altered expression of *BRE* and NF-κB is associated with apoptosis or differentiation in cells from mouse embryos,
- (2) in cells of Alzheimer's Disease and neurodegenerations with immunohistochemistry, Northern blotting and *in situ* hybridization; and
- (3) to determine if transfection of the *BRE* gene could induce apoptosis and/or differentiation in embryonic cells.

Since many of the cytokines are being used clinically, this modulator of TNF may have practical applications soon in regulating some of the adverse actions of cytokines in immunological function, osteopetrosis and osteoporosis, muscle damage and healing, anti-cancer and anti-aging approaches. (MD98094)

An Experimental Study to Determine the Role of Sonic Hedgehog (Shh) in Controlling Neuronal Differentiation in the Neural Tube

- ☐ 1 September 1998
- CUHK Mainline Research Scheme

The main aim of this study is to determine why the secondary neural tube fails to undergo neuronal differentiation.

During mammalian embryogenesis, the neural tube, which is the primordium of the central nervous system, is formed largely by the process of primary neurulation. However, caudal to the future lumbosacral region, the neural tube is formed by a distinct process, secondary neurulation. Interestingly, the lumbosacral region is the most common site of spina bifida. The recent results have shown that although the secondary neural tube initially expresses several neuron precursor genes in domains equivalent to the primary neural tube, it does not undergo further differentiation and subsequently regresses.

The notochord is the primary source of Sonic hedgehog (Shh), a secreted signaling molecule critical for the correct differentiation of the overlaying neural tube. The researchers have observed an intriguing difference in the relative position of the notochord to the primary and secondary neural tubes. The notochord is intimately associated with the primary neural tube, but is physically separated and located at a distance from the secondary neural tube. This finding leads them to propose the hypothesis that absence of neuronal differentiation may be due to a lowering in the level of Shh protein that can reach the secondary neural tube from the notochord because of the gap between these two tissues. The main objective of this project is to test this hypothesis by raising the local concentration of Shh both in vitro and in vivo to determine whether this can drive neuronal differentiation in the secondary neural tube. (MD98007)

A Study to Determine the Role of Glutamic Acid Decarboxylase (GAD) in the Pathogenesis of Caudal Agenesis Associated with Diabetic Pregnancy

- ☐ 1 October 1998
- ❖ CUHK Research Committee Funding

Caudal agenesis is a congenital malformation which is highly associated with diabetic pregnancy. The reason for this linkage is unclear. Recently, by studying a mouse model of caudal agenesis established in the P.I.'s laboratory, the gene glutamic acid decarboxylase (GAD), which has a primary role in the synthesis of y-aminobutyric acid (GABA), has been identified. It was found that GAD specifically expressed in the tail bud that contains precursor cells for forming various caudal structures of the embryo, but was switched off in embryos that developed caudal agenesis. Since it has been suggested that the development of insulin-dependent diabetes mellitus is due to destruction of islets cells in the pancreas mediated by autoantibodies against GAD, this leads the researchers to propose a hypothesis that caudal agenesis is most common in babies of diabetic mothers because maternal autoantibodies against GAD will cross the placenta, bind to and inhibit the function of GAD in the tail bud of the embryo. The effect is similar to switching off the GAD gene in their mouse model that develops caudal agenesis. The main aim of this study is to test the above hypothesis using mouse as an animal model. The specific objectives include:

- (1) *In vitro* exposure of the mouse embryo to GAD antibodies to determine whether this will lead to caudal agenesis;
- (2) Immunohistochemical detection of GABA to determine if it is synthesized by GAD in the tail bud of the embryo.

(MD98028)

MPTP-Induced Neurotoxicity in Metallothionein-I, II Knock Out Mice

- □ 7 April 1999
- CUHK Research Committee Funding

Metallothionein (MT) is a low molecular weight, cysteine-rich, heavy metal-binding protein. The MT-I and MT-II isoforms are present in many tissues, in the brain it is located in the astrocytes. The MT-III isoforms occur only in Zn-rich neurons in the brain. There are several physiological functions of MT, this include metal detoxification and sequestration, the control of zinc and copper metabolism, and free radical scavenging. There is increasing evidence that excessive production of free radicals is involved in the pathogenesis of Parkinson's Disease (PD). PD is characterized by the decrease in dopamine (DA) in the striatum and the massive cell loss of DA neurons in the substantia nigra (SN) of the brain. A selective 1-methyl-4-phenyl-1, 2, neurotoxin 3. tetrahydropyridine (MPTP) had been shown to produce pathologies and syndromes in non-human primates and mice which resembles that of PD. MPTP has been widely used as a PD model in the studies on the etiology of this disease.

Given the antioxidant properties of MT, the present study aims to examine the role of MT in its ability to protect against MPTP-induced neurotoxicity. MT-I, II knock out mice and their wild type 129/Sv controls will be used to ascertain whether the lack of MT will render the brain more susceptible to MPTP-iniduced oxidative injury. Animals will be injected with a single dose of 30mg/kg MPTP s.c. All animals will be sacrificed at 1, 3, 7 days post-treatment. Different brain regions will be dissected, the DA and metabolite contents as well as the no. of tyrosinehydroxylase positive DA cell loss will be used as an index of MPTP-induced injury. The level of MT protein and levels of the antioxidant, glutathioine will be measured. Furthermore, nitric oxide (NO) synthase activity as well as peroxynitrite formation will also be examined to elucidate whether MT can inhibit the generation of NO. (MD98095)

Neural Plasticity in the Auditory Midbrain: A Combined Histological and Electrophysiological Study

- □ 1 November 1998
- CUHK Research Committee Funding

Abstract: It has long been known that stimulation of an area in the nervous system during development may affect the architecture and physiological function of that area. In this study, we will analyse the physiological and anatomical changes in the developing auditory midbrain of the neonatal rat subsequent to a pure tone exposure of 4 kHz, 60 dB SPL, 12 hr/day during postnatal days 7-14. Three weeks later, single cell recordings of the neurons in the inferior colliculus will be obtained. The pattern of response and the proportion of FM and AM sensitive cells will be analysed. Anatomical and immunohistochemical studies will typify the morphological changes, the density and distribution of excitatory and inhibitory neurons. This study will determine the neuroplastic alterations in the developing auditory midbrain as a result of early sound exposure. This is a collaborative research project in which the physiological experiments will be performed in Taiwan and the brain specimens will be fixed and mailed to our laboratory for immunohistochemistry and golgi silver studies. (MD98030)

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

Edition	<u>Title/Investigators</u>
1995-96	A Study of Glycoproteins and Extracellular Matrix of the Normal, Dysplastic and Neoplastic Prostates of the Noble Rat (CU95622) ∠ CHAN Leung Franky • HO Shuk Mei*
1997-98	A Study of Prostatic Secretory Protein of 94 Amino Acids Expression in Normal, Castrated and Hormone-Treated Rat and Mouse Prostate Glands (MD97035) CHAN Leung Franky • XUAN Jim W.*
1995-96	Axon Guidance in the Development of Mammalian Retinofugal Pathways (CU94643)
1995-96	Investigations of the Cellular Mechanisms Underlying the Turning of Uncrossed Retinal Axons at the Midline of the Optic Chiasm(MD95110) CHAN Sun On
1996-97	Identification of the Molecular Determinants in the Retina that Govern Axon Pathfinding in the Chiasm of Mammals (CU96623) CHAN Sun On
1997-98	Mechanism of Glutamate Induced Neurotoxicity in Retina (MD97032)

- 1997-98 The Role of SPARC, an Extracellular Matrix-Associated Protein, in Ovarian Tumor Growth and Invasion (CU97610)

 ∠ CHAN Wood Yee MOK S. C.*
- 1997-98 The Role of Endothelin-1 in the Development of the Mouse Embryo (MD97033)
 - ∠ CHAN Wood Yee
- 1997-98 Development of a Novel Diagnostic Kit for Early Detection of Human Cervical Cancer: Identification and Generation of a Monoclonal Antibody (MD97003)
 - ∠ CHEW Eng Ching LEE Chuen Kwun Joseph (School of Chinese Medicine) CHEW CHENG Siew Boon (Physiology) LIU Le-he*
- 1997-98 Application for Development of a Novel
 Nuclear Matrix Laboratory for Both
 Research and Teaching at Prince of
 Wales Hospital (MD97008)

 CHEW Eng Ching
- 1996-97 Long Term Culture of the Whole Retina of Adult Hamsters as a Model to Study Regeneration of Retinal Ganglion Cells (CU96632)
 - CHO Yu Pang Eric
- 1996-97 The Ampullary Gland, Ventral Prostate and Embryogenesis (BL96033)
 - ∠ CHOW Pak Ham Patricia O Wai Sum*
- 1996-97 Male Accessory Sex Glands and Fertility: The Role of Apoptosis and Angiogenesis During Early Development (BL96031)
 - ∠ CHOW Pak Ham Patricia

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 Xianjin#
- 1996-97 Neurotoxicity of Type I Ribosomeinactivating Proteins (BL96032)
- 1996-97 The Role of BMP and MSX Genes in the Control of Programme Cell Death in the Limbs of Normal and Hammertoe Mutant Embryos (MD96122)

1997-98	∠ LEE Ka Ho Kenneth • MUNEOKA Kenneth* Bmp2 and Alk6 Gene Interaction During Programme Cell Death in the Limbs of Mouse Embryos (MD97036) ∠ LEE Ka Ho Kenneth • MUNEOKA Kenneth* • NGO-MULLER Valerie*	1996-97 1997-98	The Effects of Prenatal Heroin Exposure on Postnatal Brain Development and Behavior in Rats (CU96615)
1996-97	Mechanisms Underlying the Immunomodulatory and Antitumor Activities of Selected Lectins (CU96667) ∠ LIU Wing Keung Ken • NG Tzi Bun (Biochemistry) • OOI Vincent E. C. (Biology) • CHANG Shu Ting (Biology)	1994-95	Apoptosis in the Developing, Diseased and Aging Nervous Systems (MD95061) YEW Tai Wai David • CHAN Wood Yee • CHO Yu Pang Eric • DIXON John Stuart# • LEUNG Ping Chung (Orthopaedics & Traumatology) • SHUM Sau Wun Alisa • GOSLING John Arthur# •
1997-98	The Effect of Mushroom Extract on the Tumor Vascular System in Inbred Mice - A Scanning Electron Microscopic Study (MD97102)	1995-96 1997-98	YU Mang Chung Aging Changes in the Human Central Nervous System (MD95185) Z YEW Tai Wai David Limbal Stem Cell Identification in a
1997-98	A Study of the Molecular Basis of Diabetic Embryopathy and Interaction of Maternal Diabetic Milieu with Genetic or Environmental Factors (CU97691) SHUM Sau Wun Alisa • COPP A.		Rabbit Model (BL97007) YEW Tai Wai David • AU Yue Kong (Ophthalmology and Visual Sciences)#
1997-98	J.* The Role of Wilms' Tumor Gene (WT1) and Apoptosis in the Development of Renal Agenesis (MD97106) ✓ SHUM Sau Wun Alisa • HASTIE Nicholas D.* • TSE K. W. Herman • MENKE Aswin*	1997-98	Microglial Reaction Pattern in Normal and SCID (Severe Combined Immunodeficient) Mice (MD97103) YEW Tai Wai David • SCHUMACHER U.* • LORKE D. E.*

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RESEARCH PROJECTS

Cloning of Common Carp Metal Regulatory Element Binding Proteins

- CHAN King Ming
- ☐ 1 January 1999
- **&** CUHK Research Committee Funding

To understand how metal ions regulate gene expression, fish metallothionein (MT) gene promoter is used as a model to delineate the molecular mechanism of how divalent metal ions act on cisacting elements in the 5'-flanking regions of MT genes. The researchers have obtained MT gene fragments with their 5' flanking regions, from different fish species including common carp, tilapia, and zebrafish. The 5' flanking regions of these MT genes are being subcloned into reporter gene system to study their function and responsiveness to heavy metal ions in primary cultures of fish hepatocytes. Among these MT genes, the 5' flanking region of the common carp MT gene is well characterized in this laboratory, and is now confirmed to exert its metal induction via several cis-acting metal regulatory elements (MREs). The MRE binding factors (transacting elements) are more complicated than they anticipated, with studies in mouse and human MT genes recently revealed multiple MRE binding factors. Several models have been proposed to explain how metal ion controls MT gene transcription so far with limited information from mice. The researchers used electrophoretic mobility shift assay to confirm that all the MREs could bind to protein components of nuclear extracts prepared from both un-induced and zinc- induced carp livers and hence support the repression model, among several other models, of molecular mechanism on how metal ions regulate gene transcription. The identities and functions of the fish MRE binding proteins will provide new insights on how metals regulate MT gene transcription in fish, and perhaps in the future, on whether MT gene transcription could be related to metal tolerance in different fish species. Screening of a common carp liver cDNA library (un-induced) using oligonucleotides of MREs have isolated five putative clones which express protein(s) to bind the relevant MRE (MREc, proximal MRE to TATA box). Using one of the positive clones as probe, the researchers have further isolated 24 associated clones from the same library. The first goal of this proposal is thus to reveal the nucleotide sequences (full length) of all the isolated cDNAs for MRE-binding factor(s) and to study their binding activities with different MREs in the presence of different metal ions. The isolated clones express protein that bind strongly with one of the MREs, MREc, and thus other MREs must have other specific binding factors likely to be induced by metal ions but yet to be identified.

Therefore, the second goal of this proposal is to isolate metal inducible cDNA clones expressing proteins to bind with other MREs in the common carp MT gene promoter region. (BL98005)

IGF Gene Expression Studies in Fish

- ∠ CHENG Hon Ki Christopher
- ☐ 1 January 1999
- CUHK Research Committee Funding

Previous research work from the researchers' laboratory includes the cloning of the complementary DNA (cDNA) and the gene of a particular type of IGF from common carp, a fish species widely cultured in southern China as well as in other parts of the world. Based on their ground work, the researchers propose to study the molecular biology of IGF gene expression in fish. The first objective is to further their work on the cloning of the cDNAs and genes of other types of IGFs in common carp. The second objective is to study the regulation of IGF gene expression in common carp, both in vivo and in Knowledge thus gained on the gene multiplicity and the regulation of IGF expression would contribute significantly towards the basic understanding and expand the application potential of these important growth factors in fish. (BL98006)

Biochemical Characterisation of Mas Oncoprotein and its Interactions with RAMP

- ∠ CHEUNG Wing Tai POYNER David*
- ☐ 1 April 1999
- UK/Hong Kong Joint Research Scheme, the British Council

The mas oncogene was originally isolated from a human tumour, and sequence analysis indicates that it encodes a protein consisting of seven hydrophobic segments. Functional studies have suggested that the mas oncogene enhances angiotensin responses, but the molecular mechanism and its physiological roles are yet to be determined. In the present study, efforts will be made to elucidate the functional roles of the mas oncogene and identify the cellular proteins that interact with it. In particular we will examine possible interactions between mas, the angiotensin receptor and members of the RAMP family; proteins which have been shown to modulate the expression and binding properties of other receptors. (BL98030)

Glucose transporter as an anti-tumour target

- ☐ 1 September 1998

* Research Grants Council

Cellular glucose uptake is mediated by glucose transporter proteins. In humans, six glucose transport isoforms have been identified. They exhibit tissuespecific distribution, but overexpression of isoforms type 1 and 3 has been observed in many types of cancers. Recently, overexpression of type 5 isoform which is primarily a fructose transporter has also been found in breast cancer. Insofar as cancer cells depend mainly on glucose for energy supply and for growth, the overexpression of glucose transporter confers upon them a decided advantage in their competition for glucose supply vis-a-vis their normal counterparts. In the present study, we will examine the possibility of developing a new therapeutic mode in cancer management by suppressing the active glucose transport system of the cancer cells. Antisense nucleic acids of glucose transporter types 1,3 and 5 will be used to effect down-regulation of glucose transporter genes. Since glucose transport is feedback regulated by phosphoribosyl pyrophosphate (PRPP), the PRPP-enhancers will be tested for their probable anti-cancer activities. Furthermore, the effects of some newly developed glucose transport inhibitors on the cancer growth will also be scrutinized. The effects of the above-mentioned agents on the growth of multidrug resistant cancers will be examined. It is hoped that from this study a novel anticancer mode using the glucose transport system of cancer cells as a target will be developed. (CU98148)

Mechanistic Study of the Anti-tumour Effect of Step-down Hyperthermia

- ☐ 1 October 1998
- **&** CUHK Research Committee Funding

Hyperthermia is a new treatment modality by applying heat to the tumour sites. Whole body heating or heat generated by microwave or by laser have been on trials in treating various tumours. Like other anti-tumour regimens, prolonged hyperthermia (≥43°C) also exhibits adverse side-effects. Recently, a hyperthermic protocol on cultured tumour cells named "step-down hyperthermia (SDH)" has been introducted. In SDH, a relatively short exposure to a high temperature (≥43°C) sensitizing treatment increases the heat cytotoxic effect of a lower temperature (≤42°C) test treatment on tumour cells. In present project, the cytotoxic mechanism of SDH will be elucidated using cultured human hepatoma (HepG2) and leukemia (HL-60) cell lines and mice bearing Ehrlich ascites tumour cells. The probable effects of SDH on the inhibition of induction of heat shock proteins or antioxidant enzymes in tumour cells will be tested. The actions of SDH on the changes of free radical induction and glucose

transport system in tumour cells will also be examined. The results might shed light on a better design in treatment protocol when step-down hyperthermia is applied to patients in future. (MD98031)

Organization of 8th International Symposium of Society of Chinese Bioscientists in America

- FUNG Kwok Pui TSANG David Sau Cheuk
 (Biochemistry) WONG Ricky* WAYE Mary
 Miu Yee KONG Siu Kai (Biochemistry) •
 CHAN King Ming FONG Wing Ping
 (Biochemistry) TSUI Kwok Wing WONG
 Raymong* CHAN Vivian* CHUNG
 Stephen* WU Rudolf* CHAU F. T.*
- ☐ 1 February 1999
- ❖ Industrial Support Fund, Industry & Technology Development Council

There is increasing interest among industralists in Hong Kong on drug manufacturing. Drugs such as Traditional Chinese Medicine (TCM), generic antibiotics and vaccines are important fields to be developed in Hong Kong. R & D personnels in the industrial and acadmic sectors in Hong Kong are eager to be kept abreast with recent research in health issues, especially to understand the etiology, diagnosis and treatment of diseases which are common in Hong Kong, for example, hepatoma, nasopharyngeal cancer, avian flu, hepatitis etc., so nutraceutical intervention, diagnostic development and drug treatment can be designed. The up-to-date information from overseas are most important for Hong Kong industrialists to determine directions for future investments Biotechnology industry. In order to promote the dialogues among local industrialists and overseas research experts, Department of Biochemistry, The Chinese University of Hong Kong and Society of Chinese Bioscientists in America (SCBA) propose to organize the 8h International SCBA symposium in the Convention Centre of Hong Kong from August 14-19, 1999. Renowned researchers including Nobel Laureates will be invited to deliver lectures. Industrialists and R & D personnels in Hong Kong and the Mainland will be invited to participate. It is expected that this Symposium can upgrade the standard in manufacturing drugs and other Biotechnology industries in Hong Kong. (BL98024)

The Role of Mitochondria in the Response of Cells to Anticancer Drugs

- □ 1 October 1998
- CUHK Research Committee Funding

Two sublines, A5A and A10A, were selected for doxorubicin resistance from human squamous carcinoma A431 cells. Genes differentially expressed in the parent and the drug resistant cells were identified by RT-PCR based differential display and confirmed by Northern blot analysis. One of the clones was found to have sequence homology with part of the cytochrome C oxidase subunit II gene and the other two clones were homology with NADH dehydrogenase 3 gene. These two genes were downregulated in the doxorubicin resistant cells. Mitochondria are currently believed to play a central role in the process of apoptosis. Since both cytochrome C oxidase and NADH dehydrogenase are mitochondrial enzymes, it is therefore hypothesized that mitochondrial enzyme complexes may be important in determining the response of cells to anticancer drugs. In this proposal, the activity and the expression of mitochondrial enzyme complexes will be examined in the parent and the drug resistant Furthermore, the influence of A431 cells. doxorubicin on mitochondrial enzyme activity and gene expression in relation to drug induced apoptosis will also be measured. The results may confirm the important role of mitochondria and its enzyme complexes in drug resistance and apoptosis. (BL98008)

Isolation and Characterization of Ribosome -Inactivating Proteins with Novel Features

- NG Tzi Bun
- ☐ 1 September 1998
- * Research Grants Council

Ribosome-inactivating proteins (RIPs) are a group of proteins which can attack ribosomes and catalytically cleave the N-glycosidic bond at A4324 in rat 28S RNA resulting in inhibition of protein synthesis. The other biological actions of RIPs included antiproliferative, antitumor, immunosuppressive, antifertility, antiviral and anti-human immunodeficiency virus (anti-HIV) activities.

RIPs are divided into type I (consisting of a single chain) and type II (consisting of an A chain with RIP activity and a B chain with lectin activity which facilitates binding to galactose-containing receptors on cell surface and subsequent entry into cells). Type I RIPs have a molecular weight (MW) in the range of 26-32 kilodaltons (kDa). Type II RIPs and around 60kDa in molecular weight. Recently, a group of Chinese investigators in Shanghai reported the isolation of small RIPs with a molecular weight of approximately 10kDa from the seeks of the bitter ground "Momordica Charantia" and the sponge ground "Luffa cylindrica." The small RIP from the latter plant was structurally very dissimilar from the MW 28 kDa RIP from the same plant. It is deemed worthwhile to isolate and further characterize this novel type of RIP from the seeds of plants belonging

to Family Cucurbitaceae. Another objective of the proposed project is to isolate and characterize RIPs from plants belonging to Family Papilionaceae. This family has not previously been examined. (CU98331)

Characterization of the Human 14-3-3 Epsilon Protein

- ☐ 1 January 1999
- CUHK Research Committee Funding

14-3-3 proteins belong to a highly conserved family of small proteins that associated with cell cycle and cell death regulators, oncogenes, and signaling molecules. A number of functions have been proposed for 14-3-3 proteins, including inhibition of protein kinase C (PKC), activation of Raf-1 protein kinase, regulation of the biosynthesis of neurotransmitters and determination of the timing of cell division. Since 14-3-3 proteins associate with a number of proto-oncogenes and oncogenes, they might play an important role in tumor development. To date, 14-3-3 proteins are suggested to be a multifunctional regulator of cellular signals mediated by two types of Ca²⁺-dependent protein kinases: PKC and calmodulin-dependent protein kinase (CaM kinase). We have cloned the epsilon isoform of human 14-3-3 proteins (h1433ɛ) from a heart cDNA library. We have also mapped the h1433 ϵ gene to human chromosome 17p13, which contains a number of cancer related loci and a common hot spot for translocation and mutation in breast cancer. In this project, we plan to study the structure and functions of h1433ε. The effect of h1433ε on the activity of CaM kinase will be determined. To study the change in cellular localization during the cell cycle, a fusion construct with green fluorescent protein will be prepared. Finally, the h1433e gene will be finemapped using radiation hybrid panel to determine whether it is located within any well-established cancer loci. These studies should provide useful information on the role of 14-3-3 proteins in tumor development and cell regulation mediated by calmodulin and CaM kinase. (MD98032)

The role of pre-synaptic motor neuron acetylcholinesterase in neuromuscular synaptogenesis

- ☐ 1 September 1998
- * Research Grants Council

Acetylcholinesterase (AChE. EC 3.1.1.7) is a major enzyme of the neuromuscular synapse responsible for the rapid hydrolysis of acetylcholine released from the nerve terminals. This enzyme is very important in the synaptogensis of neuromuscular junction as exemplified by the differential expression of various molecular forms of acety lcholinesterase which are highly sensitive to neural activities. The elucidation of the regulation of AChE expression in neuromuscular junction is therefore crucial for the understanding of neuromuscular degenerative diseases such as muscular distrophy and muscle paralysis. Conventionally, the postsynaptic expression of AChE in muscle myotubes are thought to be the prominant species in the neuromuscular junctions, and their expression in muscle coincides with the stages in neural development. However, several lines of evidence indicate that the presynaptic motor neurons are able to synthesize and secrete AChE at the neuromuscular junctions. contribution of presynaptic AChE to synaptogenesis is presently not very well characterized. In this project, we propose to characterize the expression of various forms of AChE in presynaptic motor neuron during different stages of neuromuscular development and muscle degeneration. The results of this study should provide further insight into the role of presynaptic AChE in vetebrate synaptogenesis. (CU98140)

The Biological Significance of the Adenine Auxotrophic Heterozygosity in the Obligate Diploid Fungus Candida Albicans

- □ 1 November 1998
- ❖ CUHK Research Committee Funding

As one of the remaining enigmas in mycology, a number of natural isolates of the obligate diploid fungus Candida albicans can be induced to give arise strain-specific, recessive auxotrophic mutants at the frequency as high as few percent of total surviving cells. Recently the researchers have discovered that one of such isolates C. albicans CA12 is heterozygous for one of the purine biosynthesis genes, ADE2. The parental strain CA12 carries one copy of wild-type allele ADE2 and one copy of mutant allele ade2 which bears a 1.1 kb deletion in its promoter and coding regions; while all of the adenine auxotrophic derivatives of CA12 examined carry the mutant allele only. Their discovery has therefore presented the strongest and most direct proof to demonstrate that in those strains that prone to recessive mutants, one of the two homologous alleles involved was congenital defective and the occurrence of auxotrophic mutants was due to the illegitimate segregation of the mutant allele.

Having also tailored and improved the existing genetic and molecular biology techniques for the study of the fungal heterozygosity, the researchers believe that they are in an advantageous position to explore the physiological significance of this intriguing and fundamental biological process. They plan to characterize (1) the distribution and frequency of adenine heterozygosity in the clinical isolates of *C. albicans*; (2) the genetic mechanism that preserves *ade2* allele; and (3) the competitiveness of the fungal strains heterozygous at *ADE2* allele. (BL98011)

Establishment of a Catalogue of Genes Expressed in Human Liver Cancer and Mental Diseases

- WAYE Mary Miu Yee LEE Cheuk Yu FUNG Kwok Pui TSUI Kwok Wing JOHNSON Philip James (Clinical Oncology) LIEW Choong Tsek (Anatomical & Cellular Pathology) XUE Hong* SMITH Michael* LING Victor*
- □ 1 July 1998
- ❖ Industrial Support Fund, Industry & Technology Development Council

This project aims at establishing a catalogue of genes expressed in human liver cancer and mental diseases. It will be an additional resource incorporated into the Hong Kong Bioinformatics Centre. A project to be conducted in collaboration with the British Columbia (BC) Cancer Agency/BC Cancer Foundation, it will provide a central resource for developing cancer diagnosis and treatment modalities for the Hong Kong biotechnology community. The deliverables will be a catalogue of genes from samples of patients with liver cancer or mental diseases. The objectives include identification of genes that are useful as markers of liver cancer and mental diseases. The target users will be industrial partners who are interested in developing services or diagnostic kits for individuals with liver cancer or mental diseases or individuals who have genes predisposing them to these diseases. Those industrial partners can market their kits to health care providers, independent laboratories or organizations who are capable of performing the tests in cases where the complexities of the assays and the interpretations require skills not available to ordinary consumers. The benefits of predictive genetic tests for liver cancer and mental diseases are substantial, involving a target consumer population of more than 13 million. Thus new markers for the prediction of development of liver cancer and mental diseases are urgently needed for this enormous market. The net amount requested is \$9,906,000 over a three year period. (MD98069)

Molecular Study of FHL2 – a Four and a Half LIM-Domain Protein Specifically Expressed in Heart

- WAYE Mary Miu Yee
 LEE Cheuk Yu
 FUNG Kwok Pui
 TSUI Kwok Wing
- ☐ 1 November 1998

CUHK Research Committee Funding

LIM domain protein family is an important new family of proteins which carries a cysteine-rich zincbinding domain called the LIM domain. This protein family is found in mammals, amphibians, flies, worms and plants, and they may be involved in cell identity, differentiation, growth control and developmental regulation. While the researchers sequenced more than 7000 ESTs from a human heart cDNA library, they have cloned and characterized five cDNAs coding for novel LIM-only proteins. One of them-FHL2 is of particular interest because it is expressed specifically in the human heart. They have used a yeast two-hybrid system and discovered two interesting protein partners that interact with FHL2. They have raised an antibody against the FHL2 and demonstrated by in vitro binding assays that FHL2 can bind to its protein partners. They plan to use site-directed mutagenesis to delineate the domains involved in interaction of FHL2 and its protein partners. In situ hybridization. immnohistochemical studies and Green Fluorescent Protein (as a tag) will be used to study the localization of FHL2 and protein/protein interaction in both fixed and living cells. By understanding the molecular mechanisms of gene regulation in heart development, we hope to improve the diagnosis and treatment of heart diseases. (BL98012)

Study on the Expression of LIM-Domain Proteins in Human and Animal Myocardial Tissues

- WAYE Mary Miu Yee
 ZIMMERMANN Rene*
 Andreas KAMPMANN*
- □ 1 March 1999
- Germany/Hong Kong Joint Research Scheme

The LIM domain protein family is an important new family of proteins which carries a cysteine-rich zincbinding domain called the LIM domain. This protein family is found in mammals, amphibians, flies, worms and plants, and they may be involved in cell differentiation, growth control identity. developmental regulation. hCLIMl is a LIM domain protein originally cloned in our laboratory while we sequenced more than 7000 Expressed Sequence Tags (ESTs) from a human heart cDNA library and previous works in our laboratory found that it is associated with the cytoskeleton (Kotaka et al, 1998). Other researchers have shown that the rat homologue CPL36 is reduced during hypoxia and therefore it is interesting to find out whether the human CLIMl is changed in its expression in heart diseases such as dilated cardiomyopathy or in experimental system such as the pig myocardium subjected to coronary microembolization. We plan to study the hCLIMI mRNA levels by Northern blot analysis and the protein levels by immunohistochemistry. Other LIM-

domain proteins found during the sequencing process include FHL1 (Lee et al, 1998), FHL2 (Chan et al, 1998), and FHL3 will also be studied. These proteins are characterized by four and a half LIM-domains and information about their gene localization in the human chromosomes and interacting protein partners have been obtained in Dr. Waye's laboratory. (BL98034)

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

Title/Investigators

Edition

Lamon	Title/investigators		
1997-98	Molecular Mechanism of Metallothionein Gene Regulation (BL97018)		
1990-91	Comparative Endocrinology of Prolactin, Growth Hormone, and Their Receptors (BP88031)		
1996-97	Structure-function Studies on Fish Growth Hormone and Prolactin: A Protein Engineering Approach (CU96320) CHENG Hon Ki Christopher • CHAN King Ming • NG Tzi Bun		
1997-98	Xanthine Oxidase: Enzyme Inhibition Studies (BL97019)		
1997-98	Oligonucleotide Combinatorial Library: Application in Diagnostic and Therapeutic Drug Development (BL97005) CHEUNG Wing Tai • HO Walter K. K. (Biochemistry) • WAN Chi Cheong David		
1995-96	Mechanism of Combination Treatment of Tumour Necrosis Factor-α and Hyperthermia on Tumour Cells (CU95316) FUNG Kwok Pui		
1996-97	Formulation of Preservation Solution for Transplantation of Heart and Other Organs (MD96002)		
1996-97	Search for Treatment Strategies to Enhance the Cytotoxic Effect of Free- radical-mediated Antitumour Drugs on Tumour Cells and to Lower Their		

	Adverse Side Effects on the Host (CU96311) FUNG Kwok Pui		 ✓ NG Tzi Bun • WONG Nai Ching Henry (Chemistry) • FONG Wing Ping (Biochemistry) • WAN Chi Cheong David • YEUNG Hin Wing
1996-97	Tumour Necrosis Factor-α: Biological Activities and Action Mechanism in		(Biochemistry)#
	Health and Diseases (MD96127)	1997-98	Natural Products with Anti-Human Immunodeficiency Virus Activity (CU97688)
	Ki Christopher • CHOY Yuen Min (Biochemistry) • KONG Siu Kai (Biochemistry) • KWOK Tim Tak • LEUNG Kwok Nam (Biochemistry)		∠ NG Tzi Bun • WAN Chi Cheong David • FONG Wing Ping (Biochemistry) • Yeung Hin Wing*
	WAN Chi Cheong David	1997-98	Biological Activities of Milk Proteins (MD97038)
1997-98	Establishment of a Hong Kong Bioinformatics Centre (BL97001)		∠ NG Tzi Bun
	 \overline{\text{FUNG Kwok Pui} \cdot \text{LEE Cheuk Yu} \cdot \text{WAYE Mary Miu Yee} \cdot \text{TSUI} \text{Kwok Wing} \cdot \text{SMITH David Keith*} \cdot \text{XUE Hong*} \cdot \text{ZHU Guang*} \] 	1997-98	Studies on the Terminal Differentiation of Cardiac Myocytes (BL97024) Z TSUI Kwok Wing
		1997-98	Structural and Functional Studies of
1997-98	Low density lipoprotein as carrier for targeted delivery of antitumoral drugs (CU97309)		Human 14-3-3 ε Protein (BL97041)
	▼ FUNG Kwok Pui	1996-97	Characterization of Isoforms of Endothelin Converting Enzyme in
1997-98	Discovery of Traditional Chinese Medicine (TCM) - Derived Saponins with Anti-Tumour and Cardiotonic		Cultured Endothelial Cells (BL96008) Man Chi Cheong David
	Activities for Use as Health Food Supplements or Therapeutics (MD97085) FUNG Kwok Pui • WONG Nai Ching Henry (Chemistry) • CHANG Yen Albert# • HUI Yongzheng* •	1997-98	Molecular and Immunological Characterization of Endothelin Coverting Enzymes (CU97320) WAN Chi Cheong David
	YU Biao*	1996-97	Molecular Cloning and Characterization of Human Heart cDNAs Coding for LIM
1997-98	Effect of Glucose Transporter Antisense Nucleic Acids on Human Tumour Cells (MD97111)		Domain Containing Proteins (CU96313)
		1997-98	Cloning of the Mouse FHL2 Gene
1997-98	Gain of Function by p53 Mutation: Induction of Drug Resistance (BL97022)	1,,,,,0	(BL97011)
		1997-98	Cognona Analysis of the CLIM1/FILL 1)
1995-96	Sequence Analysis of Human Heart cDNA Clones (CU95642) ELEE Cheuk Yu • WAYE Mary Miu	1997-96	Sequence Analysis of the SLIM1(FHL1) Gene (BL97017)
	Yee ● FUNG Kwok Pui		
1997-98	Atherosclerosis Genes (MD97037) ∠ LEE Cheuk Yu • WAYE Mary Miu Yee • FUNG Kwok Pui	1997-98	Study on the Expression of HSP 27L in Animal & Model Systems (BL97015) WAYE Mary Miu Yee ZIMMERMANN Rene*
	100 V I ONO KWOK I UI		ZIMINIZAMIN KUR
1995-96	Natural and Synthetic Anti-human Immunodeficiency Virus and Anti- Lymphoma Compounds (BL95036)		

RESEARCH OUTPUTS AND PUBLICATIONS

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- <P981419> Collins, R.A.; T.B. Ng; W.P. Fong; C.C. Wan and H.W. Yeung. "Anionic Polysaccharides from Chrysanthemum Morifolium Inhibit Mechanistic Assays of Human Immunodeficiency Virus Type 1 Replication". International Symposium on "the Worldwide Herbal Industry: Present and Future" Program & Abstracts p.9. Hong Kong, 1998.07.
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RESEARCH PROJECTS

The Role of Mitogen-activated Protein Kinases (MAPK) in Regulating Apoptosis of Eosinophils in Allergic Inflammation

- ∠ LAM Wai Kei Christopher
 ◆ WONG Chun Kwok
 ◆ HJELM Nils Magnus
- □ 1 November 1998
- CUHK Research Committee Funding

Eosinophils are the principal effector of late-phase inflammation in allergic diseases. In response to allergen sensitisation, cytokines IL-3, IL-5 and GM-CSF not only activate eosinophils but also prolong their life-span by inhibiting apoptotic cell death. Mitogen-activated protein kinases (MAPK) are a family of>12 kinases that mediate eukaryotic cell signal transduction. Among them ERK, JNK and p38 MAPK have been shown to affect apoptosis. It is possible that cytokines regulate eosinophilic growth and function via intracellular MAPK pathways.

This project aims to utilise our established eosinophil culture techniques to elucidate the role of MAPK pathways in regulating eosinophilic apoptosis in allergy, thereby linking and providing mechanisms for cytokine activation, eosinophilia and allergic inflammation. It will study the (1) activation of ERK, JNK and p38 MAPK in cultured and peripheral blood eosinophils by cytokines IL-3, IL-5 and GM-CSF, (2) relationship between the above MAPK activities and eosinophilic apoptosis, and (3) effect of MAPK inhibitors on apoptosis of eosinophils.

Elucidation of these intracellular controlled mechanisms will explain the immunopathogenesis of allergic diseases, and provide further biochemical basis for the design of pharmacological agents for treatment of allergy. (MD98033)

Novel Analyte Assay in Experimental and Human Cataract

- ∠ LAM Wai Kei Christopher PETERS T J*
- □ 31 December 1998
- UK/Hong Kong Joint Research Scheme, the British Council

Cataract is a major cause of morbidity World Wide. The importance of identifying risk factors, pathogenic mechanisms and preventative strategies has recently been reviewed. If a factor/therapy could be identified which delayed the onset by 10 yrs, the number of annual cataract operations World Wide has been estimated to decrease by 40%. We have recently shown that male alcohol misusers have an 8-fold higher risk for developing cataracts than control subjects. Various hypotheses have been put forward for the development of these cataract. These include

the accumulation of sugar alcohols. The GC-MS facilities developed by Professor NM Hjelm and colleagues in the Department of Chemical Pathology, Chinese University of Hong Kong will allow detailed analysis of normal and cataract lens extracts for these substances.

Experimental cataract will be induced by galactose feeding in mice (this model is established in the Department of Anatomy, Hong Kong University) and by chronic ethanol feeding in rats (this model is established in the Department of Clinical Biochemistry, King's College, London). Low molecular analytes including thiol, aldehydes, sugar alcohols will be extracted from the isolated lenses using methods to minimize degradation. After a preliminary purification using ion exchange resin/gel filtration, the concentrated extracts will be analysed and assayed using the state of the art GC-MS facilities in the Chinese University of Hong Kong. (MD98089)

Evaluation of Molecular Markers for Solid Organ Rejection

- ∠ LO Yuk Ming Dennis HJELM Nils Magnus PANG Chi Pui Calvin (Ophthalmology and Visual Sciences) YEUNG Chung Kwong (Surgery) CHAN Albert Yan Wo* TONG Kwok Lung*
- ☐ 1 September 1998
- CUHK Research Committee Funding

We have recently described the presence of donorspecific DNA in the plasma of liver and kidney transplant recipients. As plasma DNA has been postulated as a marker of cell death, our observations open up the possibility that detection and quantitation of donor-specific DNA may be used as a novel marker for graft rejection. This project involves the development of new methods for donor-derived DNA quantitation and its correlation with rejection episodes following liver and kidney transplantation. The relationship between plasma donor-derived DNA with various immunosuppressive regimes and HLA mismatch between the donor and recipient will also be elucidated. The potential establishment of plasma DNA as a rejection marker will contribute significantly towards the monitoring of liver and kidney transplant. It has the advantage of being noninvasive, safe and rapid and represents a major step forward from conventional methods such as liver and kidney biopsy. (MD98034)

Non-Invasive Prenatal Diagnosis

- ∠ LO Yuk Ming Dennis
- ☐ 1 September 1998
- ISIS Innovation Limited

This project aims to utilise the recent discovery that cell-free fetal DNA exists in the plasma and serum of pregnant women to develop new methods for non-invasive prenatal diagnosis. Efficient methods for DNA extraction from plasma and serum will be developed. Sensitive and quantitative polymerase chain reaction (PCR) based detection methods for fetal DNA will then be developed. These methodology will then be used to develop a system for the prenatal determination of paternally-inherited genetic polymorphisms in the fetus. This method may ultimately help to improve the safety of prenatal genetic diagnosis. (MD98115C)

Genetic Predisposition to Breast Cancer in Chinese: Study of Mutations and Genotypes of BRCA1, Estrogen Receptor and Estradiol 17 Betadehydrogenase II Genes

- ∠ TANG Leung Sang Nelson
 ◆ YEO Winnie (Clinical Oncology)
- □ 1 May 1999
- CUHK Research Committee Funding

This project studies the role of genetic predisposition in breast cancer among Chinese. Inherited mutations in high penetrant genes, like BRCA1 and BRCA2 confer an high absolute risk of breast cancer, and the life-time risk for breast cancer among mutation carriers is up to 85%. In addition, there are other cancer predisposition genes, which lead to a modest increase in cancer risk in the magnitude of 2 to 3 folds. Some of these candidate genes were identified by studying genotypes in case-control studies.

From our previous limited investigation, some novel mutations in BRCA1 were found in Chinese patients. We propose to study the prevalence of these BRCA1 mutations in an extended sample of Chinese patients. In addition, the association of two other candidate genes, which are involved in estrogen bioactivity, and breast cancer risk will also be determined in a case-control study.

(MD98096)

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

Edition Title/Investigators

1996-97 Clinical Usefulness of a Novel Serum Marker, 1,5-anhydroglucitol in Monitoring Glycaemic Control (MD96111)

ARUMANAYAGAM Manoharan • COCKRAM Clive Stewart (Medicine & Therapeutics)

- 1997-98 Combined Effects of Thyroid Hormone and Insulin on Na⁺,K⁺-ATPase Isoform Expression in Rat Skeletal Muscle: A Possible Animal Model for Thyrotoxic Hypokalaemic Periodic Paralysis (MD97045)
 - ARUMANAYAGAM Manoharan COCKRAM Clive Stewart (Medicine & Therapeutics)
- 1996-97 Development and Application of an *in situ* PCR Method for the Detection of Mutations and DNA Polymorphisms in Single Intact Cells (MD96052)
 - ∠ HJELM Nils Magnus
 ◆ LO Yuk Ming Dennis
- 1997-98 Telemedicine Project (MD96202)
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 ELE Chuen
 ENUM Joseph (School of Chinese
 Medicine) ◆ TONG Fuk Kay
 Franklin (Information Engineering) ◆
 TSUI Hung Tat (Electronic Engineering) ◆
 ZHANG Yuanting (Electronic Engineering)
- 1996-97 Molecular Epidemiology of Diabetes Mellitus: Detection and Prevalence of a Mutation in Mitochondrial DNA (MD96109)
 - ∠ LAM Ching Wan PANG Chi Pui Calvin (Ophthalmology and Visual Sciences) TSANG M. W.* HJELM Nils Magnus
- 1997-98 Mutation Screening of a New Oncogene: The Human Smoothened (SMO) in Sporadic Basal Cell Carcinoma (MD97112)
 - ∠ LAM Ching Wan XIE J* MCCORMICK F* TO Ka Fai (Anatomical & Cellular Pathology) YUEN W. F.* LEE K. C.*
- 1997-98 Activation of Eosinophils in Allergy (MD97043)
 - LAM Wai Kei Christopher HJELM Nils Magnus
- 1997-98 Trafficking of Nucleated Cells between Fetus and Mother (CU97670)
 - LO Yuk Ming Dennis CHANG Mang Z. Allan (Obstetrics & Gynaecology) • HJELM Nils Magnus
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 Chi Pui Calvin (Ophthalmology and
 Visual Sciences) KING Wing
 Keung Walter (Surgery) HJELM
 Nils Magnus
- 1997-98 The Role of Androgen Receptor and Vitamin D Receptor Genotypes on the Risk of Prostate Carcinoma and Patient Prognosis in Chinese Patients (MD97046)
 - ∠ TANG Leung Sang Nelson ◆ PANG
 Chi Pui Calvin (Ophthalmology and
 Visual Sciences) ◆ CHAN Lung Wai
 (Surgery) ◆ TO Ka Fai (Anatomical
 & Cellular Pathology)

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- **see also** <P974966>, <P974967>, <P974969>, <P974970>, <P974971>, <P974976>, <P981077>, <P981079>, <P982505>, <P982510>, <P982557>, <P982716>, <P982717>, <P982752>, <P982963>, <P982964>, <P983324>, <P983451>, <P983459>, <P983466>, <P983467>, <P983770>, <P983771>, <P983859>,

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<P983934>, <P983943>, <P984021>, <P984025>, <P984041>, <P984128>, <P984161>, <P984162>, <P984898>, <P984942>, <P990051>, <P990394>, <P990583>, <P990592>, <P990610>, <P990660>, <P990691>, <P990927>, <P990929>, <P990946>, <P990949>, <P990950>, <P991087>, <P991108>, <P991110>, <P991132>, <P991543>, <P991764>, <P991882>, <P992450>
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A Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Effect of Cisplatin / Epinephrine Injectable Gel (Product MPI 5010) When Administered Intratumorally for Achievement of Treatment Goals in Recurrent or Refractory Squamous Cell Carcinoma of the Head and Neck

- ∠ CHAN Anthony Tak Cheung LEUNG Wai Tong Thomas MOK Shu Kam Tony YU Simon* JOHNSON Philip James
- □ 1 July 1998
- * Matrix Pharmaceutical Inc.

The main objectives of this trial are to compare the effect of MPI 5010 to placebo gel on local tumor volume, to assess achievement of an identified improvable primary treatment goal selected for the most troublesome tumor in patients with recurrent or refractory squamous cell carcinoma of the head and neck following up to 6 weekly intratumoral cisplatin/epinephrine of (cisplatin/adrenaline) gel (MPI 5010) compared to treatment with placebo gel, to compare the time to response and the time to progression for the most troublesome tumor after local treatment with MPI 5010 as compared to placebo gel, and to assess improvement or stabilization in quality of life as measured by FACT-H&N. (MD98011)

Specific Inactivation of a Suppressor Gene PML in Small Cell Lung Cancer

- CHAN Yeuk Hon John
- ☐ 1 November 1998
- * Research Grants Council

Tumor suppressor genes are known to play crucial roles in the pathogenesis of many types of cancer. We have recently analyzed the protein levels of the growth and transformation suppressor gene, PML (Promyelocytic Leukemia), in human lung cancer immunohistochemical staining. preliminary studies demonstrated that expression was almost completely absent in all of the small cell lung cancer (SCLC) samples examined, while enhanced expression was found in adeno- and squamous cell carcinomas of the lung, and moderate expression was found in normal lung. The specific inactivation of PML may be an obligatory step in the tumorigenesis of SCLC. We propose to: (1) confirm if the expression of the PML protein is suppressed in a larger cohort of SCLC tissues and cell lines; (2) determine if the levels of mRNA and the structure of the PML gene are altered in SCLC; 3) transfect the wild-type PML cDNA into SCLC cells in order to

determine if this suppressor would specifically inhibit cell growth and the transformed phenotypes of SCLC. The identification of this molecular defect may permit the development of new strategy for early diagnosis and therapy of one of the most common neoplasms in Hong Kong and Southern China. (CU98280)

Analysis for Chromosomal Anomalies in Hepatocellular Carcinoma by Conventional Cytogenetics and Comparative Genomic Hybridization

- ∠ JOHNSON Philip James WONG Nathalie •
 LAI Bo San Paul(Surgery)
- ☐ 1 October 1998
- * Research Grants Council

Chromosomal aberrations associated hepatocellular carcinoma (HCC) have received very little investigation to date. This is largely due to the low mitotic index of cultured hepatocytes and the poor chromosome morphology obtained that rendered banding analysis difficult. So far, only two complete karyotypes of HCC have been reported. With the recent development of comparative genomic hybridization (CGH) it is now possible to detect losses, gains and amplifications of DNA sequences in tumours in the absence of cell culture. The technique of CGH has been developed within our department, and we now propose to employ CGH to the investigation of genomic imbalances in HCC. detection However. the of chromosomal translocations and the ability to distinguish between different sub-clones are limited in CGH, and such analysis remain the strength of conventional The cytogenetics team of the karyotyping. Department of Clinical Oncology has recently achieved much success on the cell culture and chromosomal analysis of HCC. Successful HCC culture was attained in all cases attemped, and chromosomal anomalies of both numerical and structural were identified. We therefore propose in the present investigation to perform CGH and conventional karyotyping simultaneously on HCC This parallel study of CGH and karyotypic analyses is expected to provide us with a comprehensive and complementary insight into the genetic alterations that are involved in HCC. (CU98264)

The Study of Genomic Alterations in Breast Cancer by Comparative Genomic Hybridization

- ✓ JOHNSON Philip James WONG Nathalie TANG Leung Sang Nelson (Chemical Pathology)
- ☐ 1 April 1999
- CUHK Research Committee Funding

The incidence of breast cancer is rising rapidly in Hong Kong and promises soon to reach the epidemic proportions seen in the West. There are, however, several marked differences in the cancer epidemiology and age-specific incidence of breast cancers in the Chinese and those from the West. A higher proportion of cases is found to present before the age of 45 in the Chinese population, while in most Western countries, the incidence of breast cancer amongst aged 55-64 is three times that of 35-44. Published literature have suggested frequent deletions of 8p, 16q, 13q, 17p and 18q in breast cancer, however the genetic changes underlying the development and progression of this malignancy is not well understood. Conventional cytogenetics can provide an overall view on the genetic aberrations present. Although the success rate and sensitivity of G-banding analysis on breast cancers have improved during the last years, the frequency of aberrations may still be underestimated because of the inability to obtain analysable metaphase cells from some tumours. Comparative genomic hybridization (CGH) is a molecular cytogenetic technique that allows a rapid survey of the entire tumour genome for region of DNA sequences gains and losses without the need of cell culture. We therefore propose, in the present study, to apply CGH analysis to the study of genomic aberrations in breast cancers of Hong Kong. A better understanding on the genetic alterations of our local breast cancers should have important implications in diagnosis, prognosis and treatment strategies. (MD98098)

A Specific Isoform of Alpha-fetoprotein for the Diagnosis of Hepatocellular Carcinoma

- ✓ JOHNSON Philip James POON Chuen Wai
- □ 7 June 1999
- Oxford GlycoSciences

Alpha-fetoprotein (AFP) is a glycoprotein that is widely used as a serum tumour marker in the diagnosis of hepatocellular carcinoma (HCC or 'hepatoma'), a common and highly malignant tumour in China, including Hong Kong. If detected early, HCC can often be cured by surgery. Measurement of the serum total AFP level is the only currently available routine biochemical assay for the diagnosis of HCC. However, because over 80% of HCCs arise in patients with a cirrhotic liver, a condition which may, by itself, also lead to the elevation of serum total AFP, the specificity of serum total AFP for early diagnosis of HCC is low. To help overcome this shortcoming we have previously examined the qualitative nature of AFP. AFP has a constant protein core with heterogeneous carbohydrate sidechains, which define different AFP glycoforms. Some of these glycoforms appear relatively specific for HCC ("hepatoma specific-AFP" (HS-AFP)). We successfully developed a technique involving

isoelectric focusing (IEF) to detect HS-AFP. We now plan to develop a quantitative assay with improved diagnostic specificity, which can measure the serum levels of HS-AFP, and thereby differentiate between the cirrhosis and HCC. (MD98128)

Universal DNA Amplification by Degenerate Oligonucleotide-Primed PCR in the Study of Genomic Aberrations in Nasopharyngeal Carcinoma

- MOK Shu Kam Tony ◆ WONG Nathalie ◆ TO Ka Fai (Anatomical & Cellular Pathology)
- ☐ 1 September 1998
- CUHK Research Committee Funding

Nasopharyngeal carcinoma (NPC) is a common tumour in southern China, including Hong Kong. It is characterised by a strong association with Epstein-Barr virus (EBV) and has a young peak incidence. The genetic changes underlying the development and progression of NPC are still not well understood, although molecular studies have revealed frequent deletions on chromosomes 3p, 9p, 11q and 14q. Cytogenetic information on NPC has been little. This is largely due to the poor tumour growth in vitro. A better understanding on the genetic changes of NPC is believed to have important implications in diagnosis, prognosis and treatment strategies. Comparative genomic hybridization (CGH) is a powerful molecular cytogenetic technique that allows a rapid survey of the entire tumour genome for region of DNA sequences gains and losses without the need of cell culture. The technique of CGH is well established within our department. Attempts to carry out CGH analysis on primary NPC tissues have, however, been hampered by the normal lymphocytes infiltration, a well-known phenomenon associated with EBV-related carcinomas. We therefore propose, in the present study, to microdissect the malignant NPC colonies from tissue sections and to universally amplify this small amount of target DNA by Degenerate Oligonucleotide Primed (DOP)-PCR reaction before subsequent CGH analysis. In this way, we aim to reduce the amount of contaminating normal DNA within the tumour genome and inturn be able to study the genomic imbalances without interference. (MD98037)

OGT 719-003 HCC Study

- ☐ 1 February 1999
- Oxford Glycosciences (UK) Ltd.

The is a phase I/II study to investigating the efficiency of OG7-711 is treatment of advanced HCC. (BL98040)

A Randomized Phase II Study of Gemcitabine Plus Oral Etoposide Versus Gemcitabine Plus Cisplatin in Treatment of Advanced Non-Small Cell Lung Cancer

- MOK Shu Kam Tony
- ☐ 1 February 1999
- Eli Eilly

This is a randomized study of cisplatin versus noncisplatin based treatment using gemcitabine, a relatively less toxic novel cytotoxic drug. The primary endpoint is toxicity and quality of life and secondary endpoint includes response and survival. Development of this randomized study is based on the results of our last phase II study on use of gemcitabine and oral etoposide in treatment of advanced non-small cell lung cancer. (MD98144)

A Prospective Study Using Sequencing Analysis to Determine Mutation Variants of Hepatitis B Virus (HBV) Genome and their Incidence in Cancer Patients with HBV Reactivation during Chemotherapy

- YEO Winnie STEINBERG Joyce Leta# •
 ZHONG Sheng TAM Siu Lun John (Microbiology) CHAN Yeuk Hon John •
 JOHNSON Philip James
- ☐ 1 January 1999
- CUHK Research Committee Funding

Background: In Hong Kong, up to 15% of the population are hepatltis B carriers. Patients who are chronic carriers of the HBV with a mutation in nucleotide (nt) 1898 (G to A) in the precore (preC) region often develop more severe liver disease. This is thought to be due to rapid selection and enhanced replication ability of the mutant strain. In addition, previous reports have also suggested that the promoter region and HBx of HBV genome appears to be associated with fulminant disease in chronic carriers. In cancer patients undergoing cytotoxic therapy, reactivation of the hepatitis B virus (HBV) is a well described complication of chemotherapy which sometimes leads to hepatic failure. There is very little Information published about chemotherapy patients reactivating HBV with a mutant form of the virus. With cancer as the major cause of mortality in this area, many patients who are hepatitis B carrier will be exposed to cytotoxic therapy as part or all of the treatment, it is important to establish the role of viral B mutants in the process of HBV reactivation during chemotherapy.

Objectives: (1) To identify the type of viral genome mutations and to estimate their incidence in chronic hepatitis B carriers who develop HBV reactivation during chemotherapy. (2) To correlate the laboratory findings of individual mutation in relation to the clinical outcome, i.e. the severity of hepatic impairment. (3) To establish a background information for future investigation into the role of these mutant viruses in relation to the mechanisms of HBV reactivation during chemotherapy.

Methods: We propose to apply direct DNA sequencing of the polymerase chain reaction products of the precore (pre C), promoter and HBx regions of the HBV-DNA on serum samples of patients who develop HBV reactivation during chemotherapy. Laboratory findings will then be correlated with clinical outcome of individual patient. (MD98038)

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

Edition Title/Investigators

- 1995-96 Hepatocellular Carcinoma Health Care Services (MD95174)
 - CHAN Anthony Tak Cheung YEO
 Winnie JOHNSON Philip James •
 HAZLETT Clarke Blaine (Office of Educational Services)
- 1996-97 Cell Kinetic Studies in Undifferentiated Nasopharyngeal Carcinoma and the Implications for Clinical Management (CU96636)
 - ∠ CHAN Anthony Tak Cheung TEO Man Lung Peter LEUNG Wai Tong Thomas CHANG Alexander Russell (Anatomical & Cellular Pathology) JOHNSON Philip James
- 1997-98 Detection, Purification and Identification of Isoforms of Serum Glycoproteins: Use as Diagnostic and Dedifferentiation Markers in Cancer (CU97654)
 - ∠ CHAN Anthony Tak Cheung
 JOHNSON Philip James
 ← HJELM
 Nils Magnus (Chemical Pathology)
 ← HO Chung Shun (Chemical Pathology)
- 1997-98 An Open-Label Phase II Study of a 28day Oral Regimen of 5-Fluorouracil Plus 776C85 in Patients with Advanced Nasopharyngeal Carcinoma (FUMB2011) (MD97180)

- CHAN Anthony Tak CheungLEUNG Wai Tong ThomasJOHNSON Philip James
- 1997-98 The Role of Biological Markers as Prognosticators in Undifferentiated Nasopharyngeal Carcinoma (MD97114)
 - ∠ CHAN Anthony Tak Cheung HO
 King Wah Stephen* TEO Man
 Lung Peter CHIU Kwok Wing
 Samuel JOHNSON Philip James
- 1997-98 Functional Analysis of a New Gene (BRE) Responsive to DNA Damage and Retinoic Acid, and its Interactions with the TNF Receptor (CU97672)

 © CHAN Yeuk Hon John
- 1997-98 Aberrant Telomerase Activity in Malignant Tumors (MD97041)

 CHAN Yeuk Hon John
- 1996-97 Novel Mutations in HBV PreS2/S Gene in Hepatocellular Carcinomas: Potential Induction of the Transactivator Function During Oncogenesis (MD96044)
- 1997-98 A Pilot Study of 5-Azacytidine in Patients with Relapsed and/or Refractory EBV-Associated Malignancies (MD97011)
 - JOHNSON Philip James •
 AMBINDER R* WICKHAM
 Nicholas William Rupert# LEUNG
 Wai Tong Thomas CHAN
 Anthony Tak Cheung MOK Shu
 Kam Tony CHOW John Hei Sing
 (Anatomical & Cellular Pathology) •
 FLINN I* MANN R*
- 1997-98 T-Cell Immunotherapy for Advanced Nasopharyngeal Carcinoma: A Pilot Study of Immunisation with LMP2 Peptide Epitopes Presented on Autologous Dendritic Cells in Patients with Metastatic or Locally Recurrent Nasopharyngeal Carcinoma (MD97144)
 - ✓ JOHNSON Philip James CHAN
 Anthony Tak Cheung •
 RICKINSON Alan B.* LEE
 Steven P.*
- 1997-98 The Prognostic Significance of Serum Levels of Soluble ICAM-1 in Patients with Primary Extranodal Non-Hodgkin's Lymphomas (MD97040)
 - ✓ JOHNSON Philip James LEI Ieng-Kit Kenny*

- 1996-97 The Application of Comparative Genomic Hybridisation for the Detection of Genomic Imbalances in Nasopharyngeal Carcinoma (CU96637)
 - ∠ LEUNG Sing Fai WONG Nathalie
 HUANG POON Wai Sin Dolly
 (Anatomical & Cellular Pathology) •
 TSAO George* JOHNSON Philip
 James
- 1997-98 Alterations of the Growth and Transformation-Suppressor PML in Hepatocellular Carcinoma and Nasopharyngeal Carcinoma (CU97653)
 - ∠ LEUNG Sing Fai CHAN Yeuk
 Hon John CHAN Anthony Tak
 Cheung LIEW Choong Tsek
 (Anatomical & Cellular Pathology) •
 JOHNSON Philip James
- 1996-97 Randomised Trial of Radiotherapy Alone Versus Concomitant Radiotherapy and Chemotherapy in Locoregional Advanced Nasopharyngeal Carcinoma (MD96152)
 - ∠ LEUNG Wai Tong Thomas CHAN Anthony Tak Cheung • TEO Man Lung Peter • LEUNG Sing Fai
- 1996-97 A Phase II Study of Temozolomide (SCH 52365) in the Treatment of Patients with Advanced Nasopharyngeal Carcinoma (MD96220C)
 - ∠ LEUNG Wai Tong Thomas CHAN Anthony Tak Cheung
- 1996-97 An Open Label Phase II Study to Evaluate a 28 Days Regimen of Oral 5-Fluorouracil (5FU) Plus 776C85 in Patients with Inoperable Hepatocellular Carcinoma (MD96156)
 - ∠ LEUNG Wai Tong Thomas JOHNSON Philip James LAU Wan Yee Joseph (Surgery) MOK Shu Kam Tony CHAN Anthony Tak Cheung YEO Winnie LAM Shun Chiu Dennis (Ophthalmology and Visual Sciences)
- 1996-97 Phase III Randomised Trial of ⁹⁰Yttrium-Microspheres Selective Internal Radiation Versus Systemic Doxorubicin in the Treatment of Inoperable Hepatocellular Carcinoma (MD96157)
 - ∠ LEUNG Wai Tong Thomas LAU
 Wan Yee Joseph (Surgery) •
 JOHNSON Philip James HO S.* •
 CHAN M.* CHAN Anthony Tak

Cheung • YEO Winnie • MOK Shu Kam Tony • LEUNG Nancy*

- 1997-98 A Two Stage Phase II Safety and Efficacy Study of Intradose (Cisplatin/Epinephrine) Injectable Gel (MPF 5010) Administered to Patients with Unresectable Primary Hepatocellular Carcinoma (MD97013)
 - ∠ LEUNG Wai Tong Thomas
 JOHNSON Philip James
 YU S.*
 LAU Wan Yee Joseph (Surgery)
 CHAN Anthony Tak Cheung
 MOK Shu Kam Tony
 YEO Winnie
 TANG Mei Yee
- A Multicentre, Randomised, Phase III Study Comparing the Combination of Recombinant Human Interferon-β 1a and 5-Fluorouracil to Standard Therapy in the Treatment of Advanced Colorectal Cancer (MD97145)
 - ∠ LEUNG Wai Tong Thomas CHAN Anthony Tak Cheung
- 1997-98 A Randomised Open-label Phase III
 Study of a 28-day Oral Regimen or
 776C85/5-Fluorouracil Versus
 Intravenous 5-Fluorouracil Plus
 Leucovorin as First-time Therapy in
 Patients with Advanced Colorectal
 Cancer (Protocol No.FUMB3002)
 (MD97178C)
 - ∠ LEUNG Wai Tong Thomas JOHNSON Philip James CHAN Anthony Tak Cheung YEO Winnie
- 1996-97 Investigation of Possible Subtypes of Prostatic Specific Antigen Related to Prostatic Cancer and Benign Prostatic Hypertrophy by Isoelectric Focusing Technique (MD96045)
 - MOK Shu Kam Tony LEUNG
 Wai Tong Thomas HO Stephen K.
 W. CHAN Siu Foon Peter (Surgery)
 ● JOHNSON Philip James
- 1996-97 Phase II Study of Gemcitabine and Oral Etoposide in Treatment of Advanced Non-small Cell Lung Cancer (MD96154)
 - MOK Shu Kam Tony ◆ CHAN Anthony Tak Cheung ◆ YEO Winnie
 ◆ YIM Ping Chuen Anthony (Surgery) ◆ HUI P.* ◆ JOHNSON Philip James
- 1997-98 Phase I/II Study of Topotecan and Oral Etoposide in Treatment of Small Cell Lung Cancer (MD97012)

- MOK Shu Kam Tony ◆ CHAN
 Anthony Tak Cheung ◆ YEO Winnie
 ◆ YIM Ping Chuen Anthony
 (Surgery) ◆ JOHNSON Philip James
- 1997-98 Molecular Prognostication of Therapeutic Response of Liver and Lung Cancers (MD97082)
- 1996-97 Detection of Genetic Imbalance in Multiple Myeloma by Comparative Genomic Hybridization (MD96047)
 - WONG Nathalie ◆ NG Heung Ling Margaret (Anatomical & Cellular Pathology)
- 1997-98 The Application of Comparative Genomic Hybridization to the Analysis of Genetic Changes During Development and Progression of Hepatocellular Carcinoma (MD97042)
 - ∠ WONG Nathalie

 JOHNSON Philip
 James

 James

 ✓ Monda Nathalie

 JOHNSON Philip
 James

 Johnson

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- 1996-97 Application of Reverse Transcriptase Polymerase Chain Reaction in the Detection of Circulating Tumour Cells in Peripheral Blood (MD96048)
 - ∠ YEO Winnie WONG Hing Nam (Anatomical & Cellular Pathology) JOHNSON Philip James
- 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 (Anatomical & Cellular Pathology) KING Wing
 Keung Walter (Surgery)
- 1997-98 Adjuvant Tamoxifen Longer Against Short (ATLAS) (MD96216)
- 1997-98 Detection and Characterization of Circulating Hepatocellular (HCC) Cells for Predicting HCC Metastasis and Monitoring Treatment of HCC Patients (CU97656)
 - ✓ YEO Winnie WONG Hing Nam (Anatomical & Cellular Pathology) •
 JOHNSON Philip James • LEUNG Wai Tong Thomas • LAU Wan Yee Joseph (Surgery) • HO King Wah Stephen* • CHAN Sai Yu Michael

- (Diagnostic Radiology & Organ Imaging)#
- 1997-98 Phase II Study of Taxotere and Epirubicin for Metastatic Breast Cancer (MD97177)
 - ✓ YEO Winnie MOK Shu Kam Tony • LEUNG Wai Tong Thomas • CHAN Anthony Tak Cheung • JOHNSON Philip James • KWAN W. H.* • LAM K C* • TSE K. K.* • CHIU K W*
- 1997-98 Phase II Trial to Document the Efficacy and Tolerability of Daily Dose of 2.5mg
 Femara in Postmenopausal Chinese
 Women with Advanced or Metastatic
 Breast Cancer as Second Line Hormonal
 Treatment after Tamoxifen (MD97165)
- 1997-98 A Randomized Open-Label Phase III Study of a 28-Day Oral Regimen of 776C85/5-Fluorouracil Versus

- Intravenous 5-Fluorouracil Plus Leucovorin as First Line Therapy in Patients with Advanced Colorectal Cancer (MD97166)
- ∠ YEO Winnie

 JOHNSON Philip James

 LEUNG Wai Tong Thomas

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- 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
- 1997-98 Phase II Trial to Document the Efficacy and Tolerability of Daily Dose of 2.5mg Femara in Postmenopausal Chinese Women with Advanced or Metastatic Breast Cancer as Second Line Hormonal Treatment After Tamoxifen (FEM-HK-01) (MD97179)
 - ∠ YEO Winnie KWAN Wing Hong
 MOK Shu Kam Tony LEUNG
 Wai Tong Thomas CHIU Kwok
 Wing Samuel JOHNSON Philip
 James

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Andec Supplementation Trial – A Randomized Controlled Trial of the Effect of Milk Supplementation on the Rate of Bone Accretion in Chinese Children (Aged 9-10 years) in Hong Kong

- ∠ LAU Edith Ming Chu WOO Jean (Medicine & Therapeutics) CHENG Chun Yiu Jack (Orthopaedics & Traumatology) FOK Tai Fai (Paediatrics)
- ☐ 1 April 1999
- New Zealand Dairy Board

The study was designed to measure the effects of calcium supplementation (in the form of high calcium milk powder) on bone accretion in Chinese children. Study subjects (boys and girls aged 9-10) will be randomly assigned to 3 groups:- 40g of high calcium milk powder (equivalent to 650mg of calcium; 80g of high calcium milk powder (equivalent to 1,300mg of calcium) or no supplement. Supplementation will last for 18 months, and bone mineral density at the hip, spine and total body will be measured at baseline, 6 months, 12 months, 18 months and 33 months. The rate of bone accretion in the 3 groups will be compared. (MD98087)

Work-Related Factors and Risk of Incident Low Back Pain in Hong Kong Nurses – A Cohort Study

- ∠ LAU Edith Ming Chu LEUNG Arran* CHAN Eric* WONG C. M.* LAM Dicky*
- ☐ 12 April 1999
- Health Services Research Fund, Hospital Authority

Objectives: To investigate the prevalence, cost and occupational and lifestyle risk factors for low back pain in female nurses working in acute care and rehabilitative care for the elderly in Hong Kong.

Design: A cross-sectional survey to study the prevalence and cost of low back pain, and the cohort of nurses to be followed-up for a year to investigate how current work practice predispose to the development of low back pain.

Setting: Acute care hospitals and rehabilitative hospitals in Hong Kong.

Subjects: 1200 female nurses working in various specialties in the hospitals.

Methods: Observations will be made in several hospitals at work to identify work practice which may be associated with low back pain. Such observations will be applied to modify a questionnaire (which has been developed) to measure how occupational practice predispose to low back pain. In the cross-sectional phase of the study, 1200 nurses will be interviewed to measure the 1 year and life-time

prevalence of low back pain. The cost of low back pain in nurses will also be estimated.

The frequency of transferring, moving and lifting patients manually with or without mechanical aids will also be measured at baseline. Other factors as vitality and mental health (as measured by the SF 36), job satisfaction (as measured by the McClosky Scale), body weight and height, cigarette smoking and participation in sports activity will also be assessed. The study subjects will then be followed up for a year for the development of back pain.

Statistical methods: The percentage prevalence and 95% confidence intervals of low back pain will be calculated. Discrete-time logistic normal survival modelling will be used to study risk factors for low back pain in this cohort of nurses. (MD98078)

Collagen Type I Alpha I Gene, Estrogen Receptor Gene, and Lifestyle Factors in the Etiology of Osteoporosis in Chinese

- LAU Edith Ming Chu HO CHAN Suzanne •
 WOO Jean (Medicine & Therapeutics) •
 CRITCHLEY Julian A J H (Medicine & Therapeutics)
- □ 1 May 1999
- CUHK Research Committee Funding

Osteoporosis (thinning bones) is presenting as an epidemic in Hong Kong Chinese. Both genetic and environmental factors contribute to osteoporosis. In 1995-96, we were awarded an Earmarked Grant by the RGC to study the role of the vitamin D receptor gene in determining bone mineral density (BMD) in 250 postmenopausal Chinese women. We have found that this gene could only account for a small proportion of the variation in BMD. Recently, the estrogen receptor gene (ER) and the Collagen type I Alpha 1 (COLIA 1) gene have been found to be associated with BMD in Caucasians. We proposed to study the relationship between the ER and COLIA 1 gene and BMD in the 500 Chinese women. DNA has been extracted and stored. In this study, polymorphism in intron 1 of the COLIA 1 will be detected by polymerase chain reaction restriction fragment length polymorphism by established laboratory methods. Polymorphisms in Intron 1 and Dinucleoticle repeat polymorphism upstream of the polymorphism upstream of the ER gene will be studied by PCR amplification using the appropriate primers. BMD in the ER genotypes (PPxx, ppXX and heterogygotes for P and X), and COLIA 1 genotypes (SS, Ss, ss) will be compared. (MD98099)

Manual Handling and Low Back Pain among Nursing Home Staff in Hong Kong

- ∠ LAU Edith Ming Chu LEUNG Ping Chung (Orthopaedics & Traumatology) • WONG Louisa* • LEUNG Arran* • CHAN Wai Sing*
- ☐ 1 June 1999
- Occupational Safety and Health Council Research Grant

The objectives of the study are to observe and describe manual handling practices of staff working in nursing homes in Hong Kong. The relationship between 'at risk' practices and the occurrence of low back pain will be studied. Guidelines on 'proper manual handling procedures to prevent injury' will be produced for elderly health care workers in Hong Kong.

A cross sectional survey will be conducted on a random sample of 300 nursing homes in Hong Kong (200 subvented and 100 private). The total number of staff surveyed will be around 1200. On site observation will be made on manual handling practices (using a standard protocol), and all workers will be interviewed on the prevalence of low back pain and frequency of manual handling. Other life style factors for low back pain (in the previous year) and the frequency of manual handling as well as other life style factors will be studied. Based on the study results, guidelines on 'Safety Recommendations on manual handling'. (MD98114C)

Smoking and Health in Hong Kong Women

- ∠ LAU Edith Ming Chu WOO Jean (Medicine & Therapeutics) HEDLEY A J* LAM T H* AU T K* YAU Helen* IP Shirley*
- □ 1 June 1999
- ❖ Hong Kong Council on Smoking and Health

A random sample of women aged 18-24 and 50-69 will be surveyed by telephone. The smoking habits, exposure to environmental tobacco smoke, attitudes to smoking and other health information will be gathered. The prevalence of smoking and reason for smoking uptake will be studied. A subsample of smokers and non-smokers will be followed up to study the health effects of smoking on cardiovascular, bone and reproductive health. (MD98119C)

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

Edition <u>Title/Investigators</u>

1997-98 Interactive Multimedia Health Web Pages (MD97167)

- ∠ CHAN Shiu Yee Cynthia CHAN Keith*
- 1997-98 Computer-Assisted Interactive Tutorials on Clinical Problem Solving in Family Medicine (MD97022)
 - CHAN Shiu Yee Cynthia WUN Yuk Tsan Kyran Patrick • CHAN Keith*
- 1997-98 Qualitative Study of HIV/AIDS Risk Behaviour among Hong Kong's Teenage "Street Roamers" and Approaches for Harm Reduction (MD97094)
 - CHAN Shiu Yee Cynthia TANG Shao Fen Joyce
- 1997-98 Developing Problem Based Learning Tutorials in Family Medicine (MD97130)
 - ∠ CHAN Shiu Yee Cynthia
 ◆ WUN
 Yuk Tsan Kyran Patrick
 ◆
 DICKINSON James Arthur
- 1995-96 A Study of Bone Mass and Bone Loss in Chinese Perimenopausal Women (MD95065)
 - ∠ HO CHAN Suzanne WOO Jean (Medicine & Therapeutics) CHAN Shiu Yee Cynthia LEUNG Ping Chung (Orthopaedics & Traumatology) CHAN Sieu Gaen#
- 1996-97 Habitual Physical Activity, Health Fitness and Behaviour among Adult Population in Hong Kong (MD96011)
 - ∠ HO CHAN Suzanne LEE Shiu
 Hung CHAN Sieu Gaen#
- 1996-97 The Relationship between Sex Hormones and Bone Mass in Chinese Perimenopausal Women (MD96041)
 - ∠ HO CHAN Suzanne LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) WOO Jean (Medicine & Therapeutics) CHAN Shiu Yee Cynthia CHAN Sieu Gaen#
- 1996-97 Asian Osteoporosis Study (AOS) (MD96193)
 - ∠ LAU Edith Ming Chu
 ∠
- 1996-97 A Randomized Controlled Trial of the Effect of Milk Supplementation on the Rate of Bone Loss in the Post Menopausal Women in Hong Kong (MD96136)
 - LAU Edith Ming Chu

- 1997-98 A Randomized, Parallel-group Study to Compare the Effects on Bone Density of Oral Alendronate or Placebo in Postmenopausal Women with Osteoporosis (MD97009)
 - ∠ LAU Edith Ming Chu WOO Jean (Medicine & Therapeutics) LEUNG Suk Fong Sophie (Paediatrics)#
- 1997-98 A Randomized, Parallel-Group Study to Compare the Effects on Bone Density of Oral Alendronate or Placebo in Elderly Chinese Men and Women with Vertebral Fractures (MD97099)
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- 1997-98 A Randomized, Parallel-Group Study to Compare the Effects on Bone Density of Oral Alendronate and Calcium Supplementation or Calcium Supplementation Dose in Chinese Patients on High Dose Inhaled Steroid (MD97098)
 - ∠ LAU Edith Ming Chu WOO Jean (Medicine & Therapeutics) LAI Kei Wai Christopher (Medicine & Therapeutics)
- 1996-97 Level of and Reasons for Utilising Accident and Emergency Services by Non Urgent Patients (MD96022)
 - ∠ LEE Albert LAU Fei Lung* HAZLETT Clarke Blaine (Office of Educational Services)

- 1997-98 Social Costs of Drug Abuse in Hong Kong (SS97030)
 - ∠ LEE Albert CHEUNG Yuet Wah
 (Sociology) CHIEN James M. N.*
 LEE Shiu Hung LAM K C*
- 1997-98 "How do Physicians' Effort and Quality of Services Differ in Public and Private Sector?" (MD97081)
 - ∠ LEUNG Chi Ming Michael
- 1997-98 A Survey of Patients' Knowledge, Attitude and Behaviour on Drug Prescriptions (MD97115)
 - WUN Yuk Tsan Kyran Patrick •CHAN Shiu Yee Cynthia •DICKINSON James Arthur
- 1996-97 Occupational Noise Exposure and Hearing Impairment Among Employees in the Service Industry in Hong Kong (MD96025)
 - ∠ YU Tak Sun Ignatius WONG Tze Wai
- 1997-98 Conducting a Review of the Situation Regarding Occupational Health Research and Occupational Health Services in Hong Kong (MD97007)
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Please refer to previous issues of this publication for more details of the following ongoing research at the department:

Edition <u>Title/Investigators</u>

1996-97 Magnetic Resonance Signal Changes in Processed and Fresh Frozen Bone Allografts: An *in vitro* Study (MD96053)

> KEW Jacqueline • KUMTA Shekhar Madhukar (Orthopaedics & Traumatology) • GRIFFITH James Francis • METREWELI Constantine
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The Effect of Irbesartan on Morbidity and Mortality in Hypertensive Patients with Type II Diabetes and Diabetic Nephropathy

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The prevalence of type 2 diabetes is reaching epidemic proportion worldwide and in our local population. In particular, diabetic nephropathy is the major cause of renal failure and accounts for 30% of patients requiring dialysis. In this multicentre study, the effect of irbesartan, an angiotensin II (AII) antagonist, is compared to amlodipine, a calcium channel blocker and placebo in a large group of type 2 diabetic patients with nephropathy. This will be a 2-year study with clinical end points defined as all cause mortality, dialysis and 2 times baseline plasma creatinine. In this multicentre study, there will be an Asian component involving centres from Hong Kong, Singapore and Taiwan. The divisions of clinical pharmacology and endocrinology of CUHK at PWH has a strong track record in the research of diabetic nephropathy and will be participating in this multicentre study.

Data collected from this study will contribute to the overall analysis of the multi-centre database. These data will also be analysed together with that collected from similar studies conducted locally, which examine the effects of other AII antagonists and angiotensin converting enzyme inhibitor in our local Chinese type 2 diabetic patients with renal impairment. Thus, we will have unique information on the protective effects of inhibition of the renin angiotensin system on the progression of renal function and clinical end points in these high risk patients.

(MD98086)

Screening for Mutations in the Glucokinase and Hepatocyte Nuclear Factor-1a Genes in Chinese Patients with Early-onset Type 2 Diabetes and A Positive Family History

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- ☐ 1 April 1999
- CUHK Research Committee Funding

Diabetes mellitus is a common disease occurring in about 10% of our general population, with type 2 diabetes being the predominant form. Genetic factors have been implicated in this disease as 40% of these patients have a positive family history.

Type 2 diabetes is genetically and phenotypically heterogeneous. Recently, mutations in hepatocyte nuclear factor (HNF)- 4α , HNF- 1α , HNF- 1α , glucokinase and insulin promoter factor-1 genes have been associated with maturity onset diabetes of the young (MODY), a subtype of diabetes characterized by age of onset before 25 years and autosomal dominant inheritance. HNF- 1α and glucokinase gene mutations accounted for>50% of Caucasian MODY families and 9% of Japanese early-onset type 2 diabetics. Mutation in HNF- 4α gene was rarely found. However, mutations of these genes have not been reported in Chinese.

Our previous study has found a prevalence of 10% autoimmune type 1 diabetes in 150 early-onset diabetic patients (≤ 35 years) although 50% of them have positive family history. This suggests a role of genetics in the aetiology of the disease. In this study, we aim to identify mutations/polymorphisms in the glucokinase and HNF-1α genes by direct sequencing in 250 patients with early-onset type 2 diabetes and positive family history. Gene mutations identified will be screened in family members of the affected probands as well as in 100 age-and sex- matched healthy Chinese controls. The phenotypic characteristics subjects with mutations/polymorphisms will be examined. These data will significantly improve our understanding of the pathogenic mechanism of diabetes and allow early identification of high-risk individuals for prospective evaluation.

(MD98100)

Mapping Genes for Young Onset Diabetes, Obesity and Diabetic Nephropathy

- ∠ CHAN Chung Ngor Juliana CRITCHLEY Julian A J H TOMLINSON Brian CHAN Yan Keung Thomas COCKRAM Clive Stewart NG Chor Yin LEE Shao Chin LEE Suk Kuen THOMAS Neil G METREWELI Constantine (Diagnostic Radiology & Organ Imaging) WONG Wing Kin Gary (Paediatrics)
- ☐ 1 June 1999
- CUHK Strategic Research Program

The prevalence of diabetes, obesity and related diseases are reaching epidemic proportions in Hong Kong Chinese. Family history is a particularly important factor in the development of young onset diabetes (<40 years). Amongst these young patients, 58% gave a positive family history. Our preliminary findings suggest that 10% of these patients with familial diabetes had various gene mutations, which may contribute to disease manifestation. Obesity is also an important determinant for the development of diabetes. In this respect, there is a high prevalence of childhood obesity in Hong Kong. Diabetes is the leading cause of kidney failure, which is also the leading cause of death amongst our local diabetic

patients. Genetic predisposition to this complication has been demonstrated in several populations. The genetic mapping of these disease genes will lead to a more scientific approach to define diseases by their mechanisms rather than clinical appearance and to the development of drugs designed to modify the biochemical pathways involved in these diseases. The ability to intervene early in the course of the disease will shift the attention of health care to disease prevention and away from sustaining life in patients with end stage disease, the latter being costly in terms of both money and human suffering. In this collaborative project, the research team aims to use the state-of-the-art techniques to identify these gene markers and their interactions with environmental factors in disease manifestations. (MD98116)

A Multicenter, Double-blind, Parallel Group Study Comparing the Efficacy and Incidence of Gastroduodenal Ulcer Associated with SC-58635 100MG BID with that of Diclofenac 50MG BID Taken for 12 Weeks in Patients with Osteoarthritis or Rheumatoid Arthritis in Hong Kong

- ∠ CHAN Ka Leung Francis SUNG Joseph Jao Yiu LI Kwok Ming Edmund WOO Jean
- □ 1 June 1999
- . G. D. Searle & Co

This double-blind prospective randomized study sought to test the efficacy and safety of a new class of NSAID, celecoxib, for patients with rheumatoid or degenerative arthritis. (MD98149)

A Study on the Drug-Related Death Cases in Hong Kong

- ∠ CHAN Yan Keung Thomas CRITCHLEY Julian A J H CHAN Tai Wai David*
- 1 November 1998
- ❖ Action Committee Against Narcotics

Very little is known about the incidence and pattern of drug abuse related deaths in Hong Kong. Deaths under such circumstances are particularly tragic because mostly young people are involved and help would have been readily available from various treatment and rehabilitation programmes. This is a retrospective study of all patients who died of poisonings with drugs or substances of abuse between January 1994 and December 1998. The objectives are:

- (1) to provide an overview of drug abuse related deaths and a trend analysis of these cases;
- (2) to analyse the characteristics of the cases, which include the type of drugs involved, reasons for

- taking the drugs, where such drugs were obtained, and whether the affected subjects received any treatment programmes;
- (3) to assess as far as possible whether the deaths were caused by unexpected increase in purity of heroin, suicidal attempts, lack of understanding of the properties of the drugs, or otherwise.

The research findings will provide a quantitative basis for reference in the formulation of preventive education and publicity programmes to increase the awareness of the community (including health care professionals) to the dangers of drug abuse. Also, insight may be gained as to how co-ordinated efforts among various parties involved can be carried out, taking into account the characteristics we identify. We shall also determine the best, feasible way of monitoring drug abuse related deaths in Hong Kong. (MD98080)

Effect of Alendronate on Patients with Primary Hyperparathyroidism

- ∠ CHOW Chun Chung Francis COCKRAM
 Clive Stewart LI J. K. Y.* CHAN W. B.* •
 KWOK Chi Yui Timothy SO W Y*
- □ 31 January 1998
- Merck Sharp & Dohme (Asia) Ltd

Primary hyperparathyroidism is initially described in 1920s in patients with osteitis fibrosa cystica. While this severe form of presentation appeared rarely, other mild forms of bone disease exist and cause concern. In a community health survey, the risk of fracture was found to be raised before the diagnosis of primary hyperparathyroidism was confirmed in these patients. Primary hyperparathyroidism was found to be significantly associated with vertebral fracture. Bone mineral density studies using dual photon absorptiometry showed significant bone demineralization in patients with the disease and this bone loss appeared to be irreversible despite showing improvement after parathyroidectomy. Bisphosphonates had first been used to treat osteoporosis in 1970s. The older generation bisphosphonate, etidronate, was used initially with poor result. However, two decades later, the use of intermittent cyclical etidronate was shown to improve vertebral bone mineral content and reduce fracture rate in postmenopausal osteoporotic women. Etidronate and clodronate had both been shown to have good effect in suppressing bone resorptive activity in patients with primary hyperparathyroidism. Alendronate, being the most potent bisphosphonate, aroused great excitement recently because of its significant improvement in bone mineral density and reduction in fracture in postmenopausal osteoporosis. postmenopausal women with hyperparathyroidism, the effect of bisphosphonate on bone mineral density and fracture rate has not been established. The primary objective of this project is

to determine whether oral administration of 10mg Alendronate will increase bone mineral density significantly when compared with placebo in postmenopausal women with primary hyperparathyroidism.

(MD97175C)

IND Filing and Phase I Clinical Trial of a Malaria Vaccine TBV25H - Phase I Clinical Trial Component

- □ 1 July 1998
- Industrial Support Fund, Industry & Technology Development Council

This grant is to enable us to carry out the next phase of the development of a novel malarial vaccine, *TBV25H*. It will involve the filing of an Investigational New Drug (IND) application to the Department of Health and performing Phase I clinical trials in the Clinical Pharmacology Studies Unit of the Division of Clinical Pharmacology, Department of Medicine and Therapeutics. The deliverables of this Project will include:

- (1) human safety and tolerance data of a malaria vaccine which has the potential to prevent over 500 million people from contracting malaria and 2 million people from dying in a year worldwide:
- (2) the first IND application for a novel human healthcare product ever filed in Hong Kong;
- (3) the first Phase I human clinical trial of a vaccine under GCP guidelines ever performed in Hong Kong. Using vaccine produced by the Hong Kong Institute of Biotechnology's GMP pilot plant the staff of the Clinical Pharmacology Studies Unit will evaluate the pharmacokinetics pharmacodynamics and safety of TBV25H in man.

These studies will be performed in collaboration with Dr. Louis Miller of the NIH and the WHO. A final report will be produced for the HKSAR Government and we hope to help pave the way for the HKSAR to establish a globally competitive biotechnology industry. (MD98005)

Genome-wide Search for Diabetes-associated Genes in Chinese Patients with Type 2 Diabetes Characterized by Insulin Deficient or Non-insulin Resistance in Hong Kong

- ☐ 1 April 1999

CUHK Research Committee Funding

Type 2 diabetes is a disorder with complex etiology involving environmental and genetic factors. Candidate genes isolated so far account for a small percentage of affected patients with a rare form of early onset type 2 diabetes. Recently, a genetic locus contributing to type 2 diabetes has been mapped on chromosome 7 in Pima Indians. We have already analyzed the same locus in Hong Kong Chinese type 2 diabetic patients with the microsatellite markers spanning this region. In this project, we aim to assess the linkage of this locus with diabetes in 100 Chinese families with early-onset type 2 diabetes and perform DNA sequence analyses of candidate genes located in this locus. Specifically, we will investigate whether there are mutations associated with type 2 diabetes in the paraoxonase (PON2) and pyruvate dehydrogenase kinase (PDK4) genes mapped to this region. Because of the putative linkage of type 2 diabetes to chromosome 7q, we choose to analyze two candidate genes at this locus which are functionally involved in maintenance of glucose homeostasis. mutations identified will be screened in family members of affected probands as well as 100 age-and sex-matched healthy Chinese controls. This work will complement previous investigations at this genetic locus in other ethnic groups, such as Pima Indians and Caucasians, with different prevalences of type 2 diabetes and our data will shed light on the interethnic distribution of type 2 diabetes candidate genes.

(MD98101)

Prevalence of Sleep-Disordered Breathing and the Effects of Nasal Continuous Positive Airway Pressure on Outcome After Ischemic Stroke

- □ 7 April 1999
- CUHK Research Committee Funding

Introduction: Several studies suggest a high prevalence of Sleep disordered breathing (SDB) in patients with acute stroke but there is little data in the Chinese population.

Methods: We have prospectively studied 21 adults (9F, 12M) following their first ischaemic stroke. Sleep and Health Questionnaire, cardiovascular risk factors, Barthel Index (B1), National Institute of Health (NIH) Stroke Scale, Cerebral Tomography and Epworth Sleepiness Scale (ESS) were assessed for the patients. Ischaemic stroke classified according to the Trial of Acute Stroke Treatment (TOAST) classification. Polysomnography (Healthdyne Alice4) was performed within one week from stroke onset. Significant SDB was defined as

Respiratory Disturbance Index (RDI) ≥20/hr with results compared to a control group of 14 adults (6M, 8F).

Results: (mean±SD) Mean age 66±12yrs, mean BMI 25±5kg/m² and neck circumference 37.4±4.0cm. History of hypertension noted in 33.3%, hypercholesterolaemia 66.7%, diabetes mellitus 28.6%, recent alcohol drinking 38%, current smoking 24%, snoring 81% and excessive daytime sleepiness 33% of subjects. ESS 6±3, NIH 4.3±2.8 (out of 42), BI 15±4.

Aetiology of ischaemic stroke: Cardiac 4.8%, small vessel 14.3%, large vessel 14.4% and unknown 66.7%. RDI 29±17, Sleep efficiency 76±13% and minimum SaO2 84±7%. Significant SDB occurred in 15/21(71%) subjects with predominantly obstructive events in all subjects compared to 4/14(29%) of the control group, matched for age, BMI and ESS.

Conclusion: Our preliminary data shows a high prevalence of SDB post ischaemic stroke. Further study is needed to see if nasal CPAP will alter the outcome of these patients. (MD98102)

The Efficacy of a Community Nurse Specialist in Preventing Hospital Readmission of Older Patients with Chronic Lung Disease and Cardiac Failure

- ≪ KWOK Chi Yui Timothy WOO Jean LAU Edith Ming Chu (Community and Family Medicine) LEE Tze Fan Diana (Nursing) TANG So Kum Catherine (Psychology)
- □ 4 January 1999
- Health Services Research Fund, Hospital Authority

This is a randomised controlled trial to evaluate the effectiveness of a community nurse specialist in preventing readmissions of older chronic lung disease and cardiac failure patients. It will also investigate the causes of readmissions of these patients.

150 Residents in Shatin & Taipo areas, above 65 years old, admitted to Prince of Wales, Shatin and Taipo Nethersole Hospitals with main diagnosis of chronic lung disease and cardiac failure, having had at least one hospital admission for related problems in previous six months. They are randomised into intervention and control groups before recruitment.

The intervention group receives visits from a nurse specialist before and after hospital discharge; regular telephone contacts with nurse specialist after discharge; telephone hotline for advice, and quick access to specialist medical care; reassessment upon readmission and at six months. The control subjects have pre-discharge assessment and follow-up upon readmission and at six months.

The primary outcome measures are the proportion of subjects free of hospital admissions related to chronic lung disease and cardiac failure within twenty-eight days and that within six months. The secondary outcomes are the total hospital days after discharge and change in functional and psychological scores. Cost effectiveness analysis will be performed. (MD98075)

Association of Plasminogen Activator Inhibitor (PAI-1) Gene Polymorphism with Diabetic Nephropathy Among Type 2 Diabetic Patients in Chinese

- ∠ LI Kam Tao Philip WONG Teresa*
- □ 23 June 1999
- ❖ Hong Kong Society of Nephrology Ltd

Type 2 Diabetic nephropathy has imposed a major health burden in Hong Kong. The importance of strict metabolic and blood pressure control has been documented fully for prevention of development and progression of diabetic nephropathy in these patients. However, contributions of genetic factors remained to be defined.

Epidemiology studies showed that the non-whites Type 2 population including Chinese have a higher prevalence of diabetic nephropathy than the white patients. Despite a similar duration of disease, blood pressure and glycemic control, some diabetic patients will develop renal failure while renal function remained to be preserved in others. clustering of renal failure has been reported in several populations suggesting that genetic factors may play a role in the onset and progression of diabetic nephropathy. Understanding of contributory genetic factors in development and progression of diabetic nephropathy may give us insights into the pathogenesis of disease. This may help in the identification of high risk patients and hence add guidance in the management of these patients. However, data on genetic factors of type 2 Chinese diabetic patients is lacking. We have previously demostrated the lack of association of Angiotensin converting enzyme (DD/II) and Angiotensinogen M235T gene polymorphism with renal function among type 2 diabetic patients in Chinese. Here we aim to study the relationships between plasminogen activator inhibitor-1 (PAI-1) gene polymorphisms and type 2 diabetic nephropathy with respect to renal function, clinical features and metabolic control. (MD98126)

The Effect of Hydroxychloroquine on Serum Lipids, Apolipoproteins and Lipoprotein(a) in Patients with Systemic Lupus Erythematosus

- ∠ LI Kwok Ming Edmund TOMLINSON Brian
 LAM Wai Kei Christopher (Chemical Pathology) TAM Lai Shan
- □ 1 September 1998

CUHK Research Committee Funding

Coronary atherosclerosis is very common in SLE patients who have been treated with corticosteroid for at least 1 year. Atherosclerotic vascular disease such as coronary artery disease (CAD) or stroke is one of the most frequent causes of death in SLE. Hyperlipidaemia and elevated levels of lipoprotein(a) have been shown to be important risk factors for CAD, stroke, and other thrombotic events in these patients. Hydroxychloroquine (HCQ) is one of the most common medications used in the treatment of systemic lupus erythematosus (SLE). Its less well known effects such as the prevention of disease or complications, treatment-induced hyperlipidaemia, have been recognized to some extent in the Caucasian populations.

In this cross sectional study, we will investigate the magnitude of hyperlipidaemia in a group of SLE patients without nephritis, and study the differences in the lipid profile, if any, in those who have been on treatment with HCQ and those who have never been on this drug. (MD98039)

A Multinational, Multicentre, Randomised, Double-Blind Study to Assess the Efficacy and Tolerability of Nifedipine GITS 20 mg Compared to Placebo in Low Body Weight Patients with Mild to Moderate Hypertension

- □ 5 May 1997
- * Bayer China Co Ltd

Nifedipine GITS (extended release tablets) has been designed to provide a slow sustained release of nifedipine which is an antihypertensive drug. Recent trials in Canada have shown that approximately 75% of patients who take nifedipine GITS are controlled on 30 mg. In Asia patients have a lower body weight and a lower dose may suffice. A new dose strength of nifedipine GITS 20 mg has been designed to address this need. The study primary objective is to assess whether nifedipine GITS 20 mg is effective in lowering blood pressure when given to low body weight Asian patients. (MD96219C)

The SYMPHONY Trial: A Phase III, Multicenter, International, Randomized, Double-Blind, Aspirin-Controlled Trial to Evaluate the Efficacy and Safety of Sibrafiban (Ro 48-3657), an Oral Platelet Glycoprotein IIb/IIIa Antagonist, as Therapy for the Prevention of Secondary Vascular Events in Patients after an Acute Coronary Syndrome

- □ 26 November 1997
- Hoffmann-La Roche Inc.

This trial is a multicenter, international, randomized, double-blind, aspirin-controlled trial comparing sibrafiban in two dosage regimens to aspirin. Patients who have suffered an episode of Acute Coronary Syndrome within the prior 7 days, who are hemodynamically stable, without clinically unstable heart failure, and without ongoing ischemic chest pain will be considered for enrollment. Patients will be randomized to one of three treatment arms: sibrafiban, high-dose; sibrafiban, low-dose; or aspirin. The treatment duration is 90 days. The primary efficacy endpoint is the 90 day incidence of a composite of any of the following events: death (from any cause), myocardial infarction or reinfarction and severe recurrent ischemia. The primary safety/tolerability endpoints are the 90 day incidence of major or minor bleeds and the 90 day incidence of study drug discontinuations due to bleeding. Assessments for efficacy will continue past the 90 day treatment period and assessment of primary endpoint out to one year after randomization. Patients who undergo intracoronary stenting for either the index event or during the trial will receive aspirin/ticlopidine. sibrafiban dose/ticlopidine or sibrafiban high dose/ticlopidine placebo (double-dummy design, based on their initial randomization) for 2-4 weeks following stent placement, and thereafter continue on their previously assigned therapy. (MD97176C)

The Paragon-B Trial

- □ 9 December 1998
- Quintiles Pty. Ltd.

Paragon-B is an international multicentre, randomized, double-blind placebo controlled trial of Lamifiban in-patients with unstable angina/non Q-wave myocardial infraction. Lamifiban is new class of highly selective GP IIb/IIIa platelet inhibitor for intravenous use in acute coronary syndrome. The primary end point of the trial is 30-day incidence of a composite of death, myocardial infarction and severe recurrent leading to urgent/unplanned investigation. (MD98146)

The 2nd Symphony Trial – Sibrafiban Versus Aspirin as Therapy for the Long Term Prevention of Secondary Vascular Events Post Acute Coronary Syndromes

- SANDERSON John Elsby
- □ 28 May 1999

Hoffmann-La Roche Inc.

The 2nd SYMPHONY Trial. A Phase III, multicenter, international randomized, double-blind, aspirincontrolled trial to evaluate the efficacy and safety of two regimens with XubixTM (sibrafiban; Ro 48-3657), an oral platelet glycoprotein IIb/IIIa receptor antagonist, as theray for the long term prevention of secondary vascular events in patients after an Acute Coronary Syndrome.

(MD98125C)

Does Helicobacter Pylori Cause Or Protect Against Gastro-Esophageal Reflux In Asia

- SUNG Joseph Jao Yiu CHUNG Sheung Chee Sydney (Surgery) • NG Enders K. W. (Surgery)* • CHAN Ka Leung Francis • WU Che Yuen Justin*
- □ 1 September 1998
- Research Grants Council

Helicobacter pylori is widely recognized as the most important cause of chronic gastritis, peptic ulcer disease and gastric malignancies. Recently, there is evidence suggesting H. pylori infection may also lead to gastro-esophageal reflux disease (GERD). On the other hand, some patients received treatment for eradicating H. pylori was found to develop GERD subsequently. The relationships between H. pylori infection, gastric acid secretion, esophageal motility and gastro-esophageal acid reflux is far from clear. In Asia, the prevalence of *H. pylori* infection is higher than most Western countries. This accounts for the high incidence of peptic ulcers and gastric cancer in this locality. On the other hand, it might also contribute to the low incidence of GERD among Asian populations. Is H. pylori CAUSING or PROTECTING against the development of GERD? The present project aims to investigate the relationship between H. pylori infection, gastric acid secretion and esophageal motility in patients suffering from various gastrointestinal disorders. We will compare the prevalence of *H. pylori* infection in Chinese patients with GERD against normal control. Patients suffering from gastric or duodenal ulcers are followed up after receiving anti-helicobacter therapy to monitor changes in gastric histology, gastric, cytokines and acid secretion. Finally, patients with H. pylori-related duodenal ulcers will be studied for esophageal motility and acid reflux after receiving anti-helicobacter therapy. The results of these three studies may shed light on the relationship between *H*. pylori infection and GERD. (CU98260)

Effects of Homocysteine on Platelet Aggregation in vitro

- TOMLINSON Brian CRITCHLEY Julian A J
- 1 September 1998
- CUHK Research Committee Funding

Elevated levels of homocysteine are associated with an increased risk of atherosclerosis and thrombosis through mechanisms which are not well understood and the related literature is often controversial. Elevated levels of homocysteine may be even more common than hypercholesterolaemia, the prevalence of hyperhomocyteinemia being between 20% and 40% in different populations with vascular disease. Elevated levels of homocysteine may be normalized by supplements with folate and vitamins B12 or B6. to understand. Understanding the mechanisms of the effect of homocysteine in cardiovascular diseases should prove useful in the prevention of premature vascular disease. Possible atherogenic mechanisms of homocysteine and its derivatives include changes in coagulation factors and platelet aggregation, alteration of the vasomotor regulatory and antithrombomotic properties of vascular endothelium and stimulation of smooth muscle cell proliferation. Platelet function appears to play an important role in athero-genesis and thrombogenisis and it is possible that elevated homocysteine levels may influence this. Researchers shall investigate the effects of homocysteine and its derivatives on the platelet aggregation induced by ADP and collagen using the impedance aggregometer electric technique measuring platelet aggregation in whole blood in vitro in healthy Chinese subjects. If it appears that changes in homocysteine levels affect platelet aggregation in vitro, researchers will continue with further studies of platelet aggregation ex vivo and in vivo in order to investigate the mechanisms by which homocysteine contributes to vascular disease and this may help to develop strategies to treat or prevent vascular disease. (MD98040)

An Open-Label Study to Evaluate the Efficacy and Safety of 80 mg Simvastatin in Patients with Hyperlipidaemia

- TOMLINSON Brian TANG Leung Sang Nelson (Chemical Pathology) • CHAN, Michael*
- □ 20 October 1998
- Merck Sharp & Dohme (Asia) Ltd

This study will be performed to evaluate the LDL (LDL-C)-lowering efficacy cholesterol tolerability of 80 mg/day of simvastatin in patients with severe hypercholesterolaemia over an 8-week period. It is a single centre, open-label, study in which patients will be entered into a 2-week screening / diet / placebo run-in period followed by a

12-week treatment period which includes two phases, 40 mg/day (as a single dose for 4 weeks) and 80 mg/day (as a single dose for 8 weeks). A sub-study for investigating the cholesterol sources in the body by testing the urinary mevalonate levels will also be carried out. Total cholesterol (TC), LDL-C, high density lipoprotein cholesterol (HDL-C) and triglycerides (TG) will be measured and clinical evaluation including vital signs and physical examinations and laboratory safety tests including alanine aminotransferase (ALT), gamma glutamyltransferase (gammaGT) and creatine kinase (CK) will be performed continuously during the study. (MD98120C)

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)

- □ 20 October 1998
- ❖ Merck Sharp & Dohme (Asia) Ltd

This is a multicenter, randomized, double-blind, parallel, dose escalation study. This study will be conducted primarily to evaluate the comparative effects of simvastatin 40 and 80 mg/day versus atorvastatin 20, 40, and 80 mg/day, on high-density lipoprotein cholesterol (HDL-C) and apo A-1 and secondarily to evaluate the comparative effects of these drug doses on low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG) and their comparative safety over 36 weeks of treatment. Patients will be stratified by baseline HDL-C levels to assure balance between treatments. (MD98121C)

The Frequency and Significance of Microembolic Signals in Acute Stroke Patients with Middle Cerebral Artery Stenosis

- WONG Ka Sing Lawrence LAM Wai Man Wynnie (Diagnostic Radiology & Organ Imaging) CHAN Yu Leung (Diagnostic Radiology & Organ Imaging) METREWELI Constantine (Diagnostic Radiology & Organ Imaging) KAY Li Chi Richard
- ☐ 1 October 1998
- * Research Grants Council

Stroke is the third leading cause of mortality and a leading cause of disability in adult in Hong Kong. In Chinese stroke patient, middle cerebral artery stenosis is the most commonly found vascular lesion in patients with acute ischemic stroke. Yet the stroke

mechanism (thromboembolic or hemodynamic) in patients with middle cerebral artery stenosis remains uncertain. Recent advances in ultrasonology enable us to monitor the occurrence of microemboli signals (MES) in the cerebral circulation. Studies of MES in patients with carotid stenosis have shown that it occurred commonly in acute stroke but much less commonly in asymptomatic patients, suggesting MES may be a marker of active thrombotic process. There have been no published data on the detection of MES in acute stroke patients with middle cerebral artery stenosis. In preparation for the submission of this grant application, we performed a pilot study of twenty acute stroke patients with middle cerebral artery stenosis and found MES occurred in 15%. We propose to perform a study on 150 acute stroke patients with middle cerebral stenosis in order to document the frequency of MES and correlate its occurrence with thrombotic markers. The prognostic value of MES in relation to recurrent ischemic events will also be investigated. The finding of this study may guide us towards a better strategy in secondary stroke prevention in these high-risk patients. (CU98341)

Clinical Trial for GLYB 3001 in Acute Stroke

- MONG Ka Sing Lawrence
- ☐ 1 November 1998
- Glaxo Group Research Limited

Stroke is a leading cause of mortality and morbidity worldwide. Traditional treatment strategy composed mainly of antithrombotic and thrombolytic therapies. Recent advent in animal studies shows the benefit of neuroprotection to limit secondary brain injury after cerebral ischemia. However, early clinical trials of neuroprotection fail to confirm this benefit to human being. Glycine antagoinist is one of the most potent neuroprotant studied. In this randomized, doubleblind, placebo-controlled trial, we aim to participate in this multinational clinical trial to test the hypothesis that the use of a glycine antagonist prevent poor outcome for patients with stroke who received treatment within 6 hours of onset of symptoms. (MD98145)

Pramipexole: Efficacy, Safety and Tolerability Study in Parkinson's Disease patients, a Multinational Study

- WONG Ka Sing Lawrence KAY Li Chi Richard
- □ 1 December 1998
- Pharmacia and Upjoin Limited

Parkinson's Disease is a major cause of disability in the elderly population in Hong Kong. Current trend in therapy emphasises on the importance of adjunct therapy, especially dopamine agonist, in the treatment of Parkinson's disease. Pramipexole is a newly developed dopamine agonist with D3-preferring property. In oversea studies, pramipexole has been shown to reduce the motor fluctuation complication of Parkinson's disease in Western countries. However, the efficacy and tolerability in Asian populations have not been established. The proposed study is a multicentered, study in Hong Kong and Taiwan. It aims to study the safety and tolerability of pramipexole in patients with Parkinson's disease. The primary endpoint is measured by the change from the beginning of the study in Unified Parkinson's Disease Rating Scale II and III, compared to the baseline visit. A maximum of 150 patients will be recruited from Hong Kong and Taiwan. This study will take 10-12 months for the recruitment and follow-up phase and another 6 months for analysis. (MD98085)

Quality of Life Assessment for Palliative Care

- WOO Jean

 LO See Kit Raymond*
- □ 1 July 1998
- Society for the Promotion of Hospice Care Limited

The project is an extension of a successful pilot study of quality of life of palliative care patients in Shatin Hospital. The present proposed project is a longitudinal study, aiming to assess quality of life of palliative care patients in Shatin Hospital from admission to death, or from admission to discharge and post discharge in community depending on their survival. The assessment tool will be translated version of McGill Quality of Life questionnaire, which was designed and validated specially for palliative care patients. The project will provide very informative data of QOL of palliative care patients, and the changes as their illness proceeds. It will also highlight different perceptions of different patient groups. It will evaluate the practicability and suitability of routine application of a QOL questionnaire. Deficiencies in current care can be identified for continuous quality improvement and auditing. Staff awareness of importance of QOL as main goal in palliative care will be heightened, and further research can be promoted locally. (MD98003)

A Multicenter, Double-Blind, Randomized, Parallel Group Study to Compare the Antihypertensive Efficacy of Losartan Versus Candesartan Cilexetil in Patients with Mild to Moderate Hypertension

- ∠ WOO Kam Sang SANDERSON John Elsby •
 CHIU C. W.* YIP Thomas* KWONG S. K.*
- ☐ 1 October 1998

❖ Merck Sharp & Dohme (Asia) Ltd

Hypertension is one of the most common adults disease. It is a major determinant of stroke and coronary artery disease and blood pressure reduction has been clearly demonstrated to significantly reduce the incidence of these disorder as well as total mortality.

The renin angiotension system (RAS) plays an important role in the regulation of blood pressure and volume homeostasis, and angiotension (AII) is the active mediator, mostly through its interaction with the AT-1 isoform of the angiotension II receptor. Blockage of this RAS can be achieved by angiotensin converting enzyme inhibitor or by inhibition at the angiotension II receptor site. The former has been useful in treatment of hypertension, but its utilization is often limited by high incidence of drug induced cough, necessitating drug withdrawal. A new class of specific, selective and orally active AT-1 receptor antagonists has been developed; Losartan and Candesartan Cilexetil are the two agents demonstrated to have a potent antihypertensive effect and good side effect profile in preliminary trials.

The current study is designed to evaluate the antihypertensive efficacy of Losartan either as monotherapy 50-100mg daily, or in combination with hydro-chlorothiazide (12.5mg) versus Candesartan monotherapy 8-16mg daily in patients with mild to moduate essential hypertension. Patients with diastolic blood pressure (DBP) (95-115) mHg and systolic blood pressure<170 mHg after 4 weeks' placebo washout will be randomized to take either losartan 50 mg or Candesartan Celexetil 8 mg on double blind parallel fashion, allowing titration up to Losartan 100mg daily, Candesartan 16mg daily or Losartan 50mg + hydrochlorothiazide 12.5 mg daily if DBP > 90mHg after 6 weeks. The total treatment period is 12 weeks. Routine biochemistry profile will be closely monitored, as well as drug-related adverse experiences, and the numbers of patients discontinuing between the treatment arms after 12 weeks of double-blind therapy will be compared. (MD98088)

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

Edition <u>Title/Investigators</u>

1997-98 Cost-effective Approaches to Gastrointestinal and Antihypertensive Drug Prescribing: An Economic Impact Study of Intervention Mechanisms in the Inpatient and Out-patient Setting (MD96023)

CHANG Sophie (Pharmacy)# ◆ CRITCHLEY Julian A J H

Organ Imaging)

Relationship between Air Quality and

Tejbhan (Diagnostic Radiology &

1997-98 A Multicentre Study to Examine the Renoprotective Effects of Losartan, an Angiotensin II Antagonist Versus Placebo in Type 2 Diabetic Patients (MD97168)

- CHAN Chung Ngor Juliana
 COCKRAM Clive Stewart
 CRITCHLEY Julian A J H
- 1997-98 Phenotypic and Genotypic Characterisation of NIDDM (Type 2 Diabetes Mellitus) and their Interactions with Environmental Factors (CU97682)
 - ∠ CHAN Chung Ngor Juliana

 YEUNG Tok Fai Vincent

 CHOW

 Chun Chung Francis

 COCKRAM

 Clive Stewart

 CRITCHLEY Julian

 A J H

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 CHOW

 C
- 1997-98 NSAID-Induced Peptic Ulcer Bleeding: Protection at a Lower Cost? (MD97004)
 - CHAN Ka Leung Francis SUNG Joseph Jao Yiu
- 1997-98 Helicobacter Pylori Infection, Cyclo-Oxygenase, and Gastric Carcinogenesis (MD97116)
 - ∠ CHAN Ka Leung Francis SUNG

 Joseph Jao Yiu LEUNG W. K.* •

 TO Ka Fai (Anatomical & Cellular

 Pathology)
- 1996-97 The Role of the Renal Kallikrein-kinin System in the Regulation of Sodium Balance and Blood Pressure in Chinese Subjects in Relation to a Family History of Hypertension, Low/Normal Renin Hypertension or NIDDM Albuminuric Status (CU96675)
 - ∠ CHAN Yan Keung Thomas CHAN
 Chung Ngor Juliana YOUNG
 Robert Peter# TOMLINSON Brian
 • CRITCHLEY Julian A J H
- 1997-98 Matrix-Metalloproteinases (MMPs) and their Specific Inhibitors (TIMPs) in Tuberculous Pleural Effusions (MD97132)
 - ∠ HUI Shu Cheong David LAI Kei Wai Christopher HOHEISEL Gerhard*
- 1996-97 Pilot Study of Clomethiazole in the Treatment of Intracerebral Haemorrhage (MD96055)
 - KAY Li Chi Richard WONG Ka Sing Lawrence • AHUJA Anil

- 1996-97 Relationship between Air Quality and Hospital Admissions for Respiratory Disease in Hong Kong (MD96056)
 - ∠ LAI Kei Wai Christopher LAU Tai Shing (Statistics) • LEUNG Chung Chuen Roland • WONG Wing Kin Gary (Paediatrics) • YAM Loretta*
- 1997-98 The Effects of an Education Programme on the Compliance with Nasal CPAP in the Treatment of Obstructive Sleep Apnoea (MD97006)
 - ∠ LAI Kei Wai Christopher HUI Shu Cheong David • LEUNG Chung Chuen Roland • CHAN Ka Wing, Joseph*
- 1996-97 Prevalence of Sleep Disorder Breathing in Young Adults in Hong Kong (MD96057)
 - ∠ LEUNG Chung Chuen Roland LAI Kei Wai Christopher
- 1996-97 The Role of Cytokine Growth Factors in the Control of Myocardial Collagen Turnover and the Development of Left Ventricular Diastolic Dysfunction in Patients with Heart Failure (CU96670)
 - ≤ SANDERSON John Elsby CHOW
 Tsun Cheung Louis (Anatomical &
 Cellular Pathology) WOO Kam
 Sang
- 1997-98 The Non-Invasive Assessment of Left and Right Ventricular Diastolic Function with Two Dimensional and Doppler Echocardiography. Colour Doppler Myocardial Imaging (CDMI) and Atrio-Ventricular Plane Displacement (MD97117)
 - SANDERSON John Elsby YIP Gabriel*
- 1995-96 A Follow-On Study to Determine the Safety and Efficacy of Long Term Lamivudine Treatment in Patients with Chronic Hepatitis B Infection (NUCB 3018) (MD95267)
- 1995-96 *Helicobacter pylori:* Mode of Transmission and Carcinogenesis (MD95255)
 - SUNG Joseph Jao Yiu ◆ CHUNG Sheung Chee Sydney (Surgery) ◆ TO

Ka Fai (Anatomical & Cellular Pathology) ◆ CHENG Fun Bun Augustine (Microbiology) ◆ LIN Sar-ren*

1996-97

- 1996-97 A Double-blind, Parallel Group, Placebo Controlled, Multi-center, Phase IIIA Study to Assess the Safety and Efficacy of Oral Famciclovir (Three Times a Day) for the Treatment of Chronic Hepatitis B in Asian Population (MD96222)
- 1996-97 Does Eradication of *Helicobacter pylori* Prevents NSAID-related Ulcers and Complications (CU96604)
- 1997-98 The Use of Endosonography and MR Angiography in Predicting the Risk of Variceal Bleeding in Portal Hypertension (CU97657)
 - Z SUNG Joseph Jao Yiu ◆ CHAN Yu Leung (Diagnostic Radiology & Organ Imaging) ◆ CHUNG Sheung Chee Sydney (Surgery) ◆ LAM Wai Man Wynnie (Diagnostic Radiology & Organ Imaging) ◆ LEE Y. T.*
- 1995-96 Identification of Risk Factors for Atheroma in Chinese Patients with Overt Peripheral Vascular Disease and Diabetic Patients with Asymptomatic Peripheral Vascular Disease (CU95649)
 - ▼ TOMLINSON Brian KING Wing Keung Walter (Surgery) LI Arthur K. C. (Surgery) LAM Wai Kei Christopher (Chemical Pathology) LOLIN Yvette Ivanka (Chemical Pathology)# CHAN Chung Ngor Juliana CRITCHLEY Julian A J H YOUNG Robert Peter# COCKRAM Clive Stewart
- 1996-97 Investigation of the Genetic Region of the Lipoprotein Lipase Gene in Families of Dyslipidaemic Patients and Relation to Blood Pressure and Insulin Resistance (MD96050)
 - Z TOMLINSON Brian ◆ CHENG
 Shuk Han (Orthopaedics &
 Traumatology) ◆ CRITCHLEY

Julian A J H • YOUNG Robert Peter#

- Study of the Metabolic Syndrome in Hong Kong Chinese: Investigations of the Phenotypic Characteristics and Underlying Genotypes in Patients with the Metabolic Syndrome Presenting with Dyslipidaemia, Non-insulin Dependent Diabetes Mellitus, Hypertension or Atheromatous Vascular Disease (MD96027)
 - TOMLINSON Brian CHAN
 Chung Ngor Juliana CRITCHLEY
 Julian A J H YOUNG Robert
 Peter# PANG Chi Pui Calvin
 (Ophthalmology and Visual Sciences)
 ARUMANAYAGAM Manoharan
 (Chemical Pathology) CHAN Yu
 Leung (Diagnostic Radiology &
 Organ Imaging) CHAN Yan
 Keung Thomas SANDERSON
 John Elsby COCKRAM Clive
 Stewart YEUNG Tok Fai Vincent
 CHOW C. C.*
- 1997-98 The Effects of Different Doses of Vitamin E on Atheroma Formation and Indices of antioxidant Activity and Oxidative Stress in Cholesterol-Fed Rabbits (MD97047)
 - TOMLINSON Brian JAMES
 Anthony Edward (Laboratory
 Animal Services Centre) BENZIE
 Iris F. F.* ARUMANAYAGAM
 Manoharan (Chemical Pathology) ●
 SAHOTA Daljit Singh (Obstetrics &
 Gynaecology) CRITCHLEY Julian
 A J H HAINES Christopher John
 (Obstetrics & Gynaecology)
- 1995-96 Regress of Cerebral Artery Stenosis Study (MD95268)
 - WONG Ka Sing Lawrence ◆ KAY
 Li Chi Richard ◆ LAM Wai Man
 Wynnie (Diagnostic Radiology &
 Organ Imaging) ◆ CHAN Yu Leung
 (Diagnostic Radiology & Organ
 Imaging)
- 1996-97 A Prospective Study of Patients with Middle Cerebral Artery Stenosis Diagnosed After First Ever Ischemic Stroke (CU96605)
 - WONG Ka Sing Lawrence KAY
 Li Chi Richard AHUJA Anil
 Tejbhan (Diagnostic Radiology &
 Organ Imaging)

- 1996-97 Regress of Cerebral Artery Stenosis Study (MD96059)
 - ∠ WONG Ka Sing Lawrence LAM
 Wai Man Wynnie (Diagnostic
 Radiology & Organ Imaging) •
 CHAN Yu Leung (Diagnostic
 Radiology & Organ Imaging) •
 KAY Li Chi Richard
- 1997-98 A Prospective Study of Asymptomatic Patients with Middle Cerebral Artery Stenosis (CU97673)
 - ✓ WONG Ka Sing Lawrence LAM Wai Man Wynnie (Diagnostic Radiology & Organ Imaging) •
 YEUNG Tok Fai Vincent CHAN Yu Leung (Diagnostic Radiology & Organ Imaging) KAY Li Chi Richard
- 1996-97 Domiciliary Pulmonary Rehabilitation Program: A Randomised Controlled Clinical Trial(MD96017)
 - WOO Jean ◆ LUM Christopher* ◆
 HUI E.* ◆ LEUNG Chung Chuen
 Roland
- 1997-98 Provision of Health Services Elderly Residents in Nursing Homes Using Telemedicine (MD97005)

- WOO Jean HJELM Nils Magnus (Chemical Pathology) • TSUI Hung Tat (Electronic Engineering) • ZHANG Yuanting (Electronic Engineering)
- 1997-98 A Nutrition Manual for Carers in Elderly Residential Homes (MD97026)
- 1997-98 An Investigation of the Roles of C-Type
 Natriuretic Peptide in Central
 Haemodynamic and Endocrine Control
 Using a Gene-Targeting Approach
 (MD97048)
 - ∠ YEUNG Tok Fai Vincent CHUI Yiu Loon (Clinical Immunology Unit) LEE Sau Tuen Susanna (Biochemistry) COCKRAM Clive Stewart

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RESEARCH PROJECTS

aminoglycoside/aminocyclitol Mechanisms of resistance in mycobacteria

- ∠ CHAN Chiu Yeung Raphael
- 1 August 1998
- Research Grants Council

Tuberculosis, especially those caused by multi-drug resistant isolates of Mycobacterium tuberculosis, and infections caused by mycobacteria other than tuberculosis (MOTT), have become important uprising problems in infectious diseases worldwide. Aminoglycosides/aminocyclitols, including streptomycin, kanamycin and amikacin, have been the key drugs in the first-, second-, and third-line therapeutic regimens for these infections. Numerous reports have recently been published concerning clinical isolates of mycobacteria resistant to Although the aminoglycoside aminoglycosides. resistance mechanisms involving the production of aminoglycoside modifying enzymes (AME), barrier effect and target site modification have been elucidated in Gram-negative bacteria, studies on such mechanisms in mycobacteria have been scarce. Our research laboratory, having received support from a UGC-direct grant three years ago, has started pioneer work on the screening of aminoglycoside modifying enzymes in mycobacteria and to elucidate the *in vitro* enzyme activities in relation to resistance. Since the results from our preliminary study pointed out that the resistance mechanisms may not be solely due to the presence of AMEs, in this proposal we intend to:

- (1) examine for ribosomal resistance aminoglycoside-aminocyclitols in mycobacteria;
- (2) examine for resistance arising from reduced drug uptake in mycobacteria;
- (3) further study the relative role of aminoglycosidemodifying enzymes (AMEs) and uptake barrier in aminoglycoside resistance in mycobacteria;
- (4) determine the genetic determinants aminoglycoside-modifying enzymes in; and
- (5) identify the mutations in ribosomal resistant strains An understanding on the resistance mechanisms in mycobacteria against aminoglycosides will allow us to improve our present therapeutic regimens in the battle against tuberculosis and other mycobacterial infections. (CU98237)

TT Virus Infection in Patients with Haemophilia and Transfusion-Dependent Thalassaemia

- & CHAN Kay Sheung Paul CHIK Ki Wai (Paediatrics) • CHENG Fun Bun Augustine • LI Chi Kong (Paediatrics)
- ☐ 1 April 1999
- CUHK Research Committee Funding

Background: In 1997, a novel virus, TT virus (TTV), was identified from a patient with post-transfusion non-A, B, C hepatitis. TTV has a wide range of sequence divergence allowing classification into genotypes 1 and 2, subtypes a and b. Blood-borne transmission has been suggested based on the higher prevalence among intravenous drug users, patients with haemophilia or on maintenance haemodialysis. The limited available data also suggest TTV infection may account for a portion of acute and chronic hepatitis of unknown aetiology. While the presence of TTV viraemia in about 10% of the general population suggests a carrier stage exists, the consequences of which have not been elucidated. Study design: We propose a retrospective study on patients with haemophilia and transfusion-dependent thalassaemia. Their stored blood samples that have been obtained at intervals of 6-12 months will be sought for the presence of TTV viraemia by polymerase chain reaction. The DNA sequence will be determined by direct sequencing. Clinical data including hepatitis B, C and HIV statuses, liver function profile, use of blood and blood products will be correlated with results of TTV detection.

Objectives:

- (1) To define the prevalence and genotypic distribution of TTV infection among patients with haemophilia and transfusion-dependent
- (2) To analysis the phylogenetic relationship between isolates obtained from local patients and that from Japan, Europe and Thailand;
- (3) To elucidate the clinical course of TTV infection, in particular the duration of viraemia, proportion of chronicity, effects on liver function during the acute and chronic stages of infection.

(MD98103)

Studies on the Production of Proinflammatory Cytokines in Human Macrophages Induced by Microbial Pathogens and in Cerebrospinal Fluids from Patients with Meningitis - a Search for Interleukin 1-a

- CHENG Fun Bun Augustine CHAN Chiu Yeung Raphael
- □ 1 October 1998
- CUHK Research Committee Funding

Meningitis is a serious infectious disease with high morbidity and mortality. Traditionally, therapy for the disease is mainly on appropriate targeting of the infectious agents after rapid diagnosis has been made. However, since inflammation of the central nervous system (CNS) usually occurs after the infectious process, understanding of the pathogenic and pathophysiologic mechanisms underlying the disease is essential, and studies on the immune responses by cells in the cerebrospinal fluid after encountering the infectious agents or their products are necessary.

Cytokines, especially the proinflammatory factors, are known to play an important role in regulating the inflammatory process by maintaining a balanced homeostatic environment in the CNS so as to reduce the harmful effects on the target cells, however, the effects contributed by these compounds may become disastrous resulting in damages when they are overevoked. In this proposal researchers intend to study the expression of a cytokine (interleukin 1-α) in human macrophages (THP-1 cells) after exposure to micro-organisms and to products produced by these organisms isolated from patients with meningitis, and to study the content and levels of this cytokine in clinical specimens of cerebrospinal fluids (CSF) from patients with meningitis due to different aetiology before and after treatment. As it is likely that cytokines would be produced early in an inflammatory process, studies on the time course cytokines expressed by human macrophages to those of CSF may identify the earliest existence of the cytokines which may serve as a marker for meningitis and allow the possible development of a rapid diagnostic test for meningitis, and the late production of cytokines after infection and treatment may also serve as prognostic markers. (MD98041)

The Role of Skin Fatty Acid Profiles in the Carriage of Acinetobacter spp

- MOUANG Ting Sou Elizabeth CHU Yiu Wai • CHEUNG S. W.*
- □ 1 October 1998
- CUHK Research Committee Funding

Since 1986, Acinetobacter spp have been classified into 19 genomic species. Acinetobacter baumannii is the commonest species associated with nosocomial infections and hospital outbreaks in different parts of the world, particularly in Hong Kong. Researchers recent research shows that A. lwoffii is the commonest species (60%) recovered from skin of healthy subjects in Europe and A. baumannii is uncommon (1%). Whereas, in Hong Kong, 60% of isolates are A.baumannii. Factors that may explain the differences in our findings include Hong Kong's hot, humid climate, racial differences (e.g. patterns of skin free fatty acids (FFA)), diets, or the natural distribution of different genotypes in different geographical areas. On the other hand, researchers' work on vegetable isolates from London and Hong Kong showed the range of genospecies harboured are similar. They have also showed that different genospecies have different profiles of tolerance to different fatty acids. Researchers therefore propose to correlate skin FFA profiles with the carriage of different genospecies of acinetobacters in Londoners, Hong Kong Chinese and Hong Kong Caucasian subjects. On the forehead of each healthy volunteer, a swab for the isolation of Acinetobacter spp and 2

alcohol-soaked filter paper discs will be applied. The genospecies of acinetobacters will be determined by amplified ribosomal DNA restriction analysis together with their susceptibilities to 11 FFA. Skin FFA profiles will be obtained by gas liquid chromatography using a flame ionization or mass selective detector. Results of the study should contribute to our understanding of the natural habitat of A.baumannii in humans and its acquisition as a noscomial pathogen.

(MD98042)

Rapid Detection and Identification of Medically **Important Fungi by Molecular Methods**

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 Paul • CHENG Fun Bun Augustine
- 1 November 1998
- CUHK Research Committee Funding

fungal infection is an important complication in immunocompromised patients. Due to the vast range of etiological organisms which stretches from yeast to filamentous fungi, the use of conventional methods for detection and identification have been difficult and time consuming. Often, clinicians face the dilemma on initiation of empiric antifungal therapy which is often toxic and requires prolonged therapy without an established diagnosis. The objective of this study is to establish a rapid diagnostic molecular method applicable to routine clinical laboratory and to evaluate its feasibility and value in the clinical settings. The target organisms involve medically important fungi which are commonly found in immunocompromised host. Several known methods for extraction of DNA in fungal cells will be evaluated. Extracted DNA from fungal cells will be amplified by polymerase chain reaction using conserved primer sets based on the 18S ribosomal RNA sequence. Various methods including restriction fragment length polymorphism, hybridization and Southern blot will be explored for the identification of the organism to species level. Study on simulated blood will also be performed by spiking known quantity of fungi into EDTA blood in order to evaluate its use in the clinical setting and for the monitoring of antifungal therapy. (MD98043)

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

Title/Investigators Edition

1997-98 Association of Human Herpesvirus Types 6 and 7 with Cervical Cancer (MD97050) ∠ CHAN Kay Sheung Paul • CHAN May* • LI W. H.* • CHENG Fun Bun Augustine

HOUANG Ting Sou Elizabeth • IP 1997-98 Margaret • CHU Yiu Wai *In-vitro* Activity of Tazocin Comparison with Other Commonly Used Antibiotics against Clinical Isolates 1997-98 Molecular Epidemiology of Penicillinand Multidrug-Resistant Streptococcus (MD97147) ∠ CHENG Fun Bun Augustine
 ◆ LING pneumoniae (CU97607) Kin Wah Thomas ✓ IP Margaret • LYON Donald James • CHENG Fun Bun Augustine 1996-97 A Comparison of Acinetobacter spp Distribution in Humans and in Raw 1997-98 Study of the Colonisation and Role of Vegetables in Hong Kong and London Spread of (Drug-Resistant) Streptococcus (MD96062) Pneumoniae in Elderly Day Care Centres ME HOUANG Ting Sou Elizabeth • and Residential Homes (MD97017) CHU Yiu Wai • CHENG Fun Bun & Therapeutics) • LYON Donald Augustine James • WOO Jean (Medicine & 1996-97 Ulcerative Keratitis and Contact Lens Therapeutics) • CHENG Fun Bun Related Infection in Hong Kong Augustine (MD96015) 1997-98 Identification of Genes of Extended-Spectrum β -Lactamases by Polymerase LAM Shun Chiu Dennis (Ophthalmology and Visual Sciences) Chain Oligotyping Reaction and Mark TSO On Man (MD97118) and Visual (Ophthalmology ∠ LING Mei Lun Julia Sciences)# • CHENG Fun Bun Augustine • LYON Donald James 1996-97 A Multicentre Study to Determine the Efficacy of High-Dose Interferon Alpha-1996-97 A Comparison of Acinetobacter spp 2b in the Treatment of Chronic Hepatitis Distribution in Humans and in Raw B Virus Infection in Asia (MD96180) Vegetables in Hong Kong and London (MD96019) Bun Augustine • LEUNG Nancy* ME HOUANG Ting Sou Elizabeth • PITT Tyrone Leslie* 1997-98 Cloning and Characterization of Epstein-Barr Virus (EBV) Latent Membrane 1997-98 Acinetobacter Genospecies: Their Antigen 2 (LMP-2) Genes Associated Distribution in Hong Kong and with Nasopharyngeal Carcinoma Evaluation of PCR Identification (MD97049) Methods (CU97625) ∠
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 HOUANG Ting Sou Elizabeth • Sheung Paul • CHENG Fun Bun

RESEARCH OUTPUTS AND PUBLICATIONS

CHU Yiu Wai • PITT Tyrone

The Study of Antimicrobial Resistance in

Leslie*

Acinetobacter (MD97010)

1997-98

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Augustine

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see also <P974973>, <P975031>, <P982507>, <P982513>, <P982552>, <P982563>, <P982586>, <P982871>, <P984219>, <P984358>, <P990411>, <P990441>, <P990443>, <P990825>, <P991272>, <P991697>

RESEARCH PROJECTS

Decision-Making Preferences of Hong Kong Chinese People

- MENDERSON Amanda Jane CHIEN Wai Tong
- ☐ 1 January 1999
- CUHK Departmental Funding

Economic, Social, ethical and legal concerns are motivating changes in western type health practise to encourage patients in decisions made about their health care. This study explored the degree to which H.K. Chinese patients desire participation in decision making of their treatment. Decision-making choice would be determined by asking patients to select a card from 4 picture cards from the doctor having full control to the patient having full control, Interviews were conducted to ask about why they chose a particular card. The findings are now going to be analysed. (MD98130)

The Relationship Between Women's Childbirth Expectations and Their Feelings of Control During Labour

- ∠ IP Wan Yim
- □ 1 July 1998
- CUHK Departmental Funding

Research strongly suggests that congruence between a woman's expectation for childbirth and the actual experience play an important role in influencing her perception and evaluation of the birth process. Bramadat (1990) suggested that perception of control during labour might contribute to childbirth. The purpose of this study is to explore the Chinese firsttime pregnant women's childbirth expectation, and its relationship with women's feelings of control during A prospective, correctional descriptive labour. design will be employed for this study. All Chinese first-time pregnant women during their last four weeks of pregnancy will be invited to particepates the Childbirth expectation Questionnaire and Labour Agency Scale will be used to measure women's childbirth expectations and feeling of control during labour. The results of the finding will provide information on Chinese women's childbirth expectation which will address the type of childbirth preparation needed to be provided by health professional. (MD98131)

Umbilical Cord Coiling Index and Entanglement

- □ 27 October 1998
- CUHK Departmental Funding

To establish the relationship between umbilical cord coiling index, Wharton's jelly thickness and fetal distress due to cord entanglement. (MD98013)

Evaluating the Morse Fall Scale in Medical and Geriatric Units

- ∠ LEE Fung Kam MACKENZIE Ann Elizabeth
- ☐ 1 September 1998
- CUHK Departmental Funding

Patients falls are a significant issue in patient safety as it constitutes the largest single category of patient accidents in hospitals. Falls produce adverse effects on the recovery of patients in both physiological and Falls also increase the psychosocial aspects. healthcare cost in terms of care and treatment. Therefore, prevention of falls is of utmost importance to quality care and healthcare cost-containment. Fall prevention starts with fall risk assessment. The accuracy of a fall risk assessment is basic and important for the success of a fall prevention program. The Morse Fall Scale (MFS) has been identified as a valid fall risk assessment tool in the previous literature, but it has not been validated in Hong Kong. Therefore, the purpose of the study is to evaluate the MFS in Hong Kong. A prospective - descriptive research design was employed. Samples were recruited from medical units in an acute hospital. Sensitivity and specificity of the MFS were determined. Results of the MFS were compared with nurses' clinical judgements. Cutoff point for the MFS was also discussed. (MD98132)

A Care Protocol to Reduce Hospital Readmissions of Elderly Residential Care Home Patients with Chronic Obstructive Pulmonary Disease (COPD)

- ∠ LEE Tze Fan Diana MACKENZIE Ann Elizabeth LEE Fung Kam LAI Shuet Fun, Adela* LO Lai Fong, Tammi*
- ☐ 1 November 1998
- Health Services Research Fund, Hospital Authority

The aim of this project is to evaluate the effectiveness of an experimental care protocol used by community nurses to support residential care home staff in taking care of patients with chronic obstructive pulmonary disease. A matched, randomized pretest-posttest case control design is used. The main measure outcomes

include patients' functional, respiratory and psychological well-being and hospital services utilization. Cost-effectiveness analysis will also be conducted. Results of this study will have implications for the development of an effective and practical approach for preventing the return of residential care home patients to the hospital. (MD98073)

The Qualitative Experiences of Postnatal Depression in Hong Kong Chinese Women

- ∠ LEVY Valerie Anne CHAN Wai Chi Sally LEE Tak Shing Dominic (Psychiatry) CHUNG Kwok Hung Tony (Obstetrics & Gynaecology)
- □ 2 November 1998
- Health Services Research Fund, Hospital Authority

Objectives: To examine the qualitative experience of postnatal depression in a group of Hong Kong Chinese women diagnosed as suffering from postnatal depression, to investigate the factors perceived by the women as contributing to their depression, to identify their help-seeking behaviours and to compare their experiences with a group of women diagnosed with non-postnatal depression.

Design: Qualitative descriptive survey, using in-depth interviews

Setting: In psychiatric clinic or participant's home Participants: 50 Hong Kong Chinese women diagnosed as experiencing minor or major postnatal depression, 20 Hong Kong Chinese women diagnosed with non-postnatal depression.

Conclusions: Themes identified from the data will be used to illuminate the lived experience of postnatal depression in this group of women and will contribute to the development of guidelines for nurses and other health professionals in identifying and caring for Chinese women in Hong Kong with postnatal depression.

(MD98066)

The Clinical Management of Chemotherapy-Induced Nausea and Vomiting with Adjuvant Progressive Muscle Relaxation Training and Imagery Techniques in Breast Cancer patients

- MOLASIOTIS Alexandros ◆ YUNG Ha Ping Hilary ◆ MOK Shu Kam Tony (Clinical Oncology) ◆ YAM Bernard Man Chung
- □ 6 July 1998
- Health Services Research Fund, Hospital Authority

This study is designed to assess the effectiveness of progressive muscle relaxation training (PMRT) in the clinical management of chemotherapy-related nausea

and vomiting as adjuvant intervention to standard antiemetic treatment.

Design: Randomised controlled trial.

Subjects / setting: 92 breast cancer chemotherapy naï ve patients in the outpatient oncology unit of a university hospital in Hong Kong.

Intervention: PMRT 1 hour prior to chemotherapy administration and daily thereafter for another 5 days (total of 6 PMRT sessions). Each session lasts for 25 minutes followed by 5 minutes of imagery techniques. Main outcome measures: Chinese versions of Profile of Mood States, State-Trait Anxiety inventory, Morrow Assessment of Nausea and Vomiting scale, short structured interview. Conclusion: It is anticipated that the findings will provide a better understanding of the role of PMRT in the control of nausea and vomiting ie cancer patients after chemotherapy, and will enhance the care of cancer patients who experience chemotherapy, side-effects. (MD98006)

Nursing Management of Peripheral Intravascular Access Devices

- □ 22 February 1999
- Health Services Research Fund, Hospital Authority

Peripheral intravascular access devices (PIVAD) are commonly used in Hong Kong for the delivery of medical therapeutics. It is an important part of hospital practice for the administration of fluids, nutrients, medications, blood products, and to monitor haemodynamic status of patients. Their use can be complicated by a variety of local and systemic causes. Maintenance of these devices by use of specific guidelines can improve both patient and hospital outcomes. The purposes of this study are to introduce a nursing guideline for the management of PIVAD and to identify changes in nursing knowledge and practice after the implementation of the guideline. A pre and post-intervention design will be used to compare the approach to the nursing management of PIVAD. The study will be conducted in two major hospitals in the New Territories. A total sample of 1572 (786 control and 786 cases) adult in-patients with PIVAD will be asked to participate in this study. Data will be collected using the Intravascular Device survey Tool (IVST) which assesses main outcomes measures such as insertion site and vessel condition. The findings of this study will enable the development of a sound practice protocol for use in health care settings across Hong Kong that is based on scientific evidence. The study will also serve as an impetus for further testing of nursing practice guidelines in other areas of patient care. (MD98077)

The Influence of Extrinsic and Intrinsic Factors on Uptake Rates for Cervical Screening: A **Comparison of Perceptions of Hong Kong Chinese Women and Practitioners**

- TWINN Sheila Frances HOLROYD Eleanor ADAB Peymane*
- □ 1 November 1998
- Health Services Research Fund, Hospital Authority

This study aims to investigate the influence of extrinsic and intrinsic factors on the uptake of cervical screening by Hong Kong Chinese women and to investigate the extent to which these factors compare with the perceptions of practitioners. A comparative survey consisting of two phases has been selected as the research design. Phase I will involve a survey of cervical screening provision in Hong Kong. A random survey of practitioners will be undertaken to investigate the organization of screening programmes and practitioners' perceptions of factors influencing women's attendance for screening. A semi structured interview will be undertaken with a purposive sample of respondents to examine their perception of the extent to which service factors contribute to women's reattendance for screening. Phase II of the study will consist of focus group interviews with women who have participated in a large telephone interview survey currently being completed with HSRC funding. The data obtained from the interviews will be used to compare with that obtained from practitioners in the present study. The focus groups will undertake an indepth examination of factors influencing women's uptake of cervical screening, in particular their perception and assessment of level of risk and factors influencing reattendance patterns. The findings will be used to validate those obtained from the telephone survey. It is anticipated that the results of the survey will provide comprehensive baseline data of extrinsic and intrinsic factors influencing uptake of cervical cancer screening. (MD98010)

Analysis **Patient-Controlled** Comparative of Analgesia Versus Traditional Intramuscular Injection in Chinese Women Undergoing Elective **Gynaecological Surgery**

- Betty# • CHANG Anne Marie • IP Wan Yim • CHEUNG Tak Hong (Obstetrics & Gynaecology)
- ☐ 1 November 1998
- ❖ Health Services Research Fund, Hospital Authority

Objective: The purpose of this study is to examine the efficacy of the intravenous patient-controlled analgesia (PCA) for post-operative pain management using opioids for Chinese women undergoing elective gynaecological surgery as compare to traditional intramuscular injection of analgesics.

Design: A randomised control trail will be used in this study. Patients in the experimental group will administer the post-operative opioids to themselves with a PCA device whereas for those in the control group, the post-operative opioids will be injected intramuscularly by nurses. The independent variable is the method of opiate administration, either PCA (experimental) or IM method (control group). Dependent variables are patients' level of pain and satisfaction, and the amount of analgesia used.

Setting: This proposed study will be conducted in two gynaecological wards within a teaching hospital. Subjects: 150 patients scheduled for elective total

abdominal hysterectomy (TAH) and TAH with salpingo-oophorectomy will be recruited base on a medium effect size, an alpha of 0.05, and 15% attrition rate.

Interventions:

- (1) Standard pre-operative teaching for surgery and the use of PCA for the experimental group;
- (2) Standard pre-operative teaching and IMI for the control group.

Main outcome measures: Three instruments: Pain Visual Analogue Scale (VAS), Patient Satisfaction Questionnaire (PSQ) and the Multidimensional Health Locus of Control (MHLC) will be used to assess the patients' level of pain, their satisfaction with the mode of pain management and their health locus of control. The costs related to both types of pain management will be identified and assessed. Data analysis: Group comparability on demographic

data and MHLC. Differences in outcome variables will be analysed using t-test and chi-square analyses. Results: Will be submitted for publication in local and international journals.

(MD98074)

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

Edition	Title/Investigators
1997-98	Promoting Independent Learning and Clinical Competence through Implementing Contract Learning in a Clinical Context (ED97001) © CHAN Wai Chi Sally
1997-98	An Evaluation of the Implementation of Case Management in the Community Psychiatric Nursing Service (MD97084)

∠ CHAN

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MACKENZIE Ann Elizabeth

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Sally

	CHAN Oi Wah* • KU Man Wing, Betty* • LEUNG Lai To, Winnie*		Support / Counselling in Symptomatic HIV Patients (MD97093)
1997-98	Promoting Students' Critical Thinking:		MOLASIOTIS AlexandrosTWINN Sheila Frances
	The Use of Videotaped Vignettes in a Baccalaureate Nursing Programme		CALLAGHAN Patrick#
	(MD97020)	1997-98	The Lived Experience of Insulin-Treated
	 ∠ ∠ CHANG Anne Marie • LEE Fung Kam • CHAU Pak Chun Janita • 		Patients Who Worry about Diabetes Complications and Hypoglycaemia
	LEE Tze Fan Diana • WOOTTON		(MD97136)
	LAW Siu Yin ● WILLS Shuc Han Betty# ● IP Wan Yim		
1996-97	How Chinese Elders Adjust to	1996-97	Increasing Women's Knowledge of the Prevention of Cervical Cancer and the
1990-97	Residential Home Life (MD96179)		Uptake of Cervical Screening: the
	∠ LEE Tze Fan Diana		Implementation of a Nurse Led Community Outreach Programme
1997-98	Assessment of Psychosocial Adjustment,		(MD96026)
	Attitudes and Motivation towards Unrelated Bone Marrow Donation		▼ TWINN Sheila Frances • MAK Mui Hing June#
	(MD97051)		-
		1997-98	Telling Stories: A Strategy to Enhance Ethical Decision Making (MD97021) Z YUNG Ha Ping Hilary
1997-98	A Pilot Study to Assess the Effectiveness of Group Cognitive-Behavioral and Peer		

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RESEARCH PROJECTS

Prevalence and Intra-type Variation of Human Papilomavirus (HPV) Infection in Cervical Cancers: A Nationwide Perspective of China

- ☐ 1 August 1998
- * Research Grants Council

There is a substantial body of scientific evidence linking human papillomavirus (HPV) infection with the pathogenesis of cervical cancer. Among more than 77 genotypes of HPV isolated to date, types 16, 18, 31 and 33 have been identified as "high-risk" of causing cervical cancer.

Geographic and ethnic variations in the HPV genotypes isolated from cervical cancers have been reported. However, there is no data from a comprehensive well designed study using available, quality controlled method about the prevalence of HPV infection in cervical cancers in China nor the HPV genotype.

With reunification, it is more feasible to conduct and co-ordinate a major research project from Hong Kong involving several centres in China. We propose a nationwide study of HPV infection in cervical cancers by selecting 5 geographic regions of China: Hong Kong, Shanghai (Eastern China), Beijing (Northern China), Sichuan (Western China) and Guangdong (Southern China) Provinces. Polymerase chain reaction (PCR) and DNA sequencing-based HPV assays that afford specific detection of different HPV genotypes will be used.

This information would be important to assess the significance of HPV infection in cervical cancers in China. The data obtained from this nationwide survey will also provide valuable information pertinent to the development of HPV diagnostic probes and development of vaccination strategies in the future to prevent HPV infection and by logical extension, cervical cancer. (CU98248)

Pro-apoptotic and Anti-apoptotic Regulators in Cervical Neoplasm: Expression of Both Bcl-2 and Caspase Family Members (Bcl-2, Bcl-X, Bax, Mcl-1, Caspase-3 and Caspase-7)

- ☐ 1 December 1998
- ❖ CUHK Research Committee Funding

Apoptosis is a distinct mode of genetically controlled programmed cell death that appears to be an

important safeguard against tumour development and progression. Several genes in the Bcl-2 family have been identified as possible apoptotic regulators. They may be pro-apoptotic: Bax, Bak, Bad, Bcl-X_s, Bid Bik *etc.*, or anti-apoptotic: Bcl-2, Bcl-X_L, Bcl-_w, Mcl-1, A1, Brag-1 *etc.* In addition, current evidence suggests that Caspases are essential components of the proteolytic cascade that is triggered in response to a death stimulus. These may have roles in both the regulation and execution stages of apoptosis. Recently it has been reported that the apoptotic index significantly decreases as degree of cellular abnormality in cervical neoplasia increases. However the role of apoptotic regulators in the genesis of cervical neoplasm remains unclear.

In this project, researchers propose to examine the expression of 6 apoptotic regulators in cervical neoplasm including cervical intraepithelial neoplasia (CIN) and invasive squamous cell carcinoma of immuno-histochemical uterine cervix using techniques. The information obtained from this study may contribute to the understanding of the association between the alterations of apoptotic regulators and the pathogenesis in cervical neoplasm. This information may further enable us to find new prognostic markers for cervical neoplasm and to develop therapeutic interventions targeting specific apoptotic regulators with the aim of accelerated death of cervical neoplastic cells.

This is a collaborative study with The Burnham Institute, La Jolla, USA, which is an internationally recognized leading center for the study of apoptosis and cell death.

(MD98044)

Evidence for Oxidative Stress and Apoptosis in the Brain Following Perinatal Hypoxicischaemic Insults

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 HAINES Christopher John FISCUS Ronald Ray (Physiology) JAMES Anthony Edward (Laboratory Animal Services Centre) STADLIN Alfreda (Anatomy) WONG Yick Fu ROGERS Michael Scott
- □ 1 January 1999
- * Research Grants Council

We propose that minor perinatal hypoxic-ischaemic (H-I) insults may cause subtle brain injuries which are not detectable at birth. These injuries may result in behavioural or learning difficulties later in life. Premature infants are more susceptible to perinatal H-I insults and may develop lesions different from those in a term foetus.

This study will investigate the relationship between oxidative stress and resulting cell death after minor perinatal H-I insults. We have established a 3-day-old rat model which will reflect the type of brain injury seen in a 24-26 week human foetus. This model will be used to clarify the type and site of

lesions that develop in the preterm brain after minor H-I insults. Once the characteristic lesions have been defined, the model will be used to study the role of oxidative stress in the generation of apoptotic cell death. Follow-up behavioural studies will also be performed to determine the long term effects of minor H-I injury in the preterm setting. This work will contribute to the development of mechanisms by which a preterm foetus could be protected against H-I injury.

(CU98251)

A Study of the Role of Prostaglandin in the Pathogenesis of Diabetic Embryopathy Using Explanted Rat Embryos

- ∠ LAU Tze Kin PRATTEN Margaret K.*
- □ 1 July 1998
- * CUHK Mainline Research Scheme

The incidence of congenital malformation is higher among diabetic mothers. Although both hyperglycaemia and low insulin level have been found to be important factors in inducing these malformations, the exact underlying mechanism is still unknown. Recent studies suggested that a deficiency in prostaglandin level might be the intermediate step in the pathogenesis of diabetic embryopathy. The objectives of this study is to test whether supplementation of prostaglandins prevents malformations induced by high glucose level or low insulin level.

Whole rat embryo will be explanted at 9.5 day gestation and cultured *in vitro*. Embryos will be exposed to either high glucose or low insulin environment, with or without the addition of exogenous prostaglandins. The incidences of malformation among different groups will be assessed and compared with a control group. The result of this study will provide more information in the pathogenesis of diabetic embryopathy. (MD98009)

Relationship of Birth Weight and Chorionicity of Placenta - Retrospective Study

- ∠ LEUNG Tak Yeung TAM Wing Hung
- □ 7 September 1998
- CUHK Departmental Funding

The difference of birth weight between twins are compared with respected to the chorionicity of placenta. (MD98014)

MRI Growth Curves

- □ 21 July 1998
- CUHK Departmental Funding

A cohort of normal women were scanned using a Magnetic Resonance scanner. The volume of internal fetal organs was then derived from each of the MRI image sets produced. Multilevel modelling is then to be applied to analyse longitudinal measurements of brain, liver, lung anf fetal volume for generation of normograms which in turn can be used prospectively. (MD98019)

Computerised Estimation of Cellular Profilerative Index in Placental Tissue

- □ 21 July 1998
- * CUHK Departmental Funding

Computerised estimation of cell proliferation using by neural network classification of stain in placental tissue. Samples of placental tissue have been stained using H&E stain to identify profliferating cells. Sample images were obtained and used to train a self organising map neural network. The proliferative index was calculated for each slide and compared with that derived by conventional counting. (MD98020)

Customised Growth Assessment in the Local Ethnic Chinese Population

- □ 1 June 1999
- CUHK Research Committee Funding

Fetal growth and weight gain during pregnancy has been shown to be one important indicator for fetal well being. One measure of the assessment of fetal growth is the birthweight. The birthweight whilst being gestational dependent, has also been found to be related to socio-economic factors. In addition, the birthweight has also been found to be dependent on the physical characteristics of the mother such as her height, booking weight, ethnicity and her previous obstetrics history.

Recently published studies have documented the relationship of birthweight and maternal characteristics in other Asian ethnic communities. However, there is no information available to show how birthweight is related to these parameters in the local host community and whether obstetric outcome is worse in those babies that fail to reach their own growth potential.

The aims of this study are, firstly, the establishment of a local customised birth chart which can be adjusted for individual maternal characteristics for each pregnancy. Secondly the assessment of the screening accuracy of the growth curve in correctly identifying those small for dates babies and the comparison of the subsequent neonatal morbidity in this group.

(MD98104)

A Comparison of the Effect of Dydrogesterone and Medroxyprogesterone Acetate on the Serum Lipid Profile and Plasma Total Antioxidant Capacity in Chinese Post-Menopausal Women on Oestrogen Replacement

- ☐ 1 October 1998
- CUHK Research Committee Funding

Objective: To determine whether dydrogesterone has a different effect on the lipid profile and is more cardioprotective when combined with oestrogen 17β oestradiol for hormone replacement therapy as compared to medroxyprogesterone acetate.

Design: Prospective randomised study.

Setting: Prince of Wales Hospital, The Chinese University of Hong Kong.

Population: One hundred post-menopausal, non-hysterectomised, women who are not receiving hormone replacement therapy will be recruited when they are first referred for hormone replacement therapy.

Methods: Patients will be randomised into two groups. Group will receive 17 oestradiol 2mg daily for 28-days cycle in a month, with dydrogesterone 10 mg added to the last 14 days of each cycle. Group 2 will receive 17 oestradiol 2mg daily for 28 days a month combined medroxyprogesterone acetate 5 mg for the last 14 days of each cycle for 12 consecutive months. Blood samples would be taken before the replacement therapy, and thereafter at 1,3,6 and 12 monthly intervals for the assay of serum HDL-C, LDL-C, triglyceride, total cholesterol and Lp(a) and TAOC.

Implications: The purpose of this study is to determine whether hormone replacement with estrogen combined with newer progestogen will optimise the cardioprotective effect on postmenopausal women.

(MD98017)

Is Bat Quasi-monomorphic Tract a Prognostic Indicator for Endometrial Cancer? A Translational Study of a Biomolecular Marker to Clinical Utility

- ∠ WONG Yick Fu CHUNG Kwok Hung Tony •
 CHEUNG Tak Hong
- □ 1 December 1998

& CUHK Research Committee Funding

Microsatellite instability (MI) is a hallmark of DNA replication error phenotype (RER+). It has been reported that RER+ tumours has a better prognosis compared to RER tumours. RER would appear to be a potential biomolecular prognostic marker. However, different studies reporting MI have used varying number and type of microsatellite loci. The number of unstable microsatellite observed to define a tumour as RER+ also varied in different studies. Recently, it has been shown that poly(A) tract BAT-26, a repeat of 26 deoxyadenosines localized in an intron of mismatch repair gene hMSH2, is quasi-Simple typing of this may be monomorphic. sufficient to confirm RER+ status in human tumours. In this project we propose to test 4 BAT poly(A) tracts for establishing a polymerase chain reaction (PCR)-based, simple, low-cost, and rapid method to screen for RER status and correlate it with prognosis in endometrial cancer. There is also potential application in other gynaecological and other human malignancies.

This is a collaborative study with Prof. G. Hampton, University of California San Diego. His team is world renowned in research on RER status in cervical cancer.

(MD98045)

Effect of Antenatal Corticosteroids Therapy on Bone Metabolism and Lipids Changes

- ∠ YUEN Pong Mo MAK Wing Lai Tony
 (Chemical Pathology) NG Pui Shan LEUNG
 Tse Ngong LAM Wai Kei Christopher
 (Chemical Pathology) CHANG Mang Z. Allan
- ☐ 1 August 1998
- CUHK Departmental Funding

The aim of the study is to investigate the effects of repeated courses of antenatal corticosteroids on maternal bone metabolism and lipid changes, including the LDL particle size and oxidisability. (MD98016)

Effect of Antenatal Corticosteroids Therapy on Maternal Hypothalamic-Pituitary-Adrenal Suppression

- YUEN Pong Mo MAK Wing Lai Tony (Chemical Pathology) PANG Man Wah Selina
 LEUNG Tse Ngong LAM Wai Kei Christopher (Chemical Pathology) CHANG Mang Z. Allan
- ☐ 1 September 1998
- CUHK Departmental Funding

The aim of the study is to investigate the effects of repeated courses of antenatal corticosteroids on

maternal	bone	metabolism	and	lipid	changes,
including the LDL particle size and oxidisability.					
(MD9801	5)	_			-

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

Edition <u>Title/Investigators</u>

- 1996-97 Methylation of p16^{INK4} Promoter in Gynaecologic Tumours (MD96126)
 - ∠ CHANG Mang Z. Allan
 ◆ WONG Yick Fu
- 1997-98 Characterization of the Up-Stream Regulators of Retinoblastoma Gene in Squamous Cell Carcinoma of Uterine Cervix (MD97052)
 - ∠ CHANG Mang Z. Allan CHEUNG Tak Hong WONG Yick Fu
- 1996-97 Prevalence and the Significance of DNA Replication Errors in Endometrial Cancer with a Geographic and Racial Comparison (MD96066)
 - ∠ CHUNG Kwok Hung Tony
 ◆
 WONG Yick Fu
- 1996-97 Postnatal Depression in Hong Kong Chinese (MD96014)
 - ∠ CHUNG Kwok Hung Tony LEE
 Tak Shing Dominic (Psychiatry) •
 LEUNG Yip Shing Tony (Psychiatry)
 • NG Kee On* WONG Chung
 Kwong (Psychiatry)
- 1997-98 Postnatal Depression Epidemiology (MD96206)
 - CHUNG Kwok Hung Tony YIP Shing Kai Alexander
- 1997-98 Intratype Variation of Human Papillomavirus Infection in Cervical Cancer: A Regional Perspective in China (MD97054)
 - ∠ CHUNG Kwok Hung Tony
 ◆
 WONG Yick Fu
 ◆ CHEUNG Tak
 Hong
- 1997-98 Hypoxic-Ischemic Induction of Apoptosis in the Newborn Rat (MD96210)
- 1997-98 A Comparison of Two Stimulation Protocols for Poor Responders in IVF (MD97155)

- ∠ HAINES Christopher John
 CHEUNG Lai Ping LEUNG Tak
 Yeung LOONG Edward Ping
 Leung
- 1997-98 The Effect of Sex Steroids on Neuronal Apoptosis (MD97156)
 - HAINES Christopher John
 CHUNG Kwok Hung Tony
 CHANG Mang Z. Allan
- 1997-98 Evidence of Oxidative Stress and Apoptosis after Perinatal Hypoxic-Ischaemic Insults on the Rat Brain (MD97053)
 - HAINES Christopher John
 CHANG Mang Z. Allan
 FISCUS
 Ronald Ray (Physiology)
 JAMES
 Anthony Edward (Laboratory
 Animal Services Centre)
 STADLIN Alfreda (Anatomy)
 WONG Yick Fu
- 1997-98 Two Way Cell Trafficking: Elective LSCS (MD96209)
 - ∠ LAU Tze Kin FUNG Tak Yuen# CHANG Mang Z. Allan LO Yuk Ming Dennis (Chemical Pathology)
- 1997-98 Oxygen Free Radicals in Amniotic Fluid Sample in Second Trimester of Pregnancy (MD97119)
 - ∠ LAU Tze Kin FUNG Tak Yuen* ROGERS Michael Scott
- 1996-97 Measurement of Maternal Plasma Corticotrophin Releasing Hormone (CRH) in the Prediction of Abnormal Pregnancy Outcome (MD96067)
 - ∠ LEUNG Tse Ngong CHUNG Kwok Hung Tony
- 1997-98 Placental Apoptosis in Normal Pregnancy and Pregnancies Complicated with Preterm Labour, Pre-Eclampsia, or Intrauterine Growth Retardation (MD97152)
 - ∠ LEUNG Tse Ngong TO Ka Fai (Anatomical & Cellular Pathology) SAHOTA Daljit Singh CHANG Mang Z. Allan
- 1997-98 Psychosexual Function after Childbirth in Hong Kong Chinese Women (MD97120)
 - ∠ LEUNG Tse Ngong LEE Tak Shing Dominic (Psychiatry) •
 TANG So Kum Catherine (Psychology) CHUNG Kwok Hung Tony YIP Shing Kai Alexander LAU Tze Kin

- 1997-98 A Study of Feto-Maternal Haemorrhage after External Cephalic Version at Term Using PCR Method (MD96203)
 - LO Wing Kit LAU Tze Kin LO
 Yuk Ming Dennis (Chemical
 Pathology) ROGERS Michael
 Scott
- 1997-98 Comparative Study of GnRHa (Enantone vs Decapeptyl) in Treatment of Endometriosis (MD97154)
 - ∠ LO Wing Kit CHEUNG Tak Hong• LAU Woon Chung#
- 1997-98 A Study of Actocardiogram in Patients with External Cephalic Version at Term (MD97148)
 - ∠ LO Wing Kit LAU Tze Kin SAHOTA Daljit Singh LEUNG Tak Yeung ROGERS Michael Scott
- 1996-97 Effects of MTAP Antisense Oligonucleotides on Chemosensitivity of Gynaecologic Cancer Cells *in vitro* (MD96069)
- 1997-98 Lipid Peroxidation in Fetal Sheep: Relationship between Peroxides, Anti-Oxidants and Purine Metabolism (MD97160)
- 1997-98 Lipid Peroxidation in Fetal Sheep: Identification of Unique Marker of Neurological Hypoxia-Reperfusion Injury (MD97163)
- 1997-98 Comparison of Cadherin, Catenin and Integrin Expression in Endometrium, and in Invasive and Non-Invasive Endometriosis (MD97161)
- 1997-98 A Study of Changes in Lipid Peroxidation, Purine Degradation and Antioxidant Status Following Variable Hypoxic Insults in the Acutely Exteriorised Fetal Sheep (MD97121)

- ≈ ROGERS Michael Scott PANG
 Chi Pui Calvin (Ophthalmology and
 Visual Sciences) WANG Chi Chiu
 • MURRAY Henry*
- 1997-98 A Prospective Randomised Controlled Study of Using Oral Misoprostol and Vaginal Prostaglandin E₂ for Induction of Labour in Patients with Unfavourable Cervix (MD97122)
- 1997-98 Intrauterine Adhesions Following Spontaneous Abortion (MD96212)
 - ★ TAM Wing Hung
 ◆ CHEUNG Lai Ping
 ◆ CHUNG Kwok Hung Tony
 ◆ LAU Woon Chung#
- 1997-98 To Determine the Usefulness of 1,5-Anhydroglucitol in the Diagnosis and Monitoring of Gestational Diabetes and Impaired Glucose Tolerance (MD97123)
- 1996-97 Refinement of a Region of Loss of Heterozygosity at Chromosome 1 Short Arm in Cervical Cancer (MD96070)
 - WONG Yick Fu CHUNG Kwok Hung Tony
- 1997-98 Feasibility of a PCR-Based Technique of Whole Genome Amplification to Screen for Allelic Loss in Cervical Intraepithelial Neoplasia (MD97055)
 - ∠
 WONG Yick Fu CHUNG Kwok
 Hung Tony CHEUNG Tak Hong
- 1997-98 MRI of the Post-Term Cervix and Induction of Labour (MD96207)
 - ∠ YIP Shing Kai Alexander ◆ CHUNG
 Kwok Hung Tony ◆ CHAN Yu
 Leung (Diagnostic Radiology &
 Organ Imaging)
- 1997-98 Urodynamic Studies on Patients with Post-Partum Urinary Retention (MD97056)

A Collaborative Prospective Randomised Study of Oral Misoprostol and Intramuscular Syntometrine in the

1997-98

Management of the Third Stage of Labour (MD97157)

∠ YUEN Pong Mo • NG Pui Shan • TANG L. C. H.* • CHEUNG Kai
Run

RESEARCH OUTPUTS AND PUBLICATIONS

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RESEARCH PROJECTS

Sequence Alterations in the PAX 6 Gene In-Patients with Aniridia or Anterior Segment Dysgenesis and Their Predictive Value for the Development of Glaucoma

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- □ 1 April 1999
- **CUHK Research Committee Funding**

The PAX 6 gene, a highly conserved gene implicated in the control of neural crest cell migration, is expressed in discrete regions of the developing central nervous system. There are many PAX6 related ocular diseases. Heterozygous nonsense mutations in PAX 6 are responsible for both sporadic and familial aniridia. Missense mutations may give rise to anterior segment dysgenesis, Peter's, Axenfeld's and Rieger's anomalies. Glaucoma, a frequent complication leading to irreversible visual loss, occurs in 50% of these patients due to developmental anomalies of the angle structures that obstruct the trabecular meshwork. However, the development of glaucoma does not correlate with the degree of structural abnormalities and cannot be reliably predicted clinically. In view of the high risk of patients with aniridia or anterior segment dysgenesis to develop glaucoma and the lack of data on PAX 6 gene mutations for Chinese patients, we propose to study sequence alterations in the PAX6 gene in such patients. The coding exons and splice sites of PAX6 will be analysed by polymerase chain reaction, single strand conformation polymorphism, Southern hybridization, and DNA sequencing. Functions of mutant alleles will be studied by Western blotting after in vitro expression. Our results will throw light on the predictive value of PAX 6 mutations for the development of glaucoma in PAX 6 related ocular disorders. Detailed correlation of molecular and clinical data will provide important information on the genotype-phenotype relationship that may improve our understanding of the pathophysiology, and treatment of such conditions to prevent blindness. (MD98105)

Epidemiology of School Myopia in Hong Kong: Prevalence, Incidence and Risk Factors analysis

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- ☐ 1 August 1998
- Health Services Research Fund, Hospital Authority

Objectives: to determine the prevalence and incidence of myopia in primary school children in Hong Kong; and to identify risk factors of developing myopia in children with special reference to their visual tasks, family history of myopia and genetic basis.

Design: a school-based longitudinal study of school children in Hong Kong.

Setting: 19 primary schools each from one School district will be randomly selected.

Subjects: about 2100 children age 6 to 12 will be recruited in the study, 180 children and their family members will be randomly selected for genetic analysis

Interventions: None

Main outcome measures: refractive error, corneal curvature, axial ocular dimensions, visual tasks, family history of myopia and genetic basis of myopia Results: the prevalence and incidence of myopia in school children at age 6 to 12 will be known. It is also likely that relevant useful information regarding the effect of visual tasks, family history and genetic basis on the development of myopia in school children can be found.

Conclusions: Myopia is the commonest ocular problem in Hong Kong. The epidemiology data can help in health care planning. Moreover, the etiological factors identified in this study would formulate the basis from which future preventive and therapeutic methods can be directed. (MD98004)

Molecular Study of Poly-adenylribose-polymerase (PARP) in Apoptotic Cell Death of Retinal Neurons after Ischemia/Glaucomateous Insult

- ∠ LAM Tim Tak
- □ 1 November 1998
- CUHK Research Committee Funding

With the support of a current RGC grant on "Neuroual Rescurers for Apoptotic Degeneration of Retinal Ganglion Cells", researchers were able to obtain evidence showing important roles of caspases poly-adenosine-diphosphate (ADP)-ribose polymerase (PARP) in apoptotic loss of retinal neurons after ischemia/glaucomateous insult. further confirm their findings in the "molecular level" as well as to establish the necessary methodology within their laboratory for future of "RGC" grant applications, they propose to examine the (1) enzyme activities, (2) enzyme protein levels and forms by Western blotting, (3) m-RNA levels by Northern blotting and by in-situ hybridization (or in-situ RT-PCR) of PARP. This study will provide further insight into the role of PARP in apoptotic loss of inner retinal neurons and into the development of therapeutic strategy. It will also provide them with the experience in molecular studies of apoptotic modulators for further development of our research program.

(MD98046)

Study on Sequence Aberrations in the Mitochondrial Genome in Leber Hereditary Optic Neuropathy (LHON) and determination of their Predictive Value for Clinical Course and Outcome

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Leber Hereditary Optic Neuropathy (LHON) is an acute or sub-acute bilateral loss of vision with variable age of onset, disease progression, extent of vision recovery and association with other disorders. Diagnosis based on clinical presentation is unreliable. LHON is caused by mutations in the mitochondrial genome (mtDNA) and so far 18 causative mutations have been identified. Some are primary mutations. Some interact with other mutations environmental factors for clinical manifestations. Disease severity, ancillary disorders and clinical course are mutation related. The 3460, 11778 and 15257 mutations account for most LHON in North Europe while over 95% of Japanese LHON are caused by the 11778 mutation. However, family linkage studies have revealed the complex genetics of LHON which is not a clearly defined mitochondrial Recently we have shown maternal transmission of the 11778 mutation with complete penetrance in 2 Chinese LHON families. In view of the unclear etiology of LHON and the need to establish an unequivocal diagnostic test, we propose investigate sequence aberrations in the mitochondrial genome in 50 Chinese families with LHON. We plan to identify all mtDNA mutations by polymerase chain reaction and direct DNA We shall delineate the pattern of sequencing. inheritance of these mutations in LHON families and to establish their predictive value for clinical course and outcome of LHON. Detail correlation of molecular and clinical data will provide important information on phenotype-genotype relationship. Results of our study will also lay a foundation for indepth investigation of the molecular etiology of LHON. (MD98036)

Effects of Genetic Variants of Lipoprotein Lipase on Coronary Heart Disease and Familial Combined Hyperlipidaemia

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- □ 1 January 1999

* Research Grants Council

Lipoprotein lipase (LPL) is a key enzyme in lipid metabolism in man. Deficiency in LPL activity may lead to hypertriglyceridaemia, which is a risk factor for coronary heart disease (CHD). The LPL gene is located on chromosome 8 comprising 10 exons and spanning 30kb. Over 60 LPL gene mutations leading to LPL deficiency have been found and are recognized as risk factors for hypertriglyceridaemia and CHD. During the last three years we have investigated 160 Chinese hypertriglyceridaemic subjects for base aberrations in the LPL gene. We have found 6 novel and 2 previously reported LPL which co-segregated with mutations hypertriglyceridaemia in the families as well as 4 novel and 2 reported polymorphisms which may be associated with lipid disorders. We therefore propose an in-depth study on these mutations. We shall continue to search for novel LPL mutations and polymorphisms in more hyperlipidacmic subjects. The mutant alleles will be characterized by in vitro expression studies and the catalytic functions and stability of the mutant LPL proteins will be investigated. The structure-function relationship of the mutant LPL enzyme will be examined. We shall also investigate CHD patients for these LPL mutations and polymorphisms to ascertain those which may be a genetic risk factor for CHD, as some heterozygotes may initially have normal lipid profiles and require secondary factors, such as obesity, to modulate their phenotypic expressions. The LPL genotype will be correlated with lipid profiles in these subjects. (CU98282)

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

Title/Investigators

1997-98	Corneal Stem Cell and Amniotic			
	Membrane (MD97162)			
	∠ LAM Shun Chiu Dennis • LAU Tze			
	Kin (Obstetrics & Gynaecology)			
1997-98	Molecular Marker for Familial			
1777 70				
	Adenomatous Polyposis (FAP) and			
	Predictive Value of Congenital			
	Hypertrophy of the Retinal Pigment			
	Epithelium (CHRPE) in FAP (MD97062)			
	LAM Shun Chiu Dennis • PANG			
	Chi Pui Calvin • TANG Leung Sang			
	Nelson (Chemical Pathology) • LAU			
	Wan Yee Joseph (Surgery)			
1007.00				
1997-98	Diagnostic Kits for Early Detection of			

Genetic Eye Diseases for Blindness

Edition

1995-96	Prevention and Genetic Counselling (MD97092)	1996-97	Biochemical and Genetic Markers for Breast Cancer (MD96147) PANG Chi Pui Calvin • KING Wing Keung Walter (Surgery) • TANG Leung Sang Nelson (Chemical Pathology) • LAW Lap Kay (Chemical Pathology)
1996-97	Neuronal Rescuers for Apoptotic Degeneration of Retinal Ganglion Cells (CU96673) LAM Tim Tak • TSO Mark On Man#	1996-97	Molecular Genetics of Alzheimer Disease (MD96148)
1997-98	Ultrastructural Studies of Rod and Cone Degeneration in Transgenic Mouse and Pig Models of Retinitis Pigmentosa (MD97025)	1997-98	Interactions between Smoking, Diabetes Mellitus and Genes Affecting Lipoprotein Coronary Heart Disease Risk Factors (MD97172) ✓ PANG Chi Pui Calvin • JANUS E.D.* • MASAREI J R L*
1997-98	Therapeutics for Apoptotic Loss of Retinal Neurons in Glaucoma (CU97639) ∠ LAM Tim Tak • TSO Mark On Man#	1997-98	Study of the Enzymic Properties of Lipoprotein Lipase (LPL) Variants and their Effects on Hyperlipidaemia (MD97113) PANG Chi Pui Calvin
1996-97	The Lipoprotein Lipase Gene in Hyperlipidaemia (MD96146) ✓ PANG Chi Pui Calvin • TOMLINSON Brian (Medicine & Therapeutics)		TOMLINSON Brian (Medicine & Therapeutics)

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see also <P964286>, <P982715>, <P983173>, <P983177>, <P983741>, <P984015>, <P984021>, <P984024>, <P984026>, <P984027>, <P984028>, <P984029>, <P984030>, <P984031>, <P984032>, <P984033>, <P984037>, <P984038>, <P984136>, <P984757>, <P990890>, <P990926>, <P990929>, <P990930>, <P990931>, <P990933>, <P990934>, <P990947>, <P991108>, <P992006>

RESEARCH PROJECTS

The mechanims of delayed healing and chronic disorders in tendons - Characterization and regulation of proteoglycans of patellar tendon in a rat model

- ∠ CHAN Kai Ming LEE Kwong Man Simon
 (Lee Hysan Clinical Research Laboratories) •
 QIN Ling CHAN Barbara P.
- □ 1 September 1998
- * Research Grants Council

Chronic Achilles and patellar tendon disorders are common in clinical practice. The true incidence is not known, due to an inconsistency on definitions. It is often described in terms of "overuse injury". In operated series however, up to 30% of the cases were not related to vigorous physical activity. Various extrinsic or intrinsic factors are suggested to be associated, but the literature fails to support. literature, pathogenesis refer to "tendinitis or tendinosis", and to "degeneration" in chronic cases, despite the lack of histopathologic evidence of inflammation and sparse data on the healing potential of the disordered tendon. The most common management is the application of anti-inflammatory drugs although inflammation is absent from these tendons. In biopsies from operated human Achilles tendons, we have recently quantified an increased amount of proteoglycans, indicating a disturbed synthesis, which could be a key etiologic factor in the development of chronic tendon disorders. Further characterisation by capillary electrophoresis support these data. An animal model simulating the changes in proteoglycan profile of the human disordered tendons, is the key to open up the opportunities to therapeutic management. In our laboratory, we have established a rat patellar tendon injury model inducing an elevated proteoglycan stainability.

In this study, the profile of proteoglycan in a rat patellar tendon injury model will be characterized. Secondly, down-regulation of the proteoglycans will be studied by local injections of

- (1) IL-1, decreasing proteoglycan synthesis,
- (2) TGF-β1, stimulating proteoglycan degradation, and
- (3) a combination of the optimal dosages of these two factors which may have a synergistic effect in decreasing proteoglycans.

The outcome of this study may

- (1) facilitate understanding of the etiology of chronic tendon disorders; and
- (2) potentiate further studies on the therapeutic management of chronic tendon disorders associated with proteoglycan matrix disturbances. (CU98255)

A Cellular and Molecular Study of the Capacity of Cytokines to Promote Tendon and Ligament Healing Following Injury

- ∠ CHAN Kai Ming
 LEE Ka Ho Kenneth (Anatomy)
- ☐ 1 September 1998
- * Research Grants Council

Tendon and ligament injuries are extremely common conditions in orthopedic medicine. These connective tissues are notorious for their inability to heal properly following damage - resulting in considerable disability to patients. In this proposed study, we will focus on the capacity of various cytokines to enhance tendon healing, using the rat patellar tendon as an experimental model. Specifically, we will examine the influence of basic Fibroblast Growth Factor (bFGF), Hepatocyte Growth Factor (HGF), Platelet Derived Growth Factor (PDGF-BB) and Bone morphogenic protein (Bmp) -12 and -13 on the behaviour of tendon cells at the cellular and molecular levels. In vivo, we will incorporate these cytokines into biocompatible alginate gels and transplant them into experimentally created wounds in the rat patellar tendon. Prior to experimentation, the release profile of these cytokines from the alginate gel will be characterized using ELISA to quantify the amount of cytokines released to the surroundings. To determine the effectiveness of the cytokines on tendon healing, 3 parameters will be tendonocyte proliferation, analyzed (1) tendoncyte migration and (3) collagen type I and type III gene expression by in situ hybridization and competitive RT-PCR. (CU98256)

Enhancement of Spinal Fusion with Osteoinductive Growth Factors Proactived HATCP

- ∠ CHENG Chun Yiu Jack GUO Xia LAU L P*
 QU S X* ZHANG X D* LI J*
- □ 1 July 1998
- CUHK Departmental Funding

Autograft was the gold standard in posterior spinal fusion. The limited supply of autograft tissue and the potential of pathogen transfer with allografts have inspired surgeons and engineers to search for synthetic bone substitutes. Porous HA-TCP ceramics have been shown to have osteoconductive effect in filling bone defects. Bone morphogenetic proteins (BMPs) can enhance bone fracture healing and are capable of inducing ectopic bone formation from skeletal muscles. Aim of the present study was to determine the influence of osteoinductive bone morphogenetic protein proactivated HA-TCP on the outcome of posterior spinal fusion.

Posterolateral lumbar intertransverse process fusion was performed on two groups of 12 New Zealand white rabbits. Group I acted as control group with HA-TCP blocks as implant material. In group II, the experimental group, HA-TCP blocks were augmented with bovine-derived osteoinductive bone protein extract before the implantation. The fusion masses were evaluated 7 weeks postoperatively. The fusion masses were prepared into undecalcified sections and evaluated with microradiography, fluorescence microscopy and light microscopy. (MD98139)

Molecular Cloning and Expression of Bone Morphogenetic Protein 2 (BMP-2) in Bacterial System

- □ 1 September 1998
- CUHK Departmental Funding

It was believed that bone morphogenetic proteins (BMPs) play an important role in bone repair and maintenance. Although, it was known that crude BMPs extract could be isolated from cow bone, the quality and quantity being one of the major problems. Therefore, the aim of the current study is to produce a pure and functional recombinant BMP-2 for further studies.

The cDNAs encoding full-length and functional domain (C-terminus) of the BMP-2 were cloned into expression plasmid respectively. The cloned plasmids were transformed into bacteria. transformants were selected and induced to express BMP-2. The expression of BMP-2 was checked by SDS-PAGE. The expression was verified by Western blot. The expressed BMP-2 and functional domain were recovered by electro-elution method. recovered BMP-2 and functional domain were dissolved in 6 M guanidine and refolded by dissolvedilution-refolding strategy with refolding buffer. The refolded product was then tested for its activity in redirection of the differentiation pathway of myoblastic cell into osteoblast pathway. (MD98135)

Low Volumetric Bone Mineral Density in Adolescent Idiopathic Scoliosis

- ∠ CHENG Chun Yiu Jack QIN Ling GUO Xia

 LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) NG S W Edmond*
- ☐ 1 September 1998
- CUHK Departmental Funding

Previous studies indicated total body low areal bone mineral density (aBMD) associated with AIS, which suggested a intrinsic disturbance in bone development in AIS patients. However, DEXA measured ABMD can not differentiate disturbance of calcification (osteomalacia) from bone with loose structure (osteopenia). PQCT is a non-invasive technique which can measure volemetric BMD(vBMD). Aim of this study was to further investigate the vBMD in AIS patients.

This study investigated bone mineral status in 75 AIS patients of 12-14 years of age and compared with 94 age and maturity gender matched normal control subjects. ABMD of the lumber spine (L2-L4) and bilateral proximal femur were measured using DEXA and vBMD of the non-dominant distal radius and bilateral distal tibiae were measured with pQCT. Severity of the spinal deformity (Cobb's angle) were also evaluated and correlated with BMDs. (MD98136)

Expression of Bone Morphogenetic Protein 4 (BMP-4) in Myoblasts Leading to Osteoblast Formation

- □ 1 September 1998
- CUHK Departmental Funding

Bone morphogenetic proteins (BMPs) are a subgroup of proteins belonging to the transforming growth factor- β (TGF- β) superfamily. They were initially identified by their ability to induce bone formation at ectopic sites, such as in some soft tissues. To understand if BMP-4 can re-direct the soft tissue cells to differentiate into osteoblastic cells, the myoblastic (C2C12) cells was transfected with plasmid harbouring BMP-4 encoding sequence. Then the morphologies and one of the osteoblastic marker of the transfectants were studied.

The full-length BMP-4 cDNA was engineered to add six histidine tag on the C-terimus and amplified by Polymerase Chain Reaction (PCR). The PCR product was introduced into the mammalian expression vector, pCI-neo vector, using restriction cloning technique. Both of the pCI-neo plasmid and the pCI-neo-BMP-4 plasmid were transfected into the C2C12 myoblasts separately, with the former as an empty vector control. A day after, the positive clones were selected by incubating with 800 µg/ml antibiotic G-418 sulfate containing medium for a week. Different mono-clones were collected continuously grown in selection medium forever. The expression of BMP-4 in cells was confirmed by immunocytochemistry using anti-BMP-4 monoclonal antibody and anti-histidine antibody. The detection of alkaline phosphatase (ALP) was used as a marker for osteoblast differentiation. (MD98137)

Evaluation of the Quality of Posterior Spinal Fusion with High Resolution 3D-QCT

- ☐ 1 September 1998
- CUHK Departmental Funding

destructive evaluation Non in vivo microarchitecture of bone and quantiative measurement of trabecular bone have become available through the recently introduced high resolution 3D-QCT. Aim of the present study was to test the capacity of this new technique in evaluating the quality of posterior spinal fusion in an animal model.

Unilateral intertransverse process fusion of L5-L6 level was performed on two New Zealand White rabbits. One used a corticocancellous allograft, the other porous hydroxyapatitea tricalciumphosphate ceramic as graft. Seven weeks post implantation, the lumbar spine was biopsied together with the grafts. The samples were stored in 70% ethanol. 3D-QCT images were obtained by using a special purpose low-dose 3-D OCT localized in University of Zurich, Switzerland. The specimen then were embedded in PMMA and prepared into 100 mm undecalcified section for microradiography. The results of 3D-QCT imaging were compared with the microradiography. (MD98138)

Study of the Mechanical Properties of Bone-Hydroxyapatite Tricalcium Phosphate (HATCP) Interface by Nanoindentation

- ∠ CHENG Chun Yiu Jack GUO Xia LEUNG Y* GUO L H*
- □ 1 September 1998
- CUHK Departmental Funding

Interface mechanical properties are important criteria for evaluating the integration ability of a biomaterial with host bone. The mechanical properties of the bone-implant interface measured by conventional mechanical tests are determined by both the composition as well as the structural organization. Though the morphological and chemical composition of bone-implant interface has been extensively studied, little is known about the intrinsic mechanical properties and its relationship with the interface composition. Nanoindentation has been used in combination with histomorphology in this study to evaluate the hardness and elastic properties of different composition in the bone-HATCP interface. Experimental lumbar posterolateral intertransverse process fusion using porous HA-TCP as bone graft substitute was conducted in a rabbit model. Seven weeks postoperatively, the specimen were biopsied, embedded in PMMA and then prepared into undecalcified sections with a thickness of 50 m. The composition of the bone-HATCP interface was identified using light microscopy. The regional micromechanical properties of each composition, including hardness and Young's modulus, were measured by multiple nanoindentation tests. (MD98142)

Outcome of Treatment of Congenital Pseudarthrosis of the Tibia - PWH Experience

- ∠ CHENG Chun Yiu Jack NG B K W* LAM
 C Y*
- ☐ 1 March 1999
- CUHK Departmental Funding

Congenital pseudarthrosis of the tibia is one of the most difficult problems in orthopaedics. Treatment is often associated with many complications. The aim is to study the outcome of a series congenital pseudarthrosis of the tibia treated in Prince of Wales Hospital. This is a retrospective review of all cases of congenital pseudarthrosis of the tibia followed up in a special clinic. The records and X-ray films were retrieved. The course of treatment and the occurrence of complications during treatment were reviewed. Patients were assessed for ranges of motion of the knee and ankle, muscle power, shortening and deformity of the involved leg at the final follow-up. (MD98134)

Correlation Study on Calcaneal Ultrasound with Bone Mineral Density, Structural and Strength Indices of Weight Bearing Distal Tibia and Non-Weight-Bearing Distal Radius

- ∠ CHENG Chun Yiu Jack HUNG Wing Yin Vivian QIN Ling AU Sze Ki CHOY Wing Yee LEUNG Ping Chung
- ☐ 1 March 1999
- CUHK Departmental Funding

Quantitative ultrasound (QUS) and peripheral quantitative computed tomography (pQCT) are used to measure bone structure properties. The aim of this study was to investigate the correlation between weight bearing and non-weight bearing skeletons above two measurement modalities. QUS(Paris, Norland) and pQCT (Densiscan 2000, Scanco) were used to study the correlation between the broadband ultrasound attenuation (BUA) and velocity of sound (VOS) of heel by QUS and the volumetric bone mineral density (BMD) and content (BMC), bone cross-sectional area (CSA) and bone strength indices(BSIs) of both cortical and trabecular components of the non-dominant distal extremities (radius and tibia) by pQCT.

(MD98140)

Surgical Treatment of Recurrent Patella Dislocation in Children – PWH Experience

- ∠ CHENG Chun Yiu Jack NG B K W* MOK WY*
- □ 1 March 1999
- CUHK Departmental Funding

Recurrent dislocation of patella is an uncommon problem in paediatric patients. This study reviewed the outcome of those paediatric patients that was treated with proximal soft tissue realignment procedure.

It is a retrospective review. 11 patients and 13 knees were operated from 1985-1996, all were treated with radical lateral release and quadriceps realignment. Post-operation, they were allow to weight bear and were immobilized in long leg cast for 6 weeks and then protected with hinge brace for 6 weeks more with gradual increase in flexion of the knee. 2 incisions were used in 7 knees, single midline incision was used in 6 knees. Mean age at operation was 8.4 (5-14) years old. Mean length of follow up was 4.9 (0.8-12) years. They were assessed clinically and with X-rays.

(MD98141)

The Use of Allograft in Posterior Spinal Fusion in Scoliosis Surgery

- ∠ CHENG Chun Yiu Jack NG B K W* FU
 LLK*
- ☐ 1 March 1999
- CUHK Departmental Funding

Autologous iliac crest bone graft is the "Gold standard" for the posterior spinal fusion (PSF) with both successful fusion rates and low immunological rejection. However, autograft has the disadvantage of limitation in quantity. In long fusion and neuromuscular scoliosis, allografts has been used to supplement the bone graft which is necessary to enhance the spinal fusion. This study aims at studying the efficacy, safety and the effect on PSF in paediatric and adolescent scoliosis patients using deep frozen allogeneic femoral head allografts. From 1996 to 1999, deep frozen allogeneic femoral heads were used in 39 cases of PSF on patients with scoliosis. There are 29 girls and 10 boys with average age of 12.8 in girls and 13.7 in boys. The allogeneic femoral heads were collected from elderly patients with fracture neck of femur and undergoing hemiarthroplasty. Investigations including HIV, HbsAg, HCV, and CMV were conducted to exclude virus infection. Bacterial culture has been done to exclude contamination of aerobic and anaerobic bacteria as well as fungi. The femoral heads were

stored in -85°C freezer. The femoral heads were prepared into bone chips directly during the operation. The average postoperative follow-up period was 15.4 months. (MD98143)

Production of Recombinant Bone Morphogenetic Protein 4 for the Treatment of Bone Defects and Disorders

- ∠ CHENG Chun Yiu Jack LI Ming
- □ 20 March 1999
- UK/Hong Kong Joint Research Scheme, the British Council

Previous studies have proved that the BMP family may be a group of very important regulators in bone repair, bone formation and normal maintenance of bone tissue. The most practical application of BMPs is in clinical medicine, as a therapeutic drug for the treatment of patients with big bone defects, incurable bone fracture and bone disorders where the bone implantation becomes necessary. Repairing large bone defects created by massive trauma, excisions of tumours and congenital malformations. reconstructing bone stocks worn off by an implanted endo-prosthesis and healing delayed fractures are all formidable challenges to orthopaedic surgeons today. Therefore, our present research proposed study is aimed to produce recombinant BMP-4, which is so engineered with a 6-histidine tag fused with the Cterminus of BMP-4 that purification of the engineered BMP-4 can be achieved in just one step using affinity chromatography. Then the purified BMP-4 will be refolded into functional BMP-4 in vitro. The function of this purified and refolded recombinant BMP-4 will be tested both in cell culture and in vivo system by promoting the ectopic bone formation. The functional recombinant BMP-4 will be used in the study of improved treatment of scoliosis by spinal fusion enhanced by Morphogenetic proteins. (MD98091)

Osteopenia in Adolescent Idiopathic Scoliosis - A Study of the Genetic Markers, Bone Mineral Turnover and Their Correlation with the Severity and Progression of the Spinal Deformity

- ☐ 1 April 1999
- CUHK Research Committee Funding

Scoliosis is a serious deformity that can affect any parts of the spine. Among the various causes the most common group is Adolescent Idiopathic Scoliosis (AIS) which typically affects the growing

adolescent girls of the age of 10 to 16. Scoliosis deformity when not treated or improperly treated may deteriorate progressively leading to significant cosmetic problems and functional disabilities. In severe cases increased mortality rate can result from the associated early onset cardiopulmonary failure.

The prevalence of AIS in Hong Kong was found to be 3.08% of all adolescents. Our recent study has revealed an alarmingly high percentage (58.7%) of AIS patients had significantly lower bone mineral density (BMD). Such lower BMD status was not secondary to the scoliosis deformity itself nor related to the bracing treatment. To look into more detail scientifically on the possible link of osteopenia to AIS we proposed this study. The main *Objectives* are to identify the potential factors that can contribute to the lower BMD in AIS patients, and to investigate whether osteopenia is one of the risk factors affecting the progression of scoliosis deformity.

The outcome of the proposed study will shed light on the etiology and pathogenetic mechanisms of osteopenia in AIS. This may lead to a novel approach in the monitoring, prognostication and treatment of AIS. In those AIS with osteopenia, one may be able to alter the natural history of the scoliotic deformity by non-invasive interventional treatment to improve the bone mineral status. (MD98106)

Efficiency and Tissue Safety of Transdermal Iontophoresis Treatment of Scar Tissues

- ☐ 1 April 1999
- CUHK Research Committee Funding

Wound healing is invariably associated with scar formation, which is particularly severe after burn injuries, forming hypertrophic scars or keloids, and is a particular problem affecting the local population (Lewis & Sun 1990). Besides causing disfigurement, scar tissues also deform joints, limit movements or growth, and cause constant discomfort. consequences are particularly serious for children, who ironically are more prone to scar formation after Conventional treatments include burn injuries. pressure garment treatment, topical steroid or steroid injection into the scars, surgical excision or more recently laser therapy. These modalities of treatment are prolonged, uncomfortable or inconvenient, even painful. Transdermal iontophoresis provides a means to deliver medication to scar directly. Medication penetration into the scar is promoted with a low energy electric field. It offers an attractive alternative to scar treatment: it could be applied to large surface area, it could be applied repeatedly and programmed, it is "needle-less", does not produce pain, and reduces systemic complications of treatment. Preliminary studies indicated this technique could be adapted for

treatment of scars (Zhao 1996). The aim of this study is to determine the pharmacokinetics of transdermal iontophoresis of interferon gamma, which has a down-regulatory effect on cell proliferation and collagen production in fibroblasts from hypertrophic scars, for scar treatment.

(MD98107)

A Biomechanical and Histomorphometrical Study for the Improvement of Implant Fixation on Osteoporotic Bone with Ovariectomised Female Goats

- ∠ LEUNG Kwok Sui CHOW Hung Kay, Daniel*
 JAMES Anthony Edward (Laboratory Animal Services Centre) QIN Ling CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)
- ☐ 1 October 1998
- * Research Grants Council

Osteoporosis is common among old people. Osteoporotic bone fractures easily. They are associated with serious complications of which include death, loss of mobility and independence. Early operative treatment offers the best chance for these patients in minimizing these complications, in the control of pain and prevents deformity. Fixing osteoporotic fractures remains a major challenge to orthopaedic surgeons. Implants are commonly used in treating these fractures. Most of the available implants are designed to fix normal bone in young adults. The use of these implants to fix osteoporotic fractures often results in "bone failures" where the poor bone quality makes stable fixation difficult during the operation and leads to loosening of the implants and hence loss of fixation in the postoperative periods. This proposed project is designed to study the currently available implants with ovariectomised female goats as the osteoporotic animal model. The interaction between the implant and the bone will be studied by histomorphometry and biomechanical testing after implantation into the osteoporotic bone. Different augmentation techniques, which include the use of the most recently available biomaterial, will also be studied. The results of the study will then be used to improve the design of implants and surgical technique. It will ultimately lead to improvement of fixation for osteoporotic fractures and hence decrease the complications in treating these common and yet difficult fractures. (CU98270)

Intervention Prevention for Fast Bone Losers Identified with a High Accurate Imaging Peripheral Quantitative Computed Tomography

∠ LEUNG Ping Chung • QIN Ling • LAU Edith Ming Chu (Community and Family Medicine) • DAMBACHER M. A.*

□ 1 May 1999

CUHK Research Committee Funding

The prevalence of osteoporosis in Hong Kong, as evidenced by osteoporotic fractures is high. Osteoporotic fractures have become the 5th most commonly occurring medical condition in Hong Kong. It is estimated that with appropriate prevention more than 50% of these fractures could be avoided.

The present consensus is that one of the high-risk group of osteoporosis are people who suffer from an annual trabecular bone loss of over 3% - as defined as fast bone losers. Since bone loss is at its peak in the first decade after menopause, early effective diagnosis and monitoring of treatment effects for the fast bone losers are important. A newly developed high precise pQCT has been proven to be able to full fill this task. This pQCT can measure the trabecular and cortical BMD separately in a true volumetric density compared with other available conventional 2-dimensional densitometers, such as DEXA. This pQCT enables us to detect 1% BMD changes within one year and identify fast bone losers within 6 months. The high resolution imaging feature of the pQCT also enables us to perform qualitative evaluation of both cortical and trabecular bone structure and degree of bone mineralisation. We propose to use this new advanced technique to conduct a non-invasive direct BMD measurement in pre- and post-menopausal women aged of 50-58. After identifying the fast bone losers, the subjects will participate in intervention prevention programs clouding participating in programmed Tai Chi, a popular physical exercise among the elderly in our oriental culture and in a proven anti-resorptive Beyond measuring BMD, muscle medication. strength and balance capacity will be monitored. The outcome of this study may provide new scientific data for promoting physical exercise programs for prevention of osteoporosis and fall-induced osteoporotic fracture so as improving the quality of life of the elderly. (MD98108)

A Study of the Effect of Cartilaginous Tissues on Endothelial Cells in Angiogenesis of Tumour

- ∠ QIN Ling LEUNG Kwok Sui FUNG Kwok
 Pui (Biochemistry) LEE Kwong Man Simon
 (Lee Hysan Clinical Research Laboratories) •
 CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)
- ☐ 1 February 1999
- CUHK Research Committee Funding

Osteosarcoma is a primary malignant tumor of bone. Clinically, it is observed that osteosarcoma hardly invades through cartilaginous tissues, including growth plate and articular cartilage. Our previous

study showed that chondrocytes did not exert any direct cytotoxic or cytostatic effect on osteosarcoma cells. On the other hand, some biochemical factors are characterized such as anti-angiogenesis factor from rabbit costal chondrocyte conditioned medium cartilaginous tissue and chondrocyte-derived inhibitor from bovine articular cartilage exhibiting inhibition of collagenase activity. Thus it is postulated that cartilaginous tissue may retard tumor spread by inhibiting the sprouting of new blood vessels that provide nutrients for tumor growth.

This project is designed to investigate the effect of growth plate and articular chondrocytes on the proliferation, viability and migration of endothelial cells *in vitro*. Hamster cheek pouch model will also be established to study the anti-angiogenesis effect *in vivo*. Results from this study will help us to clarify the inhibition mechanism of cartilaginous tissues on angiogenesis during tumour growth. It is hoped that the isolation of the inhibitor(s) can be applied in clinical practice to control tumor spread. (MD98109)

Lower Limb Amputation in Local Chinese Population

- □ 1 July 1998
- CUHK Departmental Funding

Lower limb amputation is a common sequelae of diabetes mellitus and peripheral vascular disease. With advances in vascular reconstruction, improved awareness of energy consumption, better prosthetic designs and use of more distal amputation levels, satisfactory to good surgical and rehabilitation outcome has been reported. The local Chinese population suffers from a different propensity towards peripheral vascular disease and diabetes as compared to other races. Our social and psychological behavior are certainly also different. Whether the same results apply to us remains to be verified.

This research project is a prospective review of 242 consecutive lower limb amputations performed in 1994 to 1996. Information pertaining to demographic data, contributing medical conditions, vascular assessment and intervention, indications for surgery, level of amputation, surgical and rehabilitation outcome parameters, contra-lateral limb outcome and mortality are collected. Telephone interviews are made to assess their two year outcome in terms of contralateral limb risk, activities of daily living score, ambulatory status and survival.

Data collected will be compiled and analyzed. The epidemiology of Chinese lower limb amputation will be compared and contrasted with previous literature reports on other ethnicity. Prognostic factors affecting short and long term outcomes will be identified.

(MD98012)

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

Edition <u>Title/Investigators</u>

- 1996-97 An *in vivo* Study of the Change in Type I and Type III Collagen in Healing Rat Patellar Tendon the Effect of Growth Factors (MD96072)
 - CHAN Kai Ming CHAN Pui Barbara • LEE Ka Ho Kenneth (Anatomy)
- 1996-97 Health Benefits of Programmed Physical Exercise on the Prevention of Bone Loss in Postmenopausal Women (MD96021)
 - ∠ CHAN Kai Ming QIN Ling LAU Edith Ming Chu (Community and Family Medicine) WOO Jean (Medicine & Therapeutics) LEE Shiu Hung
- 1997-98 A Cellular and Molecular Study of the Potential Application of Growth Factors in the Enhancement of Tendon Healing Following Sports Injury (MD97057)
 - ∠ CHAN Kai Ming LEE Ka Ho Kenneth (Anatomy) CHAN Pui Barbara FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) QIN Ling CHENG S. H.*
- 1996-97 Dual Energy X-Ray absorptiometry in Lower Limb Callotasis Lengthening (MD95259)
 - ∠ CHENG Chun Yiu Jack

 MAFFULLI N.*

 NG B.*
- 1997-98 Coraline Hydroxyapatite as a Bone Substitute to Enhance Spinal Fusion (MD96200)
 - ∠ CHENG Chun Yiu Jack ◆
 YURIANTO Henry# ◆ GUO Xia ◆
 LEE Kwong Man Simon (Lee Hysan
 Clinical Research Laboratories)
- 1997-98 The Clinical Patterns of Presentation of Congenital Muscular Torticollis in Infants and Children (MD97138)
 - ∠ CHENG Chun Yiu Jack CHEN Tracy M. K.* TANG S. P.* LEE Sandra*
- 1997-98 Abormal Somatosensory Evoked Potential in Adolescent Idiopathic

- Scoliosis Where is the Site of the Abnormality? (MD97140)
- ∠ CHENG Chun Yiu Jack GUO Xia
 • SHER Hing Leung Andy (Lee
 Hysan Clinical Research
 Laboratories)#
- 1997-98 Correlation between Curve Severity, Somatosensory Evoked Potential and MRI in Adolescent Idiopathic Scoliosis (MD97141)
 - ∠ CHENG Chun Yiu Jack GUO Xia
 • SHER Hing Leung Andy (Lee Hysan Clinical Research Laboratories)# CHAN Yu Leung (Diagnostic Radiology & Organ Imaging) METREWELI Constantine (Diagnostic Radiology & Organ Imaging)
- 1997-98 Application of Bone Morphogenetic Protein-Hydroxyapatite Composite Implant in Un-Decorticated Posterior Spinal Fusion (CU97669)
- 1997-98 Injectable Hydroxyapatite-Tricalciumphosphate for Orthopaedic Use (MD97058)
 - ∠ CHENG Chun Yiu Jack GUO Xia
- 1997-98 Outcome of Surgical Treatment of Congenital Muscular Torticollis (MD97182)
 - ∠ CHENG Chun Yiu Jack TANG S.
 P.* NG B K W*
- 1997-98 Correction of Lower Limb Deformity in Children An Early Outcome Analysis (MD97183)
 - ∠ CHENG Chun Yiu Jack NG B K
 W* FUNG P W*
- 1997-98 Scoliosis and Abnormal Postural Balance (MD97137)
 - ∠ CHENG Chun Yiu Jack CHOW Hung Kay, Daniel*
- 1996-97 Analysis of *Tlx* Gene Functions in Oncogenesis and Development Using Gain-of-function and Loss-of-function Mutants in Transgenic Mice (CU96662)

 © CHENG Shuk Han
- 1995-96 Effect of the Muscular Regeneration Regulated Factors on Myoblasts Transfer

Duchenne Muscular Therapy in Dystrophy (MD95228) 1995-96 Biochemical Events of The Regeneration of Osseous Tissue Under Tension and Compression Stress - A • CHAN Kai Ming Study with Callotasis Model in Goat 1993-94 Distraction Lengthening of Upper Limb (CU95655) Anormalies in Children (MD94145) ∠ LEUNG Kwok Sui • LEE Kwong HUNG Leung Kim • CHENG Chun Man Simon (Lee Hysan Clinical Yiu Jack Research Laboratories) • FUNG Kwok Pui (Biochemistry) 1994-95 Outcome Study of Nerve Injuries and the Role of Sensory Re-education (MD95094) 1996-97 The Effect of Reaming Technique on ∠ HUNG Leung Kim

◆ CHENG Shu Intramedullary Pressure and Marrow Fat Kei Andy* Embolisation - A Quantitative Study (CU96631) 1996-97 Iontophoresis with Pulsed-short Circuit-∠ LEUNG Kwok Sui • CHEN Zhen Yu (Biochemistry) • WONG Wan pulsed Direct Current (PSPDC) Device: Tissue Effects and Drug Permeation Nar Margaret • FUNG Kwok Pui (Biochemistry) (MD96073) ∠
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 1996-97 Yuanting (Electronic Engineering) • Identification of TGF-beta Induced ZHAO Li • WU Hay Tong Genes During Chondrogenesis in Rabbit Periosteal-derived Cells Using mRNA 1996-97 Neurotrophic Factors Derived from Differential Display Analysis (MD96076) Schwann Cells in a "Pre-degenerated" ∠ LEUNG Kwok Sui • CHAN Chun Peripheral Nerve Wai (Lee Hysan Clinical Research Environment Temporal Changes and Clinical Laboratories) applications (MD96075) ∠
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 √ 1996-97 A Study to Correlate the Hand Function KWONG Wing Hang (Anatomy) • with the Physical and Physiological WU Hay Tong Structure of the Cervical Spine in Cervical Myelopathy (MD96169) 1996-97 Interleukin-1 ∠ LEUNG Kwok Sui • LEE Yuen Lun and Interleukin-8 Expression in Burn Wound - in vivo and 1997-98 in vitro Studies (MD96074) Study of Relationship between Femoral Neck Bone Density and Failure of Screw Fixation in Femoral Neck Fractures • CHENG Chi Wa# • FUNG Ming Chiu (Biology) (MD96197) ∠ LEUNG Kwok Sui • WONG Chin 1997-98 Quantitative Studies of P-Glycoprotein Hong* • LI Kit Yee* and Related Biochemical Markers to 1997-98 Monitor Drug Resistance in Malignant Prospective Study and Review of Intramedullary Nailing in Fractures of Musculoskeletal Tumours (MD97061) KUMTA Shekhar Madhukar • Humerus (MD96198) ∠ LEUNG Kwok Sui • WONG Chin LEUNG Kwok Sui • WONG Wan Nar Margaret • LEE Kwong Man Hong* • LI Kit Yee* Simon (Lee Hysan Clinical Research Laboratories) • FUNG Kwok Pui 1997-98 Fixation of Radial Neck Fracture Using (Biochemistry) Forked Plate (MD96199) ∠ LEUNG Kwok Sui • WONG Chin 1993-94 The Establishment of a Coordinated Hong* • LI Kit Yee* Research Programme on Cytogenetics Molecular 1997-98 Biology A Study of Physeal Retardation to

Musculoskeletal Tissue (MD93115)

Research Laboratories)

∠ LEUNG Kwok Sui • LEUNG Ping

Chung • CHAN Kai Ming • HUNG

Leung Kim • LEE Yuen Lun • YIP

Man Hing Kevin# • LEE Kwong

Man Simon (Lee Hysan Clinical

Osteosarcoma Growth: Its Significance in

Clinical and Basic Studies in Tumour

∠ LEUNG Kwok Sui • FUNG Kwok

Pui (Biochemistry) • LEE Kwong

Man Simon (Lee Hysan Clinical

Research Laboratories) • CHAN

Spread (MD97059)

	Chun Wai (Lee Hysan Clinical		
	Research Laboratories) • CHEUNG	1997-98	Identification of Fast Bone Losers
	Wing Hoi		Measured with the Most Accurate pQCT
			(Densiscan 2000) and Specific Bone
1997-98	A Comparative Study of the Mechanical		Turnover Biochemical Markers
	and Histological Properties of Bone to		(MD97060)
	Bone Union and Bone to Tendon Healing		
	(MD97015)		CHAN Kai Ming ◆ NEFF M.*
	∠ ∠ ∠ ∠ ∠ ∠ ∠		
	CHONG Wai Sing Wilson	1996-97	Epidemiological Study on Foot and
			Ankle Disorders (MD96170)
1995-96	Biosynthesis and Implantation of		■ WONG Wan Nar Margaret •
	Artificial Growth Plate Using Population		LEUNG Ping Chung
	of Proliferative Chondrocytes Cultured		
	on a Collagen Matrix (CU95656)	1997-98	A Comparative Study of the Mechanical
	∠ LEUNG Ping Chung • LEE Kwong		and Histological Properties of Bone to
	Man Simon (Lee Hysan Clinical		Bone Union and Bone to Tendon Healing
	Research Laboratories) • OOI		- A Goat Model (CU97668)
	Vincent E. C. (Biology) • FUNG		
	Kwok Pui (Biochemistry)		Ling • LEUNG Kwok Sui •
			ZHANG Yuanting (Electronic
1996-97	Cartilage Elastography (MD96128)		Engineering)
	Ø QIN Ling ● MAK F. T. Arthur* ● MOW Van C.*		

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RESEARCH PROJECTS

Randomized Comparison of Cefpodoxime Versus Cefuroxime Axetil as Follow on Treatment of Pneumonia

- ▼ FOK Tai Fai SUNG Yn Tz Rita YU Chung
 Wah
- □ 20 July 1998
- Sankyo Co Ltd

Cefpodoxime proxetil is a newer oral broad spectrum cephalosporin with high resistance to inactivation by beta-lactamases. Its pharmacokinetics supports a twice daily dosing regime and its daily cost is lower than cefuroxime or cefaclor. This clinical study is designed to evaluate the safety and efficacy of cefpodoxime versus cefuroxime for follow on treatment of pneumonia in children. (MD98127C)

Effects of Oxygen Toxicity on Megakaryocytopoiesis

- ☐ 1 November 1998
- **&** CUHK Research Committee Funding

Oxygen toxicity is an important cause of lung injury in preterm infants receiving mechanical ventilation for life support. Thrombocytopenia is another common complication of these infants. In a pilot study, researchers have established a hyperoxia neonatal rat model and shown that these animals had low circulating platelets, indicating that oxygen toxicity could down-regulate megakaryocytopoiesis. Researchers hypothesize that oxygen toxicity induces the consumption of lung megakaryocytes, leading to thrombocytopenia and a feedback mechanism regulated by the cyokine thrombopoietin (TPO) and its receptor. Using this premature rat model of hyperoxic lung injury, they shall perform a randomized controlled study to investigate the mechanism of megakaryocytopoiesis at multiple levels. The formation of megakaryocyte progenitors in the bone marrow will be measured by the assays of colony forming units (CFU-MK). The circulating thrombopoietin (TPO), a megakaryocyte-specific cytokine, will be quantified by enzyme-linked immunosorbent assays (ELISA). The TPO receptor (c-mpl) gene expression in bone marrow cells will be analysed by RT-PCR. The morphology and megakaryocytes of lung tissues will be studied by staining with acetyl-choline esterase (AchE). Neonatal thrombocytopenia could be associated with complications such as hemorrhage of the central nervous system. This study would contribute to the understanding of oxygen-induced deregulation of

megakarycytopoeisis and the possible prevention and better management of neonatal thrombocytopenia and platelet disorders.

(MD98047)

Novel Molecular Defense-mechanism Against Tuberculosis: Enhanced Expression of the Inflammation-associated Gene *PML*

- ∠ HUI Hon Lam Stephen CHAN Yeuk Hon John (Clinical Oncology) CHOW Louis Tsun Cheung (Anatomical & Cellular Pathology)*
- ☐ 1 October 1998
- CUHK Research Committee Funding

The promyelocytic leukemia (PML) is known to be induced by signals of stress and inflammation including interferons, hormones and DNA damages. This research is aimed at elucidating the role of PML during TB infection in lung tissues. Researchers' preliminary data showed enhanced expression of the inflammation-associated gene PML in TB tissues and, thus, PML may play an important role in cellular response to defend against the bacteria infection. Researchers propose the following: (1) to confirm their preliminary findings in a larger cohort of samples if enhanced expression of PML is associated with TB infected lung tissues; (2) to determine by double labeling techniques with the macrophagespecific marker kp1 and β- galactosidase, if the activated macrophages over-expressed PML, and to determine if the drug-resistant TB cases are defective in PML inductions. (MD98048)

Effect of Interleukin-13 on Eosinophil Activation, Degranulation and Survival in Chinese Patients with Multitransfused Thalassaemia

- ∠ LEUNG Ting Fan LI Kwai Har Karen CHIK
 Ki Wai LI Chi Kong
- □ 1 November 1998
- **&** CUHK Research Committee Funding

Previous reports found that patients with multitransfused thalassaemia had immunomodulation involving T and B lymphocytes as well as NK cells. On the other hand, Caucasian patients with transfusion-dependent thalassaemia were described to have lower prevalence of allergic diseases. The reason for this observation was not clear. These patients were also at risk of iron overload and its related multi-organ dysfunction. There has also been no report on the eosinophil functions in this group of patients. In this study, researchers investigate on *in vitro* eosinophil functions including activation, degranulation and survival in response to interleukin-13 stimulation in patients with multitransfused thalassaemia. Interleukin-13 was a cytokine secreted

by helper T 2 lymphocytes which had widespread effects on different immune cells. In addition, we examine eosinophil functions in thalassaemic patients after bone marrow transplantation. From this study, researchers can obtain information on abnormalities of eosinophil functions and also analyze their correlation with iron overload in Chinese patients with multitransfused thalassaemia. (MD98049)

Human Stem Cell Technology: ex vivo Expansion of Cord Blood Stem/Progenitor Cells and Applications

- ∠ LI Kwai Har Karen HUANG POON Wai Sin Dolly (Anatomical & Cellular Pathology) •
 TSANG Kam Sze Kent (Anatomical & Cellular Pathology)*
- ☐ 1 January 1999
- ❖ Industrial Support Fund, Industry & Technology Development Council

The prime objective of this project is to develop the biotechnology of cord blood stem cell expansion. Cord blood contains high quality stem cells. The major problem of its application is the small volume available in each collection, thus limiting its use mostly for children. In addition, the recovery period of the blood system of patients after cord blood transplant is usually lengthy, resulting in morbidity and high hospital cost. To resolve this constraint, we shall establish the ex vivo growth of cord blood stem cells in the laboratory prior to transplant, in order to expand the scope of their application to adults. We develop the use of reagents/techniques on blood cell volume reduction, cryopreservation and growth factor stimulation for stem cell expansion. Target users of this project include patients suffering from malignancy or blood cell and genetic disorders, cord blood banking and transplant institutions, the personalized banking industry and the stem cell-based technological industry. The application of ex vivo expansion of stem cells could be extended to areas of bone marrow and peripheral blood cell transplant (for reducing cancer cell contamination). This technique is also required in the worldwide development of gene corrective therapies using blood stem cells. (MD98070)

WHO/GSTF Maternity Advice Study

- ☐ 1 June 1999
- ❖ Norwegian SIDS Society

The study is based on the hypothesis that SIDS may be an unrecognised but significant problem in countries where prone sleeping for infants is prevalent. A previous study noted a relatively high rate of prone sleeping in Buenos Aires, Argentina, together with a significant incidence of SIDS. This prompted a successful low-cost "Link" programme between New Zealand and Argentina to raise awareness of SIDS. This highlighted the potential for similar low-cost interventions to be implemented in other countries. Therefore the SIDS Global Strategy Task Force recommended that an international study be undertaken in collaboration with WHO to determine what infant sleep position advice is given to new mothers in selected countries in Europe and Latin America. Country coordinators will be responsible for liasing with Health Departments and for distributing a questionnaire to each participating maternity hospital. The questionnaire seeks information on how babies are placed for sleep in the special care units and normal care units, whether the hospital recommends a best sleep position for babies, and whether there is printed information and a written policy on this. Data entry and check programmes are available in English and Spanish (Epiinfo statistical software, CDC). Any country, where advice to sleep infants prone is common, will be examined further to establish whether SIDS may be a significant but unrecognised problem. If indicated consideration will then be given to setting up "Link" programmes between these countries and countries experienced in SIDS risk reduction campaigns. Implementation of the study to other WHO regions will be considered at a later stage.

(MD98123)

The Effect of Postnatal Systemic Corticosteroids on Serum Leptin Concentration in Preterm, Very Low Birth Weight Infants

- ✓ NG Pak Cheung LAM Wai Kei Christopher (Chemical Pathology) FOK Tai Fai WONG Wing Kin Gary
- ☐ 1 October 1998
- ❖ CUHK Research Committee Funding

High dose systemic corticosteroids have been successfully used antenatally to prevent and to lessen the severity of respiratory distress syndrome, and also postnatally for treatment of bronchopulmonary dysplasia and to facilitate weaning from respirator in preterm, very low birth weight infants. However, systemic corticosteroids have been associated with many serious adverse effects, and one of the most important side effects is an increase in resting metabolic expenditure and nitrogen loss due to enhancement of protein and fat catabolism. Researchers have previously reported a marked increase in blood urea concentration and alterations in plasma aminogram secondary to structural protein

breakdown following dexamethasone treatment. However, the interaction between the neuroendocrine system and their target organs (skeletal muscles and adipose tissue) leading to severe catabolism is not fully understood.

Leptin, a newly discovered hormone, has been shown to involve in the regulation of body weight by controlling appetite and energy expenditure. It has been proposed that leptin acted through specific receptors in the hypothalamus and provided a vital link between the neuroendocrine system and the adipose tissue. As the clinical importance of leptin remains uncertain in human and, thus far, no report has attempted to delineate its biological effects in preterm infants, this study is designed to compare the serum leptin concentrations in VLBW infants who did and did not receive postnatal systemic dexamethasone treatment. The result will enable better understanding of the inter-relationship between the hypothalamic-pituitary-adrenal axis, the insulin pathway and the leptin-adipose tissue hormone system. (MD98050)

CTLA-4 Gene Polymorphism in Childhood Graves' Disease

- ☐ 1 September 1998
- **❖** CUHK Research Committee Funding

CTLA-4 gene is a recently described T-cell surface molecule important in controlling stimulatory signals, blocking function and suppression of antibody responses. HLA genes have also been confirmed to confer susceptibility and protection for Graves' disease in Chinese. Graves' disease is a common autoimmune disease in Chinese children. Researchers propose in this study to analyse the CTLA-4 allele distribution in a group of patients with childhood Graves' disease along with a control group. This study may help to clarify the genetic predisposition of childhood Graves' disease in Chinese. (MD98051)

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

Edition <u>Title/Investigators</u>

1997-98 Molecular Analysis of *MLL* and *TEL*Gene Abnormalities in Paediatric
Leukaemia (MD97063)

∠ CHIK Ki Wai • YUNG Chung Ming Edmund

- 1996-97 To Provide Gestation-Specific Standards on Physical Measurements on Chinese Newborns (MD96165)
 - ✓ FOK Tai Fai LAU Tak Fai Joseph
 (Centre for Clin. Trials & Epidemiological Research) SO Hung Kwan
- 1996-97 Enterobacter Septicaemia in Newborns: Analysis of Risk Factors (MD96166)
 - ✓ FOK Tai Fai LEE Cheuk Hon •
 WONG Ming Chung (Centre for Clin. Trials & Epidemiological Research) LYON Donald James (Microbiology) NG Pak Cheung
- 1997-98 A Controlled Study of Obstructive Sleep Apnea Syndrome in Obese Children in Hong Kong (MD97002)
- 1997-98 Determination of Local Oxygen Consumption by Healthy and Diseased Lungs in a Rabbit Model (MD97064)
 - FOK Tai Fai ◆ GU Jia Shi ◆ XU Feng# ◆ YIN Ai Tsang Jane
- 1997-98 To Provide Gestational Age-Specific Standards of Physical Measurements for Local Chinese Newborns (MD97086)
 - ∠ FOK Tai Fai LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research) NG Pak Cheung CHANG Mang Z. Allan (Obstetrics & Gynaecology) LEE Wai Hong* CHOW Chun Bong*
- 1997-98 Vincristine Neurotoxicity in Children with Acute Lymphoblastic Leukaemia (MD97016)
 - ∠ LEUNG Ting Fan YEUNG Wai Lan • CHIK Ki Wai
- 1997-98 Haematopoietic Stem Cells: Characterization and Retrovirus-Mediated Gene Transfer (MD97096)
 - ∠ LI Kwai Har Karen LI Chung Leung*

Suk

Fong

- 1997-98 Cross Cultural Comparison of Child Care 1996-97 Identification of Genetic Related Sids Risk Factors (MD97105) Environmental Risk Factors Childhood Asthma in Hong MELSON Edmund Anthony Severn Kong • SCHIEFENHOEVEL Wulf* (CU96609) WONG Wing Kin Gary • LEUNG 1997-98
 - The Pituitary-Adrenal Response in Chung Chuen Roland (Medicine & Preterm Very Low Birth Weight Infants Therapeutics) • LAI Kei Wai after Treatment with Multiple Courses of Christopher (Medicine Antenatal Corticosteroids (MD97024) Therapeutics) • LAU Tak Fai Joseph ✓ NG Pak Cheung • LAM Wai Kei (Centre for Clin. Trials
 - Christopher (Chemical Pathology) Epidemiological Research) WONG Wing Kin Gary • FOK Tai Fai • LEE Cheuk Hon 1997-98 Bone and Collagen Turnover in Preterm Neonates with Dexamethasone Treatment
- (MD97065) 1997-98 A Study on Cytokines and Cell Adhesion Molecules Expression in Respiratory Syncytial Virus Bronchiolitis (MD97067) Cheung • LAM Wai Kei Christopher (Chemical Pathology) • FOK Tai Fai LAM Stephen Wai Kei
- Christopher (Chemical Pathology) 1996-97 The Correlation between Graft-versus-CHAN Grace* Host Disease and Cytokine Profiles in Bone Marrow and Peripheral Blood Stem 1995-96 The Epidemiology of Childhood Diabetes Cell Transplantation (CU96663)
 - in Hong Kong (MD90205) ∠ YUEN Man Pan Patrick • CHIK Ki WONG Wing Kin Gary • LEUNG Wai • LI Kwai Har Karen • PONG Sophie# Nga Hin Henry OPPENHEIMER Stephen James#

and

for

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RESEARCH PROJECTS

Cellular Mechanisms Involved in the Excitatory Actions of Prostanoid EP₃-and IP-Receptor Agonists

- ∠ JONES Robert Leslie GURNEY A. M.* •
 KWAN Yiu Wa KENNEDY C.* SNEDDON
 p.*
- □ 1 July 1998
- UK/Hong Kong Joint Research Scheme, the British Council

The project involves the investigation of the receptors and cellular mechanisms involved in two prostaglandin-mediated actions: (1) contraction of vascular smooth muscle elicited by prostanoid EP₃-receptor agonists, and (2) excitation of sympathetic neurones in the vas deferens elicited by prostanoid IP-receptor agonists. The work is relevant to the clinical use of prostanoids in man. (BL98001)

Characterization of Muscarinic Receptors in Rat Isolated Pulmonary Artery and Thoracic Aorta

- 🗷 KWAN Yiu Wa
- ☐ 1 October 1998
- **❖** CUHK Research Committee Funding

Pulmonary circulation is a low-resistance, lowpressure system. Muscarinic receptors as well as acetylcholinesterase have been found in the pulmonary vasculatures. However, the physiological functions of cholinergic system in the pulmonary vasculatures are not known. In the lungs, there is a heterogeneity of muscarinic receptors and whether the opposite effects of acetylcholine in the pulmonary vasculatures are dependent on activation of distinct muscarinic receptor subtypes has not been resolved. Compared to the acetylcholine-induced EDRFdependent relaxation response, the physiological significance of acetylcholine-induced pulmonary artery contraction has received little attention. In the literature, information regarding the type of muscarinic receptors involved in acetylcholinemediated contraction of pulmonary artery are confusing. In this study, a range of selective muscarinic subtype receptor agonists and antagonists will be examined in rat isolated pulmonary artery and aorta, in the presence of thoracic acetylcholinesterase inhibitor neostigmine. Results obtained from this study will provide information of the type(s) of muscarinic receptors present in the pulmonary artery and thoracic aorta which may be important in the undertstanding pathophysiology of pulmonary vascular disease e.g. Eisenmenger's syndrome. (MD98052)

Studies on Anti-inflammatory Neuropeptides in Rat Knee Joints

- ∠ LAM Fu Yuen
- □ 1 January 1999
- CUHK Research Committee Funding

Sensory neurones apart from conveying pain messages to the central nervous system, could also release multiple neuropeptides from peripheral terminals to exert local effects. The released neuropeptides have different actions on peripheral tissues. One group of sensory neuropeptides is proinflammatory in nature and they mediate neurogenic inflammation in a variety of tissues including the joints. Another group of sensory neuropeptides possesses anti-inflammatory actions but their physiological roles, especially in joints, are not well understood.

The proposed research investigates the actions of anti-inflammatory neuropeptides in normal and diseased joints. Their therapeutic potentials in the treatment of inflammatory joint diseases will also be examined.

(MD98053)

Functional Characterisation of Mast Cells Cultured from Human Cord Blood

- ∠ LAU Hang Yung Alaster OBATA Toru* •
 NAGAKURA Toshikazu*
- ☐ 4 January 1999
- CUHK Research Committee Funding

Mast cells are widely distributed thorough the body and are pivotal in the pathogenesis of inflammation and allergy. Hence a thorough understanding of the mechanisms of mast cell activation and how it can be modulated pharmacologically is important for designing effective drug treatments of inflammatory and allergic diseases. Current knowledge on mast cell activation was derived almost entirely from studies using rodent mast cells. However, it is now well established that mast cells from different anatomical locations and from different animal species are indeed different and data obtained from the rodent cells cannot always be directly extrapolated to the human. Although significant advances have been achieved in the biology of human mast cells using the enzymatically isolated tissue mast cells, the advance of future research is limited by the difficulties in obtaining large number of homogeneous population of human mast cells using this protocol. Recently, homogeneous populations of human mast cells have been successfully cultured from human umbilical cord blood by a few laboratories. In collaboration with Jikei University School of Medicine of Japan, the current project is to

further characterise the functional responses of these cultured mast cells. Once they are found to be an appropriate substitute for the enzymatically isolated human lung mast cells, proper characterisation of pharmacological receptors and their underlying mechanisms of actions in these cells will be initiated in future projects. (MD98054)

Neuropharmacological Investigations into the Role of Prostaglandin-Receptors in the Emetic Reflex

- ☐ 1 September 1998
- CUHK Research Committee Funding

Prostaglandins are involved in the nausea and vomiting induced by changes in metabolism, bacterial infection, ingestion of certain foods, chemotherapy and irradiation treatment. Moreover, the therapeutic use of Prostaglandin (PG) E and PGF₂₀ and their analogues, in obstetric medicine, is associated with the unwanted side effects of nausea and vomiting in at least 20-80% of patients. There are five major types of prostaglandin receptor (DP-, EP-, TP- and IP-receptors; some of the receptors are further sub-divided, particularly the EP-receptor) but their involvement in the emetic reflex is unknown. The studies will determine the anatomical location and identity of the prostaglandin receptor(s) involved in the emetic reflex to provide a rationale for the use of selective PG-receptor antagonists to act as antiemetic drugs. The studies will also develop models to determine the optimal anti-emetic therapy to prevent the emesis induced by the clinical use of prostanoids in obstetrics and gynaecology. The studies should also provide novel models to test the in vivo activity of new prototypic PG-receptor antagonists. At the very least, the proposed studies should provide new information relative to a more effective treatment of emesis induced by the use of prostanoids in the clinic. (MD98055)

Investigation into the Mechanism of Action of Corticosteroids to Antagonise Cisplatin- and Motion-Induced Emesis

- RUDD John Anthony YEUNG Hok Keung John
- □ 14 September 1998
- * Research Grants Council

Corticosteroids used in combination with other antiemetic drugs play an important role in the management of acute and delayed chemotherapyinduced emesis in man. However, the mechanism of action of the corticosteroids to improve the control of emesis is unknown. The project will use two animal models that may be capable of elucidating the antiemetic activity of corticosteroids like dexamethasone. These models are the recently developed model of acute and delayed chemotherapy-induced emesis using the ferret and a provocative motion-induced emesis model using Suncus murinus. The models will enable a range of corticosteroids to be investigated that have dissociated properties to determine the mechanism that relates to the antagonism of the emesis. The studies will use reference anti-inflammatory agents including selective inhibitors of COX-2, an enzyme that may be induced during the delayed phase of emesis. The studies will also address the role of leukotrienes to acute and delayed emesis and provocative motion-The role of cortisol and induced emesis. corticotrophin, an endogenous hormone that is suppressed by anti-emetic doses of corticosteroids. will also be assessed by immunoassays. Investigation of the corticosteroids and related agents in the presence of cortisol synthesis inhibitors and corticosteroid receptor antagonists will assess the role of negative feedback mechanisms to anti-emesis. The studies may lead to the introduction of a new and important range of potent and selective anti-emetic drugs.

(CU98049)

Metabolic Studies of a Series of Drugs in Horses

- ☐ 1 March 1999
- Hong Kong Jockey Club

The project is a joint research in which the Racing Laboratory, Hong Kong Jockey Club and Department of Pharmacology and Department of Chemistry, CUHK will provide academic and scientific input. The project aim is to investigate the metabolism of a series of drugs in horses. *In vitro* and *in vivo* studies will be carried out in the isolation and characterization of drug metabolites using different analytical techniques.

(MD98082)

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

Edition <u>Title/Investigators</u>

Wa

1997-98	Modulatory Effects of Extracellular ATP on Delayed Rectifier K ⁺ Channels of Guinea-Pig Single Sino-Atrial Nodal Cells (MD97072) KWAN Yiu Wa	1997-98	Identification of Brain Areas Involved in Emesis in the Ferret by c-fos Immunocytochemistry (MD97070)
1996-97	Evaluation of Anti-inflammatory Agents in Animal Models of Arthritis (MD96088) & LAM Fu Yuen	1997-98	Assessment of Prostanoid Receptor Stimulated Coupling of Gs to Adenylyl Cyclase (MD97001) WISE Helen
1995-96	Neuropeptide Induced Mediator Release from Mast Cells: Effects of Non-peptide Antagonists of Neurokinins (MD95114) ∠ LAU Hang Yung Alaster • PEARCE Frederick Lawrence*	1997-98	The Role of Prostacyclin Receptors in Pain Modulation (CU97601)
1996-97	Prostanoid Receptors on Mast Cells (CU96627) ∠ LAU Hang Yung Alaster • JONES Robert Leslie	1996-97	Detection of Enzyme Induction During Anti-tuberculosis Therapy by a Novel Monoclonal Anti-6β-hydroxycortisol Antibody-based ELISA Method (MD96090) YEUNG Hok Keung John • LAI Kei
1997-98	Chloride Influx and Mast Cell Activation (MD97069) £ LAU Hang Yung Alaster		Wai Christopher (Medicine & Therapeutics) • TAI Kwok Ping*
1995-96	Investigation into the Mechanism of Metabolism-induced Hepatotoxicity of the Pyrrolizidine Alkaloid: Clivorine, and the Prevention of Such Hepatotoxicity Using Glycyrrhizin (CU95639)	1996-97	Pharmacogenetics of Trimethylamine Noxidation in Chinese, and Associated Studies on Regulation of the Flavincontaining Monooxygenase in Animals (MD96115) ✓ YEUNG Hok Keung John • DAMANI Lyaquatali A. (Pharmacy)# • LIN Ge
1997-98	Chemical and Pharmacological Studies of Beimu, a Commonly Used Antitussive Traditional Chinese Medicine (CU97632) ∠ LIN Ge • KWAN Yiu Wa • HO Yee Ping (Pharmacy) • LI Ping*	1997-98	Effects of Polysaccharide Peptide (PSP) on Glutathione-Related Enzymes in the Mouse (MD97071) Z YEUNG Hok Keung John

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RESEARCH PROJECTS

Controlled Production of Spray-dried Drug Microparticles for Pulmonary Delivery

- ∠ CHOW Hee Lum Albert LIN Ge (Pharmacology) CHAN Chak Keung*
- ☐ 1 January 1999
- * Research Grants Council

An Investigation of the experimental and operational conditions governing the production of micron-sized salbutamol particles of pulmonary delivery in a laboratory-scale spray dryer (Buchi B-191) is Salbutamol is a widely-used antiproposed. asthmatic drug commonly administered through the inhalation route. The proposed research involves particle production inside the spray dryer, physical and chemical characterization of particles, and evaluation of extent of particle deposition in rat lungs Spray drying is widely following inhalation. employed in the pharmaceutical industry in microencapsulation, film coating and the production of powders and granules. The technique involves atomization of a feed solution to form droplets; evaporation and drying of the droplets in a gas stream to effect particle formation; and separation of particles from the gas stream. A thorough understanding of the physical and chemical factors affecting the spray drying process is crucial to the production of powders with uniform properties. Studies will be conducted to systematically investigate the influence of solvents, additives, flow conditions and heating/drying conditions on particle morphology, size distribution, surface properties and Particles will be physically crystallinity. characterized by such techniques as scanning electron microscopy, X-ray diffractometry, thermal analysis, surface adsorption (BET) analysis and Coulter sizing analysis. The extent of deposition of spray-dried particles in rat lungs after inhalation will also be Through a detailed study of various operational and physicochemical parameters in spray drying on particle morphology and properties (and ultimately on particle delivery to the lungs), technology criteria for manufacturing uniform drug powders with high respirable fraction upon inhalation will be established. The proposed research is a concerted effort to develop a prototype technology for the production of novel drug microparticles in Hong Kong. (CU98244)

Establishment of a Certified Drug Evaluation Unit for Assessing the Quality of Oral Generic Drugs in Hong Kong

∠ CHOW Sing Sum Moses • CHOW Hee Lum
Albert • HO Yee Ping • TOMLINSON Brian

- (Medicine & Therapeutics) LEE Kwing Chin Kenneth
- ☐ 1 January 1999
- ❖ Industrial Support Fund, Industry & Technology Development Council

The prime objective of the present project is to provide certified bioavailabilities (BA) and bioequivalence (BE) evaluation for the locally produced oral generic drugs to enable them to meet the internationally recoginzed standards of quality. Through collaborative efforts of the CUHK Department of Pharmacy and Division of Clinical Pharmacology, the present project seeks to (a) establish a Drug Evaluation Unit that will meet the internationally recognized standards of Good Clinical Practice (GCP) and Good Laboratory Practice (GLP) for BA/BE studies and drug product testing; and (b) provide BA/BE testing of 20-24 oral drug products from local manufactures requiring valid BA/BE data for marketing and export purposes. The justifications for the proposed Drug Evaluation Unit to be set up in Hong Kong, and in particular at CUHK, are: (1) there are presently no established BA/BE study centres in Hong Kong and its neighbouring region which meet both GCP and GLP standards; (2) CUHK is the only tertiary institution in Hong Kong with an established Pharmacy School staffed by expert personnel in all aspects of drug evaluation; and (3) CUHK has a well established medical school with experienced clinical investigators to collaborate in certain aspects of BA/BE study. The deliverables of the project are: (a) in- vitro drug evaluation covering stability, content uniformity and dissolution; and (b) clinical drug evaluation, i.e. BA/BE studies on 24 oral products in healthy human subjects over the first three years. The target users will be the 50 plus local pharmaceutical manufacturers of "western" oral generic medicines. In the long term, the proposed BA/BE service will contribute to the growth and economic success of the local pharmaceutical industry leading to (1) less expensive but equally efficacious drug products; and (2) export of local generic products to developed countries. (MD98071)

Chemical and Pharmacological Study on Herbs Used for Functional Drinks

- ZHU Min ◆ LI Yawei ◆ ZHANG Jinnan
- □ 10 September 1998
- Bacardi-Martini Asia Pacific Ltd.

Herbal wines and plant-derived soft drinks are very popular in China and Asia countries for promotion of human health and for the treatment of certain chronic diseases, e.g. rheumatism. However, research related to the chemical nature of these herbs and associated pharmacological effect as well as any changes of ingredients during manufacture have not been conducted extensively. In this project, several herbs that are commonly used for preparation of functional drink are selected to investigate their chemical properties and pharmacological effects regarding anti-inflammation, anti-oxidation and immunomodulation. (BL98038)

Quality Control of Ganoderma (Lingzhi) Products

- ∠ ZHU Min QIAN Tianxiu (Chinese Medicinal Material Research Centre)
- ☐ 4 March 1999
- Vita Green Pharmaceuticals (HK) Ltd.

Quality control of herbal medicine is one of the major concerns for study of Chinese medicine that involved not only chemical but also pharmacological investigations. In this study, *Ganoderma* (Lingzhi) was selected and an array of examinations have been designed including isolation and structural identification of major components, establishment of quantitative measurements for active principles, pharmacological tests on active fractions and individual isolates and *in-vivo* pharmacokinetic study on *Ganoderma*. As a result, a set of analytic methods will be developed using different chromatographic techniques for the verified *in-vivo* bio-markers. (BL98039)

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

Edition <u>Title/Investigators</u>

1997-98 Formulation and Evaluation of Oral Traditional Chinese Medicines (TCMs) (MD97023)

- CHOW Hee Lum Albert LEE Kwing Chin Kenneth HO Yee Ping
 HO Suk San Susan LIN Ge (Pharmacology)
- 1997-98 Hygroscopic Growth of Pharmaceutical Aerosols (MD97134)
 - ∠ CHOW Hee Lum Albert CHAN Chak Keung* CHEN Guo Hua*
- 1995-96 Prospective Pharmacokinetic Dosage Adjustment of Aminoglycoside Therapy Based on Drug Blood Level Data (MD95196)
- 1996-97 Assessing the Pharmacokinetics and Pharmacodynamics of Drugs with Nonlinear, Input Rate-dependent Dispositions (MD96087)
- 1997-98 Study on Antiulcer Effect of *Hippophae rhamnoides* (BL97040)
 - ∠
 ZHU Min LI Chi Keung Ronald#

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RESEARCH PROJECTS

Research in Epithelial Cell Biology

- - WONG Patrick Yee Ding YAO Xiaoqiang
- ☐ 1 October 1998
- CUHK Strategic Research Program

The epithelium is a continuous layer of cells that covers external body surface and forms lining of body cavities such as the lung, the pancreas, intestines and all glands with exocrine function. The epithelium plays an important role in maintaining the normal functions of various organs and glands. Defective epithelial function has been found responsible for some of the diseases such as cystic fibrosis, Young's syndrome, anhidrosis and some unexplained cases of male infertility. In addition, epithelial cells, which undergo frequent apoptosis, are the origin of most types of cancer. This program aims to promote research in epithelial cell biology by encouraging collaboration to work on a number of different epithelial cells including epididymal cells, endometrial cells, Markel cells and tumor cells of epithelial origin so that problems of different disciplines (e.g., reproductive biology, developmental biology, tumor biology) can be addressed and tackled at various levels (molecualr, cellular, tissue and organ) and different aspects (receptors, ion channels and signaling pathways). This program may also function to promote exchanges with China and other parts of the world. The long term goal of this program is to establish a main stream of research in the field of epithelial cell biology in this region. (MD98084)

Modulation of Sperm Ca⁺⁺-Activated K⁺ Channels by Angiotensin II Receptors

- ∠ CHAN Hsiao Chang
- □ 1 May 1999
- CUHK Research Committee Funding

Ca2+ -activated K+ channels (Kca) have been implicated in a number of sperm functions including sperm activation and gamete interaction; however, direct characterization of the channel and its regulation has been precluded by the small size of sperm. We have recently demonstrated functional expression of this channel in *Xenopus* oocytes by injection of RNAs of the germ cells isolated from the rat testes. Co-expression of other receptors have also been observed. The present study aims to further investigate the modulation of the Kca channel by angiotensin II (AII) since AII is known to be present in seminal fluid and affect sperm motility. Using the *Xenopus* oocyte system and voltage-clamp technique,

modulation of the Kca channel will be investigated in conjunction with the use of specific agonist and antagonist of AII receptors. Signalling pathways involved will also be investigated to confirm specific AII receptor subtype involved. The expression of mRNA of particular receptor subtypes, AT_1 or AT_2 , in spermatogenic cells will be confirmed by RT-PCR and their localization by immunohistochemistry. The proposed study will elucidate the underlying mechanism by which AII affects sperm motility. (MD98110)

Ultrastructural Identification of Apoptotic Cells by Direct Immunogold Detection of Digoxigeninlabeled Genomic DNA in Semithin Sections

- ∠ CHEW CHENG Siew Boon
- □ 1 October 1998
- CUHK Research Committee Funding

Apoptosis is a procss of physiological cell death, distinct from necrosis, which plays a crucial role in a large number of physiological and pathological processes. It occurs during development, normal adult tissue maintenance and some disease processes. This active response is initiated by a definable physiological stimulus and the appearance requires de novo gene expression. Chromatin cleavage has been considered by many to be the biochemical hallmark of cell undergoing apoptosis. Fragmented DNA with 200-250 bp is followed by internucleosomal digestion to 180-200 bp fragments which could be detected by routine gel electrophoresis as the characteristic "ladder" pattern. On the other hand, the TUNEL method at the light microscopic level was widely used as a histochemical technique to detect internucleosomal DNA fragmentation at the levels of individual cells. However, the resolving power of light microscopy is limited. In the present study, a method of recognizing early apoptotic cells at an electron microscopic level will be established. The progressive of different stages of apoptotic cells can then be recognized in situ quantitatively by looking at the intensity of the labeled gold particles which act as a marker.

(MD98056)

Mechanism of Atrial Natriuretic Factor (ANF)induced Inhibition of DNA Fragmentation and Increased Expression of c-fos, junB and Ornithine Decarboxylase (ODC) Genes in NG108-15 Cells

- ☐ 1 October 1998
- CUHK Research Committee Funding

Alzheimer's disease, brain ischemia following a stroke and certain other neurological diseases involve the loss of neural functions because of apoptotic cell death of neurons. In the case of Alzheimer's disease, neuronal apoptosis is believed to result, at least in part, from toxic effects of β -amyloid peptide $(A\beta)$ and loss of neurotrophic effects of secreted form of β -amyloid precursor protein (β -APP^S). laboratory has shown that the neuroprotective effects of β -APP^S is mediated by elevation of cyclic GMP (cGMP) and activation of cGMP-dependent protein kinase (PKG) in neurons. Atrial and brain natriuretic peptides (ANF and BNP) were also found to elevated cGMP and inhibit DNA fragmentation (early step in apoptosis) in PC12 and NG108-15 cells. currently funded Direct Grant studies neuroprotective effects of BNP in PC12 cells (catecholaminergic neuron model) and role of superoxide dismutase (SOD). The proposed project will investigate ANFinduced inhibition of DNA fragmentation in NG108-15 cells (cholinergic neuron model) and role of increased gene expression of ornithine decarboxylase The Working Hypothesis is that ANF increases survival of stressed cholinergic neurons by:

- (1) activating cGMP/PKG signal transduction pathway,
- (2) increasing phosphorylation of the transcription factor CREB,
- (3) increasing expression of c-fos, junB and ODC genes, and
- (4) thereby increasing production of polyamines that protect DNA from cleavage by endonucleases.

Expression of c-fos, junB and ODC gene will be assessed by RT-PCR and Northern blot analysis. Involvement of PKG and CREB will be assess by using specific activators and blockers of PKG and antibodies against the phosphorylated form of CREB. The results of this project should provide valuable new information about the cellular and molecular mechanisms of the inhibition of DNA fragmentation and c-fos, junB and ODC expression induced by ANF in cholinergic neurons. (MD98057)

Physiological Role of Membrane Potential in Regulation of Resistance Arterial Tone

- ∠ HUANG Yu CHAN Leung Franky (Anatomy)
 NELSON Mark T.* GOLLASCH Maik*
- ☐ 1 August 1998
- * CUHK Mainline Research Scheme

Intravascular pressure causes many resistance arteries to develop myogenic tone which is further regulated by both vasoconsctrictors and vasodilators. Myogenic tone is an important contributor to basal arterial tone as well as to autoregulation which is responsible for maintaining constant blood flow in the brain during blood pressure changes. Recent attention has focused on the potential role in the resistance vasculature, in particular, how this mechanism could contribute to the increased vascular resistance which is a characteristic of hypertension. The aim of the

proposed study is to investigate the myogenic tone in coronary and cerebral arteries of normotensive and spontaneously hypertensive rats, and the modulatory role of the endothelium and some newly identified vasoactive rats, and the modulatory role of the endothelium and some newly identified vasoactive neuropeptides (adrenomedullin and pituitary adenylate cyclase-activating peptide) in the vascular tone in vessels from both types of rats. These studies should provide new insights into the mechanisms of regulation of coronary and cerebral artery tone and autoregulation and probably a better understanding of the defects in coronary and cerebral flow regulation in the case of hypertension and stroke. (MD98008)

Study on Mechanisms of Vasodilator Action of Berberine

- ∠ HUANG Yu
- ☐ 1 October 1998
- CUHK Research Committee Funding

The cellular and ionic mechanisms underlying the antihypertensive action of berberine is largely unknown. The projected proposal will specifically examine the following hypotheses using several experimental approaches:

- (1) To investigate what endothelium-derived vasoactivate factors (nitric oxide, endothelium-derived hyperpolarizing factor and prostacyclin) are involved in berberine-induced vasorelaxation;
- (2) To investigate whether berberine can inhibit plasma membrane calcium channels and calcium influx;
- (3) To investigate whether berberine can stimulate intracellular second messenger systems such as cyclic AMP and cyclic GMP to induce relaxation or inhibit protein kinase C-mediated vasoconstriction.

This will be the first detailed study to investigate the possible ionic and cellular mechanisms underlying the vascular response to berberine. This study should provide useful and novel information regarding the beneficial effect of berberine on cardiovascular function.

(MD98058)

Study on Calcium Sparks in Smooth Muscle Cells

- □ 1 June 1999
- Germany/Hong Kong Joint Research Scheme

Calcium ions play an essential role in the regulation of many forms of cellular activity including muscle contraction. The cell has access to two sources of signal calcium: extracellular calcium influx and intracellular calcium release from the endoplasmic or sarcoplasmic reticulum. The plasma membrane provides the three major pathways for calcium influx on the basis of their regulatory mechanism: voltagesensitive Ca2+ channels, receptor-operated Ca2+ channels, and store-operated Ca2+ channels. With advanced electrophysiological techniques, the former two types of channels have been pharmacologically characterized, while the latter is currently being intensively studied. At least two intracellular channels control release of calcium from the internal stores, the IP₃ receptors and ryanodine receptors. In this study, we specifically propose to (1) investigate the role of IP₃ and ryanodine-sensitive calcium release in agonist-induced oscillations of muscle tone using selective inhibitors. These experiments should generate useful information which will direct subsequent experiments on calcium signalling in single smooth muscle cells; (2) to identify the main source that triggers calcium sparks which are likely responsible for the global increase in [Ca2+], and the contractile phase of rhythmic activity in vas deferens smooth muscle; (3) to investigate interaction between calcium sparks and the activity of K_{ca} channels using simultaneous measurement of calcium signal and whole-cell K⁺ currents. This series of experiments should yield useful results regarding the possible link between calcium sparks and sarcolemmal ion channels as well as the ionic basis for noradrenalineinduced rhythmic contractions in vas deferens smooth muscle.

(MD98117)

Simultaneous Measurements of Intracellular pH and ATP-evoked Anion Secretion in Cultured Equine Sweat Gland Epithelia

- □ 1 November 1998
- CUHK Research Committee Funding

The presence of P_{2Y2} (P_{2II} -purinergic) receptors in the apical membrane of the cultured equine sweat gland epithelia allows extracellular adenosine 5'triphposphate (ATP) and uridine-5'-triphosphate (UTP) to evoke anion secretion when the cells were grown under conditions that favoured development of the polarized phenotype seen in vivo. Activation of the anion secretion has been attributed to a rise in intracellular free calcium concentration These studies on [Ca²⁺]_i measurement, $([Ca^{2+}]_i).$ however, were carried out in single cells grown on glass coverslips that cannot reveal the mechanisms by which nucleotides activate anion channels in intact epithelia. With the advent of a new technique that has been recently developed in Hong Kong which allows us to measure transepithelial ion transport and fluorescent signals simultaneously in polarized epithelial cells, our data suggested that there is a far more complex regulatory mechanism of anion secretion by $[Ca^{2+}]_i$. Other factors such as basoalteral K^+ permeability and its regulation by intracellular pH (pH_i) may also be involved. The purpose of the experiments set out in this project proposal is to clarify this mechanism by developing a new approach in which both pH_i and anion secretion are monitored simultaneously. (MD98059)

Ca²⁺ Signaling in Polarized Epithelial Cells

- □ 1 June 1999
- ❖ Germany/Hong Kong Joint Research Scheme

Epithelial cells characteristically grow as distinct sheets that form the anatomical boundaries between the relatively stable internal environment of the body and the constantly changing environment of the outside world. Many epithelia have become specialized to permit the controlled secretion and/or absorption of salt and water. These transport processes can be controlled by hormones and neurotransmitters binding to specific cell surface receptors and so evoking the production of second messenger signals within the cell. A very prominent "second messenger" in epithelial function is the intracellular Ca2+ activity ([Ca2+]i). An agoniststimulated [Ca²⁺], increase is usually composed of an initial InsP₃-mediated intracellular Ca²⁺ store release and a subsequent activation of transmembrane Ca2+ influx. In some polarized epithelia, stimulation with agonists from the luminal or basolateral side lead to differential activation of transport processes.

The aim of the project is to investigate the Ca²⁺ signaling pathways activated by luminal and basolateral agonists (e.g. ATP) and its differential effect in regulating various transport processes in polarized epithelia using microspectrofluorimetric technique, video-microscopy and laser-scanning confocal microscopy.

(MD98118)

The Function of Merkel Cell as a Touch Sensory Receptor

- LEUNG Man Sing
- ☐ 1 April 1999
- **CUHK Research Committee Funding**

Molecular biological techniques will be used to find out the possible candidates of neurotransmitters being synthesized in Merkel cells (MC) which might finally be released onto the adjacent nerve terminals. This can provide evidence for the role of Merkel cells as a force transducer in addition to its force transmission properties. All the available information about the transmitters is obtained from immunohistochemical studies, suggesting the presence of VIP, CGRP, met-

enkephalin like substances in the granules of Merkel cell. The Merkel cells from vibrissal sinus hair of the rat are used for this study. The total RNA is extracted with the Qiagen RNeasy mini kits and subject to reverse transcription - polymerase chain reactions (RT-PCR) to obtain cDNA. Selective primers like VIP, CGRP, pro-enkephalin, neuropeptide Y, substance P, etc. are used for the PCR. Quantitative PCR is performed to determine the relative abundance of mRNAs for different candidates. The sequence of the PCR products is analysed by an autonomic sequencer to confirm the correct DNA products. Since it is extremely difficult to isolate only Merkel cells from the surrounding cutaneous tissue for the experiments, a primary culture techniques will be developed to obtain a pure monolayer of Merkel cells. Such cultures can provide pure Merkel cells for other studies like programmed cell death (PCD) in these cells. Merkel cell neuroendocrine carcinoma is important due to its aggressiveness and similarity to the small cell carcinoma of the lung. (MD98111)

Changes in the Localization and Expression of Angiotensin Receptors in the Chronic Hypoxic Rat Carotid Body

- ∠ LEUNG Po Sing
- ☐ 1 June 1999
- CUHK Research Committee Funding

The mammalian carotid body is predominantly involved in sensing changes in oxygen, carbon dioxide tension and hydrogen ion concentrations and inducing compensatory reflexes in respiratory and cardiovascular control. It has been known that the carotid body is enlarged several folds and its chemoreceptors, the glomus cells also increase in number during exposure to long-term oxygen deprivation (chronic hypoxia). This chronically hypoxic treatment could alter the cardiorespiratory function. The specialized preneural type I glomus cells contain multiple putative neurotransmitters including the biogenic amines, norepinephrine, acetylcholine and neuropeptides. It is believed that sensory transduction in the carotid body involves type I glomus cells which activate closely apposed carotid sinus nerve endings by releasing excitatory neuroactive agents. Recent evidence indicates that some vasoactive peptides interact directly with the carotid body, independently of alteration in blood These include atrial natriuretic peptide, endothelin and angiotensin II. Angiotensin II is well known as a circulating humoral and tissue-based regulator of fluid and electrolyte homeostasis and cardiovascular function. It is also known that systemic angiotensin II levels are increased during hypoxia. However, the role of angiotensin II in the response to altered respiratory function is less well studied. Interestingly, it has been recently demonstrated that angiotensin II receptor, type I (AT₁) may modulate the excitation of rat carotid body chemoreceptor afferent activity.

The aim of the proposed project is to study the precise localization and expression of angiotensin II receptors, AT_1 and AT_2 in the rat carotid body and their changes by chronically hypoxic treatment. The study would provide useful data of the effect of chronic hypoxia on the localization and expression of angiotensin receptors and the physiological significance of angiotensin II in modulating the cardiorespiratory function. (MD98112)

Internalization and Routing of Trichosanthin

- Z TAM Michael S C
 SHAW Pang Chui
 (Biochemistry)
 ◆ CHAN Wood Yee (Anatomy)
- ☐ 1 September 1998
- * Research Grants Council

Trichosanthin TCS is a Ribosome Inactivating Protein (RIP) that has wide spectrum of biological activities. Preparation containing TCS is used in China as an abortifacient agent. It has been recently discovered that TCS inhibited replication of HIV and several tumor cells. It is generally believed that the biological effects of TCS on cells are mediated through ribosome inactivation. This means that TCS has to enter cells, and works its way to the ribosome. Nevertheless, this process has not been demonstrated. The objectives of this study are (1) to demonstrate entry of TCS into cells; (2) to work out the routing to the ribosome and (3) to find regions on TCS crucial for these processes. The outcome of this study can provide answers to many unexplained observations on TCS. For example, our preliminary data suggest that phagocytotic ability of a cell enhance internalization of TCS. This probably explains the variation in TCS potency between different cell lines. Phagocytotic cells are more sensitive than nonphagocytotic cells. If this finding is established, therapeutic use of TCS can be categorized. Strategy to reduce TCS toxicity can be designed in a way so that its entry into normal cell is impaired without affecting its entry into target phagocytotic cells. In conclusion, these studies form an important basis for TCS action. It also provides fundamental information for therapeutic use of TCS and related RIPs. (CU98243)

Study of CNG1 Channel in Vascular Endothelial Cells

- ☐ 1 October 1998
- CUHK Research Committee Funding

Vascular endothelium plays an important role in modulating smooth muscle tone and blood pressure. Stimulation of endothelial cells with vasoactive agents (e.g. bradykinin, histamine, ATP, and acetylcholine) causes an increase in intracellular Ca++ concentration as a key signal triggering the formation of two autacoids, prostacyclin (PGI2) and endothelium-derived relaxing factor (EDRF, NO), which subsequently act on neighboring smooth muscle cells (SMC) and cause vasorelaxation and a decrease in blood pressure. Ca++-permeable NSC channels are believed to be the sole Ca++ entry pathway in the vascular endothelium. We have recently cloned a 402-bp partial cDNA of rod-type nucleotide-gated nonselective cation (CNG1) channel from guinea pig mesenteric arteries and cultured vascular endothelial cells. The 402-bp cDNA has 100% nucleotide identity with the recently published rat eye CNG1 sequence. With the use of RT-PCR, northern blot analysis, and in situ hybridization, we have found that CNG1 mRNA is abundantly expressed in the vascular endothelial cells of large, medium, and small arteries. Here we propose to clone full length cDNA of CNG1 channel from vascular cells and to study the role of CNG1 channel in vasoregulation. Our research could potentially reveal the molecular identities of the main Ca⁺⁺ entry pathway in vascular endothelial cells. (MD98060)

Rod-Type Nonselective Cation Channel in Vascular Endothelial Cells

- ☐ 1 April 1999
- UK/Hong Kong Joint Research Scheme, the British Council

Vascular endothelium plays an important role in modulating smooth muscle tone and blood pressure. Stimulation of endothelial cells causes an increase in intracellular Ca++ concentration as a key signal triggering the formation of NO, which subsequently act on neighboring smooth muscle cells and cause vasorelaxation and a decrease in blood pressure. Ca++-permeable NSC channels are believed to be the sole Ca⁺⁺ entry pathway in the vascular endothelium. We have recently cloned a 402-bp partial cDNA of rod-type nucleotide-gated nonselective cation (CNG1) channel from guinea pig mesenteric arteries and cultured vascular endothelial cells. The 402-bp cDNA has 100% nucleotide identity with the recently published rat eye CNG1 sequence. With the use of RT-PCR, northern blot analysis, and in situ hybridization, we have found that CNG1 mRNA is abundantly expressed in the vascular endothelial cells of large, medium, and small arteries. Here we propose to clone full length cDNA of CNG1 channel from vascular cells and to study the role of CNG1 channel in vasoregulation. Our research could

potentially reveal the molecular identities of the main Ca⁺⁺ entry pathway in vascular endothelial cells. (MD98090)

Property and Role of Endothelial CNG Channel

- ☐ 1 April 1999
- American Health Assistance Foundation

CNG channel is a Ca⁺⁺ permeable nonselective cation channel sensitive to the modulation of cyclic nucleotides. The abundant presence of CNG channel in vascular endothelial cells suggest an important role of CNG channels in Ca²⁺ entry in vascular endothelium, therefore implicate a possible involvement of CNG proteins in the regulation of vasotone and arterial blood pressure.

Since endothelial CNG channels are potentially very important links in regulating arterial tone and blood pressure, we propose here to characterize the endothelial CNG channels and study the relationship between the activity of the channels and contractile response of the arterial vessels. Our aims are

- (1) to examine the basic electrophysiological and pharmacological properties of endothelial CNG channels using single channel patch clamp recording techniques; and
- (2) to use putative inhibitors of endothelial CNG channels to modulate the activity of the channels and examine whether the activity of these channels could affect contractile response of isolated arterial rings.

This study is set to reveal the electrophysiological and pharmacological properties of endothelial CNG channels which may be an important link in the regulation of arterial tone and blood pressure. An abnormal regulation of these channels may contribute the pathogenesis of hypertension and those diseases associated with hypertension such as myocardial infarction and stroke. Therefore, this study may eventually lead to the discovery of an important therapeutic site which can be modulated by antihypertensive drugs. (MD98122)

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

Edition	<u>Title/Investigators</u>
1997-98	Identification and Functional Studies of VEGF Receptors in Rat Testicular Macrophages (CU97663) ∠ AU Chak Leung • LEE Will M.*
1995-96	Study of Epithelial Electrolyte Transport (MD95029)

	 ∠ CHAN Hsiao Chang • WONG Patrick Yee Ding • CHEW CHENG Siew Boon • KO Wing Hung 		
1996-97	Local Paracrine/Autocrine Control of Epididymal Anion Secretion by Vasoactive Peptides (CU96612) CHAN Hsiao Chang • WONG Patrick Yee Ding • CHEW CHENG	1997-98	Testicular Hormone-Regulated Expression of the Renin-Angiotensin II System in the Rat Epididymis (CU97621) LEUNG Po Sing • CHAN Hsiao Chang
1996-97	Siew Boon • KO Wing Hung Calcitonin Gene-Related Peptide (CGRP) and Nitric Oxide Interactions in Vascular Smooth Muscle: Cellular Mechanisms	1997-98	Expression and Localization of the Pancreatic Renin-Angiotensin System in the Rat (MD97073) £ LEUNG Po Sing
	and Involvement in Endotoxin Shock (CU96644)	1997-98	Expression & Regulation of Renin and Angiotensin Converting Enzyme in the Rat Pancreas (MD97104) LEUNG Po Sing • NOBILING
1997-98	Cellular and Molecular Mechanisms of Brain Natriuretic Peptide (BNP)-Induced Inhibition of Apoptotic Cell Death in PC12 Pheochromocytoma Cells (MD97074) FISCUS Ronald Ray • CHEW	1997-98	Rainer* Development of Porcine Growth
			Hormone Immunoassays (BL97010) WONG Chun Cheung
1997-98	CHENG Siew Boon Study on Mechanisms of Vasodilator Effects of Green Tea Epicatechin Isomers	1997-98	Studies of the Renin-Angiotensin System in the Rat Epididymis (MD97100) WONG Patrick Yee Ding • CHAN Hsiao Chang
	in Spontaneously Hypertensive Rats and Normotensive Rats (CU97609)	1997-98	Anion Secretion by the Sertoli Cells from Cystic Fibrosis Transgenic Mice (MD97108) W WONG Patrick Yee Ding •
1997-98	Interaction between G Protein and K+ Channels in Rat Pituitary GH3 Cells		CUTHBERT Alan W.*
	(MD97101)	1997-98	Tissue Distribution and Characterization of a cGMP-Gated K Channel (MD97075) ∠ YAO Xiaoqiang
1997-98	Electrolyte Transport Mechanisms Underlying the Formation of Seminiferous Tubular Fluid by Rat Sertoli Cells (CU97640) KO Wing Hung • CHAN Hsiao Chang	1997-98	The Nigral GABAergic Inhibitory Pathway as an Endogenous Control System of Epileptic Seizures: An Electrophysiological Study (CU97626) Z YUNG Wing Ho
1997-98	Apical P ₂ Receptors and the Control of Anion Channel Activity in Epithelial Cells (MD97107)		

RESEARCH OUTPUTS AND PUBLICATIONS

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RESEARCH PROJECTS

Cytochrome P450 2D6 Genotyping and Movement Disorders in Schizophrenia

- ∠ LAM Chiu Wa WAYE Mary Miu Yee (Biochemistry) • UNGVARI Gabor Sandor • CHIU Fung Kum Helen
- □ 1 October 1998
- CUHK Research Committee Funding

Movement disorders are commonly observed in patients suffering from schizophrenia. All forms of movement disorder constitute disabling effects. It could cause life-threatening respiratory distress in severe forms. The prevalence of tardive dyskinesia (a type of chronic movement disorder) in patients on longterm antipsychotic medication is about 10% in Chinese populations. However, apart from basic demographic characteristics, no risk factor for iatrogenic and spontaneous movement disorders has been ascertained.

Recent development in pharmacogenetics has identified the role of hereditary predisposition in drug metabolism and idiosyncratic reactions. cytochrome P450 2D6 isoenzymes are involved in the metabolism of most psychotropic medications. Variations in genotypic constituents of this isoenzyme system have led to different phenotypic presentations and changes in enzyme activity. It is possible that poor metabolism with prolonged accumulation of psychotropic drugs in the body may contribute to the higher incidence of severe side effects like movement disorders. Some studies also implicated a significant contribution of mutant alleles in cytochrome P450 2D6 gene in Parkinson's disease and dementia of the Lewy body. Both disorders are characterized by occurrence of abnormal movements. It is thus possible that the gene may also be implicated in the development of spontaneous movement disorders in schziphrenia.

Researchers' project aims to study the genotypic representation of the cytochrome P450 2D6 isoenzyme system in schizophrenic patients and the association between specific alleles and movement disorders. It is hoped that the result will generate important information to the mechanism underlying movement disorders in schizophrenia and provide a biologic marker for patients requiring psychotropic medication.

(MD98061)

Outcome and Cultural Context of Anorexia Nervosa in Hong Kong

- ∠ LEE Sing HSU L. K. George*
- ☐ 1 January 1999
- * Research Grants Council

Anorexia nervosa is clearly becoming more common among females in Hong Kong. It is a severe psychiatric disorder characterised by rigid food refusal, marked weight loss, cessation of menstruation, and social dysfunction. Long-term outcome studies have indicated that 14% of anorexic patients die as a result of suicide or physical complications of the illness, while about one third of them continue to manifest eating disturbance, depression, and social impairment. The condition was once thought to be confined to women of Western societies, and was un-heard-of in Chinese societies. As a result of societal modernization and the changing and often conflicting roles of women in contemporary Hong Kong, however, an increasing number of young Chinese females who are afflicted with this condition have been reported since about a decade ago. Although clinical experience indicates that severe social impairment and death do occur among Chinese anorexic patients in Hong Kong, no outcome study of anorexia nervosa has ever been conducted in a Chinese society. This is regrettable because a systematic study of its course, outcome and prognostic factors can give clinicians a proper perspective and focus in treatment, evaluate the efficacy of existing treatment, and clarify the nature of anorexia nervosa from a cross-cultural perspective. It can also help health professionals plan the necessary health services as eating disorders predictably come to affect more young females in Hong Kong in the years to come. Since anorexia nervosa in Chinese patients is not always grounded in the fear of fatness, the present study, by combining psychiatric and cultural anthropological methodologies, may also shed light on how cultural factors shape the social course, local meaning, and symbolic function of morbid food refusal in a modern Chinese society. (CU98029)

A Randomised, Controlled Trial of Educational Counselling on the Management of Women Who Suffered Suboptimal Outcomes During Childbirth

- ∠ LEE Tak Shing Dominic CHUNG Kwok Hung Tony (Obstetrics & Gynaecology) • CHIU Fung Kum Helen • CHEUNG Lai Ping* • TAM Wing Hung (Obstetrics & Gynaecology) • LEE Albert (Community and Family Medicine)
- ☐ 1 September 1998
- Health Services Research Fund, Hospital Authority

In Hong Kong , suboptimal medical outcomes occurring in public medical service have become an increasing focus of public attention. Each year, in HA alone, there are around 5,000 parturients who have an unexpected suboptimal outcome. It is recognised that suboptimal outcomes during childbirth is relatively high risks areas in terms of patient satisfaction and

grievances. Even in the absence of medical mismanagement, formal complaints and legal actions are not infrequent. Occurring at a time of anticipated joy, these unexpected outcomes also precipitate major psychological problems for the parturients and their families. Given the commonness and the potential deleterious consequences of the condition, if educational counselling programme provided by midwife is shown to be effective in reducing psychological morbidity and in promoting patient satisfaction, the programme will be highly applicable in other obstetric units in Hong Kong. Ultimately, the concept of proactive, systematic, interventionist educational counselling may also be applicable in the management of suboptimal outcomes amongst other medical specialities. (MD98002)

A Study to Look into the Risk and Protective Factors for Drug Related Deaths in Hong Kong

- ∠ LEE Tak Shing Dominic LAU Tai Shing (Statistics) YIP Paul* HALLIDAY Peter* CHAN Kong Hei* CHAN Choi Ha*
- ☐ 1 December 1998
- ❖ Action Committee Against Narcotics

An alarming increase in trend of drug related deaths has been suggested by recent Coroners Report. In 1996, there were 182 drug-related deaths examined by the coroners, representing an increase of more than 100% over the past four years. As yet, to the best of our knowledge, there is no study of drug related death in Hong Kong. Such kind of study has been carried out in the United States, the United Kingdom and Australia and they provide important information concerning the nature and the causes of drug related death. These studies provide also important information on how to design and implement preventive intervention to reduce drugrelated death. In view of the findings of the Coroners Report, an in-dept analysis of trend of drug related deaths in Hong Kong is very timely. (MD98079)

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

Edition <u>Title/Investigators</u>

- 1996-97 Pharmacokinetics of Tricyclic Antidepressant Treatment: An Integrated Phenotype and Genotype Approach (MD96114)
 - ∠ CHIU Fung Kum Helen WING Yun Kwok CHOW Lok Yee
- 1997-98 A Study on Factors Affecting Drug Abuse Trend in Hong Kong (MD97091)
 - ∠ LEE Tak Shing Dominic LAU Tai Shing (Statistics) SO Man Pui* •
 LEE Albert (Community and Family Medicine) TANG Leung Sang Nelson (Chemical Pathology)
- 1997-98 Research on Effectiveness of Voluntary Residential Drug Abuse Treatment Programme in Hong Kong (MD97133) ∠ LEE Tak Shing Dominic
- 1997-98 The Effectiveness of Piracetam on ECT-Induced Memory Disturbances (MD97124)
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 - ✓ WING Yun Kwok LEE Sing •
 CHEN Char Nie CHOW Chun
 Chung Francis (Medicine & Therapeutics)
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RESEARCH PROJECTS

The Use of Octreotide in Adhesive Small Bowel
Obstruction - A Prospective Double-Blinded
Randomized Controlled Trial

- ∠ CHAN Chi Wai Angus CHUNG Sheung Chee
 Sydney LEE Wai Hung Danny NG Enders
 Kwok-wai LAU Yun Wong James WONG
 Kin Hung Simon LAW Ka Bo Bonita Angela
- □ 1 May 1999
- **CUHK Research Committee Funding**

Patients with previous abdominal surgery are prone to develop intestinal obstruction due to bowel adhesion and 50% of them may require another surgery to relieve the obstruction. And yet, they are vulnerable to have recurrent attack of obstruction. It would be beneficial to these patients if surgery could be avoided by other non-surgical means. somatostatin synthetic analogue, Octreotide, has been reported with success in the treatment of adhesive intestinal obstruction and was shown to reduce the need of surgery in these patients in uncontrolled trials. We proposed to evaluate the effectiveness of octreotide in reducing the need of surgery in patients suffered from adhesive bowel obstruction in a prospective double-blinded randomized controlled trial.

(MD98113)

Helicobacter pylori infection and intragastric N-nitrosation in gastric carcinogenesis

- ☐ 1 December 1998
- * Research Grants Council

the association between Helicobacter pylori infection and stomach cancer is indisputable, how the bacterium causes cancer remains unclear. It is now generally believed that gastric carcinogenesis results from a combination of bacterial virulence of H. pylori, the host responses, and coexistence of certain environmental factors. Epidemiological studies suggest that preserved food and a high salt intake predispose to gastric cancer. Preserved food contains large amount of nitrates. In the presence of proteins these compounds can be converted to nitrosoamino acids by bacteria colonizing the stomach. It has been postulated that increased in vivo formation of nitroso compounds may cause neoplastic changes of the stomach. In this study we aim to investigate the relationship between H. pylori, nitrosamines, and pre-neoplastic mucosal

changes of the stomach through a seris of clinical and laboratory studies. (CU98218)

The Bioenergetic Basis of Liver Regeneration Following Partial Hepatectomy in Man - A ³¹P Magnetic Resonance Spectroscopy Study

- ∠ LAU Wan Yee Joseph Darren Vivian MANN
 METREWELI Constantine (Diagnostic Radiology & Organ Imaging) HJELM Nils Magnus (Chemical Pathology) LAM Wai Man Wynnie (Diagnostic Radiology & Organ Imaging)
- □ 1 September 1998
- * Research Grants Council

Hepatocellular carcinoma (HCC) is one of the commonest malignancies in Hong Kong with an annual incidence of 30 per 100,000 population. Where feasible, surgical resection is the treatment of choice (and currently the only chance of cure) although it can be offered in only 10-15% of cases. The suitability of an individual patient for surgery relates to the functional condition of the liver (principally the presence of cirrhosis), since hepatic failure is the commonest cause of death after operation. When anatomically favorable, the judgment of operability is currently based on indirect assessment of liver function, with blood tests and radiological appearances being combined to estimate the risk of developing liver failure. The technique of phosphorus magnetic resonance spectroscopy (31P-MRS) allows measurement of the metabolic state of tissues, using principles similar to the more familiar magnetic resonance imaging (MRI). The advantages of 31P-MRS in the study of organ metabolism include the ability to provide direct, organ-specific information in a repeated and non-invasive manner. The aim of this research proposal is to clarify the relationship between liver metabolism and postoperative recovery in patients with HCC undergoing liver resection. The 31P-MRS evaluation of liver energetics pre- and postoperatively can be compared with the more traditional indirect assessments. The information derived from this study should help refine the selection of treatment options for individual patients, and advance scientific knowledge on the metabolic processes that characterise liver regeneration and recovery after hepatectomy in man. (CU98214)

Linezolid for the Treatment of MRSA Infections: An Evaluator – Blinded Trial Comparing Linezolid with Vancomycin

- ∠ LEUNG Ka Lau LAU Wan Yee Joseph •
 LYON Donald James (Microbiology) LEUNG
 Chi Hang Bertrand
- ☐ 1 January 1999

Pharmacia and Upjoin Limited

Methicillin resistant staphylococcus aureus (MRSA) was first identified in 1961 and since then has shown increasing resistance to other beta-lactam autibiotics. MRSA is a major nosocomial pathogen worldwide. Current isolate are uniformly susceptible to the glycopeptides, primarily vancomycin. However, with the prevalence of vancomycin resistant enterococci and the presence of a vancomycin resistance gene in an extra chromosornal element, the possibility of a vancomycin resistant S. aureus may not be far in the future. Other limitations of vancomycin include a small therapeutic range, intravenous-only method of administration and lack of deep tissue penetration. Linezolid has demonstrated good activity against MRSA and can be given intravenous and orally. Therefore the purpose of this study is to evalute efficacy, safety, tolerance and health resource use of lonezolid as compared to vancomycin. (MD98083)

Differential Gene Expression of Hepatocellular Carcinoma Using Micro Oligonucleotide Arrays Analysis

- ∠ LEUNG Mun Fai LAU Wan Yee Joseph
- ☐ 1 September 1998
- **❖** CUHK Research Committee Funding

The objective of this proposal is to initiate a pilot study of the difference(s) in gene expression between the liver cancer and the normal liver tissue using a new approach of micro oligonucleotide arrays analysis. Tens of thousands sequence database of gene of known as well as unknown functions were obtained by the advancement of the Human Genome The abilities of orderly arrange oligonucleotides of this large volume of genetic information onto a matrix for screening gene expression results in the development of oligonucleotide arrays analysis. Oligonucleotide arrays analysis employs a standard molecular biology technique for detection. Thus, thousands of gene can be screened simultaneously and easily in a single test. Liver cancer is a significant disease of this region. The genetic information regarding to this disease is scare. This project will increase the knowledge of gene expression of hepatocellular carcinoma in an exponential scale as compared to that of the current methods. The understanding of the gene expression between the liver cancer and the normal tissue is important in the future development of molecular diagnostic and gene therapy of liver cancer. (MD98063)

Cerebral Haemodynamic Tests in Traumatic Brain Injury (TBI): Do Abnormalities Such as Hypoperfusion, Hyperperfusion and Impaired

Autoregulation Require Treatment? A Correlative Study with Intracerebra

- ∠ POON Wai Sang LAM Ming Kuen Joseph HJELM Nils Magnus (Chemical Pathology) LAM Wai Man Wynnie (Diagnostic Radiology & Organ Imaging) METREWELI Constantine (Diagnostic Radiology & Organ Imaging) CHAN Matthew Tak Vai (Anaesthesia & Intensive Care)
- ☐ 1 September 1998
- * Research Grants Council

Patients with traumatic brain injury are prone to develop secondary brain damage. Cerebral blood flow (CBF) and autoregulation abnormalities have been shown to be associated with poor outcome. Non-invasive cerebral haemodynamic tests using transcranial Doppler ultrasonography (TCD) have been widely employed to document these abnormalities, although systematic validation with CBF measurements such as stable xenon-enhanced computerised tomography (CT) have not been carried out.

We propose to prospectively study 60 ventilated patients with moderate to severe head injury in the intensive care unit (ICU), where continuous invasive multimodality monitoring (arterial blood pressure, intracranial pressure, end-tidal CO2, jugular bulb oxygen saturation and laser Doppler flowmetry) and twice daily TCD examination will be performed. Stable xenon-enhanced CT measurements of CBF with CO₂ challenge will be carried out on day one (when resuscitation including evacuation of intracranial haematoma is completed), day 3 and day 7, continuous intracerebral microdialysis (real time measurements of glucose, lactate, pyruvate and glutamate at 30-minute intervals) will be carried out in the frontal lobe of the side of maximum injury. This will be the first comprehensive study (1) to validate non-invasive haemodynamic tests against stable xenon-enhanced CT CBF measurements and laser Doppler flowmetry; (2) to correlate CBF abnormalities (ischaemia versus hyperemia) and autoregulation status with cerebral metabolic disturbance using real time microdialysis data and 6month clinical outcome. (CU98223)

Predicting Severe Cerebral Ischaemia (SCI)
During Carotid Endarterectomy (CEA) with
Preoperative Stable Xenon-Enhanced Computed
Tomography (XeCT) Cerebral Blood Flow
Measurement

Ronald BOET • POON Wai Sang • LAM Wai Man Wynnie (Diagnostic Radiology & Organ Imaging) • METREWELI Constantine (Diagnostic Radiology & Organ Imaging) • WONG Ka Sing Lawrence (Medicine &

Therapeutics) • KAY Li Chi Richard (Medicine & Therapeutics) • LAM J.M.K.*

- ☐ 1 October 1998
- CUHK Research Committee Funding

Carotid endarterectomy (CEA) has been shown to significantly reduce the risk of major stroke and death in patients with severe carotid stenosis, provided the operative mortality and morbidity can be kept to a minimum. Development of severe cerebral ischaemia (SCI) during carotid artery clamping occurs in 25% of these patients and is a major risk factor for postoperative stroke. Accurate prediction of patients at risk will enable intra-arterial shunting to be established before the crisis of SCI, hence minimising the operative risk. The current methods of predicting SCI are unsatisfactory. A prospective observational study in 20 patients with severe carotid stenosis will be carried out to assess the feasibility of employing acetazolamide activated xeonon-enhanced computed tomography (XeCT) cerebral blood flow (CBF) measurement to predict the development of SCI during CEA. The baseline CBF and its acetazolamide reactivity of the three vascular territories in patients who develop SCI (estimated n=5) intraoperatively will be compared with those patients who do not (estimated n=15). This will be the first pilot study using XeCT CBF methodology to predict the occurrence of intraoperative SCI duing CEA. (MD98062)

Development of a Cantonese Basic Speech Perception Test for Hearing-Impaired Children and Children with Minimal Language Ability –

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 Fai Michael • LEE Y.S. Kathy* • CHIU S. N.*
 • WONG K.C. Terence*

- □ 2 July 1999
- Health Services Research Fund, Hospital Authority

Establishing Validity and Reliability

The study aims at developing a clinical tool for objective measurement of basic speech perception for Cantonese children with hearing impairment and minimal language ability. Test construction requires enormous time and funding. The procedures include planning, construction, quantitaive evaluation and validation which are unable to be dealt with in a single project. The present project would focus on the first three stages, leaving actual validation for hte next phase. The reseach objectives are:

- (1) to identify domains of Cantonese basic speech perception;
- (2) to test the hypothesis "normal three-year-old children are able to discriminate basic Cantonese tones";

- (3) to determine vocabulary used in the test;
- (4) to construct test items according to the domains identified; and
- (5) to examine the validity and reliability of the developed test times.

Objective (1) will be achieved through a literature search, consulting a panel of experts and conducting two research studies listed under objectives (2) and (3). One of the studies is on children's vocabulary inventory and the other is on Cantonese tones. With the information obtained, test items are constructed. Two pilot studies which involve 140 normal hearing and 140 hearing-impaired subjects will be conducted on the developed items. Results obtained in the pilot studies are subject to validity and reliability check including factor analysis, factor loading, Cronbach's alpha, inter-class correlation coefficient and paired ttests. The expected outcome would be a valid and reliable assessment tool ready for actual validation process. (AL98028)

(AL98028)

A Comparative Study of the Physiological Changes with Pneumoperitoneum During Laparoscopic Surgery in Infantile Versus Adult Animals

- × YEUNG Chung Kwong AUN Sui Tee Cindy (Anaesthesia & Intensive Care) GOMERSALL Charles David (Anaesthesia & Intensive Care)#
 FOK Tai Fai (Paediatrics) LAU Wan Yee Joseph
- □ 1 September 1998
- * Research Grants Council

The great advances of minimally invasive surgery in adults has led many to assume that these techniques should apply equally well to paediatric patients with the same degree of efficacy and safety. Over the last few years there has been a rapid expansion of the list of paediatric surgical operations being performed by laparsocopic approach worldwide, usually conducted with similar equipment operative settings, e.g. intraabdominal pressure for pneumoperitoneum, as in adults. However, scientific data regarding possible differences in physiological response and stress reaction between small children and adults during laparoscopic surgery are completely lacking. A prospective, randomized study of laparoscopic versus open appendectomy in children conducted recently in our unit has revealed no significant benefits of the former approach, and indeed some possible ill effects especially in cases with gangrenous or perforated appendicitis and bacterial contamination of the peritoneal cavity. This highlights the great importance to evaluate comprehensively the differences in physiological response including haemodynamic changes, arterial and portal venous oxygen saturation, respiratory function and intestinal mucosal microcirculation between infantile and adult

subjects during laparoscopic surgery, both in a clean as well as in a contaminated peritoneal cavity, using an animal model. The results should provide very important clues to the future development of minimally invasive surgery in young children and in particular should shed light on the necessary precautions that may be required for children with compromised cardiopulmonary status. (CU98224)

Appraisal of Microchimerism, Graft Tolerance and Rejection by Plasma and Urinary DNA Following Solid Organ Transplantation

- ∠YEUNG Chung Kwong LO Yuk Ming Dennis
 (Chemical Pathology) PANG Chi Pui Calvin
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 Wan Yee Joseph
- □ 1 December 1998
- * CUHK Research Committee Funding

The observation that donor-derived cells can be detected as resident cells in the recipient years after organ transplantation, or microchimerism, has led to the hypothesis that this may account for the development of graft tolerance. However, up to present little is known about the dynamics of donor cells in the host and its correlation with graft rejection or acceptance. Researchers have recently described the presence of donor-derived DNA in the plasma of organ transplant recipients, a phenomenon researchers termed "plasma DNA chimerism". Donor DNA was found in 100% and 83% of liver and kidney transplant patients respectively. Interestingly, plasma DNA chimerism was observed even in patients where peripheral blood cellular chimerism were undetectable. As graft rejection is an important cause of cell death in a transplanted organ, researchers observation raises the possibility that the level of donor DNA in the recipient's plasma may actually be a marker for rejection. Since cellular chimerism has been proposed as a possible mechanism towards donor-specific graft tolerance, they propose to study the relationship of plasma and cellular chimerism in correlation to the allograft outcome. Furthermore, as Starzl has proposed that the graft-host relationship can be a two-way paradigm in which there is both a host-versus-graft as well as a graft-versus-host reaction¹⁰, the dynamics of this two-way model can potentially be studied by quantitative analysis of the ratio of donor-and hostderived DNA. Results from this project may very probably help us to unveil the myriad of mysteries surrounding the immunology of organ transplantation. (MD98064)

Induction of Proinflammatory Cytokine mRNA Expression in Myocardium after Clinical Cardiopulmonary Bypass

- ∠
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- ☐ 1 September 1998
- CUHK Research Committee Funding

The release of proinflammatory cytokines, such as tumor necrosis factor α (TNF-α) and interleukin (IL)-6, has been suggested to play a critical role in the complex inflammatory response following cardiopulmonary bypass (CPB) and may further lead to postoperative complications [Wan et al. Ann Thorac Surg 1997;63:269-76]. Researchers have recently demonstrated that the myocardium is a major source of TNF-α and IL-6 during CPB [Wan et al. J Cardiovasc Surg 1996;112:806-11]. Thorac Nevertheless, it is still unclear whether the endothelial cells or the myocytes are the main source of these cytokines during clinical CPB. The current prospective study is designed to explore the possible cellular source of TNF-α and IL-6 during clinical CPB. 10 to 20 patients undergoing CPB will be enrolled in the study. Myocardial biopsies will be obtained immediately after the onset and after the end of CPB from right atrium, snap-frozen in liquid nitrogen and stored for in situ hybridization using a probe cocktail to determine TNF-α and IL-6 mRNA expression in the myocytes.

This study is expected to enhance our understanding of the mechanisms involved in the cytokine reactions during CPB. (MD98065)

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

Edition <u>Title/Investigators</u>

1996-97 Neo-adjuvant Chemotherapy in Squamous Oesophageal Cancer: Prediction of Chemoresponse Using Biopsy Sample before Chemotherapy (CU96649)

 ∠ CHAN Chi Wai Angus • CHUNG Sheung Chee Sydney • LAU Yun Wong James • METREWELI Constantine (Diagnostic Radiology & Organ Imaging) • JOHNSON Philip James (Clinical Oncology) • NG Enders K. W.*

1997-98 A Double Blind, Randomized, Placebo Controlled, Parallel Group, Multicentre, Flexible Dose Escalation Study to Assess the Efficacy and Safety of Sildenafil Administered as Required to Male Patients with Erectile Dysfunction in Asia (MD97181)

- CHAN Siu Foon Peter
- 1996-97 Prognostic Factors of Breast Cancer among Women in Hong Kong (MD96101)
 - ∠ CHAN Sun Yin Eric SUEN Wang
 Ming Michael (Anatomical &
 Cellular Pathology)
- 1996-97 To Investigate the Clinical Usefulness of Arginase, Amino Acid Profile and Sialic Acid as Tumour Markers for Breast Cancer (MD96096)
 - ∠ CHAN Sun Yin Eric PANG Chi
 Pui Calvin (Ophthalmology and
 Visual Sciences) LAM Ping Kuen
 • KING Wing Keung Walter
- 1997-98 Use of Non-Confluently Cultured Keratinocytes and Fibroblasts in Fibrin and Matrix Gel Suspension as a Permanent Wound Coverage in Athymic Mice Model (MD97078)
 - ∠ CHAN Sun Yin Eric LAM Ping Kuen
- 1996-97 Reconstitution of a Human Skin Equivalent Composed of Lyophilized Allogenic Dermis, Keratinocytes and Fibrin (CU96648)
- 1997-98 Prospective Study on the Relationship of Central Venous Pressure and Blood Loss During Hepatectomy (MD96217)
 - ∠ LAI Bo San Paul CHUI Po Tong (Anaesthesia & Intensive Care) •
 LEOW Chon Kar# • LAU Wan Yee Joseph
- 1996-97 The Induction of Apoptosis of Hepatic Cancer Cells by Polyunsaturated Fatty Acids (MD96119)
 - ∠ LAU Wan Yee Joseph LAI Bo San Paul LEOW Chon Kar#
- 1997-98 The Determination of Kupffer Cell Kinetics During the Evolution of Cirrhosis and the Potential Role of Kupffer Cells in Preventing the Development of Liver Metastases in the Presence of Cirrhosis (CU97648)
 - ∠ LAU Wan Yee Joseph LEOW
 Chon Kar# LIEW Choong Tsek
 (Anatomical & Cellular Pathology) •
 LAI Bo San Paul
- 1997-98 Evaluation of the Bioenergetic Basis of Liver Regeneration Following Partial

- Hepatectomy An *in vivo* 31P-MRS Study (MD97077)
- ∠ LAU Wan Yee Joseph Darren Vivian MANN • HJELM Nils Magnus (Chemical Pathology)
- 1996-97 Repeat Endoscopic Treatment or Surgery in the Management of Rebleeding Peptic Ulcers After Initial Endoscopic Haemostasis: A Prospective Randomized Controlled Trial (MD96182)
 - LAU Yun Wong James SUNG
 Joseph Jao Yiu (Medicine & Therapeutics) CHUNG Sheung
 Chee Sydney CHAN Ka Leung
 Francis (Medicine & Therapeutics)
- 1997-98 Adjuvant Intravenous Proton Pump Inhibitor in Bleeding Peptic Ulcers Receiving Endoscopic Therapy: A Double Blind Placebo Controlled Randomized Study (MD97171)
 - ∠ LAU Yun Wong James SUNG Joseph Jao Yiu (Medicine & Therapeutics) CHUNG Sheung Chee Sydney LEE Ka Ho Kenneth (Anatomy)
- 1996-97 Innovation Technology to Develop Human Cell Lines for Biomedical Applications and Biopharmaceutical Production (MD96192)
 - ∠ LEUNG Mun Fai IP Nancy*
- 1997-98 Immune Modulating Peptides Resemble Microtubule Binding Domains (MD97125)
 - ∠ LEUNG Mun Fai
- 1996-97 Does Intensive Rehabilitation Improve the Functional Outcome of Traumatic Brain Injury (TBI)? (MD96006)
 - ∠ POON Wai Sang ◆ ZHU Xian Lun Cannon ◆ HSIANG John Nai Keung# ◆ CHAN Che Hin* ◆ IP Wei Chung* ◆ CHANG Wai Ching*
- 1996-97 Molecular Expression of Hypothalamic Atrial Natriuretic Peptide (ANP) and Anti-diuretic Hormone (ADH) in Hyponatraemia Following Experimental Head Injury (MD96103)
 - ∠ POON Wai Sang NG Ho Keung (Anatomical & Cellular Pathology) LOLIN Yvette Ivanka (Chemical Pathology)# YEUNG Tok Fai Vincent (Medicine & Therapeutics)
 COCKRAM Clive Stewart (Medicine & Therapeutics)

- 1997-98 The Comparative Impact of Videoconsultation on Neurosurgical Health Services (MD97095)
 - ∠ POON Wai Sang KWOK Po Yin Samuel JACOBS Philip*
- 1997-98 Development of a New Hyaluronic Acid Membrane Delivery System for Using the Cultured Keratinocytes as a Permanent Wound Cover (MD97126)
 - ∠ TO Wai Hei Edward KING Wing Keung Walter LAM Ping Kuen CHAN Sun Yin Eric
- 1997-98 An Open Clinical Trial of Dysport in Bilateral Masseteric Hypertrophy (MD97142)
- 1994-95 Investigations into the Aetiology and Management of Nasopharyngeal Carcinoma (MD94071)
 - VAN HASSELT Charles Andrew LEE Chuen Kwun Joseph (School of Chinese Medicine)
- 1995-96 A Phase IIB Open Labelled, Single Group Study into the Effect of mTHPCmediated PDT on Recurrent and Advanced NPC after Radiotherapy (MD95235)
 - ✓ VAN HASSELT Charles Andrew •
 WOO Kong Sang John TONG Chi
 Fai Michael LEUNG Sing Fai
 (Clinical Oncology) LEE A.* •
 CHANG Mei Kam Amy #
- 1996-97 Effect of Radiotherapy on the Cochlear and the Central Auditory Conduction Pathway in Patients with Nasopharyngeal Carcinoma (NPC) (MD96012)
 - ∠ VAN HASSELT Charles Andrew
 ◆
 TONG Chi Fai Michael
- 1997-98 Neonatal Hearing Screening Using
 Distortion Product Otoacoustic
 Emissions (DPOAEs), Steady State
 Evoked Potentials (SSEPs) and
 Impedance Audiometry A Preliminary
 Study (MD97076)
 - ✓ VAN HASSELT Charles Andrew TONG Chi Fai Michael WONG Terrence K. C.* LEUNG Eric K. C.* FOK Tai Fai (Paediatrics) McPHERSON B.*
- 1997-98 The Effect of Indoor Pollution on the Development of Rhinitis in Office Workers in Hong Kong (MD97019)

- ✓ VAN HASSELT Charles Andrew •
 TONG Chi Fai Michael TSANG
 King Yin Raymond* WOO Kong
 Sang John LAU Tak Fai Joseph
 (Centre for Clin. Trials &
 Epidemiological Research) WONG
 Ming Chung (Centre for Clin. Trials
 & Epidemiological Research) NG
 Heung Ling Margaret (Anatomical &
 Cellular Pathology) YU Tak Sun
 Ignatius (Community and Family
 Medicine)
- 1996-97 A Double Blind Randomised Placebocontrol Trial on the Efficacy of Perioperative Zithromax as Prophylactic Antibiotic for Functional Endoscopic Sinus Surgery (MD96143)
 - WOO Kong Sang John TONG Chi
 Fai Michael VAN HASSELT
 Charles Andrew KU Peter K. M.*
 CHANG Mei Kam Amy #
- 1997-98 A Comparative Study of the Physiological Changes During Pneumoperitoneum in Laparoscopic Surgery in Infantile Versus Adult Pigs (MD97080)
- 1995-96 Video Assisted Thoracic Surgery (MD92192)
 - YIM Ping Chuen Anthony
- 1997-98 Investigation of the Efficacy of External Stenting of Saphenous Vein Bypass Grafts in Preventing Deleterious Graft Wall Changes Following Coronary Artery Bypass Surgery (CU97647)
 - ∠ YIM Ping Chuen Anthony
 SANDERSON John Elsby
 (Medicine & Therapeutics)
 ◆ CHOW
 Tsun Cheung Louis (Anatomical & Cellular Pathology)
- 1997-98 Specific Inactivation of a Growth- and Transformation-Suppressor in Small Cell Lung Cancer (MD97083)
- 1997-98 Effect of Short Term Exposure of Saphenous Vein Grafts to Thapsigargin on Medial and Intimal Thickening in a Porcine Arterio-Venous Bypass Graft Model (MD97079)
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RESEARCH PROJECTS

The Effect of Analgesia on the Expression of Leucocyte Adhesion Molecules Following Injury

- □ 1 July 1998
- CUHK Research Committee Funding

Background: Alteration of the expression of leucocyte adhesion molecules will affect the inflammatory response to trauma. In some circumstances this may be beneficial as an excessive inflammatory response may result in organ failure. Both opiates and non-steroidal anti-inflammatory drugs (NSAID's) alter the expression of leucocyte L-selectin in vitro and may have a role in the prevention of excessive inflammation following injury. However there are no known reports of the effect of NSAID's or opiates in the expression of leucocyte adhesion molecules in vivo.

Objective: To investigate firstly, the effects of intravenous analgesia on the expression of adhesion molecules following limb injury, and secondly, the role of circulating catecholamines and cortisol in regulating this expression.

Study Design: Double blind, randomised trial comparing intravenous ketorolac and morphine.

Participants: Thirty adult patients sustaining painful isolated blunt injury to a limb brought to the Emergency Department of The Prince of Wales Hospital. There will be ten patients in each intervention group and ten non-randomised control subjects.

Laboratory Methods: Flow cytometry; High Performance Liquid chromatography; Radioimmunoassay

Outcome Measures: Primary outcome measures: changes n expression (percentage expression and mean channel fluorescence) of L-selectin on the surface membranes of leucocytes; correlation of the expression of L-selectin and circulating catecholamines and cortisol.

Secondary outcome measures: Correlation between pain score and circulating catecholamines and cortisol.
(MD98001)

Analgesic Efficacy and Cost-effectiveness of Morphine Compared with Ketorolac in the Treatment of Pain Following Limb Injury in an Emergency Department: A Double-blind, Randomized Controlled Trial

- □ 1 December 1998
- CUHK Research Committee Funding

Background: The current gold standard for the treatment of pain following long bone fractures is iv morphine titrated according to the patient's requirements. However such pain is frequently undertreated in Emergency Departments (ED's) possibly because of physician held beliefs of opiate side effects. Recent studies suggest that, from a physicians viewpoint, the non-steroidal antiinflammatory drug, ketorolac, may be more effective, and may have less side effects than iv morphine. However ketorolac is more expensive and although this will concern Health Administrators, the appropriate early reduction of pain within the ED may result in earlier patient discharge. Therefore, in the management of blunt limb injury in an ED in Hong Kong a cost-effectiveness analysis (CEA) of ketorolac and morphine has important financial implications in the management of pain in an ED.

Objective: To investigate whether iv Ketorolac is a more cost-effective option than iv morphine in the managment of pain in patients with limb injuries presenting to an ED.

Design: Prospective double blind randomised study. Participants: 100 subjects having sustained isolated blunt limb injury presenting to The Prince of Wales Hospital.

Main outcome measures: Pain relief and overall cost effect.

(MD98021)

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

Edition <u>Title/Investigators</u>

1997-98 Haemostasis Following Trauma (MD97109)

∠ COCKS Robert Anthony • LAM Yuk Lan • RAINER Timothy Hudson • NG Heung Ling Margaret (Anatomical & Cellular Pathology) • MAYCOCK Paula*

- <P982773> Cocks, Robert A.; Tina Y.F. Chan and Timothy H. Rainer. "Leukocyte L-Selectin is Up-Regulated After Mechanical Trauma in Adults". The Journal of Trauma: Injury, Infection, and Critical Care vol.45 no.1, pp.1-6. USA, 1998.07.
- <P982965> Rainer, T.H.; Lam N. and Cocks R.A. "Adrenaline Upregulates the Expression of L-Selection on Monocytes in vitro" Journal of Accident and Emergency Medicine vol.15 no.6, p.415. 1998.11.
- <P983072> Rainer, T.H.; N. Lam and R.A. Cocks. "Monocyte Surface L-Selectin Correlates with Post-Traumatic Multiple Organ Failure". *Journal of Accident and Emergency Medicine* vol.15 no.6, p.405. 1998.11.
- <P983073> Rainer, T.H.; R.A. Cocks; M. Tam; K. Law; P. Lam and E. Wong. "Injury Severity Scores and Prediction of Post-Traumatic Complications". *Journal of Accident and Emergency Medicine* vol.15 no.6, p.387. 1998.11.
- <P983074> Rainer, T.H.; R.A. Cocks; C.Y. Man; N.K. Cheung; P. Lam and E. Wong. "Derivation of Prediction Rules for Post-Traumatic Lung Injury". *Journal of Accident and Emergency Medicine* vol.15 no.6, pp.392-393. 1998.11.
- <P983081> Rainer, T.H.; S.Y. Chan; K. Kwok; T.K. Suen; W. Lam and R.A. Cocks. "Severe Trauma Presenting to the Resuscitation Room of a Hong Kong Emergency Department". *Journal of Accident and Emergency Medicine* vol.15 no.6, p.405. 1998.11.
- <P983099> **Moulton, Chris and Tim Rainer.** "The Recovery from Severe Alcohol Poisoning: Report of a Pilot Study". *Journal of Accident and Emergency Medicine* vol.15 no.6, pp.411-412. 1998.11.
- <P983115> Cocks, Robert A.; Timothy H. Rainer; Paula F. Maycock; Tina Y.F. Chan and Nicole Y.L. Lam. "Cyclic-AMP: The Missing Link in Neutrophil Mobilisation after Trauma?". Journal of Accident and Emergency Medicine vol.15 no.6, p.387. 1998.11.
- <P983273> Stainer T.H.; J. Griffiths; R.A. Cocks and C. Metreweli. "Implementing the Ottawa Ankle Rules in an Asian Accident and Emergency Medicine Department. What Potential for Saving?". Journal of Accident & Emergency Medicine vol.15 no.2, p.132. UK, 1998.03.
- <P983857> Rainer, T.H.; Griffiths J.; Cocks R.A. and Metreweli C. "Would the Ottawa Ankle Rules be Effective if Implemented in Hong Kong Accident and Emergency Medicine Departments?-A Preliminary Report". Hong Kong Journal of and Emergency Medicine vol.5 no.2, pp.77-80. Hong Kong, 1998.12.
- <P990488> Cocks, Robert Anthony and Siu Kau Tong. "Police Medical Support in Hong Kong". Prehospital and Disaster Medicine vol.14 suppl.1, p.S22. Madison, WI, USA: Wadem (World Association for Disaster & Emergency Medicine), 1999.
- <P990489> Law, Kam L.; Timothy H. Rainer; James F. Griffith; Constantine Metreweli and Robert A. Cocks. "Does Ultrasound Have a Role in the Clinical Diagnosis and Management of Fractured Ribs?". Academic Emergency Medicine vol.6 no.5, p.480. USA: Hanley & Belfus, Inc., 1999.05.
- <P990490> Cocks, Robert. "Yesterday's Emergency Today's Lessons". *Today's Emergency* vol.5 no.1, pp.22-24. UK, 1999.
- <P990957> Cheung, Nai K.; Timothy H. Rainer; Michael M. Tam; Wah S. Ng; Paulina S. Mak; Peggo K. Lam and Robert A. Cocks. "Efficacy and Safety of Titrated Doses of Intravenous Ketorolac Tromethamine Compared with Intravenous Morphine Sulphate after Limb Injury". Academic Emergency Medicine vol.6 no.5, p.526. USA: Hanley & Belfus Inc, 1999.05.

- <P991014> Rainer, T.H.; T.Y.F. Chan and R.A. Cocks. "Do Peripheral Blood Counts Have any Prognostic Value Following Trauma?". *Injury* vol.30, pp.179-185. UK, 1999.
- <P991343> Cocks, Robert A. "Medical Care in Civil Disorder". Trauma vol.1, pp.255-263. UK, 1999.

see also < P982724>, < P982926>, < P983157>, < P983158>, < P983244>, < P983913>, < P983950>, < P990601>

RESEARCH PROJECTS

Post-program Survey for the "AIDS and the Workplace" Project

- ∠ LAU Tak Fai Joseph SIAH Poh Chua
- ☐ 1 March 1999
- ❖ Hong Kong AIDS Foundation

The study evaluates the "AIDS and the Workplace" Project carried out by the Hong Kong AIDS Foundation, which aims at Removing misconception and AIDS-related discriminatory attitudes in the Workplace. It is also compared to a baseline Study to describe any changes that may have occurred in the past three years. (SS98071)

Evaluation of a program for Frequent Travellers Crossing the China-Hong Kong Border

- ∠ LAU Tak Fai Joseph SIAH Poh Chua
- ☐ 1 April 1999
- * AIDS Concern Foundation Limited

The study evaluates the "Cross-border Travelers" AIDS Prevention Program carried out by the AIDS Concern, which aims at reducing unsafe border sex across the border and increase AIDS-related knowledge and awareness. (MD98147)

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

Edition <u>Title/Investigators</u>

- 1996-97 Hong Kong Adult Vision Study: A Cross-Sectional Epidemiological Study of Eye Diseases in the 40 Years of Age and Over Population of Hong Kong (MD96016)
 - ∠ LAU Tak Fai Joseph MICHON
 John Joseph (Ophthalmology and
 Visual Sciences)#
- 1996-97 Hong Kong AIDS Information Net Project (MD96133) ∠ LAU Tak Fai Joseph
- 1997-98 Understanding the Adolescent Project -Pilot Implementation and Evaluation Study (ED97026)
 - ∠ LAU Tak Fai Joseph CHOI Yuen Wan* • LAI Yee Ching Kelly (Psychiatry) • OBORNE David* • HOH Ying*
- 1997-98 The Development of Indicators to Track Awareness, Attitude and Behaviours (MD97129)
 - LAU Tak Fai Joseph LEE Shiu Hung

RESEARCH OUTPUTS AND PUBLICATIONS

- <P964286> Lo, Peng Iok; Patrick C.P. Ho; Joseph T.F. Lau; Albert Y.K. Cheung; Ernst Goldschmidt and Mark O.M. Tso. "Relationship between Myopia and Optical Components A Study Among Chinese Hong Kong Student Population". Eye Science vol.12 no.3, pp.121-125. 1996.
- <P982839> **Joe, Thomas.** "Ethical Challenges of HIV Clinical Trials in Developing Countries". *Bioethics* vol.12 no.4, pp.320-327. Oxford, UK, 1998.10.
- <P983219> **Liu, Joseph L.Y. and Jin-Ling Tang.** "Doctors are Ethically Obliged to Advise Patients to Quit Smoking". *British Medical Journal* vol.317, p.1588. UK, 1998.12.05.
- <P990134> Lau, J.; W.S. Chan; Y.W. Choi; Kelly Lai; K.K. Chan; P. Lam; David Oborne; Ying Hoh and C.K. Wong. "The Re-Examination of the Scaling Properties of an Existing Large Scale Screening Instrument for Potentially At-Risk Adolescents in Hong Kong by Multilevel Method Taking Cluster and School Information". Paper presented in the 2nd International Amster 1999.03.
- <P990396> Lau, Joseph T.F.; Joseph L.Y. Liu; Jacky C.K. Cheung; Aaron Yu and C.K. Wong. "Prevalence and Correlates of Physical Abuse in Hong Kong Chinese Adolescents: A Population-based Approach". Child Abuse & Neglect vol.23 no.6, pp.549-557. USA, 1999.

<P990747> Lau, Joseph Tak-Fai and Chau-Kiu Cheung. "Public Evaluation of an Announcement of Public Interests Communicated by an AIDS Patient". *Journal of Health & Social Policy* vol.11 no.1, pp.77-90. 1999.

RESEARCH PROJECTS

Generation of Monoclonal Antibodies Against the Epstein-Barr Virus Latent Membrane Protein 1 Variants in Hong Kong Nasopharyngeal Carcinoma

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 CHUI Yiu Loon ◆ HUANG POON Wai Sin Dolly (Anatomical & Cellular Pathology) ◆
 ∠
 CHEUNG Siu Tim (Anatomical & Cellular Pathology)# ◆ LO Kwok Wai (Anatomical & Cellular Pathology)
- ☐ 1 January 1999
- * Research Grants Council

Esptein-Barr virus (EBV) is consistently found in the nasopharyngeal epithelial cancer (NPC) cells. Its role in the development of the cancer is strengthened by the finding that the virus produces a protein with known cell transformation capability inside the This protein is called the latent cancer cells. membrane protein 1 (LMP1). LMP1 proteins from different EBV isolates show sequence variation. There is evidence that some LMP1 variants which show a loss of a string of 30 nucleotides near the end of the gene can transform cells more readily than the others which do not have the loss. Indeed, the predominant LMP1 variants present in the NPC of the South China region, where the incidence of this cancer is remarkably higher than most other parts of the world, share this sequence deletion feature. Using a polymerase chain reaction technique to analyze the LMP1 gene sequence in Hong Kong NPC, we have observed a particular variant which shows a strong association with the cancer. This variant has not been described before. It has the aforementioned deletion, but in addition an amino acid change at the sequence position 335, resulting in an aspartic acid. Majority of the NPC (87%) were found to carry this variant which was harboured by less than 30% of the healthy carriers. In contrast, another almost identical variant but without this amino acid change at position 335 was found in majority of the healthy carriers, but ony 5% of the NPC. We have resolved to further this study by using monoclonal antibodies to investigate the expression and function of our Hong Kong NPC LMP1 protein variants. As the present available antibodies were raised against a LMP1 variant present in the Caucasians, and stain poorly to our NPC samples, we propose to raise a panel of monoclonal antibodies specific to the Hong Kong NPC LMP1. We are also interested in producing antibodies that have potential immunotherapeutic value to the cancer. (CU98271)

Production of Recombinant Human Telomerase and Anti-Telomerase RNA Probe to Examine Their Diagnostic Utility in Autoimmune Disease

- ∠ LIM Pak Leong LEUNG Tze Ming WONG Kong Chiu (Medicine & Therapeutics)
- ☐ 1 April 1999
- CUHK Research Committee Funding

The recent cloning of human telomerase has aroused great interest because this could enable scientists to look more critically into the biological role played by this enzyme in cancer and ailments linked to ageing, and possibly, in other disease states not looked into hitherto. We hope to exploit this discovery as immunologists and examine whether telomerase has any role or clinical use in autoimmune disease. We will produce the enzyme in our laboratory by recloning the gene and expressing this as a recombinant protein, and use the protein in an immunoassay to see whether patients with autoimmune disease such as lupus (a common disease in Hong Kong) produce antibodies to it as some of them do with other enzymes in the body. Nothing is known about this. If they do, this may be diagnostically or biologically important. We will also investigate whether the circulating leucocytes of autoimmune patients have heightened expression of the telomerase gene, and if so, what is the significance or use of this. (MD98097)

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

Edition	<u>Title/Investigators</u>
1995-96	Transgenic Study of Immunoglobulin Gene Hypermutation: Using Selectable, Chimeric <i>E. coli</i> gpt-VJ Gene Constructs to Investigate the Role of Rearranged VJ in Hypermutation (MD94123) ∠ CHUI Yiu Loon • LIM Pak Leong
1996-97	Molecular Mechanism of Immunoglobulin Gene Hypermutation: Does It Resemble the Transcription-DNA Repair System? (CU96664) ∠ CHUI Yiu Loon • LIM Pak Leong
1995-96	Cloning and Expression in Bacteriophage of Immunoglobulin Genes from Lupus (SLE) Patients Which Encode and Antidiotypic Antibody (CU95638) ∠ LIM Pak Leong • CHUI Yiu Loon • WONG Kong Chiu (Medicine & Therapeutics)

- <P980820> Lim, Pak-Leong; Frankie C.H. Tam; Yuet-Meng Cheong and M. Jegathesan. "One-Step 2-Minute Test to Detect Typhoid-Specific Antibodies Based on Particle Separation in Tubes". Journal of Clinical Microbiology vol.36 no.8, pp.2271-2278. USA, 1998.08.
- <P980993> Chan, C.L. and H.Y.A. Lau. "Effects of PGD₂ and Its Agonists on Rat Peritoneal Mast Cells Activated by Different Secretatogues". *Archives of Pharmacology* vol.358 no.1(suppl.2), pp.17-22. Germany, 1998.07.
- <P991661> Ching, Arthur Kar-Keung; Pik-Shan Li; Wood-Yee Chan; Chun-Hung Ma; Susanna San-Tuen Lee; Pak-Leong Lim and Yiu-Loon Chui. "The Strand Bias of Somatic Hypermutation is not Locally Determined by Substrate DNA Sequerce". Proceedings of the 8th International Symposium of Society of Chinese Bioscientists in America (SCBA) p.167. Hong Kong, 1999.

see also <P980930>, <P990068>

<P983306> Cheung, W.H.; K.M. Lee; S.H. Cheng; K.P. Fung and K.S. Leung. "A Study of in vitro Inhibition on Endothelial Cells by Growth Plate Chondrocytes Secretory Factors During Tumor Spreading". Proceedings of the 18th Annual Congress of the Hong Kong Orthopaedic Association pp.100-101. Hong Kong, 1998.11.

 $\begin{array}{l} \textbf{see also} < P975062>, < P982890>, < P982892>, < P983047>, < P983305>, < P984117>, < P984118>, < P984120>, < P984581>, < P984588>, < P984979>, < P990994>, < P991079>, < P991081>, < P991121>, < P991328>, < P991539>, < P992087>, < P992529> \\ \end{array}$

- <P964291> Kwok Samuel P.Y.; Clarke B. Hazlett and James Y.W. Lau. *Grand Rounds in Surgery*. vol.2, 245 pgs. Hong Kong: THC Press Ltd, 1996.
- <P982525> Hazlett, C.B. "Improving the Interface of Health Promotions and Family Practice". The Hong Kong Practitioner (The College of Family Physicians) vol.20 no.10, pp.529-531. Hong Kong, 1998.10.

see also < P982503>, < P983048>, < P990208>, < P990679>, < P990715>