

## RESEARCH PROJECTS

### Postoperative Cognitive Function in Children

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☐ 1 July 2001

❖ Research Grants Council (Earmarked Grants)

This prospective study of 120 surgical patients aged 5-12 years old will examine whether general anaesthesia affects short term or long term cognitive function in children. We hypothesize that anaesthesia may impair memory on a short term basis but no long term effect (six weeks afterwards). The surgery scheduled will be of moderate to major category expecting to last at least one hour. The anaesthetic technique is a standard anaesthesia routinely used in children consisting of premedication with 0.5 mg/kg (maximum 15 mg) midazolam, thiopentone 4-5 mg/kg, fentanyl 1 µg/kg and non-depolarizing muscle relaxant. Anaesthesia will be maintained with nitrous oxide, oxygen, isoflurane and mechanically ventilated to ensure normocapnia, and normothermia intraoperatively. All patients will be maintained at a similar depth of anaesthesia using a Bispectral index monitor. Four cognitive tests to test verbal memory, visual memory, visual matching and comprehension will be used to compare the preoperative and postoperative cognitive functions. For comparison, a control group of students of similar age and social class will be selected to receive similar cognitive function test at similar time interval. Results will be of importance to parents and health care providers alike. No evidence of cognitive dysfunction is reassuring. However, this difference from adults' findings (25.8% incidence of postoperative cognitive dysfunction) should be investigated. On the other hand, should there be impairment, the incidence and causes should be researched further.

(MD01002)

### Intravenous Magnesium Sulphate for Neuroprotection During Cerebral Aneurysm Surgery

✉ CHAN Matthew Tak Vai • GIN Tony • Ronald BOET (Dept of Surgery) • POON Wai Sang (Dept of Surgery)

☐ 30 June 2002

❖ CUHK Research Committee Funding (Direct Grants)

Proximal temporary artery occlusion is frequently required during cerebral aneurysm surgery. It facilitates surgical dissection, aneurysm clipping and hemorrhage control during inadvertent rupture. However, during the period of vessel occlusion, distal perfusion is compromised, thus placing the brain at risk of ischemic damage. Currently, there is no standard treatment for neuroprotection during cerebral aneurysm surgery. Intravenous magnesium sulphate (MgSO<sub>4</sub>), by dilating the collateral vessels and blocking the NMDA receptor, may be a better neuroprotective agent. Using changes of neurochemistry as a surrogate measure of ischemia-reperfusion injury, we plan to evaluate the neuroprotective effects of MgSO<sub>4</sub> during cerebral aneurysm surgery.

Thirty patients undergoing craniotomy for clipping of cerebral aneurysm will be randomly allocated to receive either MgSO<sub>4</sub> or saline. The study drug will be continued for another 5 days. A multiparameter parenchymal sensor and an intracerebral microdialysis catheter will be inserted into the affected cortex. Tissue oxygen, carbon dioxide, acidity and extracellular metabolites will be measured during and after temporary artery occlusion. Data will be analyzed between groups by factorial analysis with repeated measures.

In this randomized control study, we will demonstrate the neurochemical changes of ischemia-reperfusion damage due to temporary artery occlusion. We will also quantify the magnitude of magnesium-produced neuroprotection during cerebral aneurysm surgery. Results of this study contain essential information and scientific basis for a subsequent multicentre, randomized control trial evaluating the neuroprotective effects of magnesium during cerebral aneurysm surgery.

(MD01725)

### Evaluation of Ginseng on Indices of Chronic Stress in Patients with the Metabolic Syndrome

✉ CRITCHLEY Lester Augustus Hall • THOMAS Neil G (School of Pharmacy) • CRITCHLEY

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□ 1 April 2002

❖ CUHK Research Committee Funding (Direct Grants)

Recently, there has been an increase in the number of Hong Kong patients with type 2 diabetes, hypertension and/or dyslipidaemia, known collectively as metabolic syndrome. Previously, we have investigated and shown this syndrome is closely associated with obesity. Stress appears to be another key factor in its aetiology. The Chinese medicine Ginseng (*Panax ginseng*) has been valued for over 2,000 years for its revitalizing properties. It is thought to act by reducing physical and mental stress and in mice it is known to inhibit stress-induced rises in plasma corticosterone. The project is to investigate the possible actions of Ginseng in patients with the metabolic syndrome. We are particularly interested in its beneficial actions on markers of chronic stress, which will include plasma and urinary catecholamine and cortisol levels, cardiovascular responses to postural stress (head up tilting), changes in body fat distribution (subcutaneous and visceral fat depots measured by magnetic resonance imaging) and cognitive changes (questionnaire) and psychomotor tests. A randomized, double-blind placebo-controlled, cross-over study will be performed looking at the effects of Ginseng on these different factors. Our source of standardized Ginseng will be the PLA General hospital in Beijing. The study will provide important scientific evidence regarding the use of Ginseng and its possible beneficial actions. We will also obtain valuable information regarding stress in the pathogenesis of metabolic syndrome.

(MD01618)

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**Does the Enteral Administration of *Lactobacillus* Species to Critically Ill Patients Reduce the Severity of Multi-organ Dysfunction and Decrease Mortality?**

✉ Charles David GOMERSALL • CALCROFT Ross Michael\* • Gavin Matthew JOYNT

□ 17 September 2001

❖ Research Grants Council (Earmarked Grants)

In shock states, gut perfusion is compromised, leading to gut ischaemia and loss of the intestinal barrier to pathogenic enteric organisms. Bacteria and endotoxin escape from the gut and activate the host's immune inflammatory defence mechanisms leading to the auto-inflammation and tissue destruction seen in the septic response characteristic of multi-organ dysfunction syndrome (MODS). *Lactobacillus* species (LB) may provide protection to the gastrointestinal (GI) mucosa, prevent the escape of bacteria/endotoxin from the gut, and enhance the immune system. Administration of LB may decrease the severity of MODS and reduce mortality in critically ill patients. In a pilot study of 38 patients, we have shown a trend towards a reduction in mortality in critically ill patients who received LB compared to control patients. We therefore intend to test the hypothesis that LB species can decrease the incidence of MODS and mortality in the critically ill by conducting a randomised, placebo controlled, multicentre group-sequential study of a maximum of 664 intensive care patients. LB species in active and inactive forms, together with a nutrient broth solution, will be administered enterally to study group patients and control patients respectively. Outcome measures will be ICU, hospital and 30 day mortality, together with average and maximum MODS scores. A second major aim of the study will be to determine whether LB species decrease the incidence of diarrhoea in critically ill patients.

(MD01005)

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**A Randomized, Open Label, Comparative Multicenter Study of Voriiconazole versus Conventional Amphotericin B Followed By Fluconazole in the Treatment of Candidemia in Non-neutropenic Subjects**

✉ Charles David GOMERSALL • Gavin Matthew JOYNT • Sarah Jane RAMSAY

□ 8 January 2002

❖ Pfizer Corporation

A randomized open label multi-centre study of voriconazole compared with amphotericin followed by fluconazole for the treatment of candidaemia in 360 non-neutropenic patients. End-points are clinical cure and clinical improvement.

(MD01977)

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### **Establishing Patient and Health Professional Preferences for the Management of Postoperative Nausea and Vomiting: An Application of Conjoint Analysis**

✉ GIN Tony • LEE Anna

☐ 1 July 2001

❖ Research Grants Council (Earmarked Grants)

Nausea and vomiting are common problems after surgery, with incidence up to 80%. Patients think that postoperative nausea and vomiting are worse than pain. There is debate on how best to manage this complication. Previous studies have suggested that administration of an antiemetic at the end of surgery (prophylaxis) may be associated with greater patient satisfaction than a strategy of simply waiting for a patient to develop persistent symptoms before administering an antiemetic (treatment). Some patients are willing to pay for an expensive antiemetic for prophylaxis. The objectives of this project are: (1) to establish what patients prefer for their management of postoperative nausea and vomiting; (2) to determine the optimal management of postoperative nausea and vomiting from a health professional point of view. The patients to be recruited into this study will be women undergoing elective gynaecological surgery. Nurses working in the recovery room and anaesthetists will be also recruited into this study. A series of scenarios describing benefits and harms of antiemetic drugs, costs involved and decision-making processes will be given to subjects. They will be asked to choose which scenario they prefer. Conjoint analysis, a statistical technique, designed to elicit participants' views on healthcare, will be used to analyse the data. The results will be used to decide what will be the most cost-effective way of managing postoperative nausea and vomiting.

(MD01912)

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### **Educating Patients about Anesthesia: A Systematic Review of Randomized Controlled Trials of Media-based Interventions**

✉ LEE Anna • GIN Tony • CHUI Po Tong

☐ 1 June 2002

❖ CUHK Departmental Funding

This quantitative systematic review compared the effectiveness of media-based patient education about anesthesia. Fifteen randomized controlled trials (n=1506) were identified after a systematic search of electronic databases (MEDLINE, EMBASE, CINAP, PSYCINFO, The Cochrane Controlled Trials Registry), published articles and contact with authors. Outcomes assessed were anxiety knowledge, and patient satisfaction. Anxiety levels before anaesthesia were lower in subjects receiving the video and/or print information compared to those receiving no intervention (weighted mean difference of 3; 95% confidence interval [95%CI], 1 to Patients in the video group were more likely to answer all knowledge questions correctly compared to patients with no intervention (relative risk [RR] of 6.64; 95%CI, 2.05 to 21.52). The level of knowledge about pain management was higher in the video group compared to patients with no intervention (weighted mean difference of 17%; 95%CI, 9% to 25%). However, the level of patient satisfaction with the intervention (expectation versus actual anaesthetic experience) was similar between the two groups (RR of 1.0; 95%CI, 0.93 to 1.22). This systematic review supports the use of video and printed information about general process and risks anesthesia for patient education before surgery. (MD01937)

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### **Vasopressor Therapy During Spinal Anaesthesia for Caesarean Section: Comparison of Administration by Intravenous Bolus or Infusion**

✉ NGAN KEE Warwick Dean • LEE Bee Beng • KHAW Kim Sun

☐ 1 July 2001

❖ CUHK Departmental Funding

This prospective randomized will compare two regimens for maintenance of maternal arterial pressure during spinal anaesthesia for Caesarean section. Fifty non-labouring patients having spinal anaesthesia for Caesarean section will be randomized to have their arterial pressure maintained using phenylephrine by either intravenous boluses or intravenous infusion. Maternal haemodynamic changes, neonatal outcome assessed clinically and by measurement of umbilical cord blood gases, and the incidence of maternal side effects including nausea, vomiting, and dizziness will be compared.

(MD01447)

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**Randomized Controlled Trial of Remifentanil at Induction of General Anaesthesia for Caesarean Section**

✉ NGAN KEE Warwick Dean • MA Kwok Chiu (Dept of Paediatrics) • LEE Bee Beng\* • KHAW Kim Sun • WONG Sum Yee April • GIN Tony

☐ 1 October 2001

❖ CUHK Departmental Funding

This randomized double-blinded study will assess the effect of the ultra-short acting opioid remifentanil on maternal haemodynamic changes and neonatal outcome when compared with saline placebo during general anaesthesia for elective Caesarean section. (MD01465)

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**A Comparative Traditional Dose-response Study of Ropivacaine and Bupivacaine for Epidural Analgesia in the First Stage of Labour**

✉ NGAN KEE Warwick Dean • LEE Bee Beng • KHAW Kim Sun

☐ 1 January 2002

❖ CUHK Departmental Funding

Bupivacaine and ropivacaine are the local anaesthetics most commonly used for epidural analgesia in labour, but their dose-response curves have been incompletely defined. This is particularly important for comparative purposes because recent data have suggested that many of the advantages of epidural ropivacaine in obstetrics (greater differential sensory block, lesser toxicity) could be explained by lower potency compared with bupivacaine. Much of this evidence has come from simple comparisons or from the technique of up-down sequential analysis. The latter technique has been used to determine the median effective dose (ED<sub>50</sub>). However, other than a point estimate of ED<sub>50</sub>, these data do not provide information on the shape and slope of the dose-response curves, nor on the values for ED<sub>95</sub> which are closer to the doses used clinically.

In this prospective, randomized study, we will use traditional dose-response methodology to simultaneously determine the dose-response curves for ropivacaine and bupivacaine for epidural

analgesia in labour. The methodology used will follow a model we have previously developed and used. Results will yield individual data for each drug as well as a clear measurement of relative potency. Clinically, this information may be used to facilitate both dosage and drug selection and for future.

(MD01631)

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**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>
1999-00	Use of IV Lignocaine to Attenuate the Pressor Response to Tracheal Intubation (MD99131) ✉ CHUNG David Chi Wai • HO Ming Hei Anthony • TAY Beng Aik
2000-01	Evaluation of Two Traditional Chinese Medicine Formulations for the Treatment of the Metabolic Syndrome Regarding Cardiovascular Function and Insulin Sensitivity (CU00134) ✉ CRITCHLEY Lester Augustus Hall • CHAN Chung Ngor Juliana (Dept of Medicine & Therapeutics) • THOMAS Neil G (School of Pharmacy) • Brian TOMLINSON (Dept of Medicine & Therapeutics)
2000-01	Evaluation of a New Impedance Cardiograph Using an Aortic Flowmeter in Dogs (MD00816) ✉ CRITCHLEY Lester Augustus Hall • CRITCHLEY Julian A J H (Dept of Medicine & Therapeutics)# • ZHANG Ye (Dept of Medicine & Therapeutics)# • DING Baoguo (Dept of Medicine & Therapeutics)# • Anthony Edward JAMES (Laboratory Animal Services Centre)
2000-01	Correlation Between Intraocular and Intracranial Pressure in Patients with Raised Intracranial Pressure (MD20010) ✉ HO Ming Hei Anthony • Gavin Matthew JOYNT • Sarah Jane RAMSAY • CHUNG David Chi

- Wai • POON Wai Sang (Dept of Surgery)
- LAU Tze Kin (Dept of Obstetrics & Gynaecology)
- 1998-99 Ropivacaine as an Intrathecal Agent: Part I – A Dose Response Study (MD98153)  
 ✍ KHAW Kim Sun • NGAN KEE Warwick Dean • CRITCHLEY Lester Augustus Hall
- 1999-00 Haemodynamic Changes During Spinal Anaesthesia for Caesarean Section in Patients with Multiple Gestation: Quantification and Comparison with Singleton Pregnancies (MD99079)  
 ✍ NGAN KEE Warwick Dean • KHAW Kim Sun • LEE Bee Beng
- 1999-00 Randomized Comparison of Spinal and Epidural Anaesthesia for Caesarean Section in Parturients with Severe Preeclampsia (MD99076)  
 ✍ NGAN KEE Warwick Dean • KHAW Kim Sun • LEE Bee Beng •
- 1999-00 Randomized Double-blind Comparison of Obstetric Outcome After Epidural Labour Analgesia Using Ropivacaine or Bupivacaine (MD99116)  
 ✍ NGAN KEE Warwick Dean • LEE Bee Beng • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • KHAW Kim Sun
- 2000-01 Development of Effective Strategies to Reduce the Incidence of Hypotension During Spinal Anaesthesia for Caesarean Section (MD00860)  
 ✍ NGAN KEE Warwick Dean • KHAW Kim Sun • LAU Tze Kin (Dept of Obstetrics & Gynaecology)

## RESEARCH OUTPUTS AND PUBLICATIONS

- <P013092> **ZHANG Y.; LAH Critchley; JAJH Critchley; TAM Y.H.; CHUNG C.K.; CHAN W.B.; TOMLINSON B.; COCKRAM C.S. and CHAN J.C.N.** "The Assessment of Autonomic Dysfunction Using RR Interval Spectral Analysis in Diabetics with Increased Urine Albumin Excretion Rate". Paper presented in the 12th International Symposium on the Autonomic Nervous System & Clinical Autonomic Research, organized by American Autonomic Society. vol.11, p.213. California, USA, 2001.10.11.
- <P016180> **NGAN KEE Warwick Dean.** "Postspinal Hypotension". *2nd All Africal Anaesthesia Congress* Paper presented in the 2nd All Africal Anaesthesia Congress Durban, South Africa, 2001.09.23.
- <P016207> **KHAW Kim Sun; NGAN KEE Warwick Dean; WONG Lai Yi; LIU Yat Wa Justina and CHUNG Chi Keung.** "Spinal Ropivacaine for Cesarean Section". *Anesthesiology*, vol.95 no.6, pp.1346-5. USA, 2001.12.
- <P016231> **TAN Perpetua Elma, CRITCHLEY Lester Augustus Hall, JAMES Anthony Edward, THOMAS G. N., TOMLINSON Brian, CRITCHLEY Julian A J H, FOK B, TSE John Yeuk Hon, WANG Deqing, ZHANG Ye and DING B.G.** "Acute Effect of Candesartan and Ramipril on Adrenal Catecholamine Release" *3rd Cardiovascular Risk Factors, East meets West Symposium* p. 41. Hong Kong SAR, 2001.11.

- <P016478> **GARNER Alan; LEE Anna; HARRISON Ken and SCHULTZ Carl H.** "Comparative Analysis of Multiple-Casualty Incident Triage Algorithms". *Annals of Emergency Medicine* vol.38 no.5, pp. 541-548. USA, 2001.11.
- <P016775> **NGAN KEE Warwick Dean.** "Breakfast with the Experts (Obstetrics)". Paper presented in the 2nd All Africa Anaesthesia Congress South Africa, 2001.09.25.
- <P016802> **NGAN KEE Warwick Dean.** "Obstetric Anaesthesia in the Hong Kong SAR". Paper presented in the conference, organized by Obstetric Anaesthesia Society of Asia and Oceania and Society of Obstetric Anaesthesia of the Philippines Cebu, Philippines, 2001.11.12.
- <P016903> **CHEN Phoon Ping, CHEAM Wooi Su Eddy, MA M. L., LAM Kwok Key, NGAN KEE Warwick Dean and GIN Tony.** "Patient-Controlled Pethidine After Major Upper Abdominal Surgery: Comparison of the Epidural and Intravenous Routes". *Anaesthesia* vol.2, pp.1106-1112. UK, 2001.11.
- <P017144> **ZHANG Y; CRITCHLEY Lester Augustus Hall; CRITCHLEY Julian A J H; TOMLINSON Brian; TAM Y. H.; CHUNG Chi Keung; CHAN WB; COCKRAM Clive Stewart and CHAN Chung Ngor Juliana.** "Autonomic Nervous System and Baroreflex Sensitivity Impairment in Patient With Mild Hypertension: An Assessment by Spectral Analysis" Paper presented in the First WHF Global Conference Cardiovascular Clinical Trials. p.49. Hong Kong SAR, 2001.11.
- <P017246> **HUI Ki Ling; CRITCHLEY Lester Augustus Hall; KARMAKAR Manoj Kumar and LAM Kwok Key.** "Laryngeal Mask Insertion Using Alfentanil-Propofol". *Anaesthesia and Intensive Care* vol.29 no.6, pp.647-648. Hong Kong SAR: ANZCA/HKCA CSM 2001, 2001.12.
- <P017351> **RAMSAY Sarah Jane; GOMERSALL Charles David and JOYNT Gavin Matthew.** "Predicting ICU Bed Requirements from Current Referral Patterns - The Tip of the Iceberg?". *Abstract Book, Intensive Care in the New Millennium* (Proceedings of the 8th World Congress of Intensive and Critical Care Medicine). p.107 (P21). Sydney, Australia, 2001.10.
- <P017467> **NGAN KEE Warwick Dean; KHAW Kim Sun; LEE Bee Beng; WONG Man Shu Mabel and NG Fung.** "Metaraminol Infusion for Maintenance of Arterial Pressure During Spinal Anaesthesia for Caesarean Section: The Effect of Crystalloid Preload". Paper presented in the conference, organized by Obstetric Anaesthesia Society of Asia and Oceania and Society of Obstetric Anaesthesia of the Philippines. Cebu, Philippines, 2001.11.12.
- <P017493> **KARMAKAR Manoj Kumar; GIN Tony and HO Ming Hei Anthony.** "Ipsilateral Thoraco-Lumbar Anaesthesia and Paravertebral Spread after Low Thoracic Paravertebral Injection". *British Journal of Anaesthesia* vol.87 no.2, pp. 312-316. UK, 2001.08.
- <P017514> **LEE Anna; NGAN KEE Warwick Dean and GIN Tony.** "Vasopressors in the Management of Hypotension During Spinal Anaesthesia for Caesarean Section: A Meta-Analysis". *Anaesthesia and Intensive Care* vol.29 no.6, p.665. Australia, 2001.12.
- <P017549> **CHAN Matthew Tak Vai; NG Siu Keung; CHUI Po Tong; TAN Perpetua Elma and GIN Tony.** "Hemodynamic Changes and Catecholamine Release During Laparoscopic Adrenalectomy for Primary Hyperaldosteronism". *Anesthesiology* vol.95, p.A218. USA: ASA Meeting, 2001.10.

- <P017843> **AUN Sui Tee Cindy.** "Total Intravenous Anaesthesia (TIVA) in Paediatric Anaesthesia". Paper presented in the 2nd All Africa Anaesthesia Congress SASA 2001 Durban, South Africa, 2001.09.23.
- <P017880> **HO Ming Hei Anthony, Dion P, KARMAKAR Manoj Kumar, CHENG G., CHUNG David Chi Wai, DERRICK James Lachlan and TAY Beng Aik.** "A Pharmacokinetic Model for Factor VIII Dosing During Active Haemorrhage in Patients with Haemophilia A". *Anaesthesia* vol.56, pp.785-790. UK, 2001.07.
- <P017905> **CHAN Matthew Tak Vai, NG Chi Ping, LAM Ming Kuen Joseph, GIN Tony and POON Wai Sang.** "Monitoring of Autoregulation Using Intracerebral Microdialysis in Patients with Severe Head Injury". Paper presented in the 29th Annual Meeting, organized by Journal of Neurosurgical Anesthesiology p.375. USA, 2001.09.
- <P017946> **HO Ming Hei Anthony.** "'Awareness' and 'Recall' During Emergence from General Anaesthesia". *European Journal of Anaesthesiology* vol.18 no.9, pp. 623-625. Denmark, 2001.09.
- <P017974> **NGAN KEE Warwick Dean; KHAW Kim Sun; LEE B. B.; WONG Man Shu Mabel and NG Fung.** "Metaraminol Infusion for Maintenance of Arterial Pressure During Spinal Anesthesia for Cesarean Delivery: the Effect of a Crystalloid Bolus". *Anesthesia and Analgesia* vol.93, pp.703-708. USA, 2001.09.
- <P018046> **HO Ming Hei Anthony and KARMAKAR Manoj Kumar.** "Simple Formulas for Preparing Local Anesthetic Solutions for Infusion". *Regional Anesthesia and Pain Medicine* vol.26 no.4, pp. 382-383. USA, 2001.07.
- <P018050> **RAMSAY Sarah Jane; GOMERSALL Charles David; JOYNT Gavin Matthew; LAM Tung Ching Doris; Lam C and LEE Anna.** "Predicting Outcome of Patients Refused Admission to ICU". Paper presented in the 14th Annual Congress, organized by Intensive Care Medicine. vol.27 supplement 2, p.230. Germany, 2001.09.
- <P018073> **NGAN KEE Warwick Dean; KHAW Kim Sun; LEE Bee Beng; WONG Man Shu Mabel and NG Fung.** "Randomized Controlled Study of Colloid Preload before Spinal Anaesthesia for Cesarean Section". *Anesthesiology*, vol.95, p.A1054. USA, 2001.10.
- <P018454> **NGAN KEE Warwick Dean.** "Choice of Vasopressor in Obstetric Spinal Anaesthesia". Paper presented in the 2nd All Africa Anaesthesia Congress Durban, South Africa, 2001.09.23.
- <P018475> **MAINLAND Phoebe-anne; KONG Andrew S.; CHUNG D. C.; CHAN Christopher H.S. and LAI Christopher K.W. Lai.** "Absorption of Lidocaine During Aspiration Anesthesia of the Airway". *Journal of Clinical Anesthesia* vol.13 no.6, pp. 440-446. USA, 2001.09.
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- <P018624> **Charles David GOMERSALL, Gavin Matthew JOYNT, TAN Yuen Heng, Sarah Jane RAMSAY, Lam C and Wong E.** "Long-Term Outcome of Patients Refused Admission to ICU". Paper presented in the 14th Annual Congress organized by Intensive Care Medicine p.S229. Germany, 2001.09.

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- <P018701> **HO Ming Hei Anthony; KARMAKAR Manoj Kumar; CONTARDI LH; NG SSW and HEWSON JR.** "Excessive Use of Normal Saline Managing Traumatized Patients in Shock: A Preventable Contributor to Acidosis". *The Journal of TRAUMA Injury, Infection, and Critical Care* vol.51 no.1, pp. 173-177. USA, 2001.09.
- <P018769> **LEE Anna;CHUI Po Tong.** "What Outcomes Should Be Measured After Anaesthesia?". *Best Practice & Research Clinical Anaesthesiology* vol.15 no.4, pp.531-540. UK, 2001.12.
- <P018785> **TAY BA; NGAN KEE Warwick Dean and CHUNG David Chi Wai.** "Gabapentin for the Treatment and Prophylaxis of Cluster Headache". *Regional Anesthesia and Pain Medicine* vol.26 no.4, pp.373-375. USA, 2001.07.
- <P018815> **GOMERSALL Charles David and BUCKLEY Thomas Anthony.** "Validation Of A Multiple Organ Dysfunction Score As A Surrogate End Point". Paper presented in the 8th World Congress of Intensive and Critical Care Medicine, organized by Abstract Book, Intensive Care in the New Millennium p.173 (P322). Sydney, Australia, 2001.10.
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- <P018978> **NGAN KEE Warwick Dean, LAU Tze Kin, KHAW Kim Sun and LEE Bee Beng.** "Comparison of Metaraminol and Ephedrine Infusions for Maintaining Arterial Pressure During Spinal Anesthesia for Elective Cesarean Section". *Anesthesiology*, vol.95, pp. 307-313. USA: Lippincott Williams & Wilkins, 2001.08.
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- <P019052> **CHAN Ka Lai; CHAN Matthew Tak Vai; GIN Tony; Lam MK and Tong Michael.** "Is Low Level Neuromuscular Block Compatible With Intraoperative Facial Nerve Monitoring ?". Paper presented in the conference organized by Journal of Neurosurgical Anesthesiology vol.13 no.4, p.375. USA, 2001.09.
- <P019376> **JOYNT Gavin Matthew; LEE Anna; YAP Hiu Yi Florence; HO OM; BUCKLEY Thomas Anthony and GOMERSALL Charles David.** "A Prospective Study of Limitation of Life Support in Chinese Patients: Incidence, Process and Family Acceptance". *Intensive Care Medicine* (14th Annual Congress). vol.27 supplement 2, p.S185. Germany: Springer - Verlag, 2001.09.
- <P019570> **KARMAKAR Manoj Kumar.** "Thoracic Paravertebral Block". *Anesthesiology*, vol.95 no.3, pp. 771-780. USA, 2001.09.
- <P019821> **LAM DTC; NGAN KEE Warwick Dean and KHAW Kim Sun.** "Extension of Epidural Blockade in Labour for Emergency Caesarean Section Using 2% Lidocaine with Epinephrine and Fentanyl, with or without Alkalinisation". *Anaesthesia* vol.56 no.8, pp.777-798. UK, 2001.08.
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- <P021219> **HO M.H. Anthony; LIM S. Huey; YIM P.C. Anthony; MANOJ K. Karmakar and LEE Tak Wai.** "The Resolution of ST Segment Depressions after High Right Thoracic Paravertebral Block During General Anesthesia". *Anesth Analg* vol.95, pp.227-228. 2002.
- <P026244> **LEE Bee Beng; NGAN KEE Warwick Dean; LAU Wing M and WONG Sum Yee April.** "Epidural Infusions for Labor Analgesia: A Comparison of 0.2% Ropivacaine, 0.1% Ropivacaine, and 0.1% Ropivacaine With Fentanyl". *Regional Anesthesia and Pain Medicine* vol.27 no.1, pp. 31-36. USA, 2002.01.
- <P026314> **CRITCHLEY Lester Augustus Hall; CRITCHLEY Julian A J H and ANDERSON Patricia Jane.** "Gastric Emptying Rates in European and Chinese Subjects". *Annual Scientific Meeting, ANZCA Australia*, 2002.05.
- <P026561> **HO Ming Hei Anthony.** "Attending Anesthesiologist During Live Off-Pump Coronary Artery Bypass Demonstration". *Off-Pump Coronary Surgery Symposium Hong Kong SAR: Prince of Wales Hospital & Bristol Heart Institute*, 2002.04.
- <P026792> **LEE Anna; NGAN KEE Warwick Dean and GIN Tony.** "A Quantitative, Systematic Review of Randomized Controlled Trials of Ephedrine Versus Phenylephrine for the Management of Hypotension During Spinal Anesthesia for Cesarean Delivery". *Anesth Analg* vol.94, pp.920-926. USA, 2002.04.
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- <P026888> **HO Ming Hei Anthony; LEE Anna; LING Elizabeth; TEOH Kevin and WARKENTIN Theodore E.** "Comparing INR'S Measured During (On a Heparinase-Treated Sample) and after CPB". *Canadian Journal of Anesthesia* vol.44, A44. Canada, 2002.06.
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## RESEARCH PROJECTS

### The Correlation of Matrix Metalloproteinase and Recurrent Nasopharyngeal Carcinoma

- ✉ LIEW Choong Tsek • LAM PK\* • TEO Peter\*
- ☐ 1 April 2002
- ❖ CUHK Research Committee Funding (Direct Grants)

Nasopharyngeal carcinoma (NPC) is rare in most countries of the world. However, high incidence of NPC is seen in southern China and Hong Kong with a yearly incidence rate between 10 and 50 per 100,000<sup>1-4</sup>. Carcinomas are characterized by important local dissemination and regional metastases. The ability to invade tissue and establish colonies at remote sites is considered as a dynamic, complex, multi-step process, which involves detachment of malignant cells from their point of origin, traversal of the extracellular matrix and basement membranes, and invasion into lympho-vascular channels. The breakdown or proteolytic degradation of components of the basement membrane and extracellular matrix (ECM) are essential steps in the tissue invasion. Among ECM-degrading enzymes, matrix-metalloproteinases (MMPs) have an important role. Their activities are biologically-modified by specific inhibition via binding of naturally occurring tissue inhibitors of metalloproteinase (TIMPs). In this study we aim to measure and monitor the serum levels of MMP-1,2,9 and TIMP-1,2 in 40 NPC patients before and after surgery by means of ELISA determination. (MD01652)

### Characterization of the RASSF1A Gene in Nasopharyngeal Carcinoma

- ✉ LO Kwok Wai • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute) • TO Ka Fai • TSUI Kwok Wing (Biochemistry)
- ☐ 1 September 2001
- ❖ Research Grants Council (Earmarked Grants)

The high incidence of Nasopharyngeal carcinoma (NPC) in our population poses a serious health problem in Hong Kong. Over the past decade, we aim to unravel the molecular basis of NPC by

searching genetic changes and characterizing the cancer-related genes. LOH of chromosome 3p is one of the most frequent and earliest events in the tumorigenesis of NPC. Deletion mapping and functional studies have targeted the NPC-related gene(s) to 3p21.3. We have shown that the RASSF1A gene, a newly isolated tumor suppressor on 3p21.3, was frequently altered in these cancer. High incidence of aberrant methylation of the RASSF1A promoter was found in NPC samples. The RASSF1A transcript was missing in the cell lines and xenografts with complete methylation. In this proposal, we aim to intensively search for the genetic alterations, including deletion, mutation and hypermethylation of this gene in the nasopharyngeal carcinoma, precancerous lesions and histologically normal nasopharyngeal epithelia of the nasopharynx. Aberrant expression of the RASSF1A gene will be investigated by quantitative RT-PCR analysis, in-situ hybridization and immunohistochemistry. The application of the aberrant RASSF1A gene as early tumor marker will also be evaluated. The tumor suppressor function of the RASSF1A gene will be investigated in vitro by transfection and re-expression of the gene in NPC cells. To better understand the biological function, the RASSF1A associated proteins or regulated genes will be identified by the yeast two-hybrid and cDNA array analysis. Our proposed functional studies will help to reveal the properties of this new tumor suppressor and to define its role in the molecular pathogenesis of NPC. (MD01010)

### Genetic Characterization of Medulloblastomas

- ✉ NG Ho Keung • POON Wai Sang (Dept of Surgery) • PANG Chung Sean Jesse
- ☐ 30 October 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Medulloblastomas are malignant, invasive embryonal tumors of the cerebellum with predominantly neuronal differentiation that constitute 25% of childhood brain tumors. Despite advances in multi-modal therapy, the outcome of medulloblastoma is not uniformly favorable. Whilst about half of the affected children and young adults survive more than 10 years after diagnosis, the others relapse and die despite receiving identical therapy. Moreover, long-term survivors from childhood

medulloblastoma often suffer from neurocognitive sequelae that are caused by the therapy. Recent studies have suggested that histologic differentiation and subclassification of medulloblastoma correlate with survival in retrospective analysis. Little is known regarding the genetic basis of the pathogenesis of these subtypes. In this study, we will test the hypothesis that genetic subsets of medulloblastoma are associated with different histologic types. The aims of this project are: 1) to identify key aberrant chromosomal regions that are associated with medulloblastoma histologic types; 2) to test for alterations of candidate tumor suppressors or oncogenes underlying the aberrant chromosomal regions. These studies will establish the underlying genetic changes associated with the development of medulloblastoma histologic types, as well as contributing to a classification system for medulloblastoma that may more accurately reflect tumor behavior and response to therapy. Results of this project will also lead to further studies concerning functional aspects of specific genes or collaborative studies with other centers for cloning of new genes. Moreover, identification of specific genetic events may generate novel targets for pharmaceutical interventions or adjunct therapy of medulloblastomas.  
(MD01906)

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

<u>Edition</u>	<u>Title/Investigators</u>
2000-01	The Long Arm of Chromosome 6 and Non-hodgkin's Lymphomas (MD00858) ✉ CHAN Wing Yee • LIU Yong • LEI Ieng Kit Kenny (Dept of Clinical Oncology)
2000-01	Characterization of a Primary Gastric Choriocarcinoma (MD00952) ✉ CHAN Wing Yee
1996-97	Cervical Screening Programme (MD96223) ✉ 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 (Dept of Clinical Oncology) • WOO Kong Sang John (Dept of Surgery)
2000-01	Evaluation and Characterization of a New Composite Biocompatible Skin Graft Incorporated on the Noedermis of Integra in Experimental Burn Wounds (CU00153) ✉ LIEW Choong Tsek • CHAN Sun Yin Eric (Dept of Surgery)# • LAM Ping Kuen (Dept of Surgery)# • LI Hiu Ming
2000-01	Comprehensive Study of Nasopharyngeal Carcinoma Genome (CU00154) ✉ LO Kwok Wai • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute) • PANG Chung Sean Jesse • TEO Man Lung Peter (Dept of Clinical Oncology) • TO Ka Fai
1998-99	PCR-Based Microsatellite Polymorphism in Chromosomes 3, 5, 8, 10, 16,17 and 18 in Prostatic Carcinoma and Prostatic Intraepithelial Neoplasia (CU98259) ✉ MAC-MOUNE LAI Fernand • LIEW Choong Tsek • TO Ka Fai • CHAN Siu Foon Peter (Dept of Surgery)
1999-00	Genomic Study of Selected Groups of CNS Tumours: A Combined Approach with Allelotyping, Molecular Cytogenetic and Microdissection Studies (CU99277) ✉ NG Ho Keung • PANG Chung Sean Jesse • LO Kwok Wai • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute) • POON Wai Sang (Dept of Surgery)
2000-01	Genetic Mechanism of Malignant Progression in Low-grade Astrocytomas (MD00421) ✉ PANG Chung Sean Jesse • NG Ho Keung

- 1999-00 Comprehensive Analysis of Epstein-Barr Virus (EBV) Genotypes in EBV Associated Lymphoproliferative Lesions and Normal Controls (CU99301)      ✉ TO Ka Fai • CHEUNG Siu Tim# • LO Kwok Wai

## RESEARCH OUTPUTS AND PUBLICATIONS

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- <P004280> **CHENG Y.; PANG J.C.S.; NG H.K; DING M.; ZHANG S.F.; ZHENG J.; LIU D.G. and POON W.S.** "Pilocytic Astrocytomas Do Not Show Most of the Genetic Changes Commonly Seen in Diffuse Astrocytomas". *Histopathology* vol.37, pp.437-444. UK, 2000.
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## RESEARCH PROJECTS

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### Migration of Neural Crest Cells to the Bowel in Normal and Congenitally Aganglionic Mutant Mice

✉ CHAN Wood Yee • COPP A. J.\*

☐ 1 December 2001

❖ Research Grants Council (Earmarked Grants)

Hirschsprung's disease (HD, or congenital megacolon) is a birth defect with a prevalence of 1 in 5,000 live births and is the most common cause of neonatal gastrointestinal tract obstruction. The most prominent feature of HD, abnormal dilatation of a segment of the colon, is attributed to a lack or a reduction of parasympathetic enteric ganglia derived from the neural crest cells. It has been proposed from avian studies that neural crest cells emigrate from the neural tube (developing central nervous system) during embryonic development, migrate along specific pathways in the embryo to colonize the primitive gut where they differentiate into enteric ganglia. In mammals, however, the spatial and temporal information on the vagal neural crest cell migration to the gut is still scarce. In order to find out the relationship between neural crest cell migration and the formation of enteric ganglia, we propose to use two markers coupled with a tissue transplantation technique to study neural crest cell migration in both normal mouse embryos and mutant embryos from a mouse model (*Dominant megacolon*) for HD. We aim to (1) spatio-temporally map out the migration of vagal neural crest cells in the normal mouse embryos; (2) determine the anomalies in neural crest cell migration in mutant embryos; (3) ascertain whether the primary defect of the abnormal migration lies in the neural crest cells, the microenvironment through which they migrate, or in both by reciprocal tissue transplantation between normal and mutant embryos. (MD01016)

### A Study on the Use of Sertoli Cells to Promote Retinal Ganglion Cell Regeneration

✉ CHO Yu Pang Eric

☐ 31 December 2001

❖ Research Grants Council (Earmarked Grants)

The failure of axons in the central nervous system (CNS) of adult mammals to regenerate after injury has been attributed to the microenvironment of the CNS, especially at the lesion site. Various transplant strategies, mostly using neural tissue, have been employed to replace the hostile CNS microenvironment to promote regeneration. These strategies, however, may not work optimally in diverse CNS regions, mainly because of the variable responses of nerve cells in different regions of the nervous system to injury, and the technical and ethical problems associated with neural transplants. In this study, we will examine whether a non-neural cell type, the Sertoli cell which is a supporter of germ cell development, has the ability to promote axon regeneration in the adult CNS and to serve as a superior alternative to neural transplant. The rationale for studying Sertoli cells is based on their success in enhancing recovery of nerve cells in an animal model of Parkinson's disease, and their possession of many favourable transplant characteristics such as the abundant production of numerous growth factors and the ability to elicit minimal graft rejection. (MD01017)

### Effect of Male Accessory Sex Gland Secretions on the Oxidative Stress, Functional Competence and Genomic Integrity of Hamster Spermatozoa

✉ CHOW Pak Ham Patricia • O Wai Sum\*

☐ 1 September 2000

❖ Research Grants Council (Earmarked Grants)

A significant increase in ROS has been reported in male infertility to affect sperm movement, fertilization and DNA integrity of the sperm. Under normal physiological conditions, male accessory sex gland (ASG) secretions are known to protect them against ROS but whether sperm function is affected to the extent of jeopardizing fertility remains to be worked out. Our previous *in vivo* studies in the golden hamster showed that removal of the male ASG reduced fertility. This was largely due to abnormalities in the development of embryos sired, process of implantation and subsequent embryonic wastage. It is still not known how a transient coating of sperm with ASG secretions can have a long-range impact on subsequent embryo development. We hypothesize that the antioxidative enzymes present in these glands can protect the functions and genetic integrity of the sperm. We

will focus on the study of the relationships between sperm function, their DNA integrity and the possible DNA repair mechanism. Using the established animal model of surgical ablation of the major male accessory sex glands, we propose to remove the ventral prostate gland or all ASG from male hamster and to study (1) antioxidative enzymes present in the uterine fluid of females mated with them; (2) the change in sperm function in relation to exposure to different ASG secretions; (3) the incidence of double versus single strand DNA damage in sperm produced by these males; (4) the specific type of DNA damage in sperm before and after fertilization with an oocyte and (5) the vulnerability of sperm produced by these males oxidative stress.  
(BS00621)

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**Anti-Proliferative Activity of Common Mushroom Lectins on Colon Cancer Cells**

- ✍ LIU Wing Keung Ken • NG Tzi Bun (Biochemistry)
- ☐ 1 April 2002
- ❖ CUHK Research Committee Funding (Direct Grants)

Lectins are a group of carbohydrate-binding proteins of non-immune origin, which are able to agglutinate cells through sugar-specific binding sites and bind oligosaccharides of glycoconjugates without modification of their covalent structure. They are found in animals, plants, fungi, bacteria and viruses, but particularly abundant in the seeds, beans and even mushrooms. A collection of lectins has been isolated from edible mushrooms, and they have different sugar-specificities and biological activities. Some of these dietary lectins are resistant digestion and remain active in the colon, whereby inhibiting the growth and differentiation of colon cells. It is anticipated, through a study of the anti-proliferative effects of lectins from several common edible mushrooms, including button mushrooms, straw mushrooms, oyster mushrooms and monkey head mushrooms on a battery of colon cancer cell lines will provide an insight into the regulatory mechanism(s) of proliferation of malignant colon cells at cellular level.  
(MD01430)

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**A Study to Determine Whether Apoptosis and Reactive Oxygen Species (ROS) are Involved in**

**Increased Susceptibility to Vitamin A Teratogenicity in Diabetic Pregnancy**

- ✍ SHUM Sau Wun Alisa
- ☐ 1 January 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Babies of diabetic mothers have a much higher incidence of congenital anomalies than babies of non-diabetic mothers. The increased prevalence is thought to arise from the teratogenic effect of the diabetic maternal serum factors on the developing embryo. However, our laboratory has taken a different approach to determine if environmental factors, such as drugs taken in during pregnancy, can interact with maternal diabetes to increase the malformation rate. By using mouse as an animal model, we have recently established that the vitamin A metabolite, retinoic acid, can indeed interact with maternal diabetes to greatly increase the susceptibility of the embryo to develop caudal regression syndrome, a defect particularly associated with diabetic pregnancy in human. We have shown that extensive apoptosis occurred at the caudal end (tail bud) of the embryo that developed caudal regression. Since oxidative stress can be a mediator of apoptosis and the formation of reactive oxygen species is suggested to play a role in diabetic embryopathy, hence, we speculate whether apoptosis and reactive oxygen species could be involved in the increases susceptibility to vitamin A teratogenicity in embryos of diabetic mice. The specific objectives to be achieved in this proposed project are: (i) to determine if embryos of diabetic mice show increased level of apoptosis in the tail bud when compared with embryos of non-diabetic mice after retinoic acid treatment; (ii) to determine if reactive oxygen species are generated in the tail bud of embryos after retinoic acid treatment and to compare their levels in embryos of diabetic and non-diabetic mice. Results of this project would pave the way to derive preventive measure against congenital malformation associated with diabetic pregnancy.  
(MD01610)

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**Glial Immune Response After METH ('Ice') or MDMA ('Ecstasy') Treatment**

- ✍ STADLIN Alfreda • CHANG Chuen Chung Ryamong\* • FENG Zhe Hui\*

□ 1 January 2002

❖ CUHK Research Committee Funding (Direct Grants)

Methamphetamine (METH, 'ice') and 3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy') are substituted amphetamines that are widely abused globally. In Hong Kong, METH and MDMA are popular recreational drugs, particularly among young people and in the 'rave' parties. Prevalence for METH and MDMA use has dramatically escalated over the last five years. With its emerging popularity also in China, their use causes a great concern to the Hong Kong community. METH and MDMA had been shown to cause long-term damage to the brain's dopaminergic and serotonergic systems respectively. In human and animal studies, METH and MDMA have been shown to cause a depletion of dopamine and serotonin, a decrease in their uptake sites and astrogliosis. Although the mechanisms by which METH or MDMA produce neurotoxicity is not clear, it is evident from human imaging studies that prolonged METH or MDMA use results in long-term neurotoxicity. It is also well known that both METH and MDMA caused a hyperthermic response and this had been suggested to have a strong link to the neurotoxic effects of these drugs. It has been considered that the brain's immune response has a major contribution to the expansion of neurotoxicity and neurodegeneration. Of which, factors like nitric oxide (NO), prostaglandins (PGs) and cytokines have been shown to modulate thermal regulation in the brain. Therefore we hypothesize that these factors may contribute to the evolution of METH- or MDMA-induced hyperthermia and neurotoxicity. The understanding on how NO, PGs and cytokines contribute to METH- or MDMA-induced hyperthermia and drug-induced neurotoxicity will further help to delineate what are the primary and secondary injury processes resulting from METH or MDMA exposure. The aim of this study will include the use of an *in vivo* (with the use of iNOS, COX-1, COX-2 knockout mice) and *in vitro* (microglial cells) approach to explore these processes. Given that long-term damage of METH and MDMA use is evident, the understanding of the neurotoxic mechanisms that underlie this neurotoxicity will help in the development of better treatment or protective measures.

(MD01546)

### Cellular Mechanisms of Neuronal Loss During Aging

✉ YE W Tai Wai David • CHAN Wood Yee

□ 1 November 2001

❖ Research Grants Council (Earmarked Grants)

As a result of decreasing birth rate and increasing life expectancy, populations of Hong Kong, the rest of China and most other countries have been aging steadily. The age-related diseases of the nervous system are increasing with a concomitant increase in the financial burden on medical care, pressing us to pay more attention to the neurodegenerative diseases. One of the most devastating disorders of the old age is deterioration of cognitive and emotional functions, which is related to a relatively large loss of neurons during aging. However, despite the progress made in the understanding of the aging processes, the cellular mechanisms underlying this loss of neurons remain largely unclear. In the present study, in order to study the pathogenesis of increased neuronal death in elderly, Senescence-Accelerated Mice (SAM) will be used as an animal model for studying age-related neuronal degeneration. In addition, the effects of *Ginkgo biloba* extract, the herbal drug most frequently used for improving cognitive functions in aging patients, on neuronal loss will be assessed. SAMP mice have been recognized as a good model for aging because they exhibit pathological characteristics such as degenerative arthropathy, cataract, deficits in learning and memory, which are also common features in human aging. We plan to determine (1) whether neuronal loss during aging is related to apoptosis by comparing the apoptotic activity and the expression of apoptosis regulatory molecules in different brain regions of normal and SAMP mice at different ages; (2) whether nitric oxide (NO) production, as reflected by the increase in the expression of NO synthases in SAMP mice when compared to normal mice, is also related to neuronal loss; and (3) the effects of *Ginkgo biloba* extract on apoptosis and NO production. The results of the present study will give further insight into the mechanisms underlying increased cell death in the aging brain. They will also critically evaluate if *Ginkgo biloba* can be successfully administered in the treatment of neurodegenerative diseases.

(MD01023)

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

<u>Edition</u>	<u>Title/Investigators</u>		
		2000-01	Role of <i>BRE</i> , a New Modulator of TNF- $\alpha$ Action, in Skeletal Muscle Proliferation and Differentiation (MD00801) ✍ LEE Ka Ho Kenneth
2000-01	An Expression and Functional Study of a Prostatic Secretory Protein of 94 Amino Acids in Normal and Neoplastic Rat Prostate Glands (CU00131) ✍ CHAN Leung Franky	2000-01	Cloning, Sequencing and Biological Characterization of an Immunomodulatory Fungal Protein (CU00125) ✍ LIU Wing Keung Ken • NG Tzi Bun (Biochemistry)
2000-01	The Roles of Chondroitin Sulfate Proteoglycans on Axon Growth at the Mouse Chiasm (CU00132) ✍ CHAN Sun On	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. J.*
1999-00	Embryological Basis of Congenital Heart Disease: A Study of Neural Crest Cell Migration Using A Mouse Mutant and A Transgenic Marker (CU99275) ✍ CHAN Wood Yee • COPP A. J.*	1999-00	A Study of the Pathogenetic Mechanism of Renal Agenesis (CU99283) ✍ SHUM Sau Wun Alisa • WOOLF Adrian S.*
2000-01	Therapeutic Effects of Pien Tze Huang Without Natural Musk on Hepatitis (MD20021) ✍ CHAN Wood Yee • YEW Tai Wai David • KWONG Wing Hang • LEE Ka Ho Kenneth	2000-01	A Study to Determine Whether Hyperglycemia is Responsible for Increased Susceptibility to Vitamin A Embryopathy in Diabetic Pregnancy (MD00359) ✍ SHUM Sau Wun Alisa
1998-99	The Influence of Mature Astrocytes on the Survival and Regeneration of Adult Retinal Ganglion Cells (CU98265) ✍ CHO Yu Pang Eric	2000-01	Genes and Heroin Addiction in the Chinese Population: Association Studies on Receptor Gene (MD98904) ✍ STADLIN Alfreda • LEE Tak Shing Dominic (Dept of Psychiatry) • TANG Leung Sang Nelson (Dept of Chemical Pathology) • LOH El-Wui* • CHEN Chih Ken* • CHAN Pui* • Ch'ien James*
1998-99	Ampullary Gland, Ventral prostate and Embryo Implantation (CU98030) ✍ CHOW Pak Ham Patricia • O Wai Sum*		
1999-00	Effects of Ribosome-inactivating Proteins on Motor and Ganglionic Neurons (BL97043) ✍ KWONG Wing Hang	1999-00	The Effects of Prolonged Neonatal Auditory Stimulation on the Development, Maturation and Aging of the Auditory Midbrain of the Senescence Accelerated Mice (SAM) (CU99260) ✍ YEW Tai Wai David • CHAN Wood Yee • POON W.F.Paul*
1999-00	Systemic Application of Curcumin, an NF $\kappa$ B Inhibitor, to Enhance Skeletal Muscle Healing Following Traumatic Injury (MD99099) ✍ LEE Ka Ho Kenneth		



## RESEARCH OUTPUTS AND PUBLICATIONS

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- <P011747> **CHAN H.B.; WANG Z.H.; CHENG S.B.; LI H.K. and CHEW E.C.** "Alteration of Nuclear Matrix Protein Composition Induced by Arsenic Trioxide in Esophageal Carcinoma Cells *in vitro*". *Proceedings of the 11th International Conference on Second Messengers and Phosphoproteins* pp.6-42. Melbourne, Australia: Australia Organizing Committee & International Board., 2001.04.
- <P011748> **YU D.; WANG Z.H.; CHENG S.B.; LI H.K.; CHAN H.B. and CHEW E.C.** "The Effect of Arsenic Trioxide on the Expression of Hsc and HNF4 in Nuclear Matrix Proteins in HepG2 Cells". *Anticancer Research* vol.21, pp.2553-2560. 2001.
- <P011779> **MENG Chun Ling, CHOW Pak Ham Patricia and LEE Ka Ho Kenneth.** "NF-Kappa B is Essential for Zygotic Development". *Development-Growth and Differentiation/14th International Congress of Developmental Biology* Kyoto, Japan: The Japanese Society of Development Biologists, 2001.07.
- <P011860> **TSE Kam Wah Herman, WOOLF S. Adrian and SHUM Sau Wun Alisa.** "Retinoic Acid Induces Renal Agenesis by Down-Regulation of WT1". *Proceedings of 14th International Congress of Developmental Biology* p.19. Kyoto, Japan: The International Congress of Developmental Biology, 2001.07.
- <P012471> **CHEW E.C.; WANG Z.H.; YAM H.F.; CHEN H.B.; WU P.Q. and CHENG S.B.** "Experimental Studies on Metastasis". *Proceedings of 10th Electron Microscopy Conference Malaysia 2001* pp.32-33. Malaysia: Electron Microscopy Society of Malaysia, 2001.11.
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- <P016002> **LIN Ling and CHAN Sun On.** "Expression of FGF Receptors in the Retinofugal Pathway of Mouse Embryos". *Abstracts of Society for Neuroscience* vol.27 no.592.8, 1 pgs. San Diego, California, USA: The Society For Neuroscience, 2001.11.13.
- <P016009> **CHAN O C; CHOW Pak Ham Patricia and O wai Sum.** "Total Ablation Of Paternal Accessory Sex Glands Curtails Developmental Potential In Preimplantation Embryos In The Golden Hamster". *Anat Embryol* vol.204, pp.117-122. Springer - Verlag, 2001.

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- <P016727> **CHAN Wood Yee, TIU Sau Cheung, HEIZMANN C W and YEW Tai Wai David.** "Expression of S100B in Different Cortical Regions of the Developing Human Fetus". *Neuroscience Letters* pp.S17-S18. Elsevier, 2001.
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## RESEARCH PROJECTS

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### Molecular and Functional Characterization of Ghrelin and Its Receptors in Seabream

✉ CHENG Hon Ki Christopher • WOO Norman Ying Shiu (Dept of Biology) • YU K. L.\*

☐ 1 December 2001

❖ Research Grants Council (Earmarked Grants)

Growth hormone (GH) plays a crucial role in regulating body growth. GH release from the pituitary is controlled by a multitude of factors. In mammals, GH is stimulated by both GH releasing hormone (GHRH) and GH secretagogue (GHS). In fish, although GHRH and its receptor have been isolated, the low potency of GHRH in stimulating GH release limits its application in promoting growth in fish. On the other hand, the recent development of orally active GHS analogs highlights their potential application in the fish farming industry. Our initial attempts to clone the cDNAs for the GHSR in seabream have been successful. This will form the basis of studying the tissue distribution of the receptor subtypes and their regulation in fish. The differential expression and regulation would give information regarding the physiological importance of the receptor subtypes. In addition, functional expression of the cloned receptors in cultured eukaryotic cells would be performed as a means of studying their biological activities. Ghrelin, the endogenous GHS, has recently been identified in human and in rat. The structure of this important peptide in fish is not known yet. Attempts to clone the seabream ghrelin would also be made with a view to develop novel GHS analogs for stimulation of GH secretion in fish. The elucidation of the molecular structure and physiological functions of ghrelin and its receptor in seabream would shed light on the regulation of GH secretion in fish. Results of this project will lay the foundations for the future development of strategies to enhance growth in mariculture practice.

(BL01149)

### Functional Roles of Type II Angiotensin Receptor in Pancreatic Endocrine Cells

✉ CHEUNG Wing Tai

☐ 1 September 2001

❖ CUHK Research Committee Funding (Direct Grants)

Pharmacologically, angiotensin receptor can be divided into two subtypes, namely the type-I (AT<sub>1</sub>) and the type-II (AT<sub>2</sub>) angiotensin receptors. Each angiotensin receptor displays differential sensitivities towards different selective ligands and sulfhydryl reducing agents. However, most if not all of physiological effects of angiotensin are mediated by the AT<sub>1</sub> angiotensin receptor, and the physiological function of AT<sub>2</sub> angiotensin receptor remains an open question. With the use of a mono-specific anti-AT<sub>2</sub> antibody prepared by our laboratory, we found that AT<sub>2</sub> angiotensin receptor is highly expressed in the non-insulin secretory pancreatic islet cells. Lines of evidence have suggested that activation of AT<sub>2</sub> angiotensin receptor leads to inhibition of cellular response to insulin with a coincidental suppression of insulin-induced protein tyrosine phosphorylation. The aims of the present study are to explore the potential functions of AT<sub>2</sub> angiotensin receptor in pancreases by i) characterizing the exact localization of AT<sub>2</sub> angiotensin receptor with respect to various pancreatic hormones; ii) examining effect of AT<sub>2</sub> activation on insulin-induced pancreatic hormone secretion and / or gene expression. Results of present study will help us to extend our understanding in the physiological functions of AT<sub>2</sub> angiotensin receptor, and unveiling the complex links between diabetics and hypertension.

(BL01792)

### Mechanistic Studies of the Anti-tumour Effect of Arsenic Trioxide in Human Leukemia and Solid Tumour Cells

✉ FUNG Kwok Pui

☐ 1 November 2001

❖ CUHK Research Committee Funding (Direct Grants)

Arsenic trioxide (As<sub>2</sub>O<sub>3</sub>) has been used since 70's in clinical trials for treating acute promyelocytic leukemia (APL). Recently, the use of As<sub>2</sub>O<sub>3</sub> was further applied to solid tumors such as neuroblastoma, head and neck cancer and esophageal carcinoma. In the present project, different potential mechanisms involved in the action of As<sub>2</sub>O<sub>3</sub> in tumour cells will be investigated. Human leukemia cells (HL-60 and

NB4), human solid tumour cells, namely neuroblastoma cells (SHSY-5Y), glioma (U-87MG), hepatoma (HepG2), breast cancer (MCF-7) and colon cancer (Caco-2) cells will be used as targets. Through the mechanistic study, different treatment regimens will be examined to enhance the efficacy of  $As_2O_3$  in cancer therapy. Strategies to increase apoptosis include modulation of glutathione (GSH) level, antisense inhibition of Bcl-2 expression and induction of apoptotic cascade in mitochondria. The possibility of acceleration of oncoprotein degradation in potentiating the action of  $As_2O_3$  will also be studied. We will also investigate whether  $As_2O_3$ , which is smaller in size than commonly used anti-tumour drugs, can circumvent the binding by the pumping-out by the p-glycoprotein in multidrug resistant tumour cells, using multidrug resistant HepG2 (HepG2/DR) cell as a model. The results of the present project will shed light to future design of better regimens using  $As_2O_3$  to treat human leukemia and solid cancers, so that the anti-tumour effect of  $As_2O_3$  can be enhanced in both parental and multidrug-resistant tumours and its adverse side-effects in the host can be alleviated.

(BL01516)

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#### Signaling Mechanisms Underlying the Effects of Apolipoprotein E on Cell Proliferation and Apoptosis

✉ HO Yuanyuan • FUNG Kwok Pui

□ 1 January 2002

❖ CUHK Research Committee Funding (Direct Grants)

*Background:* Apolipoprotein E (ApoE), a surface component of plasma lipoproteins as well as a ligand for lipoprotein receptors, plays a crucial role in plasma lipid homeostasis. ApoE is expressed in many cell types and the three major isoforms, E2, E3, and E4 are associated with the different risk predictions of atherosclerosis and Alzheimer's disease. Biological activities of apoE other than lipid metabolism are not well characterized. Recent reports of apoE affecting cell proliferation and apoptosis indicate novel function of apoE may be involved in the development of human diseases. In addition, apoE has been shown to modify the activities of mitogen-activated protein kinase (MAPK) and protein kinase C (PKC) signaling pathways.

*Problem identified:* Mechanisms underlying the effects of apoE on cell proliferation and apoptosis are mostly uncharacterized.

*Hypothesis:* MAP kinase and PKC mediate the effects of apoE on cell proliferation and apoptosis.

*Specific Aims:* Specific Aim 1 will compare proliferative and apoptotic responses in cells with and without apoE gene expression. Specific Aim 2 will compare MAP kinase and PKC activities in cells with and without apoE gene expression. Specific Aim 3 will correlate the effects of apoE on cell proliferation and apoptosis with MAP kinase and PKC activities.

*Significance:* These studies will reveal the signaling mechanisms mediating the effects of apoE on cell proliferation and apoptosis and thus further elucidate the biological roles of apoE in cellular processes involved in major human diseases, including atherosclerosis and Alzheimer's disease.

(BL01438)

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#### Functional Analysis of a Novel Gene Over-expressed in Doxorubicin Resistant Human Cancer Cells

✉ KWOK Tim Tak • CHEUNG Wing Tai • KONG Siu Kai (Biochemistry)

□ 1 October 2001

❖ Research Grants Council (Earmarked Grants)

Cancer is one of the major "death-causing-diseases" in Hong Kong and in many other countries. Chemotherapy is a common way of cancer treatment although it is not always successful. One of the reasons for treatment failure is the development of resistance to anticancer drugs in cancer cells. There are many ways cells can develop resistance to anticancer drugs. Although some genes responsible for drug resistance have been identified, they cannot explain all known forms of resistance. Therefore, in order to increase the efficacy of cancer chemotherapy, identification of genes that cause drug resistance remains important and of potential benefit. In the course of examining the doxorubicin resistance in human squamous carcinoma A431 cells, a novel gene was found to be over-expressed in the drug resistant cells and the gene was induced upon treatment with doxorubicin. The aim of this study is to examine the biological function and the regulation of this novel gene. The results from this study will provide a greater understanding of the function of this novel gene and further serve efforts to design better drugs

or strategies in cancer therapy. Such information, in the longer term, hopefully will benefit many cancer patients, including those prevalent in Hong Kong. (MD01024)

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**Isolation and Characterization of Novel Antifungal Proteins**

- ✉ NG Tzi Bun • WANG Hexiang\* • YE Xiu Yun\*  
□ 1 October 2001  
❖ CUHK Research Committee Funding (Direct Grants)

Antifungal proteins, an important family of self-defence proteins, can be divided into various types according to their structures, including thaumatin – like proteins, chitinases, ribosome-inactivating proteins and others. The intent of the research is to isolate and characterize novel antifungal proteins from non-leguminous species and leguminous species. Legumes have proven to be rich sources of important natural products and are often dietary components in the Chinese population. The results of our previous experiments have indicated the antifungal proteins, some of which possess a novel structure, can be isolated from American ginseng, Chinese ginseng, sanchi ginseng and different legumes including French bean, cowpea, mungbean, sugar snap, red kidney bean, soybean and peanut. The aim of the investigation is to isolate and characterize antifungal proteins from additional legumes such as red bean, rice bean and broad bean, and other dicot species such as the Ceylon spinach, asparagus, Chinese chestnut and kiwi fruit. Preliminary experiments revealed antifungal activity in the extracts of the aforementioned species. Antifungal proteins with potent and stable antifungal activity will be identified from the list of isolated proteins. The presence of other exploitable biological activities in these proteins will also be investigated. (MD01640)

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**Characterization of Differentially Expressed Genes in HBV-induced Hepatocarcinogenesis**

- ✉ TSUI Kwok Wing  
□ 1 January 2002  
❖ CUHK Research Committee Funding (Direct Grants)

In Hong Kong, it was estimated that about 10% of the whole population are hepatitis B carriers. The long term consequences of chronic viral hepatitis infection, which include hepatocellular carcinoma (HCC), chronic liver disease and cirrhosis, led to 5.5% of all deaths in Hong Kong in 1995. Local studies showed that approximately 80% of patients with HCC were found to be hepatitis B carriers. Currently, the exact mechanism of HBV-induced hepatocarcinogenesis is still unclear and demand further investigations. In an attempt to better understand the mechanism, we recently embarked on the isolation of genes that are differentially expressed in the HCC tissue. After screening a subtracted HCC library by expressed sequence tag sequencing and differential hybridization, we have isolated over 60 putative differentially expressed clones. This pool of genes should contain many important factors involved in the molecular mechanism of the hepatocarcinogenesis. In this project, we propose to characterize the putative differentially expressed genes and study their relationship with the development of HCC. The elucidation of the functional roles of these genes in the HCC tissue is prerequisite for developing new diagnostic markers and effective therapies for HCC. (MD00829)

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**Natural Inhibitors Against HIV-1 Integrase**

- ✉ WAN Chi Cheong David • NG Tzi Bun  
□ 1 October 2001  
❖ CUHK Research Committee Funding (Direct Grants)

The human immunodeficiency virus type 1 (HIV-1) is known to be the causative agent of the acquired immunodeficiency syndrome (AIDS). Over the last two decades, there is great effort worldwide dedicated to both basic and clinical research, hoping to find a cure for this debilitation disease. Three enzymes are important in the life cycle of the HIV-1. HIV-1 reverse transcriptase (RT) is crucial for viral replication. HIV-1 protease (PR) processes viral polyproteins into functional enzymes and structural proteins and HIV-1 integrase (IN) mediates integration of the viral DNA into a chromosome of the host, a step essential for efficient viral replication. Chemotherapeutic agents targeted on HIV RT and HIV-1 PR have been developed. The combination therapy approach based on a cocktail of inhibitors to



RT and PR has been successfully used to treat AIDS patients which is largely responsible for the rapid decline in death rate due to AIDS since 1995. At present, inhibitors to HIV-1 IN are not readily available for clinical use. As no cellular homologue of HIV-1 IN has been found, the development of inhibitors to this enzyme could have favorable therapeutic value for combination therapy. The proposed investigation is to screen for potent inhibitors from natural sources, in particular, from Chinese medicinal herbs against HIV-1 integrase. (MD01970)

### 14-3-3 Epsilon and Calmodulin in Signal-transducing Complexes

- ✉ WAYE Mary Miu Yee
- ☐ 1 October 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

In mammals, the 14-3-3 family of proteins comprise seven small acidic proteins known to be involved in signal transduction and cell cycle regulation. Their common active entity is a dimer that can be homogeneous or heterogeneous. 14-3-3 proteins have been implicated in a wide range of biological activities from DNA damage checkpoint control to ion transport, exocytosis and the synthesis of neurotransmitters. The precise biochemical mechanism of 14-3-3 proteins is unknown. However, numerous reports have described their interaction with key enzymes and other protein molecules in signal transduction and cell cycle transition pathways. Given this, 14-3-3 proteins have been found to bind, in an isoform-specific manner, to Raf, PI3-kinase, PKC, Bcr, the insulin-like growth factor I receptor, the insulin receptor substrate I, and Cdc 25 phosphatases (among others). Recently, it has been suggested that a potential mechanism by which 14-3-3 proteins could exert such diverse functions is their ability to form heterodimers, and hence the capability to bind, in the fashion of an adaptor, two molecules from different signal transducing pathways, thereby coordinating the activities of these pathways. This hypothesized operation for 14-3-3 proteins is not dissimilar to that of an antibody molecule i.e. a flexible adaptor molecule that links and approximates the antigen target with effector molecules. We plan to test the hypothesis that 14-3-3 proteins act essentially like

adaptor molecules, i.e. they recruit calmodulin and other signal molecules to form specific ternary complexes and thereby facilitate communication between distinct signal transducing pathways. (MD01345)

### Study on the Expression of a G Patch Containing Protein (HSPC039) in Human and Animal Myocardial Tissues

- ✉ WAYE Mary Miu Yee • ZIMMERMANN Rene\*
- ☐ 1 January 2002
- ❖ Germany/Hong Kong Joint Research Scheme

Our group at The Chinese University of Hong Kong has sequenced over 11,607 Expressed Sequence Tags (ESTs) from a human liver cancer cDNA library. From this collection of novel cDNA clones, we have found a clone which code for a G patch containing protein (HSPC08). HSPC08 contains a glycine-rich sequence, which has the consensus sequence: hhx(3)Gax(2)GxGhGx(4)G. It is present in several RNA-associated proteins and in type D retroviral polyproteins; for example, 45-kDa splicing factor, LUCA15 and DRT111. LUCA 15 is a putative tumor suppressor gene, which is deleted in small-cell lung carcinoma (SCLC) and Drt111 is a cDNA from plant *Arabidopsis thaliana*. If *E.coli* *ruvC* *recG* mutant (deficient in repair DNA damage) was transformed with this gene, the bacteria showed increased resistance to UV light and other chemical DNA damaging agents. HSPC08 is also present in CD34+ hematopoietic stem / progenitor cells (hence the name-HSPC). Its cDNA has a size of 1583bp and the open-reading-frame coded for 82 amino acids protein. From its down-regulation in cancer cells, it is possible that the high level expression of the gene is involved in the inhibition of cell proliferation. The aim of this project is to study the subcellular localization of the HSPC08 protein in human and animal myocardial tissues by using histochemical staining method as well as other molecular and protein biochemical methods. (BL01855)

**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>		
		1998-99	Isolation and Characterization of Ribosome - Inactivating Proteins with Novel Features (CU98331) ✉ NG Tzi Bun
1990-91	Comparative Endocrinology of Prolactin, Growth Hormone, and Their Receptors (BP88031) ✉ CHENG Hon Ki Christopher • NG Tzi Bun • WONG Chun Cheung (Dept of Physiology)	2000-01	Isolation and Characterization of Novel Lectins From Chinese Medicinal Materials and Legumes (MD00483) ✉ NG Tzi Bun • WANG Hexiang*
1999-00	Studies on Fish Prolactin (BL99017) ✉ CHENG Hon Ki Christopher	1999-00	The Role of LIM Domain Proteins in Heart Growth and Development (CU99305) ✉ TSUI Kwok Wing • CHAN Wood Yee (Dept of Anatomy) • FUNG Kwok Pui • LEE Cheuk Yu • LEE Sau Tuen Susanna (Biochemistry) • WAYE Mary Miu Yee
2000-01	Studies on Growth Hormone Secretagogue Receptors in Fish (BL00654) ✉ CHENG Hon Ki Christopher	1999-00	Cell Cycle Control: Regulation of CDC25B Phosphatases by Calmodulin and CaM Kinase (BL99008) ✉ TSUI Kwok Wing • WAYE Mary Miu Yee • DUCOMMUN Bernard*
1997-98	Establishment of a Hong Kong Bioinformatics Centre (BL97001) ✉ FUNG Kwok Pui • LEE Cheuk Yu • WAYE Mary Miu Yee • TSUI Kwok Wing • SMITH David Keith* • XUE Hong* • ZHU Guang*	2000-01	Characterization of Differentially Expressed Genes during Terminal Differentiation of Cardiomyocytes (CU00116) ✉ TSUI Kwok Wing • FUNG Kwok Pui • LEE Cheuk Yu • WAYE Mary Miu Yee
1998-99	Glucose Transporter as an Anti-tumour Target (CU98148) ✉ FUNG Kwok Pui • LEE Cheuk Yu	1998-99	The Role of Pre-synaptic Motor Neuron Acetylcholinesterase in Neuromuscular Synaptogenesis (CU98140) ✉ WAN Chi Cheong David • TSIM Karl W. K.*
2000-01	Development of Compound Formulation Products of GMP Standard Consisting Danshen from Zhongjiang, Sichuan and Sanqi from Wenshan, Yunnan (MD20033) ✉ FUNG Kwok Pui	2000-01	Inhibitory Effects of Antifungal Proteins on HIV Enzymes (BL00637) ✉ WAN Chi Cheong David • NG Tzi Bun
1998-99	The Role of Growth Factor Signalling and c-Jun Expression in the Anti-tumor Effect of Natural Polysaccharides (CU98141) ✉ KWOK Tim Tak • CHOY Yuen Min (Biochemistry)	1997-98	Sequence Analysis of the SLIM1(FHL1) Gene (BL97017) ✉ WAYE Mary Miu Yee • BENTLEY David R.* • ROSS Mark*
1999-00	Function & Regulation of a Gene Encoding a Heat Shock-like Protein (MD99026) ✉ LEE Cheuk Yu • WAYE Mary Miu Yee • FUNG Kwok Pui • TSUI Kwok Wing		

**RESEARCH OUTPUTS AND PUBLICATIONS**

- <P004241> **KONG L.D.; ZHANG Y.; PAN X.; TAN R.X. and CHENG C.H.K.** "Inhibition of Xanthine Oxidase by Liquiritigenin and Isoliquiritigenin Isolated from *Sinofranchetia Chinensis*". *Cellular and Molecular Life Sciences* vol.57, pp.500-505. Switzerland, 2000.03.
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## RESEARCH PROJECTS

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### **Elucidation of Intracellular Signal Transduction Mechanisms Controlling the Recruitment and Degranulation of Eosinophils in Allergic Inflammation**

✉ LAM Wai Kei Christopher • WONG Chun Kwok

□ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Eosinophils are the principal effector cells of allergic inflammation and their degranulation results in the release of cytotoxic proteins including eosinophilic cationic protein (ECP) causing tissue damage. A potent eosinophil-specific chemoattractant, eotaxin, and an  $\alpha 4\beta 1$  integrin, the very late antigen-4 (VLA-4), are crucial for the recruitment of eosinophils to the inflammatory sites and the transmigration of eosinophils through epithelial cells, respectively.

This project aims to elucidate the roles of critical intracellular signal transduction regulators in controlling eosinophil trafficking and degranulation in allergic inflammation. Our recent studies have led us to hypothesise that mitogen-activated protein kinases (MAPK) and nuclear factor-kappaB (NF-kB) are important for eosinophil recruitment and degranulation. We plan to study:

(1) The roles of MAPK and NF-kB on the expression of eotaxin and adhesion-related molecules in (i) human peripheral blood eosinophils, and (ii) a human bronchial epithelial cell line (BEAS-2B cells)

(2) The effect of specific inhibitors of MAPK and NF-kB on eosinophil recruitment and degranulation.

Elucidation of the intracellular control mechanisms of eosinophil chemotaxis and degranulations will be useful for the development of novel effective and specific therapeutic strategies for treating allergic inflammation.

(MD01351)

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### **Development of Genomic Strategies for the Non-invasive Detection of Down Syndrome**

✉ LO Yuk Ming Dennis • CHIU Wai Kwun Rossa • LAU Tze Kin (Dept of Obstetrics & Gynaecology)

□ 1 April 2002

❖ 3Ben Genomics Hong Kong Limited; Gene Company Limited • Innovation and Technology Support Programme, ITF, Innovation & Technology Commission

Down syndrome is the predominant reason why many pregnant women opt for prenatal diagnosis. Unfortunately, the major methods for prenatal diagnosis, such as amniocentesis, are invasive, with a finite risk to the mother and unborn baby. Due to such invasiveness, it has been estimated that in Hong Kong Hospital Authority-run hospitals in which there is no other screening test other than maternal age, 2.5 normal babies are lost for every Down baby diagnosed prenatally. Such statistics clearly emphasise the need for the development of a new generation of non-invasive tests for Down syndrome. Our group has discovered the presence of fetal nucleic acids in maternal blood plasma. We have also filed key patent applications on this technology. In this project, we propose to use modern genomic technologies to identify molecular markers which will allow us to identify the presence of a baby affected by Down syndrome, just by analyzing peripheral blood of the mother. Genomic technologies which will be used include microarrays and large-scale epigenetic analysis. The project deliverables would represent a key step towards a safe universal screening test for all pregnant women. As such, we believe that this project represents an important development of Hong Kong-based biotechnology.

(MD01862)

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### **Is Thyrotoxic Periodic Paralysis Resulted from a Calcium Ion Channelopathy?**

✉ TANG Leung Sang Nelson • CHOW Chun Chung Francis (Dept of Medicine & Therapeutics) • Clive Stewart COCKRAM (Dept of Medicine & Therapeutics) • YAO Xiaoqiang (Dept of Physiology)

□ 1 November 2001

❖ Research Grants Council (Earmarked Grants)

Thyrotoxic periodic paralysis (TPP) is a complication of hyperthyroidism (excessive secretion of thyroid hormone). This condition is almost exclusively confined to patients of East Asian populations. A sudden onset of systemic paralysis occurs in a

susceptible thyrotoxic male patient after a high carbohydrate meal, which is also associated with hypokalaemia.

The cause of this condition is uncertain. The high degree of racial predilection and documentations of individual susceptibility to paralysis indicate that an underlying genetic susceptibility trait exists. Many of its clinical features are in common with an autosomal-dominantly inherited paralytic syndrome found in Caucasians, hypokalaemic periodic paralysis (HOKPP), which is not associated with hyperthyroidism. HOKPP is caused by mutations in a gene (CACNL1A3) encoding for a subunit of voltage gated calcium channel (VGC). Therefore, we hypothesize that TPP is a milder form of defect in this calcium channel, and the latent susceptibility to paralysis is only unmasked at the time of hyperthyroidism. This project is to study if TPP is caused by a defective VGC. As other subunits (totally five subunits form a VGC) may also cause TPP, they will be also included in this study.

(MD01035)

**Elucidation of Nitric Oxide Mediated Mechanisms Controlling the Recruitment of Eosinophils in Allergic Inflammation**

✉ WONG Chun Kwok • LAM Wai Kei Christopher • LEUNG Ting Fan (Dept of Paediatrics)

☐ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Allergic diseases such as asthma and allergic rhinitis are prevalent and have been increasing worldwide. Eosinophils are the principal effector cells of allergic inflammation, which are characterized by their accumulation and infiltration in tissues mediated by chemokine eotaxin, and adhesion molecules vascular cell adhesion molecule 1 (VCAM-1) and intercellular adhesion molecule 1 (ICAM-1) on epithelial cells. Asthmatic patients have elevated levels of exhaled nitric oxide (NO) and inducible NO synthase (iNOS) can promote allergic inflammation in airways. The primary object of this research proposal is to elucidate NO-mediated intracellular signal transduction mechanisms in the control of eosinophil chemotaxis in allergic inflammation. We plan to study (1) The effects of specific inhibitor of NOS, and NO donor on (i) the activation of NF-κB, (ii)

chemotaxis, and (iii) expression of very late antigen-4 (VLA-4) of eosinophils, and expression of ICAM-1 and VCAM-1 on an epithelial BEAS-2B cells, (2) investigation of iNOS mRNA expression and activity of human eosinophils after the treatment with platelet activating factor, TNF, IL-17 and IL-18 *in vitro*, and comparison of iNOS mRNA expression and activity in eosinophils from 40 non-steroid-treated asthmatic patients and 40 healthy sex- and age-matched control subjects, and (3) correlation between plasma concentrations of nitrate, sICAM-1 and sVCAM-1 in asthmatic patients and control subjects. Elucidation of the role of NO on the expression of adhesion molecules and eosinophil chemotaxis will be useful for the identification of new markets for diagnosis and monitoring of allergic inflammation, and development of new therapeutic strategies for treating allergic inflammation.

(MD01925)

**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>
1999-00	Mitochondrial Genome in Wolff-Parkinson-White Syndrome (MD99028) ✉ LAM Ching Wan • John Elsby SANDERSON (Dept of Medicine & Therapeutics) • WONG Lee-Jun C* • FONG Win Hon*
2000-01	Intracellular Signal Transduction for Tumor Necrosis Factor-α-induced Eotaxin Synthesis of Human Eosinophils in Allergic Inflammation (MD00783) ✉ LAM Wai Kei Christopher • WONG Chun Kwok
1999-00	Investigation into Plasma DNA Abnormalities in Pre-eclampsia (CU99255) ✉ LO Yuk Ming Dennis • HJELM Nils Magnus# • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Tse Ngong (Dept of Obstetrics & Gynaecology)

- 1999-00 Development of Plasma DNA-Based Diagnostic Technology (MD99015)  
✉ LO Yuk Ming Dennis • HJELM Nils Magnus# • Philip James JOHNSON (Dept of Clinical Oncology)
- 2000-01 Molecular Analysis of Cell-free RNA in the Plasma of Pregnant Women (MD00848)  
✉ LO Yuk Ming Dennis • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Tse Ngong (Dept of Obstetrics & Gynaecology)
- 2000-01 Enhanced Expression of a Novel Gene BRE That May Modulate Steroid
- 2000-01 Metabolism in Adrenal Gland and Testis (MD00669)  
✉ PANESAR Nirmal Singh • CHAN John Y H\*
- 2000-01 Genetic Susceptibility for Hepatocellular Carcinoma in Chronic Hepatitis B Carriers: A Study of Genetic Polymorphisms in CYP1A1, GST-M1, IL-1 $\beta$  and IL-1RN Genes (MD00880)  
✉ TANG Leung Sang Nelson • LAI Bo San Paul (Dept of Surgery) • CHAN Ka Leung Francis (Dept of Medicine & Therapeutics)

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- <P012233> **LAM Wai Kei, Christopher and WONG Chun Kwok.** "Apoptosis, Part 1: Biochemical Assessment". ed. by SPIEGEL E. Herbert. vol.36, pp.64-98. USA: Academic Press, 2001.
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- <P017957> **TANG Leung Sang Nelson; CHOY Kwong Wai; PANG Chi Pui Calvin; YEO Winnie and JOHNSON Philip James.** "Prevalence of Breast Cancer Predisposition Gene Mutations in Chinese Women and Guidelines for Genetic Testing". *Clinica Chimica Acta* vol.313 no.1-2, pp.179-185. Amsterdam, The Netherlands: Elsevier, 2001.11.
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## RESEARCH PROJECTS

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### "Studies on Anti-tumour Effect of M225, a Monoclonal Anti-epidermal Growth Factor Receptor Antibody, on Nasopharyngeal Carcinoma"

✉ CHAN Anthony Tak Cheung • Philip James JOHNSON • POON Chuen Wai • TO Ka Fai (Dept of Anatomical & Cellular Pathology)

☐ 1 November 2001

❖ Research Grants Council (Earmarked Grants)

Nasopharyngeal carcinoma (NPC) is a major public health problem in Hong Kong. Despite a high initial local control rate in locoregionally advanced disease, the rate of distant metastasis is high after radiotherapy. Patients with distant metastases have a median survival of around 12 months and new therapeutic strategies are therefore needed. Studies on other tumour types expressing epidermal growth factor receptor (EGFR) indicate that monoclonal anti-EGFR antibody can inhibit cell proliferation, increase radiosensitivity, and enhance the anti-tumour effect of cytotoxic drugs. Recently C225, a human-mouse chimeric monoclonal anti-EGFR antibody, derived from mouse monoclonal anti-EGFR M225 has become available as an anti-tumour drug. Our pilot immunohistochemical study showed that EGFR was weakly, moderately, and strongly expressed in 9%, 36% and 49% of NPC cases respectively, and work by others have shown that anti-EGFR antibody inhibited the cell proliferation of a NPC cell line, CNE-2, in vitro. C225 is thus a potentially useful drug for NPC treatment. However, how the expression level of EGFR influences the anti-tumour effect of C225/M225 in NPC and whether or not anti-EGFR antibody will potentiate radiotherapy and chemotherapy are unknown. In the proposed study, we will first identify the expression level of EGFR in NP biopsies from patients and the derived cell cultures, and then investigate the effect of the expression level on growth inhibition by M225. We will then investigate the potentiation effect of M225 on the currently available treatment for NPC, including radiotherapy and chemotherapy using cisplatin and paclitaxel. For those methods that appear to be effective in this system, a xenograft model will be used to investigate the anti-tumour

effect in vivo. The outcome of this study can potentially provide the basis for deciding the patient selection criteria for anti-EGFR antibody treatment. Ultimately the overall treatment outcome of NPC patients may be improved by offering anti-EGFR antibody together with the currently available radiotherapy or chemotherapy. (MD01039)

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### Impact on Salivary Gland Function by Intensity-modulated Radiation Therapy in Treatment of Nasopharynx Cancer: A Prospective Randomised Trial

✉ LEUNG Sing Fai • CHEUNG Kin Yin • KAM Koon Ming Michael • TEO Man Lung Peter

☐ 1 August 2001

❖ Research Grants Council (Earmarked Grants)

Nasopharynx cancer (NPC) is a commonly-occurring cancer in Hong Kong and the standard curative therapy for this cancer is radiation therapy. Dry mouth is occurs in almost all patients as both a short-term and long-term side-effect of conventional radiation therapy treatment. Intensity-modulated radiation therapy is a new modality of radiation therapy with preliminary evidence of capacity to spare the parotid glands and consequent mouth dryness of patients. However, Intensity-modulated radiation therapy is much more resource intensive and experience of its application in nasopharynx cancer is limited. A change of clinical practice need be supported by evidence from a randomised trial. The study aims to assess parotid saliva flow, mouth dryness, and quality of life of patients treated under IMRT and conventional RT in the context of a randomised trial, aiming at obtaining high-level evidence to effect a re-definition of standard clinical practice. (MD01041)

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### Integration of Serological Markers into a New Staging Classification for Hepatocellular Carcinoma; A Prospective Validation

✉ LEUNG Wai Tong Thomas • POON Chuen Wai • TANG Mei Yee#

☐ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

We have derived from a previous study, an improved staging classification for hepatocellular carcinoma (HCC) which gives more precise prognostication of the disease. By adding the following factors: TNM staging classification, serum alkaline phosphatase, total bilirubin, alpha-fetoprotein, ascites, asymptomatic disease at presentation, we were able to classify HCC patients into 3 risk groups with more distinct prognosis than the present TNM staging system. The new staging classification system is called the Chinese University Prognosis Index (CUPI). The present study aims to validate CUPI in a prospective study and also to integrate serum tumor marker profiles into the staging classification. The end result would be a validated new staging classification for HCC and new serological markers that are useful for prognostication. (MD01591)

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**Randomized, Double Blind, Controlled Trial Comparing Two Intravenous Doses of Recombinant Human Thrombopoietin (rhTPO) vs Placebo for the Reduction of the Need for Platelet Transfusions Following Myelosuppressive Chemotherapy in Adult Patients with Solid Tumor or Lymphoma**

✍ LEUNG Wai Tong Thomas • LEI Ieng Kit Kenny • HUI Pun  
 ☐ 1 November 2001  
 ❖ Pharmacia Asia Limited

Thrombocytopenia is a commonly observed complication following myelosuppressive or myeloablative chemotherapy as well as intensive radiotherapy. RhTPO has been shown to prevent the need for platelet transfusions in prior Phase II study in patients with gynecologic malignancies under high dose carboplatin chemotherapy. The objective of the present study is to test the efficacy of 2 doses of rhTPO vs placebo given by IV route, in reducing the proportion of cancer patients who require at least one platelet transfusion due to chemotherapy-related severe thrombocytopenia during one cycle of chemotherapy. This is a double blind, prospective randomized controlled multi-national, multi-center study. (MD01656)

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**A Double-blind Placebo Controlled Randomized Study on the Use of Chinese Herbal Medicine in**

**Treatment of Advanced Non-small Cell Lung Cancer**

✍ MOK Shu Kam Tony • Philip James JOHNSON • ZEE Chung Ying Benny  
 ☐ 1 November 2001  
 ❖ Research Grants Council (Earmarked Grants)

Majority of cancer patients in Hong Kong would explore the use of CHM during the course of their illness, but few (including physician or Chinese herbalist) know or understand its efficacy. Lung cancer is the most common cancer in Hong Kong and there are preliminary data from China suggesting beneficial effect. However, definitive comparative study is lacking.

In this double blind randomized comparative study we shall determine whether CHM is beneficial in patients with advanced non-small cell lung cancer. We will adopt our last study design in which eligible patients are assessed by a licensed CHM practitioner before and independent research assistant randomizes the patient to either an active treatment arm (CHM in granule, as per prescription by the CHM practitioner) or a placebo arm (nonspecific herb in granule). The primary endpoint is improvement in quality of life while the secondary endpoints include tumor response, time to disease progression, overall survival and improvement in disease related symptoms. We shall document feasibility by recording the number of patients approached to the number agreeing to enter the study, detailed analysis of compliance and comparison of perception on disease status. Detail record of herbal product used by the patients will also form an important database for future reference. (MD01043)

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**A Phase II Study of Sequential Administration of Irinotecan and Cisplatin Combination Followed by Docetaxel in Treatment of Advanced Non-small Cell Lung Cancer**

✍ MOK Shu Kam Tony  
 ☐ 23 November 2001  
 ❖ Aventis Pharma Ltd.

(1) Both irinotecan and docetaxel are active single agents in treatment of advanced NSCLC.

(2) Mechanism of action and toxicity profile is different and non-overlapping.

(3) Recent phase I/II studies on combination of irinotecan and cisplatin reported high efficacy with limited toxicity. (BJC 78:251, 1998; WCLC abstr. #89,2000)

(4) The role of docetaxel as first and second line monotherapy has been confirmed by 2 randomized comparative studies.

(5) Sequential administration of a cisplatin-based novel drug combination followed by a taxane is a novel method of administration that could augment the exposure to non-overlapping drugs.

We hypothesized that sequential administration of irinotecan and cisplatin combination followed by docetaxel is associated with more potent synergism, thus higher response rate.

(MD01922)

**A Randomized, Double-blinded, Placebo Controlled, Multicenter, Phase III Study of Tarceva Plus Chemotherapy (Cisplatin and Gemcitabine) Versus Chemotherapy Alone in Patients with Advanced (Stage III B or IV) Non-small Cell Lung Cancer (NSCLC) Who Have Not Received Prior Chemotherapy.**

✉ MOK Shu Kam Tony • HO Pui Ching • WONG Tze Ming • LAM Kwok Chi

☐ 26 March 2002

❖ Roche Hong Kong Limited

This study has the following objectives:

(1) To evaluate the effect on efficacy and safety of Tarceva in combination with chemotherapy versus chemotherapy alone

(2) To evaluate the pharmacokinetic and pharmacodynamic properties of Tarceva in combination with chemotherapy versus chemotherapy alone

(3) To evaluate the effect on QOL, time to symptomatic progression, safety and the pharmacokinetic properties of Tarceva combination with chemotherapy versus chemotherapy alone.

(4) To evaluate the correlation of EGFR expression rate (HER1) and other markers potentially predictive for response.

(MD01660)

<b>Phase</b>	<b>II</b>	<b>Trial</b>	<b>of</b>
<b>Gemcitabine-carboplatin-paclitaxel</b>			<b>as</b>

**Neo-adjuvant Chemotherapy for Operable Non-small Cell Lung Cancer**

✉ MOK Shu Kam Tony • WONG Tze Ming • LAM Kwok Chi

☐ 30 April 2002

❖ Eli Lilly (Asia) Inc.

This study has the following objectives:

(1) To evaluate the clinical response rate to neo-adjuvant chemotherapy with Gemcitabine-Carboplatin-Paclitaxel (GCP) in patients with operable early stage NSCLC.

(2) To evaluate the safety of neo-adjuvant chemotherapy with GCP with respect to toxicity of GCP, peri- and post-operative mortality and serious morbidity possibly related to GCP.

(3) To determine the pathological complete response rate.

(4) To determine the complete tumor resection rate.

(5) To evaluate time to treatment failure, time to documented disease progression, and overall survival.

(MD01571)

**Development and Application of a Novel Real Time PCR Assay for the Quantitation of HBV-DNA**

✉ Philip James JOHNSON • ZHONG Sheng

☐ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Real-time PCR (RTD-PCR) has the potential to quantify HBV-DNA in a 10-log<sub>10</sub> dynamic range, with a sensitivity of 1 copy/reaction. The aim of this study is to develop and validate an in-house real-time PCR assay for HBV-DNA quantitation based on the ultra-rapid LightCycler. PCR primers and fluorescent probes that target the conserved region of the overlapping HBV polymerase and surface antigen genes will be designed. Measurements of plasma/serum HBV-DNA obtained by the real-time PCR method will be compared to those obtained by AMPLICOR by MONITOR (monitor) and by QUANTIPLEX HBV DNA assays (bDNA) in 100 and 50 HBsAg<sup>(+)</sup> samples, respectively. If the development of novel real-time PCR assay for the quantitation of HBV-DNA is



successful, it should provide a sensitive, reproducible and rapid assay with a very wide dynamic range that may be of commercial value. As an initial application we will use the new assay to monitor "HBV reactivation" in cancer patients during chemotherapy. This may provide insights into the mechanism of chemotherapy-induced "HBV reactivation" and be an efficient tool for closely monitoring the HBV-DNA titers of the cancer patients during chemotherapy.  
(MD01561)

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### **Chromosomal Aberrations in Hepatocellular Carcinoma: A Comprehensive Elucidation by Spectral Karyotyping and Comparative Genomic Hybridisation**

- ✉ WONG Nathalie • LAI Bo San Paul (Dept of Surgery) • LEUNG Wai Tong Thomas
- ☐ 1 September 2001
- ❖ Research Grants Council (Earmarked Grants)

Chromosome abnormalities, *whether gains, losses or relocation of chromosome segments*, can perturb one or more cancer-related genes resulting in the transformation of normal cells to neoplastic. Cytogenetic analysis on solid tumors relies on the successful culture of malignant tissues. Karyotypic studies on hepatocellular carcinoma (HCC), a common and highly malignant cancer in Hong Kong, have unfortunately received little attention thus far. This is largely due to the poor tumor growth *in vitro*. We have overcome the problem of HCC culture by establishing a protocol that enabled aberrant metaphases to be obtained. However, the complete karyotypic analysis was hampered by the frequent presence of many unrecognizable chromosomal rearrangements. We propose, in this study, to enhance our studies on HCC, using conventional cytogenetics, by the techniques of Spectral Karyotyping (SKY) and Comparative Genomic Hybridization (CGH). The combined application of these techniques, whereby SKY can provide information on structural rearrangements and CGH on overall DNA sequences gains and losses, can offer a comprehensive and complementary picture into the chromosomal abnormalities in HCC. Karyotypic information derived will be correlated with clinical and pathological characteristics of the disease, and further investigated for candidate gene(s) involvement. Our underlying hypotheses are that (1)

the difference in HCC subgroups will turn out to be characterized by different karyotypic patterns, and (2) non-random chromosomal aberrations involve critical genes relevant to hepatocarcinogenesis.  
(MD01044)

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### **Investigation for Candidate Genes Expression of 1q21-q25 in Hepatocellular Carcinoma**

- ✉ WONG Nathalie • LAI Bo San Paul (Dept of Surgery)
- ☐ 1 October 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Hepatocellular carcinoma (HCC) is a highly malignant tumour that is prevalent in China, including Hong Kong, and Southeast Asia. Using comparative genomic hybridization, we and others have reported on the frequent 1q over-representations in HCC and a novel amplicon below the heterochromatic region at 1q21-q25. In breast cancer, this amplicon has also been described and was suggested to be associated with tumor metastasis. Since our first report in 1999, work on delineating this amplicon for its core region in HCC has been carried out in our laboratory. By positional mapping using interphase cytogenetic analysis, we found the amplicon 1q21-q25 to actually hold three regions of high-level gains. These regions now represented by 3 Yeast Artificial Chromosomes have greatly confined the region of interest from the initial 50Mb to approx. 4Mb. In this study, we proposed to further investigate these YACs for the candidate genes expression. We propose to perform reverse-transcription following by quantitative PCR to the estimate the expression level of each gene investigated. The information obtained from this study is expected to yield information related to candidate gene(s) that carries a poorer clinical outcome in HCC.  
(MD01498)

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### **Detection of Mitochondrial DNA Mutation in Tumour and Peripheral Blood (Cell-free) of Patients with Hepatocellular Carcinoma**

- ✉ YEO Winnie • Philip James JOHNSON • ZHONG Sheng
- ☐ 1 December 2001

❖ Research Grants Council (Earmarked Grants)

Hepatocellular carcinoma (HCC) is one of the most common malignancies in China and is the second major cause of cancer death in Hong Kong. Only 10% of the patients may be offered curative surgical resection, and even so, half of them relapsed shortly after surgery. Potentially more effective adjuvant treatment can be offered post-surgery to improve the overall prognosis of the patients. Effective serum markers may have prognostic values and may potentially enable the prediction of disease recurrence, which may aid clinicians in the pre-treatment assessments and treatment-planning.

Studies have demonstrated that tumour specific DNAs are detectable in plasma and serum of cancer patients. Recently, mutations in the mitochondrial DNA (mt DNA), has been found in the tumour tissues and the respective adjacent bodily fluids of colorectal, head and neck, bladder and lung cancers. (MD01045)

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**A Multicenter III Randomized Trial Comparing Docetaxel In Combination With Doxorubicin And Cyclophosphamide (TAC) Versus Doxorubicin And Cyclophosphamide Followed By Docetaxel (AC→T) As Adjuvant Treatment Of Operable Breast Cancer HER2NEU Negative Patients With Positive Axillary Lymph Nodes**

✉ YEO Winnie

☐ 1 January 2002

❖ Breast Cancer International Research Group

To compare disease-free survival after treatment with docetaxel in combination with Doxorubicin and Cyclophosphamide (TAC) to Doxorubicin and Cyclophosphamide followed by Docetaxel (AC→T) in operable breast cancer her2neu negative patients with positive auxiliary lymph nodes. (MD01478)

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**Open-label, Multicenter, Randomized, Controlled Study of IM or Oral Exemestane (Aromasin<sup>R</sup>) in Postmenopausal Women with Advanced Breast Cancer (ABC) Having Progressed on Tamoxifen**

✉ YEO Winnie • HO Wing M\* • KWAN Wing H\*

☐ 1 March 2002

❖ Pharmacia Asia Limited

This is an open-label, multicenter, randomized, controlled study to compare intramuscular or oral Exemestane (Aromasin<sup>R</sup>) in postmenopausal women who have advanced breast cancer having progressed on tamoxifen.

(MD01739)

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

<u>Edition</u>	<u>Title/Investigators</u>
2000-01	Biweekly Irinotecan (CPT-11), 5-Fluorouracil (5-FU) and Folinic Acid (FA) in Unresectable Liver Metastases from Colorectal Cancer: A Phase II Study (MD20018) ✉ CHAN Anthony Tak Cheung • MOK Shu Kam Tony • LEUNG Wai Tong Thomas • YEO Winnie • Philip James JOHNSON • LAI Bo San Paul (Dept of Surgery) • CHUI Ka Keung Albert (Dept of Surgery) • LAU Wan Yee Joseph (Dept of Surgery) • Hui Edwin P*
2000-01	A Multi-national, Multi-Centre, Open-label Study to Evaluate the Efficacy of Cetuximab in Combination with Carboplatin in Patients with Recurrent or Metastatic Nasopharyngeal Carcinoma (NPC) (MD00719) ✉ CHAN Anthony Tak Cheung • MOK Shu Kam Tony • YEO Winnie • LEUNG Wai Tong Thomas • Philip James JOHNSON • LEE Chi Yan Conrad
2000-01	A Randomized, Open-label, Multicenter Phase III Study of 5-Fu/Leucovorin with or without Concomitant SU5416 in Patients with Metastatic Colorectal Cancer (MD20065) ✉ CHAN Anthony Tak Cheung • MOK Shu Kam Tony • YEO Winnie • LEUNG Wai Tong Thomas • Philip James JOHNSON • HO Wing Ming

- 2000-01 Phase III Randomized Multicenter Comparatives Study of Peginterferon alpha2a vs. Roferon-A for the Treatment of Patients with Recently Diagnosed Chronic Phase Chronic Myelogenous Leukemia (CML) not Previously Treated with Interferon (MD20042)  
 ✉ LEI Ieng Kit Kenny • LEUNG Wai Tong Thomas • HUI Pun
- 2000-01 Randomized, Double-blind, Placebo-controlled Trial of Primary Prophylaxis with Recombinant Human Thrombopoietin (rhTPO) Administered to Patients Receiving DHAP Chemotherapy for Recurrent or Refractory Intermediate-grade or High-grade non-Burkitt's, non-Hodgkin's Lymphoma (NHL) (MD20067)  
 ✉ LEI Ieng Kit Kenny • LEUNG Wai Tong Thomas • HUI Pun
- 1997-98 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 of 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 • Philip James JOHNSON • CHAN Anthony Tak Cheung • YEO Winnie
- 2000-01 Neoadjuvant Systemic Chemotherapy for Operable Hepatocellular Carcinoma (MD00994)  
 ✉ LEUNG Wai Tong Thomas • Philip James JOHNSON • LAU Wan Yee Joseph (Dept of Surgery) • LIEW
- 2000-01 A Phase I/II Open Label Study of T138067-sodium in Patients with Advanced Surgically Unresectable Hepatocellular Carcinoma (MD20061)  
 ✉ LEUNG Wai Tong Thomas • MOK Shu Kam Tony • Philip James JOHNSON
- 1998-99 A Randomized Phase II Study of Gemcitabine Plus Oral Etoposide Versus Gemcitabine Plus Cisplatin in Treatment of Advanced Non-Small Cell Lung Cancer (MD98144)  
 ✉ MOK Shu Kam Tony
- 2000-01 A Double-blind Placebo-control Randomized Study of the Efficacy of Chinese Herbal Medicine in Reduction of Cytotoxic Chemotherapy-induced Toxicity (CU00109)  
 ✉ MOK Shu Kam Tony • Philip James JOHNSON • YEO Winnie • ZEE Chung Ying Benny
- 2000-01 A Randomized, Double blind, Phase III Comparative Trial of 2 Doses of ZD1839 (IRESSA™) in Combination with Gemcitabine and Cisplatin Versus Placebo in Combination with Gemcitabine and Cisplatin in Chemotherapy-naïve Patients with Advanced (Stage III or IV) Non-small Cell Lung Cancer (MD20046)  
 ✉ MOK Shu Kam Tony • CHAN Anthony Tak Cheung
- 2000-01 Phase I/II Study of a Paented Labyrinthin Peptide Base Vaccine in Patients with Advance Stage Labyrinthin Expressing Cancer (MD20064)  
 ✉ MOK Shu Kam Tony
- 2000-01 Investigation of the Cellular Factors Associated with the Resistance of Hepatocellular Carcinoma to Combination Chemotherapy, PIAF (MD00625)
- Choong Tsek (Dept of Anatomical & Cellular Pathology) • ZEE Benny\*

- ✎ MOK Shu Kam Tony • LEUNG Wai Tong Thomas • POON Chuen Wai • LIEW Choong Tsek (Dept of Anatomical & Cellular Pathology)
- 2000-01 Identification of Metastasis-related Genes in a Human Lung Cancer Cell Line Using Representational Difference Analysis and cDNA Array Technology (MD00741)  
 ✎ Philip James JOHNSON • ZHONG Sheng • Zheng Jie\* • LIU Cuiling\*
- 2000-01 A Phase III Randomized Trial Comparing Efficacy of Non-adherent Dressing Versus Gentian Violet for Treatment of Radiation-induced Moist Desquamation Wounds in Patients with Nasopharyngeal Carcinoma (BL20009)  
 ✎ Philip James JOHNSON • Alexandros MOLASIOTIS (The Nethersole School of Nursing)# • ZEE Chung Ying Benny • Mak So Shan\* • Chan Eunice\*
- 2000-01 Adenocarcinoma of the Lung in Hong Kong Chinese Females: A Genome Investigation for Underlying Genetic Alterations (CU00112)  
 ✎ WONG Nathalie • TSAO Ming Sound\* • YIM Ping Chuen Anthony (Dept of Surgery)
- 1997-98 High Dose Adjuvant Chemotherapy and Peripheral Stem Cell Transplant for High Risk Breast Cancer Patients (MD95266)  
 ✎ YEO Winnie • KWAN Wing Hong • TEO Man Lung Peter • LEUNG Wai Tong Thomas • SUEN Wang Ming Michael (Dept of Anatomical & Cellular Pathology) • KING Wing Keung Walter (Dept of Surgery)
- 1997-98 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 • Philip James JOHNSON • LEUNG Wai Tong Thomas
- 1997-98 Randomized Trial of Tamoxifen versus Placebo for the Treatment of Inoperable Hepatocellular Carcinoma (MD97169)  
 ✎ YEO Winnie • Philip James JOHNSON • LEUNG Wai Tong Thomas
- 2000-01 Lamivudine for Prevention of HBV Reactivation in HBsAg Seropositive Patients Undergoing Cytotoxic Chemotherapy (MD20031)  
 ✎ YEO Winnie • Philip James JOHNSON • ZEE Chung Ying Benny • HO Wing Ming • HUI Pun • LEUNG Wai Tong Thomas • MOK Shu Kam Tony • LEI Ieng Kit Kenny • CHAN Anthony Tak Cheung • ZHONG Sheng • CHAN Kay Sheung Paul (Dept of Microbiology)
- 2000-01 A Phase I/II Study of Weekly Paclitaxel, UFT and Leucovorin in Patients with Metastatic Breast Cancer (MD00480)  
 ✎ YEO Winnie • MOK Shu Kam Tony • CHAN Anthony Tak Cheung • LAM Kwok Chi
- 2000-01 Definition and Measurement of Methylation Index (MI) in Hepatocellular Carcinoma Tissues and Their Corresponding Non-tumor Tissues (MD00568)  
 ✎ YEO Winnie • Philip James JOHNSON • ZHONG Sheng
- 2000-01 Randomised Double-blind Trial in Postmenopausal Women with Primary Breast Cancer Who Have Received Adjuvant Tamoxifen for 2-3 Years, Comparing Subsequent Adjuvant Exemestane Treatment with Further Tamoxifen (MD00331)  
 ✎ YEO Winnie
- 2000-01 A Phase II Study of Herceptin Monotherapy Administered 3 weekly

in Women with HER 2  
Overexpression/amplification in  
Metastatic Breast Cancer (MD20044)

✉ YEO Winnie • MOK Shu Kam Tony  
• LAM Kwok Chi

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## RESEARCH PROJECTS

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### Randomised Controlled Trial of Doctor Education to Increase Cervical Screening Rates

✉ CHAN Shiu Yee Cynthia • James Arthur DICKINSON • TANG Jinling • CHIN Robert\* • FABRIZIO Cecilia\*

□ 1 November 2001

❖ Health Care & Promotion Fund, Hospital Authority

*Objective:* To measure whether a behaviour-focused, brief but intensive education workshop with a follow-up component will change smear-taking behaviour and increase the cervical screening rates of Hong Kong private primary care doctors with initially low screening rates.

*Design:* Randomised controlled trial

*Setting:* Independent private practices in Hong Kong, and Clinical Skills Learning Centre at Prince of Wales Hospital

*Subjects:* Doctors who currently undertake few or no cervical smears.

*Interventions:* Intensive 3-hour workshop, focusing on physical and consultation skills needs for persuading women to undertake a cervical smear, and to perform smears without excessive discomfort or embarrassment. The alternate intervention would be a similar workshop focused on behaviour change skills for cardiovascular disease prevention.

*Main outcome measures:* Comparison of pathology laboratory record of smears taken over six months, with comparison to numbers taken the previous year, between the intervention and alternate intervention groups. Background changes occurring among other doctors served by the laboratories will be compared. Immediate impact will be measured by a knowledge attitudes and behaviour (KAP) questionnaire conducted before and 3 months after the seminar.

(MD01952)

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### A Study on the Prevalence, Brain Pain Centre Activity, Psychological Stress and Quality of Life of Subjects with the Irritable Bowel Syndrome (IBS)

✉ CHAN Shiu Yee Cynthia • CHAN Ka Leung Francis (Dept of Medicine & Therapeutics) •

LAU Edith Ming Chu • LEE Albert • LEUNG Chi Ming (Dept of Psychiatry) • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • TANG Jinling • WUN Yuk Tsan Kyran Patrick#

□ 1 December 2001

❖ Research Grants Council (Earmarked Grants)

The irritable bowel syndrome (IBS) is a common chronic problem that is poorly understood and difficult to manage. However, new criteria for making a more positive diagnosis and new brain imaging techniques for assessing the brain-gut axis are now available. We plan to study the prevalence of IBS in the Hong Kong community and its impact on quality of life, by conducting a cross-sectional household survey using the new Rome II diagnostic criteria and the validated Chinese version of the health-related quality of life short form SF-36 questionnaire and the IBS Quality of Life questionnaire.

Randomly selected groups of IBS subjects who have consulted general practitioners or gastroenterologists, who did not consult doctors and healthy controls identified from the survey or from clinics will then undergo functional magnetic resonance imaging (fMRI), to study brain activity in response to rectal distension. This will determine if the central nervous system pain/emotion centers respond any differently to visceral pain among the above IBS-sub-groups when compared with controls. The subjects will also complete psychological questionnaires to determine whether there is any difference in distress.

This study will provide new information on the possible associations between biological responses of the brain-gut axis and the psychosocial factors affecting visceral pain perception and the quality of life of IBS patients.

(MD01046)

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### Development of Food Frequency Questionnaire and Database for Assessing Soy Isoflavones Intake in the Chinese Population

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

□ 15 September 2001

❖ Research Grants Council (Earmarked Grants)

With declining levels of estrogens, women approaching menopause have increased risks in developing osteoporosis, cardiovascular diseases, and postmenopausal symptoms. While hormonal replacement therapy is the established method for the prevention of menopausal related conditions, its use is very low in Asian women. Soy food is part of the traditional Asian diets and is also the main source of isoflavones (a major type of phytoestrogens). Increasing number of studies is investigating the potential benefits of soy on health because of the estrogenic and anti-estrogenic properties of phytoestrogens. While many of these studies are presently being conducted in the Western populations, population-based studies in Asia would be particularly revealing because of the range and variability of soy food intake. Food frequency questionnaire (FFQ) is the instrument of choice for assessing usual food and nutrient intake in large-scale epidemiological investigations. Up till present, no validated FFQ has been developed for assessing soy isoflavones exposure in the Asian setting. This study proposes to develop a food frequency questionnaire and a database for the assessment of soy isoflavones exposure in the Hong Kong Chinese population.

(MD01047)

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**A Randomized Controlled Trial of the Effect of Milk Supplementation on Bone Density in Women Aged 20-35 Years in Asia**

✉ LAU Edith Ming Chu • WOO Jean (Dept of Medicine & Therapeutics) • LEUNG Ping Chung (Dept of Orthopaedics & Traumatology)

☐ 1 January 2002

❖ New Zealand Dairy Board

The study was designed to investigate the effect of milk supplementation on bone mineral density at the hip, spine and total body among young women (aged 20-35 years). The trial will involve 200 subjects to detect a 0.75% change in the primary outcome (bone mineral density) over the two years intervention. Subjects will be women, 20-35 years old, with approximately half in the 20-27 age range and half in the 28-35 age range. Subjects will be randomized into a treatment and control group at each site by method of randomized permuted blocks. Treatment group will be given daily milk supplement (1000mg per day) and the control group will not be given any

supplement. Bone mineral density will be measured at baseline, 6, 12, 18 and 24 months. The biochemical indices of bone turnover measurements will be taken at baseline, 3 and 24 months.

(MD01501)

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**Testing the Effectiveness of an Intervention Programme in Reducing Non-urgent Utilization of Accident and Emergency Services: Pilot Study to Analyse the Feasibility and Develop the Framework of the Intervention**

✉ LEE Albert • CHENG YAM Fung Khing Frances

☐ 1 November 2001

❖ CUHK Research Committee Funding (Direct Grants)

Accident and Emergency (A&E) Department have become a popular venue for primary care delivery. The significant increase in inappropriate attendance of non-urgent patients is considered as a serious threat to the health care system in terms of inefficient utilization of resources and depriving the quality care of true emergent cases. In Hong Kong, a recent study by the principal investigator has illustrated that 57% of the accident and emergency (A&E) attendees would be appropriately managed by general practitioners (GPs). It has also demonstrated higher utilization rate by members of the higher socio-economic class, and the factor of low cost was shown to be associated with lower odds ratio of utilizing A&E services for primary care purposes. The organization of the health care delivery system plays a significant role as limitations in the availability and accessibility of comprehensive primary health care services causes patients to utilize the emergency services as alternative primary health care services. There is also good evidence suggesting that referral to primary care providers can be acceptable to patients. It has also been shown that employing GPs in A&E to manage patients' primary care needs resulted in reduced rate of investigations, prescriptions and referrals. A related study showed that primary care patients could be managed in this way at reduced cost and with no detrimental effect on outcomes.

The main question is to ask which primary care developments are more likely to result in a decrease in accident and emergency attendance and / or impatient admissions. The ultimate objective of the

full study is to test the effectiveness of structured referral back and interfacing system between A&E and GPs for a group of non-urgent A&E attendees randomly selected as intervention group, and compare with a control group. In this pilot study, it is aimed to analyse the feasibility and develop the framework of structured referral and interfacing system between A&E and GPs by qualitative methods such as focus groups study and interviews on patients, GPs, A&E physicians and health professionals, and administrators.

The long term Implication will be cost saving especially the opportunity cost, improved health status, high level of patient satisfaction, and better quality of life. Apart from resources implication, the increasing demand on A&E services would lead to prolong waiting time and delay in management of seriously ill patients. This will jeopardize the quality of health care and also the efficiency of health services.

(MD01314)

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**Provision of Training Services to Frontline Rehabilitation Personnel for the Mentally Handicapped Persons**

✍ LEE Albert • TSANG Kwong Ka • CHENG YAM Fung Khing Frances

☐ 1 January 2002

❖ Social Welfare Department, HKSAR Government

The programme is aimed to improve the standard of services provided by rehabilitation personnel. It is also aimed to improve the quality of care for chronic illness patient and enhance the concept of care in the community.

(MD01916)

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**Human Dioxin Levels in Hong Kong - A Pilot Study**

✍ WONG Tze Wai • NELSON Edmund Anthony Severn (Dept of Paediatrics) • HEDLEY Anthony J\* • LAM Tai Hing\* • FIELDING R\* • NGAI C\* • HO P C\*

☐ 1 July 2001

❖ Environmental Conservation Fund (Collaboration with The University of Hong Kong)

The study will aim to provide information on (a) Variation in breast milk concentrations of dioxin like compounds (international toxic equivalents) in a representative sample of primiparous nursing mothers recruited in several districts of the SAR. (b) The analyses will be supported by information on past geographical place of residence, usual dietary preferences and intake and other lifestyle factors. (c) Comparison will be made with comparable data from the Asia Pacific region and other data from both the east and west, industrialized and rural areas. (d) An estimate will be made of the contribution which is made to total dioxin intake in the first year of life for an average breast fed infant in Hong Kong.

(MD01395)

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**Provision of Service for Collection of Information on the Non-auditory Effects due to Environmental Noise Exposure**

✍ WONG Tze Wai • YU Tak Sun Ignatius • CHEN Weiqing

☐ 8 November 2001

❖ Environmental Protection Department, HKSAR Government

To review the non-auditory health effects caused by environmental noise, we critically appraise literature from Asian, European and North American countries. The methodology and protocol for data collection interpretation and evaluation of non-auditory effects are examined, results are summarized and the applicability in respect of transportation noise of the findings to Hong Kong is reviewed. A pilot study is conducted to study the feasibility in establishing a database and evaluating the magnitude of the non-auditory health problems in Hong Kong residents.

(MD01367)

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**Assessment of Toxic Air Pollutant Measurements in Hong Kong**

✍ WONG Tze Wai • YU Tak Sun Ignatius

☐ 1 December 2001

❖ Environmental Protection Department, HKSAR Government

To assess the potential health impact of toxic air pollutants covered in the monitoring programme in



Hong Kong, based on the measured ambient / roadside / rural concentrations with reference to overseas experience. The Principal Investigators will systematically assess any adverse effects of individual toxic air pollutants on public health at the current and the predicted concentration levels by adopting for example a time budgeting approach using measurement data from the roadside, urban and rural sites. The assessment should build upon relevant experiences overseas, and give justifications for the selected methodology and unit risk factors, acceptable risk level, recommendations, conclusive remarks, etc.

(MD01308)

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**A Comparative Study of the Effects of Air Pollution on General Practitioner Consultations in Hong Kong and London**

✉ WONG Tze Wai

☐ 28 February 2002

❖ Environmental Protection Department, HKSAR Government

This time series study on air pollution and morbidity in general practice for three years aims to compare its results with that performed in 1992-1995 in London. No other studies have been reported elsewhere. The hypothesis is that a positive association exists between daily air pollutant levels and changes in GP consultations. Because of climatic, topographical and differences in air pollution profile, the effects on health might differ in the two cities. This study will explore the effect (on health) of air pollution in Hong Kong and compare the differences (in health outcomes) in the two cities.

(MD01592)

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**A Database on Traditional Chinese Medicine Treatment for Drug Addiction**

✉ XU Min • LEE Tak Shing Dominic (Dept of Psychiatry) • LEUNG Ping Chung (Dept of Orthopaedics & Traumatology)

☐ 4 April 2002

❖ Beat Drugs Fund Association

*Objectives:* To establish a database on traditional Chinese medicine (TCM) treatment for drug addiction, and to systematically evaluate the safety

and efficacy evidence of the identified TCM treatment products and protocols.

*Method:* English and Chinese journals and literature databases will be searched by hand and computer. Researchers and pharmaceutical companies will be contacted to retrieve unpublished information. Data will be entered into a database that enabled easy and systematic retrieval. Safety and efficacy data will be evaluated and categorized.

*Outcome:* A database on TCM treatment for drug addiction.

*Potential:* This project is proposed pursuant to the Report on Review of Methadone Treatment Programme. The results will help inform governmental policy on TCM drug abuse research and service.

(MD01884)

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**Effect of Traditional Chinese Medicine on Noise Induced Tinnitus - A Randomized Controlled Trial**

✉ YU Tak Sun Ignatius • TANG Jinling • CHIU Yuk Lan

☐ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Subjective tinnitus is the perception of sound that does not exist. It is a common symptom among adults and a frequent and annoying accompaniment of occupational hearing loss. Both drug and non-drug treatments have been applied to help patients with subjective tinnitus. However, no specific treatment has been shown to cure subjective tinnitus up till now.

The current study will try to examine the effects of traditional Chinese medicine in the treatment of subjective tinnitus resulting from noise exposure. The drug to be used is a formulated prescription named Er Long Zuo Ci (ELZC) pill (耳聾左慈丸). Patients with subjective tinnitus will be recruited among employees exposed to occupational noise in Hong Kong. They will then be randomly allocated into two groups: one group will take the ELZC pills and the other will take the placebo pills. The tinnitus handicap will be measured by a standardized questionnaire. The visual Analogue Scales will be used to measure the loudness, annoyance, and awareness of tinnitus. Outcome measurements also include an audiometric test, tinnitus matching, and the

magnitude of deficiency of kidney-yin assessment. Comparing the results of the two groups will show whether the ELZC pills are effective in the treatment of subjective tinnitus.

If the ELZC pill is shown to be effective with few side effects in this trial, it can be promoted as an inexpensive alternative therapy for subjective tinnitus among workers exposed to noise at work.

(MD01307)

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

Edition      Title/Investigators

2000-01      How Well do Primary Care Physicians Communicate with Patients and is a Part-time Course in Family Medicine Effective in Improving Their Skills? (MD00831)

✉ CHAN Shiu Yee Cynthia • WUN Yuk Tsan Kyran Patrick# • James Arthur DICKINSON

1999-00      A Population-based Cohort Study on Phytoestrogens Intake and Bone Loss in Chinese Early Postmenopausal Women (MD99011)

✉ HO CHAN Suzanne • WOO Jean (Dept of Medicine & Therapeutics) • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research) • CHEN Zhenyu (Biochemistry)

2000-01      Effects of Phytoestrogens on Calcium Metabolism in Chinese Postmenopausal Women (CU00162)

✉ HO CHAN Suzanne • John J Anderson\* • LEE Simon K. M.\* • WOO Jean (Dept of Medicine & Therapeutics) • YU Chai Mei (Dept of Chemistry)

2000-01      A Pilot Investigation into the Effect of Antibiotic Use on the Development of Antibiotic-resistance in Gram Positive Cocci (MD00385)

✉ James Arthur DICKINSON • BOOST Margart\* • FRENCN Peter\*

1998-99      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 (MD98087)

✉ LAU Edith Ming Chu • WOO Jean (Dept of Medicine & Therapeutics) • CHENG Chun Yiu Jack (Dept of Orthopaedics & Traumatology) • FOK Tai Fai (Dept of Paediatrics)

1999-00      Tai Chi and Resistance Training Exercise - Would These Really Improve the Health of the Elderly? (CU99303)

✉ LAU Edith Ming Chu • CHAN Kai Ming (Dept of Orthopaedics & Traumatology) • WOO Jean (Dept of Medicine & Therapeutics) • CRITCHLEY Julian A J H (Dept of Medicine & Therapeutics)# • KWOK Chi Yui Timothy (Dept of Medicine & Therapeutics) • SO Raymond\*

1999-00      A Randomized Controlled Trial of the Effect of Milk Supplementation on the Rate of the Bone Loss in the Post Menopausal Women in Hong Kong (MD99068)

✉ LAU Edith Ming Chu • WOO Jean (Dept of Medicine & Therapeutics)

1999-00      Multi-centre Influenza Trial of RWJ-270201 (MD99128)

✉ LEE Albert • TSANG Kwong Ka • LEE Shiu Hung • Tung Wai Kit\*

2000-01      Comprehensive School Health Education Programme: Implementing the Concept of Health-promoting Schools to Enhance Quality Education (MD20016)

✉ LEE Albert • LEE Shiu Hung • TSANG Kwong Ka • TO Cho Yee

2000-01      New Initiatives for School Based Management to Promote Healthy Educational Environments: The Hong Kong Healthy Schools Award Scheme (MD00896)

- ✎ LEE Albert • LEE Shiu Hung • TO Cho Yee  
 1998-99 "Healthy Schools" and "Healthy Society": Quality Education for Children and Teachers (MD98068)  
 ✎ LEE Shiu Hung • LEE Albert • TO Cho Yee  
 2000-01 Utilization of Neuro-cognitive Science for the Improvement of Language Education in Hong Kong (MD20022)  
 ✎ TO Cho Yee • CHAN Sui Yin Agnes (Dept of Psychology) • CHAN Tin Cheung (Dept of Psychology) • CHAN Yu Leung (Dept of Diagnostic Radiology & Organ Imaging) • FOK Tai Fai (Dept of Paediatrics) • FUNG Kwok Pui (Biochemistry) • HUNG Hin Wai Joseph (Dept of English) • LAU Din Cheuk (Dept of Chinese Language & Literature) • MARK Kai Keung • MOK Ka Wai Alice# • YUE Kwan Cheuk (Dept of Japanese Studies)# • ZHANG Jingsong (School of Public Health)# • FUNG Man Lung\* • So Ting Pat Albert\* • Kwan Ting Fai\* • Chan H Y Francis\* • Chan Wing Kwong\* • Chau Wai Lap Albert\* • Fung C W Peter\* • Hoosain Rumjahn\* • Lee Hok Ming\* • Man Tin Yau Tania\* • Ng Choi Yi\* • Ng Yuk Lan Laura\* • Tang Mei Sin\*  
 2000-01 Provision of Service for Continuation Study of the Short-term Effects of Air Pollution on Morbidity in Hong Kong (MD20053)  
 ✎ WONG Tze Wai • WUN Yuk Tsan Kyran Patrick# • YU Tak Sun Ignatius • TAM Wai San Wilson  
 1999-00 Lung Cancer Mortality in Relation to Silicosis: A Cohort Study of Hong Kong (CU99328)  
 ✎ YU Tak Sun Ignatius • WONG Tze Wai • CHAN Chi Kuen Alan\* • LEUNG Chi Chiu\* • TAM Cheuk Ming\*

## RESEARCH OUTPUTS AND PUBLICATIONS

- <P004233> **LI K.T., Donald and DICKINSON James.** "A Primary Medical Care Certificate for Hong Kong". Oral Presentation at the Wonca Asia Pacific Regional Conference 2000 & Rnzcp Annual Conference - "General Practice into the New Millennium" p.248. New Zealand: WONCA, 2000.06.  
 <P008524> **CHAN C K, LEUNG C C, TAM Cheuk Ming, YU Tak Sun Ignatius and WONG Tze Wai.** "Lung Cancer among Workers Compensated for Silicosis in Hong Kong (Authors' Reply to Letters to the Editor)". *Journal of Occupational and Environmental Medicine* vol.42, p.860. USA: American College of Occupational and Environmental Medicine, 2000.09.  
 <P009485> **CHAN Charles C, CHENG J Y C, WONG Tze Wai, CHOW C B, LUIS Ben P K and CHEUNG W L.** "An International Comparison of Childhood Injuries in Hong Kong". *Injury Prevention* vol.6 no.1, pp.20-23. UK: BMJ Publishing Group, 2000.03.  
 <P010056> **DICKINSON J.A.** "Clinical Challenge: Unusual Pain in the Chest". *The Hong Kong Practitioner* vol.22, pp.616-618. Hong Kong, 2001.12.

- <P011151> **CHIU Yuk Lan and YU Tak Sun Ignatius.** "Colorectal Cancer Among Chinese Restaurant Waiters (Letters to the Editor - Authors' Reply)". *Occupational Medicine* vol.51, p.523. UK: Oxford University Press, 2001.12.
- <P011761> **CHIU Yuk Lan and YU Tak Sun Ignatius.** "Colorectal Cancer Among Chinese Restaurant Waiters". *Occupational Medicine* vol.51, pp.343-346. UK: Oxford University Press, 2001.08.
- <P011887> **YU T.S. Ignatius; YEUNG S. Simon; CHAN C.H. Chetwyn and WONG W.H. Ernest.** "Ergonomic Evaluation of Musculoskeletal Health Problems Among Aircraft Cabin Cleaners". *Occupational Ergonomics* pp.248-250. Beijing, China: Pan-Pacific Council on Occupational Ergonomics, 2001.08.
- <P011895> **CHAN Shiu Yee Cynthia, WING Yun Kwok, LEE Sing and YU Wai Man Mandy.** "Utilization of Primary Medical Care Service by Chinese Patients Diagnosed with Psychological Disorders Compared with Age-Sex Matched Controls Over a Five Year Period". *Proceedings of the 26th Congress of the World Federation for Mental Health* Vancouver, British Columbia, Canada: World Assembly for Mental Health, 2001.07.
- <P011932> **DICKINSON J.A.** "Completing the Feedback Loop: Research, Audit and Evaluation in Family Medicine". *The Hong Kong Practitioner* vol.23, pp.321-322. Hong Kong, 2001.08.
- <P011956> **DICKINSON J.A. and CHAN C.S.Y.** "Opinion Survey of Hong Kong Private Primary Care Doctors About Cervical Screening". *Hong Kong Medical Journal* vol.7, pp.284-290. Hong Kong: Hong Kong Academy of Medicine & Hong Kong Medical Association, 2001.09.
- <P011988> **WONG T.W.; WUN Y.T.; TAM W. and YU T.S.** "Association of Air Pollution and Daily GP Consultations for Respiratory Diseases in Hong Kong". *Epidemiology* vol.12 no.4, p.S69. Garmisch-Partenkirch, Germany: International Society for Environmental Epidemiology, 2001.09.
- <P011989> **CHAN C.H., Chetwyn; YU T.S. Ignatius; YEUNG S. Simon; YEUNG, Coley and WONG, Horace.** "VDT Workers' Musculoskeletal Discomfort and Ergonomic Features of Workstations". *Epidemiology* pp.200-202. Beijing, China: Pan-Pacific Council on Occupational Ergonomics, 2001.08.
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## RESEARCH PROJECTS

### Clinical and MRI Evaluation of Skeletal Changes and Growth in Well Chelated Thalassaemic Patients: Comparison of Oral Chelator with Desferrioxamine

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The standard treatment of iron overload in regularly transfused thalassaemic patients is by subcutaneous infusion of desferrioxamine. The treatment, though effective, is costly and may be associated with skeletal dysplasia and growth retardation, which are in fact the most frequent complications of desferrioxamine therapy. These complications tend to occur when excess iron is no longer available for chelation as is seen in well-chelated patients. The other disadvantage of desferrioxamine is that it requires subcutaneous infusion, which is time-consuming and uncomfortable. These factors create the need of a safe and effective oral chelating agent. 1,2-dimethyl-3-hydroxypyrid-4-one (L1) is the only oral iron-chelating agent shown to be effective in maintaining the iron balance between intake from transfused blood and the urine excretion. Nevertheless, its role in well-chelated patients has not been conclusively defined. Although L1 has the known side effect of inducing arthropathy, it is not known to associate with skeletal dysplasia and growth retardation. As such, the change of desferrioxamine to L1 may provide a means to alleviate skeletal dysplasia and growth retardation induced by desferrioxamine therapy. We hypothesize that L1 is of value in reducing skeletal dysplasia and growth retardation whilst maintaining iron balance in the well-chelated thalassaemic patients. (MD01507)

**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>
1999-00	Evolution of Metabolite Concentration and Vascular Perfusion in Late Delayed Radiation Induced Brain Injury – Evaluation on Proton Magnetic Resonance Spectroscopy and Magnetic Resonance Perfusion Imaging (MD99035) ✉ CHAN Yu Leung • LEUNG Sing Fai (Dept of Clinical Oncology) • YEUNG Ka Wai David*
1999-00	Phosphorous-31 Magnetic Resonance Spectroscopy in the Evaluation of Progressive Brain Tumour versus Radiation-induced Brain Injury (MD99091) ✉ CHAN Yu Leung • LEUNG Sing Fai (Dept of Clinical Oncology) • YEUNG Ka Wai David* • BACHERT Peter* • SCHLEMMER Heinz-Peter*
2000-01	Turbo Spectroscopic Imaging Evaluation of Dose-response Relationship in Irradiated Normal Brain Tissue after Arteriovenous Malformation Radiosurgery (CU00104) ✉ CHAN Yu Leung • CHIU Kwok Wing Samuel (Dept of Clinical Oncology) • LAM Ming Kuen Joseph (Dept of Surgery) • YEUNG Ka Wai David*
2000-01	Are Western Skeletal Age Standards Applicable to Hong Kong Chinese? (MD20014) ✉ James Francis GRIFFITH • CHENG Chun Yiu Jack (Dept of Orthopaedics & Traumatology)

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## RESEARCH PROJECTS

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### **Accelerated Atherosclerosis in Chinese Patients with Systemic Lupus Erythematosus: The Effects of Methionine Loading-induced Hyperhomocysteinaemia on Platelet and Endothelial Function and Oxidative Stress**

✉ Brian TOMLINSON • THOMAS Neil G (School of Pharmacy) • HAINES Christopher John (Dept of Obstetrics & Gynaecology) • LI Kwok Ming Edmund • YIM So Fan\* • TAM Lai Shan

☐ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Patients with the autoimmune disorder, systemic lupus erythematosus (SLE) have a substantially increased risk of vascular disease that cannot be attributed to multiple conventional risk factors. Endothelial dysfunction is an early stage in atherogenesis and is an independent predictor of future vascular events. Methionine loading produces a transient hyperhomocysteinaemia challenge to the endothelium that can exaggerate endothelial dysfunction to provide early evidence of this condition in subjects without overt dysfunction. To date, the interactions of homocysteine with platelet function, oxidative stress and endothelial function have not been described in this patient group. SLE is 4-5 times more prevalent in Hong Kong than in Caucasians. In addition, despite a similar positive relationship between homocysteine levels and cardiovascular disease, mortality from CAD in Chinese generally is 20-25% of that seen in Western countries, suggesting ethnic differences may exist. In healthy subjects, we have reported that homocysteine did not affect platelet aggregation *in vitro*, suggesting endothelial-derived factors may be important. To extend our earlier studies, we propose to investigate the *in vivo* interactive effects, not previously studied in humans, of transient endothelial dysfunction on platelet aggregation and oxidative stress following methionine loading in 12 SLE and 20 healthy Chinese subjects. Endothelium-dependent vasodilatation will be assessed using high-resolution ultrasonography and plasma markers and platelet aggregation using markers of platelet activation and flow cytometry.

This study will provide data for the first time in humans to clarify the understanding of the mechanisms by which homocysteine may promote platelet aggregation and endothelial dysfunction in SLE patients who are particularly prone to vascular disease.  
(MD01577)

### **Characterization of Obesity and Insulin Resistance in Chinese Patients with Early-onset Type 2 Diabetes**

✉ CHAN Chung Ngor Juliana • NG Chor Yin • TONG Peter Chun Yip • Clive Stewart COCKRAM

☐ 1 July 2001

❖ CUHK Research Committee Funding (Direct Grants)

This is a downsized version of an RGC Earmarked Grant application that was described as “fundable but not funded”. The original involved two cohort studies and for this direct grant project, a reduced scale of the first study will be conducted.

Base on the ‘thrifty genotype’ and ‘thrifty phenotype’ theories, we hypothesize that dramatic change in lifestyle, particularly with regards to high stress, high fat diet and physical inactivity, can result in the accumulation of visceral fat with its vascular and metabolic consequences. Obesity-associated hormonal changes may interact with genetic and intra-uterine factors to alter insulin sensitivity or pancreatic beta cell function, giving rise to diabetes and related diseases.

In this study, 150 young Type 2 diabetic patients (age of onset 40 years) followed up for 2 to 3 years will be reassessed in year 2001. various adipostatic and glucose regulatory hormones (plasma insulin, C-peptide, leptin, growth hormone, cortisol and urinary catecholamines) will be measured in blood and urine samples saved at the baseline and follow up period. This prospective study aims to investigate for the association of hormonal status, insulin sensitivity, insulin secretion with obesity and diabetes, as well as to investigate the possible changes of these hormonal factors during the course of diabetes. These phenotypic data will complement with our ongoing genetic study to provide comprehensive information on the pathogenesis of young onset diabetes.

(MD01362)

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**"Diabetes Mellitus, Obesity and Cardiovascular Risk Factors in Hong Kong Adolescents"**

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

☐ 1 September 2001

❖ Research Grants Council (Earmarked Grants)

In Hong Kong, 10-15% of childhood diabetes belongs to Type 2 diabetes with obesity and family history as major features. In this study, we aim to document the prevalence of diabetes, obesity and cardiovascular risk factors in Hong Kong adolescents. Demographic, anthropometric, lifestyle, family history and birth weight will be documented in addition to extended phenotypes including insulin and autoimmune status. The relative contributions of socioeconomic, behavioral and biological factors operating in these adolescents to the risk for diabetes and cardiovascular risk factors will be examined in a mathematical model.

This population-based study will allow us to document, for the first time, the prevalence of diabetes, obesity and cardiovascular risk factors in Hong Kong adolescents. We expect these risk factors to persist into adulthood in 50% of these adolescents followed by development of major cardiovascular and renal complications in 10-15 years in their middle age. Hence this study will provide important information for future planning of health care policy and strategies. It will also provide an invaluable resource to determine the effects of intrauterine, environment, psychosocial and biological factors and their interactions on future disease development.

(MD01055)

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**A Multicentre, Double-blind, Randomised, Placebo- and Active-controlled Parallel Study to Evaluate the Glucose and Lipid-altering efficacy and Safety of L-410198 in Patients with Type 2 Diabetes**

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

☐ 30 November 2001

❖ Merck Sharp & Dohme (Asia) Ltd

This is a multinational, double blind, randomised, placebo-controlled phase IIB study which aims to examine the efficacy and safety of a combined PPAR- $\delta$  and PPAR- $\alpha$  agonist (L-410198) in Type 2 diabetic patients. In the first 12 week, the study aims to identify the optimal dosage of L-410198 (2.5 mg, 5.0 mg, 7.5 mg and 10.0 mg) as compared to placebo tablet and 30 mg pioglitazone, another PPAR- $\alpha$  agonist. After week 12, the subjects are allocated to pioglitazone 30 mg or L-410198 5 mg for another 52 weeks. The endpoints include detailed measurements of the metabolic indices, haematological and coagulation indexes, insulin resistance and other cardiovascular risk factors. This study will involve a total of 400 subjects from different countries and our center is one of the few centers in Asia to be involved in this phase IIB (multicentre) study.

(MD01943)

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**A Comparative Efficacy and Safety Study of Nexium (esomeprazole Magnesium) Delayed-Release Capsules (40 mg qd and 20 mg qd) versus placebo for the Prevention of Gastric Ulcers Associated with Daily NSAID Use in Patients at Risk**

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

☐ 1 July 2001

❖ AstraZeneca Hong Kong Limited

The aim of this study is to investigate the efficacy and safety of a new proton pump inhibitor, esomeprazole, for the prevention of gastric ulcers associated with NSAIDs in high-risk patients.

(MD01984)

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**Cyclooxygenase-2 in Human Gastric Ulcers: Biological and Clinical Perspectives**

✉ CHAN Ka Leung Francis • LEUNG Wai Keung • SUNG Joseph Jao Yiu • SZETO Cheuk Chun • TO Ka Fai (Dept of Anatomical & Cellular Pathology)

☐ 1 September 2001

❖ Research Grants Council (Earmarked Grants)

Prostaglandins (PG) serve many important functions in the human body. By inhibiting cyclooxygenase (COX) which is the key enzyme in PG synthesis, nonsteroidal anti-inflammatory drugs (NSAIDs) relieve pain and suppress inflammation. However, NSAIDs also inhibit PG synthesis in the stomach, leading to peptic ulcers and ulcer bleeding. A new approach in preventing the gastric toxicity of NSAIDs becomes feasible with the discovery that there are 2 isoforms of COX, COX-1 and COX-2. COX-1 is normally expressed in the stomach and maintains mucosal integrity. By contrast, COX-2 is rapidly induced at sites of inflammation e.g. arthritis. Development of NSAIDs that selectively inhibits COX-2 offers the prospect of relieving pain and inflammation without causing gastric toxicity. However, the notion that COX-1 is protective and COX-2 is pro-inflammatory may be over-simplistic. There is evidence from animal experiments that COX-2, but not COX-1, is up-regulated in gastric ulcers. Inhibition of COX-2 delays experimental ulcer healing. We have shown that, unlike animal ulcer models, *both* COX-1 and COX-2 are up-regulated in human gastric ulcers. Our preliminary study also suggests that inhibition of COX-2 *alone* may not lead to a clinically significant delay in ulcer healing. These observations suggest that peptic ulcer healing is more complex in the human stomach. The current proposal aims to resolve the functional significance of COX-2 in the healing of human gastric ulcer from a biological and clinical perspective. We plan to study: 1. the relative contribution of COX-1 and COX-2 in PG synthesis in human gastric ulcer, 2. the effect of COX-2 inhibition on PG synthesis in gastric ulcers, and 3. the effect of COX-2 inhibition on ulcer healing.  
(MD01056)

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**Cyclooxygenase and Trefoil Peptides in Stomach - Biology & Clinical Diseases**

- ✉ CHAN Ka Leung Francis • LEUNG Wai Keung • YU Jun • SUNG Joseph Jao Yiu • NG Enders Kwok-wai (Dept of Surgery) • CHUNG Sheung Chee Sydney (Dept of Surgery) • TO Ka Fai (Dept of Anatomical & Cellular Pathology) • CHEN M H\* • HU P J\*
- ☐ 1 September 2001
- ❖ CUHK Strategic Research Program

Peptic ulcer disease and gastric cancer are the two most important digestive disorders in Chinese. Hong Kong has the highest incidence of bleeding peptic ulcer in the world. Furthermore, gastric cancer is amongst the leading causes of cancer death in Hong Kong and China. The socioeconomic impact of these two digestive disorders is enormous. The objectives of this strategic research programme are:

- (1) to study the roles of COX-1- and COX-2-mediated prostaglandins in the healing of human gastric ulcers;
- (2) to determine the effect of inhibition of COX-2 on the progression of pre-malignant gastric lesions;
- (3) to explore the effect of *H. pylori* infection on the expression of trefoil peptides (TFFs) in various stages of gastric carcinogenesis; and
- (4) to investigate the therapeutic potential of blocking TFF3 in gastric cancer.  
(MD01711)

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**Clinical Protocol for a Randomized, Double-blind, Placebo-controlled Study of the Efficacy and Safety of Celecoxib (SC-58635) in the Prevention of Colorectal Sporadic Adenomatous Polyps (PRESAP)**

- ✉ CHAN Ka Leung Francis • SUNG Joseph Jao Yiu • LEUNG Wai Keung • LEE Yuk Tong • CHAN Lik Yuen • WU Che Yuen Justin • HUI Yui • HUNG Cheung Tsui • HUI Aric Josun
- ☐ 14 December 2001
- ❖ Pharmacia Asia Limited

The aim of the study is to investigate the efficacy and safety of Celecoxib in the prevention of Colorectal sporadic adenomatous polyps.  
(MD01879)

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**Prevention of Ulcer Bleeding in High-risk Patients: Is the Enthusiasm for COX2 Selective NSAIDs Justified?**

- ✉ CHAN Ka Leung Francis • LEUNG Wai Keung • SUNG Joseph Jao Yiu • LUK Yiu Wing\* • LAI Moon Sing\* • LEUNG King Sun Vincent\*
- ☐ 28 June 2002
- ❖ Health Services Research Fund, Hospital Authority

Peptic ulcer bleeding is amongst the top causes of hospitalization in Hong Kong. The problem is anticipated to expand because of the increasing use of NSAIDs in our aging population. While there is much enthusiasm about the use of COX-2 selective NSAIDs, whether these drugs will prevent ulcer bleeding in high-risk patients remains uncertain. Unlike pharmaceutical industry-driven studies, the current project aims to critically evaluate the value of COX-2 selective NSAIDs in high-risk patients from clinicians' and Hospital Authority's perspectives: Are COX-2 selective NSAIDs an effective alternative to concurrent therapy of conventional NSAIDs with a proton pump inhibitor for high-risk patients? Will COX-2 selective NSAIDs provide only marginal benefits at a substantial cost? This study will provide important data to formulate better guidelines for the prevention of NSAID-associated ulcer disease.

(MD01406)

**A Multi-national, Multi-centre, Randomised, Open-labelled, Parallel Group Trial to Compare Glycaemic Control of Biphasic Insulin Aspart 30 in Combination with Pioglitazone to Biphasic Insulin Aspart 30 Monotherapy and Pioglitazone in Combination with Sulphonylurea in Subjects with Type 2 Diabetes**

✉ CHOW Chun Chung Francis • Clive Stewart  
COCKRAM • MA Ronald\* • Ozaki R\*

☐ 20 July 2001

❖ Novo Nordisk Asia Pacific Pte Ltd

The trial is a multinational, randomised, open-labelled, parallel group 18 weeks efficacy and safety comparison of BIAsp 30 b.i.d. + pioglitazone, BIAsp 30 b.i.d. monotherapy and SU + pioglitazone in inadequately controlled subjects with Type 2 diabetes. The trial will include a 2 weeks screening phase to assess subject eligibility followed by an 18-week treatment period.

*The primary objective is to:*

Compare glycaemic control as measured by HbA<sub>1c</sub> of biphasic insulin aspart 30 (BIAsp 30) twice daily (b.i.d.) + pioglitazone, sulphonylurea (SU) + pioglitazone and BIAsp 30 b.i.d. monotherapy after 18 weeks of treatment in inadequately controlled subjects with Type 2 diabetes.

*The secondary objectives are to:*

(1) Compare glycaemic control as measured by fasting whole blood glucose and 7 and 8-point blood

glucose profiles of all treatment groups after 18 weeks of treatment in inadequately controlled subjects with Type 2 diabetes.

(2) Compare the safety profile of all treatment groups as measured by the incidence of hypoglycaemic episodes, occurrence of adverse events and standard safety parameters (haematology, biochemistry) after 18 weeks of treatment.

(3) Compare cardiovascular risk factors as assessed by triglyceride, total cholesterol, LDL- and HDL-cholesterol and plasminogen activator inhibitor 1 (PAI-1) levels after 18 weeks of treatment.

(MD01549)

**Multi-centre, Multinational, Open-labelled, Randomised, Parallel, Controlled Trial in Type 2 Diabetic Subjects Inadequately Controlled on Repaglinide, to Compare the Efficacy and Safety of Repaglinide Combined with Bedtime NPH Insulin versus Twice Daily NPH Insulin**

✉ CHOW Chun Chung Francis • Clive Stewart  
COCKRAM • MA Ronald\* • Ozaki R\*

☐ 1 August 2001

❖ Novo Nordisk Asia Pacific Pte Ltd

This is a multi-centre, multinational, open-labelled, randomised (1:1), parallel, controlled trial in subjects with Type 2 diabetes, pre-treated with SU and/or metformin.

The trial includes a screening visit to assess subjects' eligibility. The subjects will be switched to repaglinide treatment, starting up with 1 mg repaglinide at each main meal, followed by a repaglinide titration phase, where dosage is gradually increased to 2 mg at each main meal. The repaglinide titration phase will last 3 to 4 weeks.

Only subjects with a FPG $\geq$ 8.0 mmol/l (144 mg/dl) when on 2 mg of repaglinide at each main meal will be randomised to one of the two treatment regimes:

(1) *Repaglinide group*: Repaglinide (2mg) at each main meal + NPH insulin at bedtime or before midnight, whichever comes first.

(2) *Insulin group*: NPH insulin twice daily, at breakfast and at dinner.

After randomisation, the insulin dosage should be adjusted based on home self monitored blood glucose measurements to achieve the following glycaemic targets: Fasting blood glucose $\leq$ 5.5 mmol/l (100 mg/dl) and post-prandial blood glucose $<$ 7.5 mmol/l (135 mg/dl).(Ref.1)

The total time from randomisation to trial end will be 26 weeks.  
(MD01661)

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**A 24 Week, Open, Controlled, Randomized, Multinational, Multicenter, Phase II b Clinical Study to Investigate the Efficacy and Safety of Lantus® Insulin Analogue (Once Daily at Bedtime) Plus Amaryl® (Glimepiride) and NPH Basal Insulin (Once Daily at Bedtime ) Plus Amaryl® in 440 Patients with Type 2 Diabetes Mellitus Who Fail Good Metabolic Control with Oral Antidiabetic Drugs (OADs)**

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

□ 10 August 2001

❖ Aventis Pharma Ltd.

This is an open-label, NPH human insulin-controlled, randomized (1:1), parallel groups, multinational, multicenter study.

The study consists of a 3/4-week screening phase and a 24 – week treatment phase, with 2 screening visits (week –4/-3, and –3/-2), 1 baseline visit (week 0), and 8 on-treatment visits (weeks 2, 4, 6, 8, 12, 16, 20, 24 or end of treatment). Patients will be switched from their previous OADs treatment to Amaryl on visit 2. within the treatment phase, insulin will be administered according to a predefined titration regimen.

To compare the effect of Lantus® insulin analogue (once daily, at bedtime) plus Amaryl® and NPH basal insulin (once daily, at bedtime) plus Amaryl®, on glycated hemoglobin (HbA1c) in insulin naïve patients with type 2 diabetes mellitus who fail good metabolic control with oral antidiabetic agents.

To compare Lantus® insulin analogue (once daily, at bedtime) plus Amaryl® and NPH basal insulin (once daily, at bedtime) plus Amaryl®, on the rate of hypoglycemia.

(MD01709)

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**A Randomised, Multi-centre, Double-blind, Double-dummy, Parallel Group Trial of Two Doses of NNC 61-0029 in Combination with Glibenclamide versus Glibenclamide Monotherapy and versus Combination Therapy of Glibenclamide and Metformin in the Treatment of Type 2 Diabetic Subjects (Phase IIIa)**

✉ CHOW Chun Chung Francis • Clive Stewart COCKRAM • SO W Y\* • CHAN W B\*

□ 1 November 2001

❖ Novo Nordisk Asia Pacific Pte Ltd

This is a 6-month multi-centre, multi-national, double-blind, double dummy, asymmetrically randomised (2:2:1:2), 4 armed-parallel group trial of two doses of NNC 61-0029 in combination with glibenclamide versus glibenclamide monotherapy and versus combination therapy of glibenclamide and metformin in patients with type 2 diabetes.

*The primary objectives are:*

(1) To compare the efficacy of two doses of NNC 61-0029 in combination with glibenclamide versus glibenclamide monotherapy and versus glibenclamide and metformin combination therapy on glycaemic control in the treatment of type 2 diabetes as assessed by HbA<sub>1c</sub>.

(2) To compare the triglyceride lowering effects of two doses of NNC 61-0029 in combination with glibenclamide versus glibenclamide monotherapy and versus glibenclamide and metformin combination therapy as assessed by triglyceride.

(MD01754)

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**A 12-week, Multi-centre, Double-blind, Randomised, Placebo-controlled Trial on Low Dose Repaglinide for the Treatment of Impaired Glucose Tolerance in Asian Subjects**

✉ CHOW Chun Chung Francis • Clive Stewart COCKRAM • MA Ronald\* • CHAN W B\*

□ 20 January 2002

❖ Novo Nordisk Asia Pacific Pte Ltd

The objectives are:

The effects of low dose (0.25mg at mealtimes) repaglinide compared to placebo in different ethnic subjects (Chinese, Indians and Malays) with IGT will be assessed after 12 weeks of treatment based on the following parameters:

(1) *Primary objective* is to assess the effect on 2 hour plasma glucose as measured by oral glucose tolerance test (OGTT),

(2) *Secondary objectives* are (a) to assess the glycaemic control as measured by OGTT profile of plasma glucose, insulin, C-peptide, serum fructosamine and HbA<sub>1c</sub>. (b) to assess lipid profile

(triglycerides, total cholesterol and HDL- and VDL-cholesterol).  
(MD01479)

**Reference Lung Function Values and the Effects of Smoking on Lung Function in Chinese Adults in Hong Kong**

✉ HUI Shu Cheong David • CHAN Tung# • CHOY Ka Leung Dominic • CHAN Pui Yu\* • LEUNG Mei Yi\* • TONG Wai Ching\*

□ 1 February 2001

❖ Hong Kong Thoracic Society

Lung function test is an important tool in the diagnosis of many respiratory diseases. Interpretation of results relies on comparison with reference values. Adult lung function reference values currently in use in HK are based on either local data obtained two decades ago or overseas data. It is therefore highly desirable to obtain a new set of lung function data from 'normal' adults in HK. Smoking is well known to adversely affect lung function according to the Caucasian data. We plan to include smokers with the aim of studying the effects of smoking on lung function decline in Chinese subjects. This is multi-center cross sectional study in HK. Random subject recruitment is performed by a telephone interviewer. The subjects will be asked to complete a questionnaire on lung health and if suitable, they will be invited to have a lung function test and blood test for haemoglobin determination at the nearest participating hospital. The American Thoracic Society questionnaire for chronic obstructive pulmonary disease will also be completed. The target sample size for the whole project is 2000 subjects, consisting of 1000 male and 1000 female subjects of various ages ranging from 18 to 80 years of age. The expected time frame of the study will be 2/2001 to 12/2002. The study is funded by the Pneumoconiosis Fund Board.  
(MD00494)

**The Effects of Nasal Continuous Positive Airway Pressure Treatment on Cardiac Structure, Function and Cardiac Natriuretic Peptide Levels in Obstructive Sleep Apnoea**

✉ HUI Shu Cheong David • John Elsby SANDERSON

□ 1 August 2001

❖ CUHK Research Committee Funding (Direct Grants)

Obstructive sleep apnoea syndrome (OSAS) is a common form of sleep-disordered breathing (SDB) affecting 2 to 4% of the middle-aged adults. Repetitive episodes of obstructive respiratory events cause sleep fragmentation, hypoxia and, in more severe cases, respiratory failure. Excessive daytime sleepiness (EDS) is a major consequence of OSAS and results from fragmented sleep and micro-arousals associated with obstructive respiratory events. Nocturnal diuresis is another common manifestation and is thought to be due to release of atrial natriuretic peptide (ANP) with some conflicting data. Brain natriuretic peptide (BNP), recently noted to be elevated in patients with left ventricular dysfunction with poor prognostic implications, has also been reported to be increased in OSAS.

Several large epidemiological studies have recently shown an independent association between SDB and systemic hypertension. While we have previously shown a high prevalence of SDB, predominantly of obstructive type, in HK Chinese patients with diastolic heart failure, there is little published data concerning the prevalence of cardiac dysfunction in patients with OSAS despite a strong epidemiological link between SDB and systemic hypertension. Both ANP and BNP promote water and salt excretion and may play a protective or compensatory role against blood pressure (BP) increases in OSAS. While there is robust evidence that nasal continuous positive airway pressure (CPAP) can improve EDS, cognitive function and quality of life in patients with OSAS, it is unclear whether long-term CPAP treatment can improve cardiac function and BP control.

This study aims to assess the cardiac structure and function in patients with OSAS by echocardiography together with concomitant measurement of cardiac natriuretic peptide levels (ANP and BNP) and 24 hour BP before, 6 and 12 months after commencing nasal CPAP treatment.  
(MD01436)

**Evaluation of Subjective Sleepiness and Prevalence of Obstructive Sleep Apnoea and Sleep Disordered Breathing in a Population of Commercial Drivers**

✉ HUI Shu Cheong David

□ 1 October 2001

❖ Health Care & Promotion Fund, Hospital Authority

According to the Hong Kong Government statistics, there have been over 14,000 Motor Vehicle Accidents (MVA) per year with a fatality rate of 33 per million of population and 39 drivers died in drink driving related accidents in 1996-1998. The local mass media and the local authority tend to attribute these accidents to over-speeding and excessive alcohol consumption with little attention paid to driver sleepiness as an underlying cause of the MVA. This large cross-sectional epidemiological study will provide data concerning the degree of subjective sleepiness and the prevalence of OSA among the commercial bus drivers. All the drivers of a major bus company will be recruited and assessed by the Epworth sleepiness scale (ESS) for their degree of subjective sleepiness, the Sleep & Health Questionnaire (SHQ) for common symptoms of OSA and the Calgary Sleep apnoea quality of life index (SAQLI) for quality of life. Basic demographics such as age, sex, body mass index, hip to waist ratio, sleep/work schedule and alcohol consumption will be recorded. Subjects who have completed the questionnaire and consented for sleep study will be randomly invited to undergo partial home sleep study with the Mesam IV device (Madaus Medizin-Elektronik, Freiburg, Germany). From the Health education and promotion point of view, the data will be most useful in providing an information base to enhance public awareness of OSA among the drivers, the medical profession, legislators and the licensing authority. If a high prevalence of OSA is found, then hopefully appropriate actions will be taken by all the parties involved in order to improve road safety. (MD01948)

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**Heart Failure in Hong Kong: Epidemiology, Aetiology and Determinants of Prognosis**

✉ John Elsby SANDERSON • WOO Kam Sang

□ 1 July 2001

❖ Institute of Heart Health Promotion

Heart failure is recognized to be increasing worldwide, to cause considerable ill health and to have a poor prognosis from the time of diagnosis. It is a common cause of hospital admissions in Hong

Kong and rising. The previous studies of patients admitted into the Prince of Wales Hospital suggested that hypertension was the commonest cause with coronary artery disease (ischaemic heart disease) a close second. However, there are no data available for the whole of the SAR on the causes of heart failure and its prognosis once diagnosed. We plan therefore to undertake a SAR-wide survey of heart failure, (in fact a heart failure registry), to obtain more accurate information on the prevalence and incidence of heart failure in Hong Kong, the main risk factors or causes, what is the outcome once it is diagnosed and what are the main predictive factors from the clinical, echocardiographic and genetic studies. We also wish to assess the relative importance of so-called diastolic heart failure (heart failure with preserved systolic function) in this community. This study will also act as a spring-board for larger treatment trials of heart failure to provide more appropriate local information on the best treatment strategies for this serious condition. (MD01892)

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**TRANSCEND - Telmisartan Randomized Assessment Study in aCE iNtolerant Subjects with Cardiovascular Disease Trial**

✉ John Elsby SANDERSON • YEUNG Leata Y.C.\* • CHAN Kit Wan Skiva • WU Eugene Brian\* • WONG John\* • CHAN Anna\* • MA Wing Yan

□ 17 June 2002

❖ Hamilton Health Sciences Corporation on behalf of Boehringer Ingelheim (Canada) Ltd.

A large, simple, randomized, double-blind, multicentre, international trial comparing the effects of Telmisartan with placebo on outcomes in patients at high risk for cardiovascular events and intolerant of ACE-I. (n=5,000)

This parallel trial is to determine if telmisartan 80 mg daily is superior to placebo in reducing the composite endpoint of cardiovascular death, MI, stroke or hospitalization for CFH. The secondary objectives are similar to those in ONTARGET, but comparing the effects of telmisartan 80 mg daily with placebo. (MD01729)

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**ONTARGET - Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial**



✉ John Elsby SANDERSON • YEUNG Leata Y.C.\* • CHAN Kit Wan Skiva • WU Eugene Brian\* • WONG John\* • CHAN Anna\* • MA Wing Yan

□ 17 June 2002

❖ Hamilton Health Sciences Corporation on behalf of Boehringer Ingelheim (Canada) Ltd.

A large, simple, randomized, double blind, multicentre, international trial comparing the effects of Telmisartan, Ramipril and their combination on outcomes in patients at high risk for cardiovascular events (n=23,400).

*Primary objectives:* To determine if (1) Telmisartan 80 mg daily and Ramipril 10 mg daily combination therapy is more effective in reducing the composite endpoint of CV death, MI, stroke or hospitalization for CHF compare with Ramipril 10 mg alone; and (2) Telmisartan 80 mg daily is at least as effective as (i.e. not less effective than) Ramipril 10 mg daily, on this endpoint.

*Secondary objectives:* To determine and effects of the treatments on incidence of newly diagnosed CHF, revascularization procedures, newly diagnosed diabetes mellitus, cognitive decline and dementia, and new onset of atrial fibrillation.

*Others:* To determine incidence of all cause mortality, non-CV death, LV hypertrophy (by ECG), changes in BP, acute ischemic syndrome, transient ischemic attack, nephropathy, microvascular complications diabetes, and changes in ankle-arm BP ratio.

(MD01796)

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**A Comparative Study of the Long-term Outcomes of Two Orthopaedic Services with and without Geriatric Liaison in Older Hip Fracture Patients**

✉ KWOK Chi Yui Timothy • WOO Jean • LAU Edith Ming Chu (Dept of Community and Family Medicine) • LEUNG Ping Chung (Dept of Orthopaedics & Traumatology)

□ 1 December 2001

❖ CUHK Research Committee Funding (Direct Grants)

Hip fracture is a major cause of disability and mortality in old age in Hong Kong. There have been few studies on outcomes of hip fractures in Hong Kong. Apart from the costs of acute hospital

care, the costs of rehabilitation and subsequent social care have not been investigated. Overseas studies suggest that coordinated interdisciplinary rehabilitation, and involvement of geriatricians (physicians for elderly) may shorten hospital stay and prevent old age home placement. We therefore propose to compare the short and long term outcomes of older hip fracture patients managed by a traditional orthopaedic service supported by physicians on request with those by a service with close liaison with geriatricians in the acute care and a geriatrician led rehabilitation programme in the convalescent phase. The medical and social costs of both groups will also be compared. A total of 530 community dwelling subjects above 64 years old will be recruited from two hospitals, and followed up prospectively for one year. The primary outcome is survival without institutionalization. The secondary outcomes are functional level, handicap, direct medical and social costs, and indirect costs. The determination of incremental medical and social costs will facilitate cost effectiveness analysis of any preventive programmes against hip fractures in Hong Kong. Jockey Club Centre for Osteoporosis Care and Control, School of Public Health, the Chinese University of Hong Kong will provide additional manpower to complete the study.

(MD01886)

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**Histologic and Cell Kinetic Changes of Premalignant Gastric Lesions with Helicobacter Pylori Eradication and Cyclooxygenase-2 Inhibition**

✉ LEUNG Wai Keung • CHAN Ka Leung Francis • CHAN Wing Yee (Dept of Anatomical & Cellular Pathology) • CHUNG Sheung Chee Sydney (Dept of Surgery) • NG Enders Kwok-wai (Dept of Surgery) • SUNG Joseph Jao Yiu • YU Jun

□ 1 September 2001

❖ Research Grants Council (Earmarked Grants)

Gastric cancer is a leading cause of cancer mortality in China. While *H. pylori* plays an important role in triggering the gastric carcinogenesis cascade, we have previously shown that eradication of *H. pylori* alone is insufficient in retarding this progression. Thus far, no treatment has been shown to effectively reverse the histological progression of premalignant gastric lesions (glandular atrophy, intestinal

metaplasia, dysplasia). Recently, there is compelling epidemiological and experimental evidence suggesting that cyclooxygenase-2 (COX-2) plays an important role in carcinogenesis, including gastric cancer. Inhibition of COX-2 appears to be a promising chemopreventive agent in cancers of the digestive tract, possibly by inducing apoptosis and inhibiting angiogenesis. In this prospective randomized placebo-controlled study, we will examine the effects of COX-2 inhibition on premalignant gastric lesions. The histological progression of intestinal metaplasia will be monitored and correlated with changes in cellular expression of COX-2, peroxisome proliferator-activated receptors (PPAR), cellular apoptosis (programmed cell death) and proliferation. The results of this study will yield important data on pathways of gastric cancer development and provide directions for its prevention.

(MD01061)

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**A Multicentre, Randomised, Double-blind, Placebocontrolled Dose-finding Phase II Study of Subcutaneously Administered Onercept in the Treatment of Patients with Active Crohn's Disease (Protocol: 22523) and Long-term Follow-up of Crohn's Disease Patients Having Completed Serono protocol 22523, Allowing for Re-treatment with Open-label Onercept (Protocol: 23054)**

✉ LEUNG Wai Keung • LEONG Rupert Wing Loong • CHAN Ka Leung Francis • HUNG Cheung Tsui

□ 1 April 2002

❖ Serono International SA

Crohn's disease is an inflammatory bowel disease of unknown etiology for which no curative treatment is available. TNF-alpha has been identified to play a pivotal role in the pathophysiology of Crohn's disease. Onercept is a recombinant form of human soluble TNF binding protein that may have an effect on active Crohn's disease. This is a multicentre, randomized, double-blind and placebo controlled study that evaluate the effectiveness of subcutaneously administered onercept in the treatment of patients with active Crohn's disease and in the re-treatment with open-label onercept.

(MD01458)

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**A Randomized, Double-blind Study of Treatment with LdT, Lamivudine, or the Combination of Both Agents in Adult Patients with HBeAg-positive Chronic Hepatitis B**

✉ LEUNG Wai Yee Nancy

□ 24 January 2002

❖ PharmaResearch Corporation

Primary:

(1) To determine which of two doses of LdT (400 mg vs. 600mg per day) produces better antiviral effects (reduction in serum HBV DNA) in adults with HBeAg-seropositive chronic hepatitis B.

(2) To characterized the safety and tolerability of four investigational treatment regimens (LdT 400mg/day, LdT 600mg/day, LdT 400mg/day + lamivudine 100mg/day, or LdT 600mg/day + lamivudine 100mg/day).

Secondary:

(1) To determine whether the combination of LdT with lamivudine produces superior antiviral effects compared to either agent alone.

(2) To compare the antiviral activity of the four investigational regimens with that of lamivudine monotherapy (100mg/day).

(3) To derive preliminary data on clinically relevant efficacy endpoints at the end of 52 weeks of treatment with the four investigational regimens (e.g. HBeAg loss and HBeAg seroconversion, HBsAg loss and HBsAg seroconversion, and ALT normalization).

(4) To determine the frequency of virologic breakthrough during 52 weeks of treatment with each of the four investigational regimens, and mutations in the HBV polymerase gene that may be associated with virologic breakthrough in each treatment group.

(MD01585)

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**Endothelial Dysfunction as an Early Index of Atheromatous Disease in Systemic Lupus Erythematosus and its Association with Markers of Oxidative Stress and Inflammatory Mediator**

✉ LI Kwok Ming Edmund • THOMAS Neil G (School of Pharmacy) • Brian TOMLINSON • TAM Lai Shan\*

□ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Systemic lupus erythematosus (SLE) presents with a wide range of clinical manifestations and is a chronic systemic disease involving multiple organs, characterised by autoantibody production and has a high burden of cardiovascular disease. In Chinese, SLE is 4-5 times more common relative to Caucasian populations. Measures of endothelial dysfunction have been shown to predict coronary heart disease (CHD) events. The inflammatory nature of SLE is thought to contribute to atherogenesis at multiple stages throughout this process and autoantibodies can cause vascular damage and modify the LDL promoting foam cell genesis. Although conventional risk factors also play an important role in this process, little is known as to the impact of autoantibodies and other inflammatory mediators on endothelial function in lupus. The identification of these associations will allow a clearer understanding of the accelerated atherogenesis in patients with SLE. Assessment of endothelial function, as a surrogate marker of atheroma, in SLE will enable a better understanding of the earlier stages in the process, rather than observing the end points in patients with vascular events, the survivors of which may not be representative of the group as a whole. Atherosclerosis is a chronic process that takes years to manifest itself and as such factors involved in the initiation of the disease may differ from those promoting endpoint events and may be masked by changes resulting from such events. These data from this study will help improve our understanding of the pathogenic mechanisms that promote the development of atherosclerosis in this patient group. (MD01333)

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**Salvage of Infarcted Myocardium by an Extract of Dagencao with Dual Effects on Angiogenesis and Cardiomyogenesis and Investigation of the Molecular Mechanism Involved in Dagencao Induced Angiogenesis & Cardiomyogenesis**

✉ LI Ming • John Elsby SANDERSON • LEE Ka Ho Kenneth (Dept of Anatomy) • LEUNG Ping Chung (Dept of Orthopaedics & Traumatology)

☐ 1 January 2002

❖ CUHK Strategic Research Program

Ischemic coronary heart disease remains the leading cause of death worldwide. Current available therapeutic approaches can relieve symptoms mainly by surgery or angioplasty. These are crude

techniques and not so effective. Ideally we require a medicine that will stimulate the growth of new vessels (angiogenesis) at due course to replace those affected by disease, stimulate the regeneration and replacement of lost myocytes and reduce scar tissue formation. The heart is composed of myocytes that have been considered as terminally differentiated cells that cannot divide. In decades, many efforts have been devoted to the research of trying to regenerate cardiomyocytes, but up to now the dead lock of cardiac myocytes still cannot be opened.

In our recent studies we identified an extract of a Chinese herbal medicine-Dagencao (ECD) that showed potent dual effects on stimulating early growth of new vessels (<24h) and myogenesis/cardiomyogenesis in rat skeletal muscle injury and rabbit acute myocardium infarction models. In comparison to the period of weeks of naturally occurring angiogenesis and angiogenesis by using growth factors, ECD induced angiogenesis takes less than 24 hours. Induction of cardiomyogenesis has long been our dreams but never been achieved no matter *in vitro* or *in vivo*. Therefore, our ECD induced early angiogenesis and cardiomyogenesis are groundbreaking findings that would doubtlessly open a new era for future research of cardiology and the development of new strategies/drugs to treat ischemic diseases. Although both early angiogenesis and cardiomyogenesis can be reproduced with the administration of our ECD, the mechanism underlying remains challenging.

There is no doubt that research in the field of myocardial regeneration has a remarkably exciting future. This is reflected by a recent statement of the special emphasis panel at the National Heart, Lung and Blood Institute in the USA, which was assigned to identify areas, which should be in the focus of cardiovascular research within the next decades (1). Therefore, the main line of the present strategic research planning is to investigate the underlying mechanism of ECD-induced early angiogenesis and cardiomyogenesis and development of new strategies/drugs for the treatment of heart diseases.

Both genomic and proteomic strategies will be used to identify the differentially expressed genes between ECD treated specimens and control specimens. PCR-select differential screening strategy will be used to identify true differentially expressed clones in the constructed subtracted cDNA libraries from above specimens. The identities of those differentially expressed protein spots from proteomic

study will be analyzed by MALDI TOF. Immunochemical histology will be used to detect the location and the timing profiles of some known angiogenesis-associated inhibitory and mitogenic factors. The possible signal transduction pathway involved in ECD induced early angiogenesis and cardiomyogenesis will also be studied using CLONTECH signal transduction pathway profiling strategy. All data obtained from above different strategies will be analyzed using bioinformatics to elucidate the mechanism involved. Clinical evaluation of the synergistic effects of ECD on heart infarction animal model will be performed, such as echocardiography, myocardial perfusion using echo-contrast agents; magnetic resonance analysis, myocardial perfusion using MR perfusion or angiography using micro-CT.  
(MD01972)

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**A Phase II Study of Lamivudine Compared to Lamivudine Plus Adefovir Dipivoxil for Patient with Chronic Hepatitis B**

- ✉ SUNG Joseph Jao Yiu • CHAN Lik Yuen • CHAN Ka Leung Francis • LEUNG Wai Yee Nancy
- ☐ 1 January 2001
- ❖ Glaxo Wellcome China Limited

This is a randomized, double blind, active controlled trial, evaluating the safety and efficacy of 52 weeks combination treatment of lamivudine and adefovir dipivoxil compared to treatment with lamivudine alone in patients with chronic hepatitis B. Subjects will be randomized to receive open label lamivudine 100mg orally once daily, plus either adefovir dipivoxil 10mg orally once daily or matching placebo.

The study objectives are to assess the antiviral effect of 16 weeks treatment of the combination of lamivudine and adefovir dipivoxil compared to treatment with lamivudine alone, in addition to assessing both the antiviral effect and clinical benefit of 52 weeks of the continued study treatment. The adefovir dipivoxil treatment will be blinded with respect to the placebo treatment for the 52 weeks of the trial.

Approximately 100 subjects (male or female),  $\geq 18$  years of age, with chronic hepatitis B will be randomized at a minimum of 10 investigational centers in North America, Europe, Australia, and

Asia. Subjects will be eligible as determined by protocol inclusion/exclusion criteria.

The primary efficacy endpoint is virologic response (HBV DNA reduction), measured as a time weighted change in HBV DNA from baseline to Week 16 (DAVG<sub>16</sub>). The principal secondary endpoint is the proportion of patients achieving serum ALT normalization by the end of treatment on two successive visits (Week 48 and 52).

Safety will be assessed by comparing clinical adverse events as well as incidence of graded laboratory abnormalities.  
(MD00505)

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**A Multi-centre, Asia Pacific, Double-blind, Placebo-controlled, Randomized, Parallel-group, Fixed Dose Study to Evaluate the Efficacy, Safety and tolerability of Zelmac®(Tegaserod) in Patients with Non-D-IBS**

- ✉ SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • LEUNG Wai Keung • WU Che Yuen Justin
- ☐ 1 April 2001
- ❖ Novartis Pharmaceuticals (HK) Ltd

The aim of the study is to investigate the efficacy, safety and tolerability of Zelmac® (tegaserod) in patients with non-D-IBS.  
(MD00601)

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**Multicenter Open Label Expanded Access Program Of Peg-Interferon Alfa 2a (Ro-25=8310) And Combination Therapy With Ribavirin (Ro-20-9963) In Patients With Hepatitis C**

- ✉ SUNG Joseph Jao Yiu • CHAN Lik Yuen • CHAN Ka Leung Francis • LEUNG Wai Yee Nancy • HUNG Cheung-tsui Lawrence\*
- ☐ 1 February 2002
- ❖ Roche Hong Kong Limited

This is a multicenter, multinational, open-label study on the use of pegylated interferon alfa-2a (Peg-IFN) and combination with ribavirin in the treatment of patients with chronic hepatitis C. Patients > 18 year old with serological and histological proven chronic hepatitis C would be recruited into the study. Co-infection with hepatitis B or HIV, severe medical or psychiatric illness and pregnancy are excluded

from the study. Patients will be allocated into group A (Peg-IFN monotherapy for 48 weeks), group B (Peg-IFN plus ribavirin for 24 weeks) or group C (Peg-IFN plus ribavirin for 48 weeks) to the discretion of the investigator. Patients will be followed up 24 weeks post-treatment. Adverse events and treatment response will be monitored regularly on follow-up. A total of 10 patients are expected to be recruited from Prince of Wales Hospital. (MD01964)

### Genomic Study of Viral Hepatitis B to Predict Development of Cancer and Response to Therapy

- ✉ SUNG Joseph Jao Yiu • CHAN Lik Yuen • LEUNG Wai Yee Nancy • MOK Shu Kam Tony (Dept of Clinical Oncology) • Philip James JOHNSON (Dept of Clinical Oncology) • TSUI Kwok Wing (Biochemistry) • WAYE Mary Miu Yee (Biochemistry) • LEUNG Kwong Sak (Dept of Computer Science and Engineering) • HENG Pheng Ann (Dept of Computer Science and Engineering) • LEE Kin Hong (Dept of Computer Science and Engineering)
- ☐ 1 April 2002
- ❖ Funding from Other Sponsors • Innovation and Technology Support Programme, ITF, Innovation & Technology Commission

Infection by hepatitis B virus (HBV) leads to chronic hepatitis, cirrhosis and liver cancer (HCC). It is a major global health problem affecting over 300 million people in the world, but mostly in Asia.

Despite strong epidemiological evidence correlating HBV infection and HCC, there is no viral marker identifying high-risk of cancer development. On the other hand, while lamivudine and other anti-viral therapy have been developed for the treatment of HBV infection, the response to these anti-viral agents and the development of mutant viral strains are unpredictable.

We aim to establish a database of viral genome and clinical data based on a large cohort of HBV infected individuals who developed HCC or who received anti-viral therapy. Data generated from this database will be used to identify genetic markers for (1) the development of liver cancer and (2) predicting response to antiviral therapy. (MD01639)

### Physiological Control of Peritoneal Permeability: A Study of the Interactions between Leukocytes, Mesothelial and Endothelial Cells

- ✉ SZETO Cheuk Chun • Li Kam Tao Philip\* • WONG Yuk Hwa, Teresa\*
- ☐ 1 October 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

*Background:* Peritoneal dialysis (PD) is the first-line renal replacement therapy in Hong Kong. PD uses peritoneum, the lining of the abdominal cavity, as the interface for removal of metabolic wastes. The permeability of peritoneum plays a critical role in the success of therapy. Peritoneal permeability is governed by a paracrine system that involves macrophage, mesothelial and endothelial cells. Recently, studies in other organ systems showed that vascular endothelial growth factor (VEGF) has a profound effect on the permeability and growth of capillary endothelium, which is the major site of peritoneal transport resistance.

*Objective:* To study the role of VEGF in the paracrine system of peritoneal macrophage-mesothelial-endothelial cells. Our experiments will focus on mesothelial and endothelial cell proliferation, collagen synthesis, and cellular expression of water channel.

*Method:* We use primary culture of rat mesothelial and peritoneal endothelial cells, and an immortalized macrophage cell line. Mesothelial production of VEGF in response to dialysis solution and inflammatory stimuli is examined by quantitative PCR and ELISA. Secondly, the effects of VEGF on mesothelial and endothelial cells, including cell proliferation and expression of water channel, are examined by co-culture experiments.

*Significance and Potential:* Peritoneum is the lifeline of renal failure patients; better understanding on peritoneal physiology would have implications on the long-term success of peritoneal dialysis. This model may also advance our understanding in bacterial peritonitis, peritoneal adhesion after surgery, and ovarian hyper-stimulation syndrome. (MD01550)

### Genetic Factors in the Etiology of Middle Cerebral Artery Stenosis in Chinese with Diabetes and Hypertension

✉ WONG Ka Sing Lawrence • THOMAS Neil G (School of Pharmacy) • Brian TOMLINSON • KAY Li Chi Richard

☐ 1 September 2001

❖ CUHK Research Committee Funding (Direct Grants)

Stroke is one of the commonest causes of disability and death worldwide. Despite the advances in the field of molecular biology, the progresses in studying the genetic factors of stroke have been limited. Furthermore, genetic study on Chinese stroke patients has not been published. Stroke is a heterogeneous condition with very different stroke mechanisms: ischemic versus hemorrhagic; cardioembolism versus large artery stenosis versus small artery disease; intracranial versus extracranial stenosis. Therefore, the phenotype of the study population need to be well-characterised. In Chinese, intracranial larger artery stenosis is the commonest vascular lesion identified in stroke patients, while extracranial carotid stenosis is the commonest lesion found in Caucasians. Genetic factors may play an important role in this observed differences. With a previous RGC-supported grant studying the prevalence of asymptomatic middle cerebral artery stenosis in Hong Kong Chinese, we have identified 100 patients with both hypertension and diabetes. We propose to recruit 200 more to study a total of 300 patients with MCA stenosis. 300 patients with both hypertension and diabetes but without MCA stenosis will be recruited as control. We plan to compare the difference in the prevalence of polymorphism of common genes.  
(MD01965)

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**Management of Atherothrombosis with Clopidogrel in High-risk Patients with Recent Transient Ischemic Attack or Ischemic Stroke: A Randomised, Double-blind Study, with 18 Months of Follow-up**

✉ WONG Ka Sing Lawrence

☐ 1 October 2001

❖ Sanofi Synthelabo Recherche

Stroke prevention using aspirin is the standard practice. Clopidogrel is a new antiplatelet agent that has been shown to be slightly better than aspirin. It

is unclear whether combination of aspirin + clopidogrel is better than clopidogrel alone.

This is a randomized, double-blind, parallel groups study, comparing the combination of clopidogrel and acetyl-salicylic acid with clopidogrel alone for preventing new ischemic event, after 18 months of follow-up in patients with a recent transient ischemic attack or ischemic stroke and at high-risk of recurrent ischemic event.

*Objective:*

(1) To evaluate whether clopidogrel in combination with acetyl-salicylic acid (ASA) is superior to clopidogrel alone in preventing new ischemic events (cerebrovascular or cardiovascular events) in patients after transient ischemic attack (TIA) or ischemic stroke (IS) and at high-risk of recurrent ischemic event.

(2) To evaluate the safety of long-term administration of clopidogrel in combination with ASA compared to clopidogrel alone.

This is an international multicenter randomized placebo controlled study. The results will have major impact to the daily clinical practice for stroke prevention.

(MD01361)

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**A Phase III, Double-blind, Placebo-controlled, Randomised Study Comparing the Efficacy, Safety, and Tolerability of Sumanriole versus Placebo or Ropinirole, as an Adjuvant to Levodopa, in Patients with Advanced Parkinson's Disease**

✉ WONG Ka Sing Lawrence • MOK Chung Tong Vincent

☐ 1 May 2002

❖ Pharmacia Asia Limited

Parkinson's disease is a common disorder in the elderly patients. Recent clinical trials suggest that dopamine agonists have neuroprotective effect in addition to the symptomatic effect by stimulating the dopamine receptors. Sumanriole is a new dopamine agonist. In this phase III, international, multicentered, double-blind, placebo-controlled, randomized study, we aim to compare the efficacy, safety, and tolerability of sumanriole versus placebo or ropinirole, as an adjuvant to levodopa, in patients with advanced Parkinson's disease.

(MD01488)

**Long Term Care for the Elderly in Hong Kong - What Constitutes Quality and What Resources are Needed to Achieve**

✉ WOO Jean • CHI Iris\* • PHILLIPS David\* • CHAN Alfred\*

☐ 1 October 2001

❖ S K Yee Medical Foundation

The profile and needs of elderly residents of a representative sample of long term care institutions in Hong Kong will be documented using a translated version of the Resident Assessment Care Instrument (to be developed as a palm top programme), and compared with other countries. Areas of quality improvement may be identified and an estimation of the resource needed for quality care may be made. (MD01402)

**A Novel Strategy to Prevent Atherosclerosis in Predialysis Renal Failure: A Clinical Model of Accelerated Atherosclerosis**

✉ WOO Kam Sang • CELERMAJER David S\* • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research) • LUI Siu Fai • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • John Elsby SANDERSON • SZETO Cheuk Chun • YU Wai Yin Alex

☐ 1 July 2001

❖ Research Grants Council (Earmarked Grants)

*Introduction:* Atherosclerosis (heart attacks and stroke) is the most important medical problem of modern society. This is particularly prevalent among chronic renal failure patients, and an accelerated atherogenic process has been implicated. We hypothesize high homocysteine blood level (a novel atherosclerosis risk factor) together with other traditional risk factors contributes to this accelerated process.

*Objectives:* To study the prevalence of hyperhomocysteinaemia and other risk factors in predialysis chronic renal failure in Hong Kong, and to evaluate the impact of oral folic acid (15mg/day) supplementation on surrogate markers of early atherosclerosis (vascular reactivity and inner wall thickness) in chronic renal failure patients with hyperhomocysteinaemia.

*Design:* Prospective double-blind randomized placebo control cross-over study. *Subjects and Methods:* 300 patients with predialysis chronic renal failure (plasma creatinine 200-500µmol/l) will be recruited and the occurrence of hyperhomocysteinaemia (fasting total homocysteine >14µmol/l) identified. Vascular reactivity (flow mediated endothelium-dependent dilation) of brachial (arm) artery and carotid (neck artery) intima-media thickness will be measured by ultrasonography and groups comparison (patients vs normal database; hyperhomocysteinaemic vs normohomocysteinaemic patients) will be made. Oral folic acid (15mg/day) supplementation or placebo capsule will be given for 12 weeks to 50 eligible hyperhomocysteinaemic patients in double-blind randomized cross-over fashion, with 10 weeks placebo washout before crossing over. Vascular reactivity test will be repeated at the end of each treatment period. Open-label folic acid (±vitamin C) will be maintained for 1 year; homocysteine assay, vascular reactivity test and carotid artery scan will then be repeated.

*Primary end-point:* Improvement in endothelial function (vascular reactivity). *Secondary end-points:* Carotid intima-media thickness and carotid atherosclerotic plaques size.

*Significance:* Successful result of this pilot project will establish a firm scientific foundation to embark on larger interventional trial and eventually the evidence-base, for long-term folic acid supplementation intervention programme for primary and secondary prevention of stroke and coronary events in predialysis chronic renal failure.

(MD01070)

**A Non-randomized Evaluation of the Multi-link Rx Vision™ Coronary Stent System in the Treatment of Patients with De Novo Native Coronary Artery Lesions**

✉ WOO Kam Sang • CHAN Wai Man Wilson • TSE Kin Kei Lawrence\*

☐ 20 August 2001

❖ Advanced Cardiovascular Systems, INC.

*Design:* Prospective, open-label, multi-center, global registry.

*Enrollment:* Enrollment of approximately 265 patients with a native, *de novo* coronary lesion in a vessel 3.0 mm – 4.0 mm in diameter and a lesion

length no longer than 25 mm (around 25 patients from Hong Kong)

*Purpose:* To demonstrate the safety and efficacy of the MULTI-LINK RX VISION™ Coronary Stent Systems (CSS) when used to treat patients with native, *de novo* coronary lesions

*Primary Endpoint:* Target Vessel Failure (TVF) at 180 days

*Secondary Endpoint:* Acute success Ischemic, hemorrhagic, and vascular complications

Major Adverse Cardiac Event (MACE) rate in-hospital and at 14 days, 30 days, 180 days, 270 days and 265 days.

TVF rate in-hospital and at 14 days, 30 days, 270 days and 365 days.

Clinically Driven Target Site Revascularization (TSR) at 180 days.

Clinically Driven Target Vessel Revascularization (TVR) at 180 days.

Angiographic in-stent Binary Restenosis ( $\geq 50\%$ ) at 180 days.

(MD01334)

**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>
1998-99	A Multicenter, Double-Blind, Randomized, Parallel, 36-week Dose Escalating Study to Evaluate the Efficacy and Safety of Simvastatin 40 and 80 mg/day Versus Atrovastatin 20, 40 and 80 mg/day in Patients with Hypercholesterolaemia (International) (MD98121C) ✉ Brian TOMLINSON
2000-01	Molecular Biology of Hypertension: A Study Investigating Genetic Markers and Possible Underlying Pathogenic Mechanisms of Hypertension in Chinese (CU00095) ✉ Brian TOMLINSON • CHAN Chung Ngor Juliana • THOMAS Neil G (School of Pharmacy)
1998-99	Mapping Genes for Young Onset Diabetes, Obesity and Diabetic Nephropathy (MD98116)

✉ CHAN Chung Ngor Juliana • CRITCHLEY Julian A J H# • Brian TOMLINSON • CHAN Yan Keung Thomas • Clive Stewart COCKRAM • NG Chor Yin • LEE Shao Chin (Dept of Clinical Oncology) • LEE Suk Kuen • THOMAS Neil G (School of Pharmacy) • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • WONG Wing Kin Gary (Dept of Paediatrics)

1999-00 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 (CU99292)

✉ CHAN Chung Ngor Juliana • NG Chor Yin • LEE Shao Chin (Dept of Clinical Oncology) • Clive Stewart COCKRAM

2000-01 Establishment of a Catalogue of Chinese-specific Genetic Markers for Obesity, Diabetes and Diabetic Kidney Disease (MD20020)

✉ CHAN Chung Ngor Juliana • NG Chor Yin • LEE Shao Chin (Dept of Clinical Oncology) • Clive Stewart COCKRAM • TONG Peter Chun Yip • Brian TOMLINSON • CHAN Yan Keung Thomas • THOMAS Neil G (School of Pharmacy) • CRITCHLEY Julian A J H#

1999-00 Laser Therapy of Hypertrophic Scars (CU99299)

✉ CHAN Hin Lee Henry • CHAN Sun Yin Eric (Dept of Surgery)# • LAU Wan Yee Joseph (Dept of Surgery)

2000-01 Effects of COX-2 Inhibition on Ulcer Healing and Prevention of Recurrent Ulcer Hemorrhage in High-risk NSAID Users (MD00881)

✉ CHAN Ka Leung Francis • SUNG Joseph Jao Yiu



- 2000-01 A Multicentre, Randomized, Double-blind, Cross-over Comparison Trial on the Long-term Glycaemic Control in a Twice Daily Regimen of Biphasic Insulin Aspart 30 (BIAsp 30) and Biphasic Human Insulin 30/70 (BHI 30/70) in Type 2 Diabetics (MD20012)  
 ✉ CHOW Chun Chung Francis • Clive Stewart COCKRAM • CHAN W. B.\*
- 2000-01 A Randomized, Double-blind Safety and Efficacy Study of Losartan Plus Hydrochlorothiazide Versus Losartan as First-line Therapy After 6 Weeks In Patients with Severe Hypertension (232-00) (MD20059)  
 ✉ CHOW Chun Chung Francis • Clive Stewart COCKRAM • Ozaki R\*
- 1999-00 Nocturnal Nasal Positive Pressure Ventilation Plus Oxygen Therapy versus Oxygen Alone in Severe Stable Chronic Obstructive Pulmonary Disease (MD99017)  
 ✉ HUI Shu Cheong David
- 2000-01 The Effects of Nasal Continuous Positive Airway Pressure on Platelet Activation, Fibrinolysis and Activities of the Sympathetic Nervous System and Renal Kallikrein-kinin System in Obstructive Sleep Apnoea (CU00147)  
 ✉ HUI Shu Cheong David • CHENG Gregory
- 1998-99 The 2<sup>nd</sup> Symphony Trial – Sibrafiban Versus Aspirin as Therapy for the Long Term Prevention of Secondary Vascular Events Post Acute Coronary Syndromes (MD98125C)  
 ✉ John Elsby SANDERSON
- 1999-00 The Effect of Adrenergic Receptor Blockade on Myocardial Collagen and Ventricular Remodeling in Heart Failure Post Myocardial Infarction (CU99340)  
 ✉ John Elsby SANDERSON • CHOW Tsun Cheung Louis (Dept of Anatomical & Cellular Pathology) •
- CHOW Sing Sum Moses (School of Pharmacy) • WOO Kam Sang
- 1999-00 The Effects of  $\alpha$ - and  $\beta$ -adrenoreceptor Stimulation on Collagen Production in Cultured Cardiac Fibroblasts (MD99104)  
 ✉ John Elsby SANDERSON • LAI Ka Bik
- 2000-01 A Randomized, Triple-blind, Two Arm Parallel Study of the Efficacy, Tolerability, and Safety of Losartan 50mg Titrated to Losartan 50mg/Hydrochlorothiazide 12.5mg, titrated to Losartan 100mg/Hydrochlorothiazide 25mg Versus Amlodipine 5mg Titrated to Amlodipine 10mg, Titrated to Amlodipine 10mg/Hydrochlorothiazide 25mg in Patients with Isolated Systolic Hypertension (MD20037)  
 ✉ John Elsby SANDERSON • Brian TOMLINSON • FUNG Wing Hong • CHIU Chun Wai Roman# • Chan Kin Yin\*
- 2000-01 Omapatrilat versus Enalapril Randomized Trial of Utility in Reducing Events (OVERTURE) (MD20068)  
 ✉ John Elsby SANDERSON • YEUNG Leata Y.C.\* • CHAN Kit Wan Skiva
- 2000-01 Identification and Isolation of a Chinese Herbal Medicine that Could Enhance Cardiac Muscle Revascularization and Healing Following Heart Muscle Infarction (MD00667)  
 ✉ John Elsby SANDERSON • LI Ming
- 1998-99 The Efficacy of a Community Nurse Specialist in Preventing Hospital Readmission of Older Patients with Chronic Lung Disease and Cardiac Failure (MD98075)  
 ✉ KWOK Chi Yui Timothy • WOO Jean • LAU Edith Ming Chu (Dept of Community and Family Medicine) • LEE Tze Fan Diana (The Nethersole School of Nursing) •

	TANG So Kum Catherine (Dept of Psychology)	1999-00	A Double-blind Placebo Controlled Clinical End-points of Lamivudine in Patients with Hepatitis B Related Cirrhosis (MD98164)
2000-01	Clinical Evaluation of A Ben-chair Monitoring System in Rehabilitation 'Wards for the Elderly (MD20023) ✉ KWOK Chi Yui Timothy • WOO Jean • TSUI Hung Tat (Dept of Electronic Engineering)		✉ SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • TSANG W. C. Steven* • CHAN L. Y. Henry* • HUI Y.*
2000-01	Quality of Life and Handicap of Stroke Survivors in Hong Kong (MD20055) ✉ KWOK Chi Yui Timothy • WOO Jean • KAY Li Chi Richard • YU Ly Mee Ashley (Centre for Clin. Trials & Epidemiological Research) • LEUNG Kwok Fai* • Lo Raymond*	1999-00	Gastric Cancer – A Study on Genetic and Bacterial Mechanisms (MD99092) ✉ SUNG Joseph Jao Yiu • YU Jun • Peter Malfertheiner* • Matthias Ebert*
2000-01	Trefoil Peptides, Cyclooxygenase-2 & Gastric Carcinogenesis (MD00526) ✉ LEUNG Wai Keung • CHAN Ka Leung Francis • SUNG Joseph Jao Yiu	2000-01	Eradication of H. Pylori in Gastro-esophageal Reflux Disease: A Clinical and Pathophysiological Study (MD00307) ✉ SUNG Joseph Jao Yiu • WU Che Yuen Justin • CHAN Ka Leung Francis
2000-01	Elucidation of the Production and Action Mechanisms of Novel Proinflammatory Cytokines IL-17 and IL-18 in Systemic Lupus Erythematosus (MD00306) ✉ LI Kwok Ming Edmund • LAM Wai Kei Christopher (Dept of Chemical Pathology) • WONG Chun Kwok (Dept of Chemical Pathology)	2000-01	A Randomised, Double-blinded, Placebo-controlled Trial of Lamivudine Treatment in HbeAg Negative Chronic Hepatitis B Patients (in Asia) (MD20060) ✉ SUNG Joseph Jao Yiu • CHAN Lik Yuen • CHAN Ka Leung Francis • LEUNG Wai Yee Nancy • HUI Y.*
2000-01	Purification of a Novel Muscle Healing Protein That Enhances Muscle Repair and Regeneration (MD00386) ✉ LI Ming • CHAN Kai Ming (Dept of Orthopaedics & Traumatology) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)	2000-01	Correction of Metabolic Acidosis in Continuous Ambulatory Peritoneal Dialysis Patients with Borderline Dialysis Adequacy-effect on Nutritional Status, Systemic Inflammatory Response & Patient Morbidity (MD20027) ✉ SZETO Cheuk Chun • Li Kam Tao Philip*
2000-01	Relationships of Peroxisomal Proliferator Activated Receptor- $\gamma$ Gene Polymorphisms with Insulin Resistance and Obesity in Chinese Patients with Type 2 Diabetes Mellitus (MD00615) ✉ NG Chor Yin • CHAN Chung Ngor Juliana • Clive Stewart COCKRAM • CRITCHLEY Julian A J H#	2000-01	Spatial Redistribution of Signaling Molecules Following Insulin Stimulation in Rat Skeletal Muscle Cells (MD00720) ✉ TONG Peter Chun Yip • LEE Shao Chin (Dept of Clinical Oncology)
		2000-01	Epidemiology of Cardiovascular Problem in Chinese Continuous Ambulatory Peritoneal Dialysis Patients: Prevalence, Severity & Risk Factors (MD20005)

- ✎ WANG Yee Moon Angela • John Elsby SANDERSON • CHAN Kam Wing (Dept of Diagnostic Radiology & Organ Imaging) • LUI Siu Fai
- 1998-99 The Frequency and Significance of Microembolic Signals in Acute Stroke Patients with Middle Cerebral Artery Stenosis (CU98341)
- ✎ WONG Ka Sing Lawrence • LAM Wai Man Wynn timer (Dept of Diagnostic Radiology & Organ Imaging) • CHAN Yu Leung (Dept of Diagnostic Radiology & Organ Imaging) • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • KAY Li Chi Richard
- 1999-00 A Pilot Study of Early and Aggressive Lipid-lowering Therapy for Atherosclerotic Stroke (MD99041)
- ✎ WONG Ka Sing Lawrence • LO See Kit Raymond\* • Brian TOMLINSON • LAM Wai Man Wynn timer (Dept of Diagnostic Radiology & Organ Imaging) • LAM Wai Kei Christopher (Dept of Chemical Pathology) • KAY Li Chi Richard
- 2000-01 A Multicenter, Open-label Study to Evaluate the Safety, Tolerability and Efficacy of Eletriptan 40mg for the Treatment of Migraine (with or without Aura) in Subjects Unsuccessfully Treated with NSAIDS (MD00343)
- ✎ WONG Ka Sing Lawrence • FU Yat Pang Michael
- 2000-01 A Prospective Study of the Long Term Outcome of Patients with Intracranial Arterial Occlusive Disease (MD00869)
- ✎ WONG Ka Sing Lawrence • LAM Wai Man Wynn timer (Dept of Diagnostic Radiology & Organ Imaging) • LI Huan# • KAY Li Chi Richard
- 2000-01 Effects of the Ultrasound Contrast Enhancing Agent Levovist on the
- Detection of Intracranial Arteries and their Stenoses by Transcranial Doppler Ultrasound (MD20054)
- ✎ WONG Ka Sing Lawrence • E. B. RINGELSTEIN\* • Tjark Hansberg\*
- 2000-01 A Randomized 26-week, Double-blind, Placebo-controlled Trial to Evaluate the Safety and Efficacy of Galantamine in the Treatment of Dementia Secondary to Cerebrovascular Disease (MD00553)
- ✎ WONG Ka Sing Lawrence • HUI Andrew Che Fai • MOK Vincent\*
- 1999-00 The Role of Phytoestrogens in Women's Health (MD99069)
- ✎ WOO Jean • LI Martin • HO CHAN Suzanne (Dept of Community and Family Medicine) • LAU Edith Ming Chu (Dept of Community and Family Medicine) • HAINES Christopher John (Dept of Obstetrics & Gynaecology) • FUNG Kwok Pui (Biochemistry) • CHAN Sui Yin Agnes (Dept of Psychology) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)
- 1999-00 A Study of the Acceptability and Effectiveness of Hip Protectors in Elderly Chinese in the Institutional Setting (MD99010)
- ✎ WOO Jean • SUM Cecilia\*
- 2000-01 Development of the Chinese MNA (MD20041)
- ✎ WOO Jean • KWOK Chi Yui Timothy • HUI E.\*
- 1999-00 Chinese Atherosclerosis in the Aged and Young (Cathay Study) (MD96224)
- ✎ WOO Kam Sang • WOO Jean • John Elsby SANDERSON • CRITCHLEY Julian A J H# • CHENG Gregory • LAM Ching Wan (Dept of Chemical Pathology) • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research)
- 1999-00 Hyperhomocysteinaemia and Arterial Endothelial Dysfunction: An Emerging

- Strategy for Prevention of Atherosclerosis (CU99282)  
✉ WOO Kam Sang • WOO Jean • John Elsby SANDERSON • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • FUNG Kwok Pui (Biochemistry) • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research)
- 1999-00 A Multicenter, Randomized, Controlled, Double-blind Trial to Investigate the Clinical Efficacy and Tolerability of Early Treatment with Simvastatin 40mg Daily for 30 Days, Followed by Simvastatin 80mg Daily thereafter in Tirofiban-Treated Acute Coronary Syndrome Patients Who have been Randomized to Receive Enoxaparin or Unfractionated Heparin in Conjunction with Aspirin. (A to Z study) (MD99072)  
✉ WOO Kam Sang • John Elsby SANDERSON • FUNG Wing Hong\* • CHAN W M Wilson\*
- 2000-01 An Open Prospectively Randomised Comparison of Hirulog Versus Heparin in Patients Receiving Aspirin and Thrombolysis (Streptokinase) for the Treatment of Acute Myocardial Infarction - The Hirulog Early Reperfusion/Occlusion (HERO-2) Trial (MD97341)  
✉ WOO Kam Sang • John Elsby SANDERSON • YIP Wai Kwok Gabriel
- 2000-01 Tolerability and Clinical Application of Platelet Glycoprotein IIb-IIIa Inhibitor (Epifibatide) Therapy in Hong Kong Chinese (MD20063)  
✉ WOO Kam Sang • John Elsby SANDERSON • CHAN Wai Man Wilson • TSE Kin Kee • CHAN C K\* • CHAN S K\*

## RESEARCH OUTPUTS AND PUBLICATIONS

- <P004185> **KO G.T.; CHAN J.C.; TSANG L.L. and COCKRAM C.S.** "Hyperfibrinogenaemia did not Improve after Treating Hyperglycaemia in Chinese Type 2 Diabetic Patients". *Annals of Clinical Biochemistry* vol.37, pp.655-661. 2000.
- <P008021> **KANG DE; PIETRZIK CU; BAUM Lawrence William; CHEVALLIER N; MERRIAM DE; KOUNNAS MZ; WAGNER SL; TRONCOSO JC; KAWAS CH; KATZMAN Robert and KOO EH.** "Modulation of Amyloid Beta-Protein Clearance and Alzheimer's Disease Susceptibility by the LDL Receptor-Related Protein Pathway". *Journal of Clinical Investigation* vol.106 no.9, pp.1159-1166. 2000.11.
- <P011537> **TAM L.S.; LI E.K.; BENZIE I.F.F.; LAM C.W.K.; ARUMANAYAGAM M.; CHUNG W.Y. and TOMLINSON B.** "Metabolic Abnormalities Associated with Microalbuminuria in Systemic Lupus Erythematosus". *Rheumatology* vol.40, pp.1193-1194. UK, 2001.08.
- <P011787> **WOO J.; LI M. and LAU E.** "Population Bone Mineral Density Measurement for Chinese Women and Men in Hong Kong". *Osteoporosis International* vol.12, pp.289-295. 2001.07.
- <P011788> **SANDERSON E. John; HAINES J. Christopher; YEUNG, Leata; YIP W.K. Gabriel; TANG, Kare; YIM So-Fan; JORGENSEN N. Lars and WOO Jean.** "Anti-Ischemic Action of

Estrogen-Progestogen Continuous Combined Hormone Replacement Therapy in Postmenopausal Women with Established Angina Pectoris: A Randomized, Placebo-Controlled, Double-Blind, Parallel-Group Trial". *Journal of Cardiovascular Pharmacology* vol.38, pp.372-383. USA: Lippincott Williams & Wilkins, Inc., Philadelphia, 2001.09.

- <P011790> **SEA Mandy.** "A Pilot Study for the Effectiveness of Weight Management Program". Paper presented in the Centre of Research and Promotion of Women's Health First Scientific Symposium: Research in Women's Health: from Knowledge to Practice, organized by The Centre of Research and Promotion of Women's Health and School of Public Health, The Chinese University of Hong Kong. Hong Kong, 2001.10.21.
- <P011842> **CHENG Alfred S L, CHAN H.L.Y., WONG Nathalie, Philip James JOHNSON and SUNG Joseph Jao Yiu.** "Inhibition of Cox-2 Induces Apoptosis in Hepatoma Cells: Possible Involvement of Fas Receptor/Ligand System". Paper presented in the American Association for the Study of Liver Diseases, 52nd Annual Meeting, Dallas, USA, 2001.11.12.
- <P011843> **RAHMAN P.; GLADMAN D.D.; UROWITZ M.B.; HALLETT D. and TAM L.S.** "Early Damage is a Predictor of Mortality in SLE". *Lupus* vol.10, pp.93-96. UK: Arnold, 2001.09.
- <P011844> **CHENG Alfred S L, GO Yin Yin, CHAN H.L.Y., SAKATA Ryuichiro and SUNG Joseph Jao Yiu.** "Roles of Cyclo-Oxygenase-2 and Prostaglandins on Proliferation of Hepatic Stellate Cells". Paper presented in the 52nd Annual Meeting, American Association for the Study of Liver Diseases. Dallas, USA, 2001.11.12.
- <P011846> **WANG Yee-Moon, Angela; SEA Man-Mei, Mandy; IP, Ricky; LAW Man-Ching; CHOW Kai-Ming; LUI Siu-Fai; LI Kam-Tao, Philip and WOO, Jean.** "Independent Effects of Residual Renal Function and Dialysis Adequacy on Actual Dietary Protein, Calorie, and Other Nutrient Intake in Patients on Continuous Ambulatory Peritoneal Dialysis". *Journal of American Society of Nephrology* vol.12, pp.2450-2457. USA: Lippincott Williams & Wilkins, 2001.11.
- <P011847> **WANG Yee Moon, Angela; WOO Jean; WANG Mei; SEA Man Mei, Mandy; IP, Ricky; LI Kam Tao, Philip; LUI Siu Fai and SANDERSON Elsby, John.** "Association of Inflammation and Malnutrition with Cardiac Valve Calcification in Continuous Ambulatory Peritoneal Dialysis Patients". *Journal of the American Society of Nephrology* vol.12, pp.1927-1936. USA: Lippincott Williams & Wilkins, 2001.09.
- <P011848> **WANG Yee Moon, Angela; MAC-MOUNE, LAI MacMoune Fernand; YU Wai-Yin, Alex; LAM Kwok Wai, Peggio; CHOW Kai Ming; CHOI Cheung Lung, Paul; LUI Siu Fai and LI Kam Tao, Philip.** "Recurrent IgA Nephropathy in Renal Transplant Allografts". *American Journal of Kidney Diseases* vol.38, pp.588-596. USA, 2001.09.
- <P011904> **LO S.K. Raymond; WOO, Jean; ZHOC C.H. Karen; LI Y.P. Charlotte; YEO, Winnie; JOHNSON, Philip; MAK, Yvonne and LEE, Joseph.** "Cross-Cultural Validation of the McGill Quality of Life Questionnaire in Hong Kong Chinese". *Palliative Medicine 2001* vol.15, pp.387-397. Arnold, 2001.
- <P012012> **SZE Kai-hoi; WONG, Eric; LEUNG H.Y. and WOO Jean.** "Falls Among Chinese Stroke Patients During Rehabilitation". *Arch Phys Med Rehabil* vol.82, pp.1219-1225. USA: American Academy of Physical Medicine Rehabilitation, 2001.09.
- <P012021> **SANDERSON J.E.; WANG A.Y.M.; WANG M.; WOO J.; HO P.; SEA M.M.; IP R.; LI P.K.T. and LUI S.F.** "Association of Inflammation and Malnutrition with Cardiac Valve

- Calcification in Patients on Long-Term Continuous Ambulatory Peritoneal Dialysis". *European Heart Journal* vol.22(Abst. Suppl), p.308. UN: European Society of Cardiology, 2001.09.
- <P012022> **BERNARDI L.; PORTA C.; BELLWON J.; SPICUZZA L.; SPADACINI G.; FREY A.W.; YEUNG L.Y.C.; SANDERSON J.E.; TRAMARIN R. and PEDRETTI R.** "Slow Breathing Increases the Arterial Baroreflex in Heart Failure". *European Heart Journal* vol.22(Abst. Suppl), p.295. UN: European Society of Cardiology, 2001.09.
- <P012103> **CHIU C.W.; WOO K.S.; LAM W.W.M.; SO N.M.C.; CHAN K.Y.; WONG T.H.; CHEUNG A.S.P.; CHAN L.L.T.; CHOOK P.; CHAN W.M.; TSE K.K.; SANDERSON J.E. and METREWELI C.** "Assessment of Apical Hypertrophic Cardiomyopathy by Magnetic Resonance Imaging". *Abstracts of the 9th Annual Scientific Congress of the Hong Kong College of Cardiology* 2nd ed., vol.9, p.94. Hong Kong, 2001.09.
- <P012108> **LI K., Edmund.** "Management of Steroid-Induced Osteoporosis". *Hong Kong Bulletin on Rheumatic Disease* vol.1, pp.15-20. Hong Kong: Medcom Ltd., 2001.07.
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## RESEARCH PROJECTS

### Association between Human Leukocyte Antigens and Progression of Oncogenic Human Papillomavirus Infection of the Cervix

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

☐ 1 October 2001

❖ Research Grants Council (Earmarked Grants)

The consequences of infection with genital human papillomaviruses (HPVs) range from spontaneously resolved cytological abnormalities to invasive cervical cancer. Scientific evidences indicate that co-factors are essential, in addition to HPV infection, for cancer development. However, none of the suspected co-factors seems to play a major role.

Clearance of virus-infected cells and tumour cells relies heavily on the host immune response. Since the human leukocyte antigens (HLAs) are important in host immunity, we hypothesize that the HLA type of an individual may be a key determinant for a successful immune clearance of HPV-associated tumour cells.

In this study, the association between HLA immunogenetics and HPV infection in the development of cervical cancer will be investigated. Our study design will address the shortcomings of available data. In addition, we will make use of the unique situation of Chinese population i.e. an unusual high prevalence of a worldwide uncommon oncogenic HPV type (HPV58). This unique epidemiology will enable us to generate data that are otherwise difficult to obtain from other parts of the world. Thus our proposed study should generate novel data with long-term significance on management of patients and vaccine development. Furthermore, the results should have direct benefits to the Chinese population.

(MD01071)

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

✉ HOUANG Ting Sou Elizabeth • LEE Albert (Dept of Community and Family Medicine) • FUNG Kitty S. C.\* • LYON Donald James

☐ 7 January 2002

❖ Health Care & Promotion Fund, Hospital Authority

*AIM 1:* To establish the incidence of household spread of MRSA from colonised patients on discharge from the hospital-A follow up study.

*AIM 2:* To identify the risk factors related to the domestic spread of MRSA-A nested case-control study.

*Design:* Survey

*Setting:* Community

*Subjects:* 414 carries of MRSA who have been discharged home, provided consent has been obtained from patients and their household members.

*Methods:* Over a period of 2 months, questionnaires will be used at home visits to record demographic, personal hygiene practices, visits to healthcare institutions, inter-current illnesses and domestic settings of the patients, his/her household members over a period 2 months. Screening samples for MRSA will also be taken at the same time from carriage sites and domestic environments.

*Results:* Positive swab results for MRSA will be compared with the scores of questionnaire answers, demographic features and hygienic practices of the household and domestic settings.

*Conclusions:* The incidence of household spread, patient risk factors associated with positive homes, domestic setting risk factors associated with secondary cases in the household, and secondary case personal risk factors associated with acquisition of MRSA in secondary cases will be determined. Thus, evidence-based advice to patients after discharge to minimise household spread can be formulated.

(MD01743)

### Study of Pneumococcal Bacteraemia - A Multicentre Observational Study

✉ IP Margaret • HUI Shu Cheong David (Dept of Medicine & Therapeutics) • YU Victor\*

☐ 1 December 1998

❖ Infectious Disease Section, Veterans Administration Medical Centre, University of Pittsburgh

*Streptococcus pneumoniae* is the most common cause of community-acquired pneumonia. Blood cultures are positive in 15-30% of pneumococcal pneumonia cases, depending on the population studied, and to a lesser extent the serotype. The incidence of pneumococcal bacteraemia is extremely high among patients with HIV and other risk factors include alcoholism, liver cirrhosis, and splenectomy. Penicillin has been the antibiotic of choice for pneumococcal infections. In the last decade, *in vitro* resistance by pneumococci intermediately or highly resistant to penicillin have become established in many parts of the world. However, there is little evidence to suggest penicillin-resistant pneumococcal infections outside the central nervous system (bacteraemia and pneumonia) respond poorly to therapy with penicillin. Patients infected with strains of *S. pneumoniae* with 'intermediate' *in vitro* susceptibility (MIC 0.1 to 1.0ug/ml) have not been shown to have poorer outcome as compared to patients infected with susceptible strains (Pallares 95, Baquero 96). Few reports have included comparison of outcome in patients infected with penicillin-resistant (MIC  $\geq$  2.0 ug/ml) versus penicillin-sensitive pneumococci (Friedland 1995), nor dealt with the impact of therapy on outcome. The objectives of the study are to determine the patients' risk factors for acquiring penicillin-sensitive and penicillin-resistant pneumococcal infections; to correlate *in vitro* antibiotic susceptibility of the antibiotics including the new macrolides administered to clinical outcome in patients with pneumococcal bacteraemia, and to assess the relationship between serotypes and resistance among invasive isolates and AIDs patients. (MD98694)

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#### The Epidemiologic Typing of Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Hong Kong

- ✉ IP Margaret • CHENG Fun Bun Augustine • LYON D.J.\* • ENRIGHT M\*
- 15 September 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important pathogen in many hospitals around the world and has become a major global concern. Hospital MRSA infections are serious threats to patients, being associated with high morbidity and

mortality, and represent a significant burden to health care resources. In addition, the emergence of vancomycin-resistant *Staphylococcus aureus* (VRSA) reported in the U.S. and Japan in recent years poses an imminent threat to the future use of vancomycin. The occurrence of VRSA had been associated with epidemic MRSA infections. MRSA is endemic in most Hong Kong hospitals. The epidemiology of MRSA for the years 1988-1999 at Prince of Wales Hospital was reviewed and indicated a changing pattern with a rise during 1995-99. This was associated with a disproportionate rise in MRSA bloodstream infection, suggestive of a change in the predominant strain types and characteristics. Strategies for control of MRSA require an understanding of its epidemiology and surveillance on the types of strains involved. Few longitudinal studies worldwide have tracked the MRSA over an extended period. It would thus be invaluable to establish a system of typing MRSA isolates in Hong Kong so as to study the evolution of the MRSA in an endemic situation over an eleven-years period. The objective of the study is to establish an effective system of typing isolates of MRSA in Hong Kong to track the MRSA types over an eleven-years period so as to identify and recognize the 'epidemic' strains of MRSA.

(MD01646)

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#### The Ability of Different Antimicrobial Agents to Induce and Select Resistant Mutants of *Escherichia Coli* and *Pseudomonas Aeruginosa*

- ✉ LING Mei Lun Julia • CHAN Wai Chi
- 8 October 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Antibiotics are probably the most commonly used group of drugs in hospital and private practice. Due to their widespread use, many microorganisms have developed resistance to almost all available antimicrobial agents. Antibiotic resistance has therefore become a major threat to the public health system in many parts of the world. Developing effective antibiotic resistance control programmes is the prime task of many organizations such as the World Health Organization and the Centres for Disease Control and Prevention. We have shown that different  $\beta$ -lactam drugs that were apparently similarly active against an organism could in fact

induce and select resistant mutants at different rates. Such resistance development rates also varied with different antibiotic-organism combinations. We therefore suggested that not only was susceptibility of the infectious agent to antibiotics important clinically, knowledge of those antibiotics that were least likely to induce or select resistant bacteria was equally important. However, this aspect is often overlooked. We therefore aimed to study the resistance induction/selection potentials of different antibiotics against two organisms frequently encountered in the community and hospital, namely, *Escherichia coli* and *Pseudomonas aeruginosa*, respectively. This study will provide basic information on the ability of drugs of choice to select for resistances in two commonly isolated bacterial pathogens. Such information is vital in the formulation of antimicrobial treatment regimens that are both effective and the least resistance inducing and will be a step forward towards the control of antimicrobial resistance.  
(MD01384)

**Development of a Molecular Typing Method for the Study of Invasive *Candida Albicans* Infection**

- ✉ Mamie HUI • CHENG Fun Bun Augustine
- ☐ 1 November 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

*Candida albicans* is usually a harmless commensal fungus found in small amount on the human body. However, when given the opportunity, it can cause diseases that range from vaginal candidiasis in healthy young women to life-threatening candidemia in immunocompromised patients. Question was often raised on whether the presence of this fungus from different body sites will predate the advent of invasive candidemia in susceptible hosts. Molecular typing methods had been widely employed in the epidemiological investigation of bacterial infections in delineating carriage and route of transmission. Pulse field gel electrophoresis karyotyping, restriction fragment length polymorphism, DNA fingerprinting, hybridization with repetitive DNA elements and arbitrarily primed polymerase chain reaction have been recently described with variable degree of success. We proposed: (1) to establish an optimal molecular typing method for *Candida albicans*; (2) to study the genetic relatedness of

*Candida albicans* isolated from different body sites of patients with *Candida* sepsis; and (3) to study whether specific genotypes are related to invasive disease. The results will provide an understanding of the genetic relatedness of clinical isolates of *Candida albicans*, as well as leading to further studies on early diagnosis of invasive candidemia in high risks patients previously colonized with *Candida albicans*.  
(MD01456)

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

<u>Edition</u>	<u>Title/Investigators</u>
2000-01	Development of a Rapid <i>in vitro</i> Drug Susceptibility Test Method for Mycobacterium Tuberculosis Using Metabolic Markers (CU00097) ✉ CHAN Chiu Yeung Raphael
1999-00	Clinical Significance of Human Herpesvirus 7 Infection in Bone Marrow Transplantation (CU99248) ✉ CHAN Kay Sheung Paul • CHIK Ki Wai (Dept of Paediatrics) • LI Chi Kong (Dept of Paediatrics) • YUEN Man Pan Patrick (Dept of Paediatrics) • CHENG Fun Bun Augustine
2000-01	Viral Load Quantification of Human Papillomavirus: Correction with Staging and Application in Post-treatment Surveillance of Cervical Carcinoma (MD00949) ✉ CHAN Kay Sheung Paul • CHEUNG Tak Hong (Dept of Obstetrics & Gynaecology) • YU Mei Yung (Dept of Anatomical & Cellular Pathology) • YEO Winnie (Dept of Clinical Oncology) • CHIU Kwok Wing Samuel (Dept of Clinical Oncology) • CHENG Fun Bun Augustine
2000-01	A Survey of Drug-resistance Genes in Clinical Isolates of Mycobacterium Tuberculosis and Its Direct Application to the Detection of Drug-resistant M.

- Tuberculosis in Clinical Specimens (CU00098)  
 ✍ CHENG Fun Bun Augustine • CHAN Chiu Yeung Raphael • Mamie HUI
- 2000-01 *In vitro* Antimicrobial Susceptibility of Linezolid (MD00793)  
 ✍ CHENG Fun Bun Augustine • LING Kin Wah Thomas
- 1999-00 Quinolone and Multidrug Resistance in *Acinetobacter* spp (CU99290)  
 ✍ HOUANG Ting Sou Elizabeth • CHU Yiu Wai • IP Margaret • PIDDOCK L. J. V.\*
- 2000-01 Characterisation and Detection of an Integron Carrying the Newly Described Carbapenemase IMP3 Gene (MD00815)  
 ✍ HOUANG Ting Sou Elizabeth • CHU Yiu Wai
- 1999-00 Mechanisms of Macrolide, Lincosamide, Streptogramin (MLS Group) Resistance in Drug-resistant *Streptococcus Pneumoniae* and Other *Streptococci* (CU99331)  
 ✍ IP Margaret • LYON Donald James • CHENG Fun Bun Augustine
- 1998-99 Surveillance of Antibiotic Resistance in the Community – an Approach to Reduce Bacterial Resistance to Antimicrobial Agents (MD98166)  
 ✍ LING Mei Lun Julia • CHAN Wai Chi • CHENG Fun Bun Augustine
- 2000-01 Mechanisms of Fluoroquinolone-resistance in *Salmonellae* in Hong Kong (CU00049)  
 ✍ LING Mei Lun Julia
- 2000-01 Development of a Rapid Diagnostic Method for Invasive Candidiasis by Detection of D/L-arabinitol Using Gas Chromatography / Mass Spectrometry (MD00737)  
 ✍ Mamie HUI • CHAN Chiu Yeung Raphael • CHEUNG Siu Wai • CHENG Fun Bun Augustine
- 2000-01 Virus Isolation in Association with a Multicentre Clinical Trial on the Safety and Efficacy of Influenza Virus Vaccine, Trivalent, Types A & B, Live Cold-Adapted (CAIV-T) in Healthy Children in Asia (MD00369)  
 ✍ TAM Siu Lun John • FOK Tai Fai (Dept of Paediatrics) • CHENG Fun Bun Augustine
- 2000-01 A Prospective, Randomized, Double-blind, Placebo-controlled Trial to Determine the Safety and Efficacy of Influenza Virus Vaccine, Trivalent Types A & B, Live Cold-Adapted (CAIV-T) in Healthy Children (MD00691)  
 ✍ TAM Siu Lun John • FOK Tai Fai (Dept of Paediatrics) • CHENG Fun Bun Augustine • NELSON Edmund Anthony Severn (Dept of Paediatrics) • NG Pak Cheung (Dept of Paediatrics) • CHAN Kay Sheung Paul • LEUNG Ting Fan (Dept of Paediatrics) • MA Kwok Chiu (Dept of Paediatrics) • CHENG Pik Shun (Dept of Paediatrics) • LI Man Chim Albert Martin (Dept of Paediatrics) • FUNG Lai Wah Eva (Dept of Paediatrics) • MOK Chi Fung Geoffrey (Dept of Paediatrics)

## RESEARCH OUTPUTS AND PUBLICATIONS

<P004255> **ADEYEMI-DORO F.A.B.; LYON D.J.; LING T.K.W. and CHENG F.B. Augustine.**  
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- <P012015> **CHAN Kay Sheung Paul, TAM Wing Hung, CHANG Alexander Russell and CHENG Fun Bun Augustine.** "Pregnancy and Cervical Human Papillomavirus Infection : A Case Control Study on Hong Kong Chinese Women". Paper presented in the 19th International Papillomavirus Conference. Brazil, 2001.09.
- <P012016> **LING Kin Wah Thomas, TAM P.C., LIU Z.K. and CHENG Fun Bun Augustine.** "Evaluation of VITEK 2 Rapid Identification and Susceptibility Testing System Against Gram-Negative Clinical Isolates". *Journal of Clinical Microbiology* vol.39 no.8, pp.2964-2966. USA, 2001.08.
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- <P012612> **IP, Margaret.** "Moxifloxacin". *Medical Progress* pp.45-48. Hong Kong, 2001.
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- <P020181> **LING Mei Lun Julia, CHAN Wai Chi and CHENG Fun Bun Augustine.** "Are Community-Acquired Organisms Less Resistant to Antibiotics?". *Clinical Microbiology and Infection* vol.8 (Suppl 1), p.198. Italy, 2002.
- <P020183> **MARGARET Ip; LYON Donald J.; YUNG W.H., Raymond; TSANG Lily and CHENG F.B., Augustine.** "Introduction of New Clones of Penicillin-Nonsusceptible *Streptococcus Pneumoniae* in Hong Kong". *Journal of Clinical Microbiology* vol.40 no.4, pp.1522-1525. USA: American Society for Microbiology, 2002.

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- <P020343> **CHAN K.S., Paul; CHIK Ki-Wai; TO Ka-Fai; LI Chi-Kong; SHING Matthew M.K.; NG King-Cheung; YUEN M.P., Patrick and CHENG F., Augustine.** "Case Report: Human Herpesvirus 7 Associated Fatal Encephalitis in a Peripheral Blood Stem Cell Transplant Recipient". *Journal of Medical Virology* vol.66, pp.493-496. USA: Wiley-Liss Inc., 2002.
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- <P020368> **FUNG Sau Chun Kitty, LAM Tin Keung Edman and LYON Donald James.** "Comparison of Methods for Screening of Methicillin-Resistant *Staphylococcus Aureus* (MRSA)". Paper presented in the 10th International Congress on Infectious Diseases, organized by the International Society for Infectious Diseases. Singapore, 2002.03.
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- <P02542> **TAM S. John.** "Influenza a (H5N1) in Hong Kong: An Overview". *Vaccine* vol.20, pp.S77-S81. England, 2002.
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- <P027658> **CHAN Kay Sheung Paul; LAM Ching Wan; CHEUNG Tak Hong; LI William WH; LO Keith WK; CHAN May YM; CHEUNG Lai Ken Jo and CHENG Fun Bun Augustine.** "Association of Human Papillomavirus Type 58 Variant with the Risk of Cervical Cancer". *Journal of the National Cancer Institute* vol.94 no.16, pp.1249-1253. USA, 2002.

- <P02801> **CHAN Kay Sheung Paul, LAM Ching Wan, CHEUNG Tak Hong, LI W.W.H., LO K.W.K., CHAN M.Y.M., CHEUNG Lai Ken Jo, XU Liying and CHENG Fun Bun Augustine.** "Human Papillomavirus Type 16 Intratypic Variant Infection and Risk for Cervical Neoplasia in Southern China". *GenBank - National Centre for Biotechnology Information* AF478132-AF478167. USA: National Center for Biotechnology Information, 2002.03.27.
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## RESEARCH PROJECTS

### Adherence to Phase II Cardiac Rehabilitation Programme & Psychosocial Outcomes of Clients with Acute Coronary Syndrome

- ✉ CHAN Dominic Shung Kit • CHANG Anne Marie# • CHAU Pak Chun Janita
- ☐ 1 November 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Heart disease continues to be the second cause of death in Hong Kong. A better understanding of the psychosocial status of clients following acute coronary syndromes can assist health professionals in promoting the health of coronary disease survivors. Only a small proportion of eligible clients participated and completed in cardiac rehabilitation programmes. It is therefore, imperative to determine factors that enhance client's decision to participate and their adherence to cardiac rehabilitation programmes. Identification of possible barriers may facilitate health professional to develop strategies to increase client's participation. It is envisaged that the results of this study will also assist health professional in the continual development of cardiac rehabilitation programmes.

*Objectives:* Assess the psychosocial outcome of clients following acute coronary syndromes, and investigate factors contributing to clients' participation in cardiac rehabilitation programmes.

*Design:* Longitudinal study design, data to be collected on 2 occasions from subjects over a period of 6 months following initial hospital admission.

*Setting:* A regional major hospital.

*Subjects:* 168 patients admitted with acute coronary syndromes to the major hospital.

*Main outcome measures:* Hospital Anxiety & Depression Scale (HADS) to assess anxiety and depression, Social Support Questionnaire (SSQ6) to assess social support, State-esteem Scale (SSES) to detect changes in self-esteem. Rosenberg's Self-Esteem Scale (RES) to measure trait self-esteem. Medical Outcome Study Short-Form (SF-36) to assess quality of life, and demographic data including information on clients' intention and reasons to participate in the rehabilitation programme. (MD01339)

### Effectiveness of Interventions for Reducing Breathlessness, Fatigue & Anxiety in Chinese Patients Undergoing Lung Cancer Radiotherapy in Hong Kong

- ✉ CHAN YIP Carmen Wing Han • CHANG Anne Marie# • LEUNG Sing Fai (Dept of Clinical Oncology) • Mak So Shan\*
- ☐ 1 April 2002
- ❖ Health Services Research Fund, Hospital Authority

*Objective:* This study will examine the effectiveness of progressive muscle relaxation (PMR), education combined with PMR and usual care on breathlessness, fatigue and anxiety experience by lung cancer patients receiving radiotherapy (RT).

*Design:* A 3-group randomized controlled trial will be used to compare outcomes among patients who receive PMR, PMR combined with education and usual care

*Setting:* Acute hospital, Oncology department where patients receive radiotherapy

*Subjects:* 184 lung cancer patients undergoing radiotherapy. There will be 61 per group.

*Intervention:* PMR and PMR combined with education.

*Main outcome measures:* VAS of breathlessness and associated distress; Revised Piper Fatigue Scale (PFS) for determining the level of fatigue, and A-State Anxiety from the State-Trait Anxiety Inventory (STAI) for anxiety levels.

*Data analysis:* ANCOVA for repeated measures will be used to compare the outcomes among the 3 groups.

*Results:* For dissemination in conferences and in local and international referred journals.

*Conclusion:* the findings will provide information on the physical and psychosocial benefits to lung cancer patients undergoing radiotherapy of PMR, PMR combined with education compared to the usual care (MD01833)

### Effectiveness of Mutual Support and Psychoeducational Group Interventions for Family Caregivers of Patients with Schizophrenia

- ✉ CHIEN Wai Tong • CHAN Wai Chi Sally • Jean Mary MORRISSEY
- ☐ 1 May 2002

- ❖ Health Care & Promotion Fund, Hospital Authority

The study aims to compare the effectiveness among mutual support group, psychoeducational group and conventional outpatient service in the care of schizophrenic patients and families on various psychosocial outcomes. A longitudinal, randomized, multigroup pretest & posttest control group design will be used. The subjects (n=102) will participate in either a treatment group or a control group for 6 months. Pre-test and 3 post-test measurements (i.e. 12 months follow-up) as outcome evaluation, and audio/video-taped sessions and semi-structured subject interviews as process evaluation, will generate data for assessing the relative impacts of the three types of interventions. The findings will indicate which group intervention will result in a comparatively significant increase in family's social support and self-efficacy to caregiving; and which intervention will result in a significant reduction of family's burden of care and unmet support service needs. The sustainable effects up to 1 year after intervention and the cost-effectiveness of the group interventions will also be examined and compared. The analysis of the group process will increase understanding of the factors influencing the success of the interventions.

(MD01337)

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#### **An Investigation of Hong Kong Chinese Women's Experience and Responses to a Diagnosis of an Abnormal Smear**

- ✉ Sheila Frances TWINN • LO S\*
- ☐ 1 August 2001
- ❖ Health Services Research Fund, Hospital Authority

Well-organised population cervical screening programmes are effective in reducing deaths from cervical cancer. However, these programmes have been shown to result in many more women being diagnosed with cervical intraepithelial neoplasia (CIN) resulting in an abnormal cervical smear. Several studies in western countries have shown high levels of psychological morbidity among women diagnosed with an abnormal smear, but to date there has been little documentation of women's response to an abnormal cervical screen or the psychological sequelae of this event locally. The aim of this study

is to investigate the responses and experiences of Hong Kong Chinese women to a diagnosis of an abnormal smear. Data collection will consist of face-to-face semi-structured interviews with three groups of women selected from the same Family Planning Association (FPA) centre. The groups will consist of women with an abnormal result who require a repeat test, women with vaginitis who require treatment and women referred for colposcopy. Total population sampling will be used for all three groups of women the study and approximately 20 will be recruited from each group and be invited to participate in the interview approximately one week after receiving their abnormal smear result. Prior to the interview, which will be tape-recorded, women will be given information about the study and asked to sign an informed consent form. Thematic analysis of the qualitative data will be undertaken to conceptualize women's responses and experiences of receiving an abnormal result. A comparison of the thematic analysis of the data from each group will be undertaken to identify any similarities and differences in the findings from the three groups.

(MD01779)

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#### **To Assess the Effectiveness of a Nurse-led Sexual Health Promotion Project amongst Hong Kong Adolescents**

- ✉ Sheila Frances TWINN • LEE Albert (Dept of Community and Family Medicine) • Eleanor Anne HOLROYD • CHENG YAM Fung Khing Frances (Dept of Community and Family Medicine) • SHIU Tak Ying
- ☐ 1 September 2001
- ❖ Health Care & Promotion Fund, Hospital Authority

The aim of this two-year project is to assess the effectiveness of a school-based nurse-led health promotion programme to promote the sexual health of young adolescents. The programme involves a multi-strategy intervention consisting of needs assessment, health education and one-to-one counseling in selected government funded secondary schools. An important component of the programme is the collaboration between nurses, doctors, teachers and adolescents and their parents. Evaluation of the programme consists of impact and process strategies. Impact includes measures of changes in sexual knowledge, behaviour, attitudes

influencing that behaviour and health locus of control. Logs, focus groups and interviews will be used for process evaluation. It is anticipated that a multidisciplinary approach from nursing, medicine and education will not only promote adolescents' sexual health but also further develop school-based multidisciplinary approaches to adolescent sexual health education.  
(ED01702)

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**Validation of Chinese Versions of Measures of Stress Incontinence and the Intrinsic Motivation Inventory**

- ✉ Violeta LOPEZ • CHANG Anne Marie# • YIP Shing Kai Alexander (Dept of Obstetrics & Gynaecology) • SIU LS Katherine\*
- ☐ 4 March 2002
- ❖ Health Care & Promotion Fund, Hospital Authority

*Objectives:* The aim of this study is to establish the reliability and validity of a Chinese version of the Symptom Severity Index (SSI) and Symptom Impact Index (SII) and Intrinsic Motivation Inventory (IMI).  
*Design:* Prospective, descriptive study.  
*Setting:* A regional hospital  
*Subjects:* Women with and without incontinence.  
*Main outcome measures:* Symptom Severity Index (SSI) and Symptom Impact Index (SII) and the Intrinsic Motivation Inventory (IMI). Additionally the Frequency and Volume Chart, and the SF-36 Health Survey will be used to determine the validity of the translated SSI, SII while Rosenberg's Self-Esteem (RSE) scale will be used to determine the validity of the translated IMI tool.  
*Data analysis:* The reliability will be tested using Cronbach's alpha coefficient with intraclass correlation coefficient for the test-retest data. Criterion validity of the SSI will be estimated from the Spearman rank correlation coefficient with the Frequency and Volume Chart. Factor analysis of and correlations between the newly translated tools and previously validated and relevant tools will be used as well as to determine construct validity. t-test will be used to compare women with and without incontinence on the SSI and SII.  
*Conclusion:* the development of reliable and valid SSI, SII and IMI will enable the testing of the effectiveness of pelvic floor muscle exercises (PFME) in an RCT under planning. A Chinese version of

the SSI and SII will provide a measure for determining the self-reported changes in women's continence state. Measurement of motivation of Chinese incontinent women's adherence to the PFME is essential in accounting for differences in treatment adherence.  
(MD01466)

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**Establishing the Validity and Reliability of the Chinese Versions of the Chronic Heart Failure Questionnaire (CHQ) and the Medical Outcome Study Social Support Survey (MOS-SSS)**

- ✉ YU Sau Fung • LEE Tze Fan Diana • WOO Jean (Dept of Medicine & Therapeutics)
- ☐ 2 January 2002
- ❖ Health Services Research Fund, Hospital Authority

*Objectives:* The aim of this study is to establish the validity and reliability of the Chinese versions of the Chronic Heart Failure Questionnaire (CHQ) and Medical Outcome Study Social Support Survey (MOS-SSS)  
*Design:* Prospective, descriptive study.  
*Setting and Subjects:* 110 chronic heart failure elderly patients admitted to the Medical unit of a general hospital and 64 healthy elderly people of a community elderly center during the study period.  
*Main Outcome Measures:* Chronic Heart Failure Questionnaire (CHQ) and Medical Outcome Study Social Support Survey (MOS-SSS). The New York Heart Association Classification, the Multi-dimensional Self-Perceived Social Support Scale, the Hospital Anxiety and Depression Scale will be used to determine the validity of the Chinese versions of CHQ and MOS-SSS.  
*Data Analysis:* The criterion and concurrent validity of the translated CHQ and MOS-SSS will be determined by the correlation with previously established criterion or validated measure. Construct validity of the Chinese versions will be established using factor analysis and correlations with previously validated tool of theoretically linked construct. t-test will be used to compare the CHQ scores between chronic heart failure patients and healthy elderly subjects for known group comparison. The internal consistency and test-retest reliability of the Chinese versions of CHQ and MOS-SSS will be established using Cronbach's alpha coefficient and the interclass correlation coefficient respectively.

*Conclusion:* Development of valid and reliable Chinese versions of CHQ and MOS-SSS is the cornerstone in a currently planned study that evaluates the effectiveness of Progressive Muscular Relaxation (PMR) in promoting the psychosocial well being of Chinese elderly people with chronic heart failure. The CHQ reveals the effect of PMR on Chinese elders' quality of life (disease-specific) while the MOS-SSS reveals the possible confounding effect of social support on the outcome measures. Thus, a more reliable and sensitive evaluation of the effects of PMR on chronic heart failure Chinese elders can be obtained.  
(MD01545)

2000-01 Preparation for Pregnancy, Labour & the Early Postpartum Period: An Evaluation of a Hospital Based Antenatal Education Program (MD20028)

✍ Eleanor Anne HOLROYD • IP Wan Yim • Sheila Frances TWINN

2000-01 Chinese Families' Experiences with Residential Care Placement of Their Elderly Relatives (CU00376)

✍ LEE Tze Fan Diana • Ann Elizabeth MACKENZIE#

2000-01 The Nursing Care Needs of Chinese Elders in Residential Care Homes in Britain (SS00804)

✍ LEE Tze Fan Diana

2000-01 Determining Research Priorities for Critical care Nurses in Hong Kong: A Delphi Study (MD00435)

✍ Violeta LOPEZ

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

Edition      Title/Investigators

2000-01 An Evaluation of the Effectiveness of a Multisensory Environment on Clients with Learning Disability (MD00708)  
✍ CHAN Wai Chi Sally • CHIEN Wai Tong • TO Yuen Fung Maggie\*

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- <P029302> **LEE Tze Fan Diana.** "Residential Care Placement of an Elderly Relative: Chinese Families' Experiences". *Proceedings of the International Conference - Traditions, Evidence and Innovations in Nursing* p.131. Phuket, Thailand: Prince of Songkla University & La Trobe University, 2002.03.22.
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- <P029747> **CHAN Dominic Shung Kit.** "Development of the Clinical Learning Environment Inventory: Using the Theoretical Framework of Learning Environment Studies to Assess Nursing Students' Perceptions of the Hospital as a Learning Environment". *Journal of Nursing Education* vol.41 no.2, pp.69-75. Thorofare, USA: Slack Inc., 2002.02.
- <P029827> **邵德英、WONG Y.M. Rebecca.** 〈從糖尿病一型及二型患者的低血糖恐懼分析取得的一些對基層醫護服務的啟示〉. Abstracts of the 5th Guangdong, Hong Kong and Macau Conference on Preventive Medicine p.78. 香港特別行政區: The Hong Kong Health Education and Health Promotion Foundation (HEP Foundation), 2002.03.
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see also <P011927>, <P012323>

## RESEARCH PROJECTS

### Global Protein Profiling of Cervical Cancer Using a Novel Protein Biochip Technology: A Pilot Study

✉ CHUNG Kwok Hung Tony • WONG Yick Fu • CHEUNG Tak Hong • MOK Samuel C.\*

□ 1 December 2001

❖ CUHK Mainline Research Scheme

Improving early detection, treatment monitoring and improving prognosis of cancer remains a big challenge. It requires rapid and high throughput detection, identification, and measurement of multiple biomarkers. A proteinchip technology (surface-enhanced laser **desorption**/ionization (SELDI) mass spectrometry) has recently been developed to facilitate protein profiling of biological mixtures. So far only a few of research centers have installed this sophisticated proteinchip (called ProteinChip) system and used this technology to explore protein signatures associated with early stage of human tumor development. Prof. S.C. Mok at the Brigham and Women's Hospital, Harvard Medical School has successfully studied protein signatures of ovarian cancer using this system, and identified three proteins to be highly expressed in ovarian cancer. Cervical cancer is a leading cause of morbidity and mortality in Hong Kong women but cervical cancer related/specific biomarkers have not been well characterized. The main aim of this project is to generate sensitive, rapid and reproducible global molecular weight protein profiles from normal cervix, early and late stage cervical cancers using SELDI ProteinChip in a collaboration with Prof. S.C. Mok's unit where this novel technology is available. This collaborative study may provide important information on applicability of this technology in our future research in biomarkers of gynecologic cancers, as well as provide important clues on searching for protein signatures of cervical cancer.

(MD01480)

### Effect of Maternal Emotional Status During Pregnancy on Neonatal Birthweight

✉ Daljit Singh SAHOTA • LAU Tze Kin • LEE Tak Shing Dominic (Dept of Psychiatry) • LEUNG Tse Ngong • YIP Shing Kai Alexander

□ 1 October 2001

❖ Research Grants Council (Earmarked Grants)

It has been suggested that differences in pregnancy outcome can be attributed to the individual characteristics and lifestyle of the mother. Recent studies suggest that a mothers' psychological state, indicated by poor scores on singular and combined psychological assessment, could adversely affect the condition of her fetus. The degree of chronic and acute maternal stress, depression and anxiety during the antepartum and postpartum period have been reported to be linked with low birthweight, impaired uterine as well as umbilical cord vessel blood flow, decreased fetal movement, prolonged fetal sleep and significant increases in fetal heart rate.

Low birthweight and small for gestational age still remains one of the primary risk factors for morbidity and mortality in otherwise normally formed neonates. Low birthweight has been linked with a later predisposition to adult diseases such coronary heart disease and hypertension.

The principal aim of this study is to determine the relationship between maternal psychometric assessment in otherwise uncomplicated pregnancies and subsequent deviation of the actual birthweight from that which would have been expected according to the mothers physical characteristics, previous obstetrics history.

We therefore propose to identify a cohort of Chinese antenatal patients with abnormal psychometric assessment, Spielberger State-Trait Anxiety, and measure fetal growth, size and uterine and umbilical cord vessel blood flow and compare them with those of a cohort with normal psychometric assessment scores.

(MD01082)

### A Study on Placental Transfer of Rosiglitazone

✉ LAU Tze Kin • YEUNG Hok Keung John (Dept of Pharmacology) • SIU Shing Shun Nelson • CHAN Yik Si Louis

□ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

The objective of this study is to investigate the potential placental transfer of a new insulin sensitising agent, Rosiglitazone, in the first trimester of pregnancy. In this study, the concentration of

Rosiglitazone in matched samples of maternal serum, amniotic fluid, extra-coelomic fluid and fetal tissue will be measured by High Performance Liquid Chromatography following two standard doses of the drug in the patient. Since diabetes is a common medical disease, the result of this study will enable better counseling of women who incidentally become pregnant during rosiglitazone therapy.  
(MD01681)

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**Evaluation of Green Tea Polyphenols in Pregnancy**

✉ ROGERS Michael Scott • CHU Kai On • HAINES Christopher John • LAU Tze Kin • PANG Chi Pui Calvin (Dept of Ophthalmology and Visual Sciences) • WANG Chi Chiu

□ 1 October 2001

❖ Research Grants Council (Earmarked Grants)

There is growing body of evidence that tea, mainly green tea, and the polyphenols therein, possess inhibitory effects against diseases and act as powerful antioxidants. Tea polyphenols with their natural antioxidant ability are widely used for the prevention of oxidative stress, in which they have also showed a synergistic effect with other antioxidants. Since the availability of commercially prepared decaffeinated green tea extract which contain enriched quantities of polyphenols, numerous animal and human studies have been conducted concerning its metabolism, bioavailability, safety, and antioxidant mechanism. However, there are no reports of its possible effect and benefits in pregnancy. We propose to evaluate green tea polyphenols and their metabolites using several animal models in order to understand their pharmacokinetics and toxicology in pregnancy. The efficacy and potency of these polyphenols in prevention of hypoxic-ischaemic damage during labour will be the principal aim of this project. From this study, we can determine whether green tea polyphenols have any teratogenic properties; can cross the placenta in adequate quantities; and cross the fetal blood-brain barrier in physiological active quantities. This information will be used to determine whether green tea polyphenols can be used in the future in clinical prophylaxis against fetal brain damage in human pregnancy.  
(MD01077)

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**To Compare the Levels of Oxidative Stress in Pregnant Women with Varying Degrees of Carbohydrate Intolerance**

✉ ROGERS Michael Scott • LI Chi Yin • NG Pak Cheung (Dept of Paediatrics) • PANG Chi Pui Calvin (Dept of Ophthalmology and Visual Sciences) • TAM Wing Hung • WANG Chi Chiu

□ 1 October 2001

❖ Research Grants Council (Earmarked Grants)

*Introduction:* Patients suffering from diabetes mellitus are often deficient in antioxidants and are prone to suffer from oxidative stress. Long term dietary advice, along with careful control of blood glucose, prevents much of the damage during pregnancy. This may not be the case where previously normal women develop diabetes as a consequence of being pregnant. Increased oxidative stress may lead to the development of pregnancy-induced hypertension (PIH) and the birth of compromised babies.

Studies are now being conducted on the role of hyperglycaemia as it relates to pregnancy, and the Prince of Wales Hospital is one of the centers for the National Institute of Health (NIH) funded Hyperglycaemia and Adverse Pregnancy Outcome study (HAPO).

*Methods:* Women will be recruited at 28 weeks of gestation and subjected to a 75g oral glucose tolerance test (OGTT). Those whose glucose tolerance results are in the range of frank diabetes will be managed as usual and not participate in the study. The study participants will receive no treatment and their obstetricians will be blinded to the results of the OGTT. The levels of antioxidants and oxidative stress, the incidence of PIH and perinatal oxidative stress will be compared between women with normal and abnormal carbohydrate tolerance.

*Anticipated Results:* Higher levels of oxidative stress and increased incidence of PIH will occur amongst women with abnormal carbohydrate tolerance, particularly where signs of insulin resistance exist.  
(MD01081)

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**The Effect of Interactions Between Genetic and Environmental Factors and History of Gestational Diabetes on the Incidence of Diabetes and Metabolic Syndrome in Hong Kong Chinese Women and Their Offspring**



✉ TAM Wing Hung • CHAN Chung Ngor Juliana (Dept of Medicine & Therapeutics) • KO Tin Choi (Dept of Medicine & Therapeutics) • NG Chor Yin (Dept of Medicine & Therapeutics) • TONG Peter Chun Yip (Dept of Medicine & Therapeutics) • Clive Stewart COCKRAM (Dept of Medicine & Therapeutics) • ROGERS Michael Scott

☐ 1 September 2001

❖ CUHK Research Committee Funding (Direct Grants)

Women with a history of GDM are at high risk of developing DM so as their offsprings are also at risk of developing DM and metabolic syndrome. Our objective are i) to determine the incidence of DM in Chinese women with a history of GDM, ii) to examine the roles of hormonal, autoimmune, genetic and environmental factors in the development of DM in these high risk women, and iii) to determine the continuous relationships between birth weight, changes in body weight and various cardiovascular risk factors as well as the effects of a maternal history of GDM on these risk factors in the offspring.

In a cohort of 942 women established in 1992-1993, among which 13% were diagnosed GDM, we aimed to perform a prospective study to document the incidence of DM amongst women with a history of GDM. 100 women with GDM in the index pregnancy and 200 controls together with the children will be recruited. We shall conduct an interview with a structured questionnaire, perform physical examination and laboratory test including OGTT, HbA<sub>1c</sub>, insulin, C peptide, lipids, cortisol, growth hormone and autoimmune markers. The role of environmental, genetic, hormonal and autoimmune factors in the development of DM in the cohort will be studied.

(MD01482)

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**A Prospective Observational Study on the Prevalence of Group B Streptococcus in Hong Kong Pregnant Women and Its Associated Factors**

✉ TSUI Hang Yuet Michelle • LEUNG Tse Ngong • IP Margaret (Dept of Microbiology)

☐ 15 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Group B Streptococcus (GBS) is the most common pathogen causing neonatal sepsis, and is associated with significant perinatal morbidity and mortality. In Hong Kong, the prevalence of GBS in our pregnant population is thought to be very low, based on studies in the early nineties. Therefore, currently no antenatal screening program for GBS is practiced in Hong Kong. However, recent clinical observations suggest that the prevalence of GBS colonization may have increased: with a rising incidence of neonatal sepsis caused by GBS, increased preterm delivery rate, as well as increase in sexually transmitted disease in our gynaecological population. Possible reasons for recent increase in prevalence include changes in lifestyle, sexual behaviour, age groups, educational levels, as well as population composition (with 25% from Mainland China) in our pregnant women in the last decade. In this study, we aim to establish the prevalence as well as identify any associated factors for GBS colonization in our pregnant population. We will also correlate the culture findings between antenatal and intrapartum swabs.

The outcome of this study will be of both local and international significance. With an established prevalence of GBS in our antenatal population, we can answer the question of whether a screening program should be implemented. Identified risk factors for colonization will also be important in determining whether universal or selective screening is preferable in our locality. Risk factors identified which are associated with the change in prevalence of GBS in an ethnically homogenous society will also be of international interest.

(MD01945)

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**Gene Expression Profiles in Cervical Neoplasms in Hong Kong Chinese Women: Analysis by cDNA Array Hybridization**

✉ WONG Yick Fu • CHEUNG Tak Hong • CHUNG Kwok Hung Tony • TSAO George\*

☐ 1 December 2001

❖ Research Grants Council (Earmarked Grants)

Cervical cancer is the leading cause of gynecological cancer death in Hong Kong and 95 % of them are squamous cell in origin. Mutation of genes along the signaling pathways controlling cell proliferation, differentiation and apoptosis, as well as disruption of genomic integrity, have been widely studied in

relation to carcinogenesis. Previously, these studies have been hampered because only a few genes or genetic events can be evaluated at any one time and the interactions of whole human genome could not be evaluated. A new technique, cDNA microarray, now allows quantitative measurement of the expression of thousands genes simultaneously. In this project we are to investigate the gene expression profiles in pre-malignant and malignant neoplasms of the cervix using cDNA array analysis. By identifying the genetic expression profile of tissue specimens collected from premalignant lesions, early and late stage cervical cancer tissues, we propose to identify genetic changes that characterized early and late events in carcinogenesis. We will also determine the presence of HPV infection and genotype in these cervical neoplasms. This research can provide unprecedented information on global genetic events in cervical neoplasms. Such basic information is necessary for understanding the gene expression differences that underlie neoplastic development, progression, and metastasis. (MD01084)

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**A Randomized Controlled Evaluator-blinded Intervention Study of Psychological Counselling on the Outcomes of Miscarriage**

- ✉ YIP Shing Kai Alexander • LEE Tak Shing Dominic (Dept of Psychiatry) • TAM Wing Hung • SHEK Tan Lei Daniel (Dept of Social Work) • CHUNG Kwok Hung Tony
- ☐ 1 November 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Miscarriage (spontaneous pregnancy loss before 24 weeks of gestation) is one of the commonest complications of pregnancy with up to one in five pregnancies aborting spontaneously. It can bring serious psychological stress as recent studies suggested up to 50% of miscarried women were found to have clinical depression.

The investigators propose to conduct a randomised controlled evaluator-blinded study involving 652 subjects to evaluate the effect of psychological counselling in reducing psychological morbidity amongst patients who have suffered a miscarriage. In addition, we propose to study the impact of miscarriage on marital relationship. The intervention group will receive specific additional

psychological counseling while the control group will receive normal care. Psychometric instruments used in this study will be: Dyadic Adjustment Scale (DAS), General Health Questionnaire (GHQ), Perinatal Grief Scale (PGS) and Beck's Depression Inventory (BDI), and these will be conducted for all patients on recruitment as baseline and repeated at 12 weeks after miscarriage. Socio-demographic data will also be collected and collated with the above data. DAS is used to assess marital relationship while GHQ, PGS and BDI are used to measure the psychological well-being, level of grief, and level of depression respectively. Changes of the DAS, GHQ, PGS, and BDI scores at different stages of the study will be compared between the two groups in order to evaluate the effects of psychological counselling. (MD01803)

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**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>
1999-00	Microsatellite Instability in the Evolution of Cervical Neoplasm (MD99093) ✉ CHUNG Kwok Hung Tony • WONG Yick Fu • CHEUNG Tak Hong* • YU Mei Yung May* • LAHR G.*
2000-01	Microsatellite Instability in the Evolution of Cervical Neoplasm and Its Clinical Association (MD00784) ✉ CHUNG Kwok Hung Tony • WONG Yick Fu • CHEUNG Tak Hong • YU Mei Yung (Dept of Anatomical & Cellular Pathology)
1999-00	A Comparison of the Antiatherogenic Properties of Estradiol with Other Cardioprotectants Used in the Treatment of Postmenopausal Women (CU99268) ✉ HAINES Christopher John • Anthony Edward JAMES (Laboratory Animal Services Centre) • Daljit Singh SAHOTA • CHOW Tsun Cheung Louis (Dept of Anatomical & Cellular Pathology) • Brian TOMLINSON (Dept of Medicine & Therapeutics) •

- PANESAR Nirmal Singh (Dept of Chemical Pathology) • BENZIE Iris F. F.\* • HUSBAND Alan James\*
- Chi Pui Calvin (Dept of Ophthalmology and Visual Sciences)
- 2000-01 A Randomized, Double-blind Placebo-controlled Crossover Study of the Effect of Livial (tibolone) on the Dyadic Relationship of Chinese Couples (MD00939)  
 ✎ LAM Po Mui • SHEK Tan Lei Daniel (Dept of Social Work) • LEE Tak Shing Dominic (Dept of Psychiatry) • CHEUNG Wai Yan Grace\*
- 1999-00 Effect of Antenatal Corticosteroids Therapy on Maternal Bone Metabolism and Lipids Changes (MD99047)  
 ✎ TAM Wing Hung • YUEN Pong Mo • LEUNG Tse Ngong • MAK Wing Lai Tony (Dept of Chemical Pathology) • NG Pui Shan • CHANG Mang Z. Allan • LAM Wai Kei Christopher (Dept of Chemical Pathology)
- 2000-01 Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study (MD98171)  
 ✎ LI Chi Yin • ROGERS Michael Scott • NG Pak Cheung (Dept of Paediatrics)
- 2000-01 Regulation of Oviduct Specific Oestrogen-dependent Glycoproteins (oviductins) mRNA Expression on vitro (MD20047)  
 ✎ LOK Hung Ingrid • Christine May BRITON-JONES • YUEN Pong Mo • HAINES Christopher John
- 1999-00 Gene Expression Profiles in Cervical Cancer Based on a cDNA Array Analysis (MD99048)  
 ✎ WONG Yick Fu • CHUNG Kwok Hung Tony • CHEUNG Tak Hong\*
- 1999-00 To Determine the Relationship between Umbilical Cord Artery Lipid Peroxide Concentrations and Morbid Neonatal Outcomes (CU99329)  
 ✎ ROGERS Michael Scott • PANG Chi Pui Calvin (Dept of Ophthalmology and Visual Sciences) • FOK Tai Fai (Dept of Paediatrics) • LAU Tze Kin • WANG Chi Chiu
- 2000-01 Methylation Profiling of Gene Promoter CpG Islands in Cervical Neoplasm (MD00701)  
 ✎ WONG Yick Fu • CHUNG Kwok Hung Tony • CHEUNG Tak Hong
- 2000-01 To Assess the Predictive Value of Ultrasonic Assessment of Umbilical Cord Morphology for Intrapartum Fetal Distress (MD20007)  
 ✎ ROGERS Michael Scott • IP Wan Yim (The Nethersole School of Nursing) • LAU Tze Kin • PANG
- 2000-01 Psychosocial Morbidity Following Miscarriage: A Prospective Observational Study of Chinese Women in Hong Kong (MD00600)  
 ✎ YIP Shing Kai Alexander • LOK Hung Ingrid • LEE Tak Shing Dominic (Dept of Psychiatry) • TAM Wing Hung • SHEK Tan Lei Daniel (Dept of Social Work) • CHUNG Kwok Hung Tony

## RESEARCH OUTPUTS AND PUBLICATIONS

- <P004221> **STRACHAN Bryony; SAHOTA Daljit; VAN WIJNGAARDEN, Willem J.; JAMES David and CHANG Z.M., Allan.** "The Fetal Electrocardiogram: Relationship with Acidemia at Delivery". *American Journal of Obstetrics & Gynaecology* vol.182 no.3, pp.603-606. USA, 2000.03.
- <P004227> **CHIU T.Y. Tony; BRITON-JONES Chris M.; ROGERS Michael S. and HAINES Christopher J.** "Birth of Twins Using *in vitro* Matured Oocytes and Cryopreserved Semen from a Male with Carcinoma of the Penis". *Australian & New Zealand Journal of Obstetrics and Gynaecology* vol.40 no.4, pp.475-476. Australia, 2000.11.
- <P004228> **BRITON-JONES C.M.; LOK I.H.; CHIU T.T.; YUEN P.M.; CHEUNG L.P. and HAINES C.J.** "Variation in Oviductin mRNA Expression Throughout the Ovulatory Cycle". *ASRM 2000 56th Annual Meeting of the American Society for Reproductive Medicine* vol.74 no.3(Suppl. 1), pp.S130-S131(P-114). USA: American Society for Reproductive Medicine, 2000.10.
- <P011828> **HAINES Christopher John, CHUNG Kwok Hung Tony, YIM So Fan, LEE Tak Shing Dominic, LAM Wai Kei Christopher, LAU Edith Ming Chu, NG Heung Ling Margaret and CHIN Kien Howe Robert.** "A Prospective, Randomised, Placebo-Controlled Study of the Dose Effect of Oral Oestradiol on Menopausal Symptoms and Quality of Life in Postmenopausal Chinese Women". *Abstracts of the 29th British Congress of Obstetrics and Gynaecology* p.382. Birmingham, UK: Royal College of Obstetricians & Gynaecologists, 2001.07.
- <P011883> **CHUNG Kwok Hung Tony, LAU Tze Kin, YIP Shing Kai Alexander, CHIU Fung Kum Helen and LEE Tak Shing Dominic.** "Antepartum Depressive Symptomatology is Associated with Adverse Obstetric and Neonatal Outcomes". *Psychosomatic Medicine* vol.63, pp.830-834. USA: Lippincott Williams & Wilkins, 2001.10.
- <P011891> **CHAN L.Y.; TAM W.H. and LAU T.K.** "Venous Thromboembolism in Pregnant Chinese Women". *Obstetrics and Gynaecology* vol.98 no.3, pp.471-475. USA: Elsevier Science Inc, 2001.09.
- <P011905> **LO K.W.K.; CHEUNG T.H. and CHUNG T.K.H.** "The Value of Pelvic and Para-Aortic Lymphadenectomy in Early Stage Endometrial Cancer". *Abstracts of the 2nd World Congress on Controversies in Obstetrics Gynecology & Infertility* p.81. Paris, France: Academic Press, 2001.09.
- <P011906> **LO W.K. Keith; CHEUNG T.H.; YIM S.F. and CHUNG K.H. Tony.** "Preoperative Hysteroscopic Assessment of Cervical Invasion by Endometrial Carcinoma: A Retrospective Study". *Gynecologic Oncology* vol.82, pp.279-282. USA: Academic Press, 2001.09.
- <P011907> **LO K.W.K.; CHEUNG T.H.; YIM S.F. and CHUNG T.K.H.** "Hysteroscopic Dissemination of Endometrial Carcinoma Using Carbon Dioxide and Normal Saline: A Retrospective Study". *Abstracts of the 2nd World Congress on Controversies in Obstetrics Gynecology & Infertility* p.81. Paris, France: Academic Press, 2001.09.
- <P011927> **NG P.S.; LAI C.Y.; SAHOTA D.S. and YUEN P.M.** "Comparison of Oral Misoprostol and Intramuscular Syntometrine in the Management of the Third Stage of Labour - a Double-Blind Randomised Controlled Trial". *Abstracts of the 29th British Congress of Obstetrics and Gynaecology* Abstracts no. 283. Royal College of Obstetricians & Gynaecologists, 2001.07.

- <P011971> **LEUNG H.Y.P.; YIP S.K.; CHEON C.; LIU Y.S.J.; LAU J.; WONG H.K.T. and CHUNG K.H.T.** "A Randomized Controlled Trial of Tolterodine and Oxybutynin on Tolerability and Clinical Efficacy for Treatment of Chinese Women with Overactive Bladder". *ICS 2001* Seoul, Korea: Pharmacia Company Ltd., 2001.09.20.
- <P011972> **CHOY C.M.Y.; LAM C.W.K.; CHEUNG L.T.F.; BRITON-JONES C.; CHEUNG C.K. and HAINES C.J.** "Blood Mercury Concentrations and Seafood Consumption Among Infertile Couples in Hong Kong". *Abstracts of the 2nd World Congress on Controversies in Obstetrics, Gynaecology & Infertility* p.50. Paris, France: American Society for Reproductive Medicine, 2001.09.
- <P011973> **IP Chui Ping, Christine May BRITON-JONES, LOK Hung Ingrid, CHEUN L.P., CHIU Tak Yu Tony and HAINES Christopher John.** "Progesterone Receptor Isoforms AB and B mRNA Expression in Human Oviduct Mucosal Cells". *Proceedings of the 8th Meeting of the Chinese Reproductive Biologists--Developmental and Reproduction Biology* p.93. Beijing, China: Science Press, 2001.10.
- <P012023> **CHAN Yik Si Louis, SO W W K and LAO T T H.** "A Prospective Study to Evaluate the Effectiveness of Ultrasound-Guided Transvaginal Aspiration in the Treatment of Recurrent Endometrioma". *11th World Congress on Ultrasound in Obstetrics and Gynecology vol.18 suppl. no. p.5(CEG-02)*. Melbourne, Australia, 2001.10.
- <P012033> **LAM Po Mui, YUEN Pong Mo, LAU Tze Kin and LEUNG Tse Ngong.** "Relationship Between Birthweight and Repeated Courses of Antenatal Corticosteroids". *Australian & New Zealand Journal of Obstetrics and Gynaecology* 3rd ed., vol.41, pp.281-284. Australia: Hong Kong Government Printer, 2001.08.
- <P012078> **TAM Wing Hung, ROGERS Michael Scott, LAU Tze Kin and ARUMANAYAGAM Manoharan.** "The Predictive Value of Serum 1,5-Anhydro-D-Glucitol in Pregnancies at Increased Risk of Gestational Diabetes Mellitus and Gestational Impaired Glucose Tolerance". *British Journal of Obstetrics and Gynaecology* vol.108, pp.754-756. The Netherlands: Elsevier Science BV, 2001.07.
- <P012149> **LOK I.H.; CHAN M.T.V.; TAM W.H.; LEUNG P.L. and YUEN P.M.** "Thermal Balloon Endometrial Ablation under Patient Controlled Sedation". *Abstracts of the 29th British Congress of Obstetrics and Gynaecology* Abstracts no.252. Birmingham, UK: Royal College of Obstetricians & Gynaecologists, 2001.07.
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- <P012151> **YUEN P.M. and CHOY C.M.Y.** "A Randomised Controlled Trial of Intramuscular Syntometrine and Intravenous Oxytocin for Prevention of Post-Partum Haemorrhage". *Abstracts of the 29th British Congress of Obstetrics and Gynaecology* Abstracts no.282. Birmingham, UK: Royal College of Obstetricians & Gynaecologists, 2001.07.
- <P012152> **Daljit Singh SAHOTA, LEUNG Tak Yeung, CHAN Lin Wai Daniel, FOK Wing Yee and LAU Tze Kin.** "Measurement of Contact Surface Pressures Exerted During External Cephalic Version". *Abstracts of the 29th British Congress of Obstetrics and Gynaecology* Abstracts no.324. Birmingham, UK: Royal College of Obstetricians & Gynaecologists, 2001.07.

- <P012316> **ROGERS M.S.** "Induction and Augmentation of Labour". *Turnbull's Obstetrics* ed. by CHAMBERLAIN Geogrey and STEER Philip. 3rd ed., pp.563-579. UK: Miranda Bromage, 2001.10.
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## RESEARCH PROJECTS

### Mutations in *ABCA4* (*ABCR*) Gene in Chinese Patients with Age-Related Macular Degeneration

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☐ 1 September 2001

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Age-related macular degeneration (AMD) is one of the leading causes of blindness in elderly in Hong Kong. It is caused by lifestyle factors as well as genetic variations, whose identification may lead to prevention or treatment of this disease. Since the only genes repeatedly reported to be significantly associated with AMD are *ABCA4* and *APOE*, we decided to confirm the reported association with *ABCA4* genotype. The retina specific ATP-binding cassette transporter (*ABCR*) gene, now known as *ABCA4*, is responsible for the transport of vitamin A derivatives across the disc membrane and has been shown to be a causative gene of AMD. Mutations in the *ABCA4* gene cause Stargardt's disease, the most common hereditary macular degeneration. Similarities between Stargardt's disease and AMD led researchers to look for *ABCA4* mutations in AMD. Though some studies of Caucasians and Japanese found no association of *ABCA4* variants with AMD, the largest study to date found some *ABCA4* mutations strongly associated with at least a few percent of AMD patients. In one family, AMD was linked to chromosome 1q25-q31 but the gene has not been identified. We therefore propose a continuous case-control study on AMD patients and age matched normal control subjects to investigate the *ABCA4* mutations on the development of AMD. (MD01994)

### Endolaser and Internal Limiting Membrane Removal around Macular Holes Causing Retinal Detachment in High Myopes

✉ CHAN Wai Man • LAM Shun Chiu Dennis

☐ 1 December 2001

❖ CUHK Research Committee Funding (Direct Grants)

Myopia is a much more frequent and severe disorder in Asia than in western countries. Among the Chinese population in Hong Kong, more than 50% are myopic, and the trend is increasing. The proportion of severe myopia is high and retinal detachment secondary to a macular hole is common in these eyes. Very often the retina fails to be reattached spontaneously, leading to serious and irreversible visual impairment and even blindness. In small reported series, higher primary anatomic success rates were attained when laser or internal limiting membrane removal was employed around the macular hole. Meanwhile, no prospective study of reasonable sample size has been reported discussing the best surgical procedure to obtain optimized results. One difficulty for such study in western countries is the low number of highly myopic patients there requiring treatment. In Hong Kong, however, retinal detachment due to a macular hole is a common and serious ophthalmic problem. We therefore propose to perform a prospective interventional study with each patient receiving pars plana vitrectomy, fluid/gas exchange, with laser and internal limiting membrane removal around the macular hole. Establishment of an optimized procedure will greatly improve clinical outcome of such patients and reduce personal and social burden of this treatable ophthalmic complication. (MD01509)

### TIGR Gene Mutations and Their Association with Primary Open Angle Glaucoma

✉ CHUA Kien Han John • LAM Shun Chiu Dennis • PANG Chi Pui Calvin • FAN Shu Ping Dorothy • Lawrence William BAUM (Dept of Medicine & Therapeutics)

☐ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Primary open angle glaucoma (POAG) is the major form of glaucoma affecting about 2% of the world's population. The exact cause is unknown but genetic factor is believed to play an important role. TIGR was identified as a causative gene for POAG in 1997 and a TIGR mutation, Arg46Stop that essentially eliminates the TIGR protein has been reported to cause POAG. However, this mutation is found for the first time in non-glaucoma control subjects we screened. Our results suggest that normal aqueous

outflow may not actually require TIGR. We have also published 10 other sites of TIGR sequence alteration. Six of which change amino acids but none showed statistically significant association with POAG. Arg46Stop has been identified only in Asians and our finding of this mutation in normal subjects was unexpected. Therefore, we propose to screen for sequence alterations in the TIGR promoter/coding regions in 250 POAG and 250 normal subjects. We will observe the effects of mutations on the secretion and aggregation of TIGR and measure the effects of promoter sequence changes on TIGR expression. The results will reveal the frequency of specific TIGR sequence alterations in Hong Kong and how these alterations affect the development of POAG. (MD00631)

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**A Twelve-week, Double-masked, Parallel Group, Primary-therapy Study of the Safety and Efficacy of Travoprost 0.004% Compared to Latanoprost 0.005% in Patients With Chronic Angle-closure Glaucoma**

✉ CHUA Kien Han John • LAM Shun Chiu Dennis • LAI Shiu Ming Jimmy • THAM Chee Yung Clement • POON Shuet Yan • YEUNG Yat Ming Barry • CHIU Yee Hang Thomas • NG Wai Chung Philip

☐ 1 January 2002

❖ Alcon Hong Kong Ltd

Prostaglandin analogs represent a new class of active ocular hypotensive agents and Alcon Research Ltd has developed a new agent, Travoprost, a highly selective agonist of the FP receptor, one of the prostaglandin receptor subtypes. The drug has been approved by the FDA in the United States with clinical studies demonstrating the effectiveness and safety in patients with primary open angle glaucoma or ocular hypertension. In Asian populations angle-closure glaucoma is significantly more prevalent than in Caucasian populations. The primary objective of this study is to demonstrate that the intraocular pressure-lowering efficacy of Travoprost Ophthalmic Solution 0.004% is at least equivalent to that of Latanoprost 0.005% in patients with chronic angle-closure glaucoma. The study is a double-masked, parallel group design and active-controlled with two treatment groups. The

recruited patients will receive treatment of either Travoprost or Latanoprost for a total of 12 weeks. (MD01398)

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**A Prospective Randomized Comparative Study on the Safety and Efficacy of Argon Laser Peripheral Iridoplasty (ALPI) versus Systemic Intraocular Pressure Lowering Medications for the Immediate Management of Acute Attack of Primary Angle Closure Glaucoma (PACG)**

✉ LAM Shun Chiu Dennis • CHUA Kien Han John • LAI Jimmy S. M.\* • POON Shuet Yan • THAM Chee Yung Clement

☐ 1 July 2001

❖ Research Grants Council (Earmarked Grants)

Acute attack of primary angle closure glaucoma (PACG) is a common condition in the Asian (including Chinese) populations. The suddenly increased intraocular pressure (IOP) can cause irreversible optic nerve damage and permanent visual loss. Conventional medical treatment involves lowering the IOP by immediate intravenous carbonic anhydrase inhibitor and hyperosmolar agents. These systemic medications have many side effects of which some could be life threatening.

Argon laser peripheral iridoplasty (ALPI) is traditionally used to treat PACG 3 to 6 hours after maximal medications fail to control the IOP. It involves the placement of contraction burns on the peripheral iris that pulls open the angle mechanically and promptly lowers the IOP.

Our previous studies suggested that "immediate" instead of "delayed" ALPI an effective and safe alternative to conventional systemic medical treatment for acute PACG. The main advantages of immediate ALPI are: (1) shortening the period of high IOP, thus minimizing symptoms and nerve tissue damage; (2) shortening the period of angle closure, and thus may limit the development of permanent angle closure and chronic glaucoma; (3) not using any systemic drugs, and thus avoiding their potential systemic side effects.

The present prospective randomized controlled study aims to directly compare immediate ALPI with conventional systemic medications in patients with acute PACG. No such information is available in literature.

(MD01090)

**A Randomized Controlled Trial to Determine the Optimal Laser Power Setting for Argon Laser Trabeculoplasty (ALT) in Chinese Eyes with Primary Open-angle Glaucoma (POAG): 300 mW versus 500 mW**

✉ LAM Shun Chiu Dennis • THAM Clement Chee-yung\* • CHUA Kien Han John • LAI Jimmy Shiu-ming\* • POON Agnes Shuet-yan\*

□ 1 September 2001

❖ CUHK Departmental Funding

Primary open-angle glaucoma (POAG) is a potentially blinding eye disease. The conventional treatment includes medications, argon laser trabeculoplasty (ALT), and filtration surgery. All of which are aimed at reducing intraocular pressure (IOP), the most important risk factor for POAG.

ALT was first proposed by Wise and Witter in 1979. It involves the placement of argon laser burns to the trabecular meshwork in the drainage angle. Although the exact mechanism of IOP reduction is still not well understood, ALT has been shown to be both effective and safe for various forms of open-angle glaucoma.

In Caucasians, a power setting of 500 mW was shown to be optimum. Power levels below 500mW produced poor IOP reductions in Caucasians, while higher power used (> 900 mW) will result in more complications. Laser power from 500mW to 800mW produced IOP reductions with no statistically significant differences in Caucasians.

From our clinical experience, Chinese eyes tend to have almost universal pigment deposition over the trabecular meshwork. It has been shown that more pigment in the angle correlates with more effective IOP reduction after ALT. For this reason, we hypothesise that a lower laser power setting may be equally effective in Oriental eyes, with the added benefit of a lower risk of laser complications. We, therefore, plan to compare an ALT power setting of 500 mW with a lower setting of 300 mW in Chinese patients with bilateral primary open-angle glaucoma (POAG), using a randomised controlled trial.

(MD00727)

**Proview Eye Pressure Monitor Observational Pilot Evaluation**

✉ LAM Shun Chiu Dennis • CHEUNG Yan Yan • LAI Shiu Ming Jimmy • CHUA Kien Han John • CHIU Yee Hang Thomas • YICK Wai Fong •

NG Wai Chung Philip • LEUNG Yu Lung Dexter\*

□ 19 December 2001

❖ Bausch & Lomb Incorporated

The objectives of this investigation are to evaluate the Bausch & Lomb Proview™ Eye Pressure Monitor for monitoring intraocular pressure in ocular hypertensive patients or patients currently being treated for glaucoma, and to determine how patients view its ease of use in an in-home environment. (MD01930)

**PIR207A - A Second Year of Treatment in a One Year Multi-center, Double-masked, Placebo-controlled, Parallel, Safety and Efficacy Study of 2% Pirenzepine**

✉ LAM Shun Chiu Dennis • FAN Shu Ping Dorothy • LAM Robert Fung • CHENG Chak Kwan Arthur

□ 1 February 2002

❖ Valley Forge Pharmaceuticals, Inc.

Myopia is the commonest eye problem in Hong Kong. The health-relatedness of myopia treatment has taken on a sense of urgency because of the increasing prevalence in school children. Atropine, a nonselective antimuscarinic agent, was proven to be effective in preventing myopic progression. However, it was associated with a number of side effects including pupil dilatation, photophobia and loss of accommodation. Newer type of selective antimuscarinic agent (pirenzepine) was developed. The preliminary result on this agent was promising.

We propose to examine the safety and efficacy of pirenzepine treatment in preventing of myopic progression in school children in Hong Kong. A randomized trial will be instituted and the endpoint will be the refractive error and the axial length after 2 years of treatment. The rates of myopia progression between treated and controlled cases eyes will be compared. The principal eligibility criteria of the proposed enrollees will be 5-12 years of age with -1 to -4D of myopia (spherical equivalent refraction) but less than 1.00D of astigmatism and 1.00D anisometropia. The rate of myopia progression will be determined with cycloplegic autorefraction to determine the refractive error, ultrasound biometry to measure changes in axial length.

With data collected from this study, more information on the treatment regimes in preventing myopic progression can be obtained. Thus devastating diseases associated with myopia including open-angle glaucoma, cataracts, retinal detachment, and age-related macular degeneration can be prevented.

(MD01995)

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### Retinal Nerve Fibre and Corneal Endothelial Cell Damage in Children with Previous Systemic Steroid Therapy

✉ NG Siu King Joan • CHIK Ki Wai (Dept of Paediatrics) • LAM Shun Chiu Dennis • LEE K.P.\* • LI Randa T.H.\*

☐ 1 November 2001

❖ CUHK Departmental Funding • CUHK Research Committee Funding (Direct Grants)

Systemic steroid is the mainstay of treatment for a number of pediatric diseases. Conditions, such as nephritic syndrome, leukemia and autoimmune diseases, require repeated high dose systemic steroid treatment. One of the major ophthalmic complications of steroid is ocular hypertension that may result in irreversible ocular damage.

The results of our previous studies have shown that children will have more frequent, more severe and more rapid ocular hypertensive response to topical dexamethasone than adults. This exaggerated response to topical steroid may also present in children receiving systemic steroids.

Although steroid-induced ocular hypertension is usually reversible after discontinuation of the agent, the resulting ocular damage is irreversible, which include reduced retinal nerve fiber thickness and corneal endothelial cell count. Pediatric patients who had been put on chronic high dose systemic steroid therapy may suffer from these complications. Albeit subclinical at early stage, it may render the development of symptomatic complications in adulthood such as loss of visual field and corneal decompensation. With the introduction of new diagnostic tools including nerve fiber analyzer and specular microscopy, it allows a more precise and detail assessment of such structural damages. Therefore, the aim of this study is to investigate those children for possible development of permanent ocular damage as a result of previous high dose steroid treatment. The result of this study could

provide important clinical information for pediatricians and ophthalmologists in the early detection of ocular damage and the appropriate management of these patients.

(MD00706)

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### Identification of DNA Methylation Sites in Cancer-related Genes in Retinoblastoma Genome

✉ PANG Chi Pui Calvin • CHOY Kwong Wai • FAN Shu Ping Dorothy • LAM Shun Chiu Dennis • LO Kwok Wai (Dept of Anatomical & Cellular Pathology) • TO Ka Fai (Dept of Anatomical & Cellular Pathology) • YU Bing On Christopher\*

☐ 1 October 2001

❖ Research Grants Council (Earmarked Grants)

Retinoblastoma is the most common and severe form of ocular cancer affecting infants and young children in most populations. Early detection is vital for appropriate treatment to improve prognosis. However, patients may present late with irreversible loss of vision in one or both eyes, and even advancement with systemic spread to become life threatening. Over 90% of both heritable or sporadic forms of retinoblastoma are caused by defects in the tumor suppressing *Rb1* gene. Transmission of retinoblastoma at the cellular level is recessive and requires loss of function of both alleles at the *Rb1* locus. Methylation of *Rb1* occurs in retinoblastoma but its role in tumor development is unclear. Recently we have shown methylation of the *MGMT* gene in retinoblastoma. *MGMT* has DNA repair function and is associated with response to chemotherapeutic drugs. We therefore propose to identify commonly hypermethylated sites in the retinoblastoma genome and in other reported cancer-related genes, *p15*, *p16*, *p19*, *Rb1* and *MGMT*. We are able to collect clinical samples of retinoblastoma patients and document their clinical and histopathological features. We shall use methylation-sensitive restriction fingerprinting (MSRF), methylation-specific polymerase chain reaction (MSP), and DNA sequencing to identify common hypermethylated CpG islands in the micro-dissected retinoblastoma samples. The identified epigenetic abnormalities will be correlated with disease status, response to treatment, and tumor properties. Results of this study will contribute to the understanding of the molecular pathogenesis of



retinoblastoma and form the basis for the development of more effective diagnostic and treatment strategies.  
(MD01091)

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

<u>Edition</u>	<u>Title/Investigators</u>
2000-01	Genetic Cause of Age-related Macular Degeneration in Hong Kong (MD99333) ✉ CHAN Wai Man • PANG Chi Pui Calvin • LAM Shun Chiu Dennis • FAN Shu Ping Dorothy • KWOK Kwan Ho • Lawrence William BAUM (Dept of Medicine & Therapeutics)
2000-01	Clinical Presentation and Genome Mapping of Congenital Cataract (MD00950) ✉ FAN Shu Ping Dorothy • PANG Chi Pui Calvin • LAM Shun Chiu Dennis • LEUNG Yuk Fai
2000-01	Safety of Intravitreal Injection of Various Concentrations of Indocyanide Green Dye (MD00325) ✉ KWOK Kwan Ho • LAM Shun Chiu Dennis • PANG Chi Pui Calvin • YAM Hin Fai# • LAI Yuk Yau Timothy
1997-98	Diagnostic Kits for Early Detection of Genetic Eye Diseases for Blindness Prevention and Genetic Counselling (MD97092) ✉ LAM Shun Chiu Dennis • PANG Chi Pui Calvin
1998-99	Epidemiology of School Myopia in Hong Kong: Prevalence, Incidence and Risk Factors Analysis (MD98004) ✉ LAM Shun Chiu Dennis • CHEW Sek Jin* • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research) • FAN Shu Ping Dorothy • CHENG Hong Ming*
2000-01	Study on the Use of Single Intraoperative Mitomycin C and Conjunctival Autograft to Prevent Recurrence in the Treatment of Double Head Pterygia (MD00753) ✉ LAM Shun Chiu Dennis • YEUNG Emily Fung-yeet* • CHI Chung-chai* • YUEN Kwok-lai*
2000-01	Use of Conjunctival-limbal Autografts Versus Intraoperative Application of Mitomycin-C in Treatment of Recurrent Pterygium in Hong Kong (CU00052) ✉ LAM Shun Chiu Dennis • RAO Srinivas Kamalakara# • YU Yau Woon Edward#
2000-01	A Randomized Trial to Investigate the Ocular-hypertensive Response to Different Dosages of Topical Steroid (0.1% Dexamethasone) in Chinese Children (CU00050) ✉ LAM Shun Chiu Dennis • FAN Shu Ping Dorothy • NG Siu King Joan • YU Bing On Christopher
2000-01	Retinal Electrophysiological Changes in Patients Following Acute Angle Closure Glaucoma (MD00552) ✉ LAM Shun Chiu Dennis • LAI Timothy Yuk-yau* • CHUA Kien Han John • FAN Shu Ping Dorothy • KWOK Kwan Ho • AU Wai Hing
2000-01	Topical Anaesthesia versus Transcutaneous Anaesthetic Injection in Chalazion Surgery (MD00745) ✉ LAM Shun Chiu Dennis • LI Randa T.H.* • LEUNG Tai Shing • NG Siu King Joan • LAI Jimmy Shiu-ming*
2000-01	A One-year Multi-center, Double-masked, Placebo-controlled, Parallel, Safety and Efficacy Study of 2% Pirenzepine Ophthalmic Gel in Children with Myopia (MD00996) ✉ LAM Shun Chiu Dennis • FAN Shu Ping Dorothy • LAM Robert Fung
2000-01	A One Year Multi-center, Double-masked, Placebo-controlled,

- Parallel, Safety and Efficacy Study of 2% Pirezepine Ophthalmic Gel in Children with Myopia (MD20040)  
✉ LAM Shun Chiu Dennis • FAN Shu Ping Dorothy
- 2000-01 An Observer-masked, Parallel Group, Randomized, 7-day Environment Study of Patanol versus Loratadine in Asian Patients from Hong Kong with Perennial Allergic Conjunctivitis (MD20052)  
✉ LAW Wai Kee • LAM Shun Chiu Dennis • LEUNG Tai Shing
- 1998-99 Effects of Genetic Variants of Lipoprotein Lipase on Coronary Heart Disease and Familial Combined Hyperlipidaemia (CU98282)  
✉ PANG Chi Pui Calvin • Brian TOMLINSON (Dept of Medicine & Therapeutics)
- 2000-01 Role of the Putative Promoter of the *TIGR* Gene on Development of Primary Open Angle Glaucoma (MD00439)  
✉ PANG Chi Pui Calvin • LAM Shun Chiu Dennis • FAN Shu Ping Dorothy • CHUA Kien Han John • Lawrence William BAUM (Dept of Medicine & Therapeutics)

## RESEARCH OUTPUTS AND PUBLICATIONS

- <P016024> **PANG Chi Pui Calvin; FAN Shu Ping Dorothy; KEUNG J.W.; BAUM Lawrence William; TANG Leung Sang Nelson; LAU Wan Yee Joseph and LAM Shun Chiu Dennis.** "Congenital Hypertrophy of the Retinal Pigment Epithelium and APC Mutations in Chinese with Familial Adenomatous Polyposis". *Ophthalmologica* vol.215 no.6, pp.408-411. New York, USA: S. Karger, 2001.11.
- <P016100> **CHUA Kien Han John; THAM Chee Yung Clement; TANG W.W.; POON Shuet Yan; LAI Shiu Ming Jimmy and LAM Shun Chiu Dennis.** "Scanning Laser Polarimetry To Measure The Nerve Fiber Layer In Normal Chinese Subjects". Paper presented in the Annual Meeting of the Association for Research in Vision and Ophthalmology (ARVO) Fort Lauderdale, USA, 2001.
- <P016124> **LAI Yuk Yau Timothy, KWOK Kwan Ho, CHUA Kien Han John, AU A.W., FAN Shu Ping Dorothy and LAM Shun Chiu Dennis.** "Multifocal ERG Changes in Patients Following Unilateral Attack of Acute Angle Closure Glaucoma". Paper presented in the Annual Meeting of the Association For Research In Vision And Ophthalmology (ARVO) Fort Lauderdale, USA, 2001.
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- <P016472> **CHENG Chak Kwan Arthur; RAO Srinivas Kamalakara; YU Yau Woon Edward; LEUNG Helios Tin Chung; LAW Wai Kee and LAM Shun Chiu Dennis.** "Reproducibility of Corneal Flap Thickness in Laser in Situ Keratomileusis Using the Hansatome Microkeratome". *Journal*

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- <P019116> **LAI Shiu Ming Jimmy; THAM Chee Yung Clement and LAM Shun Chiu Dennis.** "The Efficacy and Safety of Combined Phacoemulsification, Intraocular Lens Implantation, and Limited Goniosynechialysis, Followed by Diode Laser Peripheral Iridoplasty, in the Treatment of Cataract and Chronic Angle-closure Glaucoma". *Journal of Glaucoma* vol.10 no.4, pp.309-315. New York, USA: Raven Press, 2001.08.
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- <P019284> **NG Siu King Joan; LEUNG Helios Tin Chung and LAM Shun Chiu Dennis.** "Clear Lens Phacoemulsification for Correction of High Myopia". *Journal of Cataract and Refractive Surgery* vol.27 no.12, pp.1901-1902. Fairfax, USA: American Society of Cataract and Refractive Surgery, 2001.12.
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- <P019928> **LEUNG Yuk Fai; LAM Shun Chiu Dennis and PANG Chi Pui Calvin.** "The Miracle of Microarray Data Analysis". *Genome Biology* vol.2 no.9, REPORTs4021. London, UK: Genome Biology Ltd., 2001.09.
- <P026330> **KWOK Kwan Ho; CHENG Lu Lulu; TSE Wai Ip; CHEUNG Yan Yan and LAM Shun Chiu Dennis.** "Outcomes of Primary Rhegmatogenous Retinal Detachment in Myopes of Five or More Diopters". *Ophthalmic Surgery and Lasers* vol.33 no.3, pp.188-194. Thorofare, New Jersey, USA: Slack, Inc., 2002.05.
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## RESEARCH PROJECTS

### A Study of the Potential of a Semi-purified Total Flavone Extract from Chinese Medicine Hippophae Rhamnoides in Promoting Tendon Healing

✉ CHAN Kai Ming • FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) • FUNG Kwok Pui (Biochemistry) • GAO Jin\* • LI Jingxian\*

□ 1 September 2001

❖ Research Grants Council (Earmarked Grants)

With advancing affluence in developed countries, we are seeing an increasing trend of incidence of sporting injuries arising from contusion and twisting, leading to various forms of ligament and tendon injuries. These have taken up significant health care resources in the management and rehabilitation. To date, there is relatively little understanding how the healing potential of ligaments and tendons can be improved.

For thousands of years, Chinese Medicine had been used to promote soft tissue healing. A semi-purified total flavone extract from Hippophae rhamnoides (Shaji 沙棘) (TFH) has been shown to modulate the inflammatory phase by alleviating edema, reducing the oxidative damages and promoting the healing environment with neovascularization. In our own laboratory, we have already established a validated animal model for the study of tendon healing and have demonstrated the significance of cytokines in modulating healing responses in tendon. In collaboration with the National Laboratory of Natural Drugs and Biomolecules under the Chinese Academy of Science, we would study the scientific basis of TFH with reference to the modulation of inflammatory, expression of tendon fibroblast stimulating growth factors, PDGFBB and TGF- $\beta$ , also the quality of the healing tendon by measuring the biochemical parameters of collagen synthesis and the biomechanical parameters of ultimate stress.

The outcome of this study would delineate the scientific basis of TFH on tendon and ligament healing and would have a far reaching implication in the clinical management.

(MD01092)

### To Promote Tai Chi as an Exercise to Enhance the Health Promotion Aspect of Osteoporosis

✉ CHAN Kai Ming • QIN Ling • LI Jingxian (Dept of Sports Science & Physical Education) • HONG Youlian (Dept of Sports Science & Physical Education) • LAU Edith Ming Chu (Dept of Community and Family Medicine) • WOO Jean (Dept of Medicine & Therapeutics)

□ 1 January 2002

❖ Health Care & Promotion Fund, Hospital Authority

Osteoporosis is one of the most prevalent musculo-skeletal conditions leading to significant morbidity and mortality in the elderly population. The complication of osteoporosis and related fractures such as fractures around the hip, fractures of the distal radius and fractures of the spine are common causes of prolonged hospital stay, thereby incurring a significant budget in the health care system.

Previous research findings of our team indicated that Tai Chi is a popular and implementable form of exercise to be promoted among the elderly population as a means to reduce the morbidity of osteoporosis and the attending complications of the fractures.

The main objectives of this project are (1) to enhance the awareness of Tai Chi as a preventative exercise to prevent osteoporosis, and (2) to facilitate the implementation of the promotion project and to monitor the outcome. To achieve these objectives, we will assemble a group of elderly and test several sets of Tai Chi so as to find out the most suitable form for them. We will then produce a user-friendly video on this particular set of Tai Chi and conduct a regular Tai Chi course with an integrated community care approach with health talks and workshops, thereby, creating an environment of peer support and professional health care to the elderly population in our community. As an assessment outcome, questionnaire will be designed to assess the validity of this project and to collect data on long term compliance and reasons for not continuing.

(MD01740)

### Percutaneous Intramedullary Kirschner Wiring for Displaced Disphyseal Fractures in Children

✉ CHENG Chun Yiu Jack • YUNG Shu Hang Patrick • NG Kin Wah Bobby • LAM Tsz Ping

□ 1 January 2000

❖ CUHK Departmental Funding

This is to access the results and pitfalls in treatment of children diaphyseal forearm fracture with percutaneous K-wire fixation with an average FU of 48 months. We have performed percutaneous Kirschner (K) wire fixation in 112 children with displaced forearm shaft fracture in the past 9 years, with 84 cases reviewed. 64 (76%) of them had both the radius and ulna fractured, and 10 (12%) the radius only and the other 10 (12%) the ulna only. In 60 (71%) patients we performed close reduction, while in the remaining 24 (29%) close reduction failed and an open reduction through a small incision was required before K-wire performed. The K-wire was inserted through the Radial styloid or the Lister tubercle for the radius, and through the tip of the olecranon for the ulna. All the patients reviewed were found to have good functional results, none had non-union, deep infection or premature physal closure at a mean follow-up of 48 months. If initial pre-operative radiograph showed shortening or translation of the fracture, significant higher chance of open reduction was anticipated.

(MD99476)

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**Correlation of Calcium Absorption and Homeostasis with Severity and Progression of Spinal Deformity in Growing Adolescents with Idiopathic Scoliosis**

✉ CHENG Chun Yiu Jack • LEE Tak Keung Warren • LEE Kwong Man, Simon\* • GUO Xia

□ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Scoliosis is a serious deformity that can affect any parts of the spine. The most common form of scoliosis is Adolescent Idiopathic Scoliosis (AIS) which predominantly affects adolescent girls of the age 10 to 16. scoliosis deformity if 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 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. And that there is a negative trend between BMD and the extent of spinal deformity.

In order to investigate in details whether intestinal true fractional calcium absorption, and the indices of calcium homeostasis that may contribute to the variation in body calcium retention, bone mineral acquisition, and the progression of scoliosis deformity in AIS, a 1-year follow-up study has been proposed. The outcomes of the study will shed light on the understanding of calcium and bone metabolism in AIS adolescents, and the possibility of abnormal calcium metabolism that may contribute to the pathogenic mechanism of osteopenia and the progression of scoliosis deformity in AIS adolescents. This may lead to a novel approach in the monitoring, prognostication and treatment of AIS. In those AIS adolescents with osteopenia, the natural history of the scoliotic deformity may be modified by non-invasive treatment in order to improve the bone mineral status.

*The Objectives of the study are:*

(1) To establish baseline true fractional calcium absorption (TFCA), indices of calcium homeostasis and BMD status in 10-16 years old AIS female patients. And to compare with those of the age, sex, and maturity matched normal controls.

(2) To carry out a longitudinal follow-up study to evaluate the dynamic changes of true fractional calcium absorption (TFCA), urinary calcium excretion, and indices of calcium homeostasis that may contribute to net body calcium retention, bone mineral acquisition and the progression of spinal deformity in AIS patients. And to compare with those of the age, sex, and maturity matched normal controls.

(MD99370)

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**Relationship between Postural Balance, Somatosensory Evoked Potential and the Progression of Scoliotic Deformity in Adolescent Idiopathic Scoliosis - A Longitudinal Study**

✉ CHENG Chun Yiu Jack • Hui Chan W Y Christina\* • GUO Xia\*

□ 1 April 2002

❖ Scoliosis Research Society (SRS) - Etiology Grant

*Study Background:* The association of abnormal postural control and balance with adolescent idiopathic scoliosis (AIS) has been reported, particularly in patients with severe curves. Our previous studies have demonstrated the presence of abnormal somatosensory evoked potentials (SEPs) in patients with AIS. It is unknown whether reported problems in postural control and somatosensory function are causes or effects of the scoliotic spinal deformity.

*Aims of the Study:* The aims of the study are to answer following questions:

- (1) Are postural control problems in AIS associated with disturbed somatosensory function?
- (2) Are abnormal somatosensory function and postural control problems causes or effects of scoliosis deformity?

*Materials and Methods:* One hundred new cases of AIS with mild spinal deformity and 50 age and maturity matched normal controls will be recruited into this two-years longitudinal follow-up study. Measurements of Cobb angles, SEPs and Posturography balance tests will be performed on each subject at the time point of 0, 10 and 20 months.

*Clinical Significance:* Results of the present study may help to improve our understanding of the role of somatosensory function and balance in the etiology and prognostication of AIS. The outcome of this study may help in future development of new interventional treatment program aiming at improving the postural balance and thus preventing the progression of scoliosis deformities.

(MD01864)

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### **Electromotive Antibiotic Delivery to Bone by Iontophoresis**

✉ HUNG Leung Kim • CHAN Chiu Yeung Raphael (Dept of Microbiology) • WU Hay Tong

☐ 1 January 2002

❖ CUHK Research Committee Funding (Direct Grants)

Antibiotic diffusion into infected bone is difficult and is impaired by poor vascularity, the presence of necrotic bone or dead space. Iontophoresis, a form of electromotive drug delivery, regulates drug delivery by an electric field. The use of this technique in bone infection can ensure a high local concentration of antibiotics, and systemic toxicity can

be reduced. Pilot study on iontophoresis of ofloxacin through cortical bone has shown significantly enhanced drug delivery. The technique will also be studied for vancomycin and rifampicin.

(MD01360)

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### **Bisphosphonates Induce the Healing and Consolidation of Osteolytic Secondary Bone Tumors**

✉ KUMTA Shekhar Madhukar • YEO Winnie (Dept of Clinical Oncology) • James Francis GRIFFITH (Dept of Diagnostic Radiology & Organ Imaging) • CHOW Tsun Cheung Louis (Dept of Anatomical & Cellular Pathology) • HUANG Lin • CHENG Yuen Yee#

☐ 15 December 2001

❖ CUHK Research Committee Funding (Direct Grants)

Cancers of visceral organs such as the lung, thyroid, kidney, prostate and breast often metastasize to bone causing severe pain, fractures and extreme morbidity. This is a large-scale problem all over the world. In Hong Kong there are almost 11,000 new cases of cancer diagnosed each year; 37% of these have a predilection to spread to bone. Bone provides a rich source of nutrition and growth sustaining factors that help sustain the growth of secondary tumors. However these growth factors are bound to the mineral matrix and can only be released after the mineralized matrix is dissolved by osteoclasts. Bisphosphonates are a class of drugs that have previously been used for the prevention of new metastatic lesions especially in patients with breast carcinoma. Bisphosphonates have potent effects on osteoclast cells, through many pathways, and are powerful inhibitors of osteoclast mediated bone resorption.

The conventional management of patients with secondary or metastatic tumors has been radiotherapy with or without internal fixation of the bone. Radiation weakens the bone and may predispose the bone to sustain a pathological fracture. In addition, not all secondary tumors respond to radiation, and despite radiation, progressive destruction of bone may continue to occur.

The use of bisphosphonates may prevent the progression of secondary tumors in bone by preventing the release of growth sustaining cytokines. Our proposed study aims to investigate the effect of

bisphosphonates on metastatic lesions in bone. Preliminary work has revealed that a combination of amino and non-amino bisphosphonates has promoted the healing and re-calcification of metastatic skeletal lesions. This indirect means of manipulating the microenvironment around tumors is a relatively novel but effective strategy and may also extend the survival of patients with metastatic disease. Our proposed study is a clinical trial in which we aim to study the bone healing effects of bisphosphonates (Pamidronate and Clodronate) in patients affected by secondary neoplasms.

(MD01649)

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**The Biological Mechanism of Neo-Angiogenesis with Callotaxis - A Study of the Effect of External Mechanical Stimulation on Biological System and Its Potential in Clinical Modulation**

✉ LEUNG Kwok Sui • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • FUNG Kwok Pui (Biochemistry) • LUI Po Yee Pauline#

☐ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Lengthening of bone by inducing new bone formation under tension stress has been successfully applied to treat clinical problems related to limb length discrepancies and bone loss due to trauma. The treatment course consists of three distinct phases: the first phase is the surgical procedure to break the bone and preparation for distraction with the application of external distractor; the second phase is the actual lengthening of the bone by distraction with the rate of 1 mm per day and the third phase is the consolidation and remodeling of the newly formed bone to become normal bone. While the clinical results have been satisfactory, complications are common. Most of the complications are related to the prolonged applications of the external distraction device and the long duration of hospitalization. Although the biological events during various stages of distraction have been characterized within the scientific investigations which our team has been actively involved in the past eight years, the mechanism of neo-osteogenesis induced by external mechanical force during distraction phase has not been explored yet.

In this proposal, we plan to study the effect of external mechanical stimulation on biological system in a subcellular level and its potential in clinical modulation. The aims are to shorten the duration of bone lengthening and to enhance bone formation and maturation. With the external mechanical stimulation, this very well orchestrated biosynthetic events that lead to complete tissue regeneration is activated and sustained. In this very complicated biological process, the activation of cyclo-oxygenase 2 (COX-2) pathway is critical. In the first phase of the proposal, critical modulators of this pathway, namely COX-2 inhibitors and PGE2 (one of the downstream effectors of (COX-2), will be injected into our well-established rabbit distraction model for evaluating their effects on distraction rate and consolidation. The expression profile of growth factors, TGF-beta and bFGF, which we have shown in the previous RGC-grant projects to have anabolic effects during distraction osteogenesis, will also be examined under these external interventions. In the second phase of this investigation, the direct effect of COX-2 pathway on the biological activities of osteoblast and endothelial cell culture systems, which are key players of distraction osteogenesis, will be examined by direct application of these COX-2 pathway modulators during mechanical stimulation. The effect of cyclic and continuous step-up stretching protocols on the anabolic response of osteoblasts and endothelial cells will also be compared. Results obtained from this project will help us to modify clinical treatment protocol, which leads to an increase in the rate of distraction and hence decreases the complications. The information obtained will also improve our understanding on the growth stimulation and control of the bony tissue in fracture healing and in the regeneration of bone by distraction osteogenesis.

(MD01806)

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**Herbal Formula for Prevention and Treatment of Osteoporosis - A Rat Model**

✉ LEUNG Ping Chung • FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) • FUNG Kwok Pui (Biochemistry) • QIN Ling • SHI Yin Yu\* • XU Min (Dept of Community and Family Medicine)

☐ 1 November 2001

❖ Research Grants Council (Earmarked Grants)

We have good experience on the use of a Herbal formula (YYH) for the control of osteoporosis in an experimental model and in the human (pilot study) we are now ready to engage in more in deep study on the same YYH formula. The scope of research would include:

- (1) Densitometer changes in the bones of a rat model with induced osteoporosis - in response to YYH and placebo;
- (2) Work out the different combinations with YYH to give the best effects; and
- (3) Work on the abstract and ingredients of YYH and its combined formula; which might give the major therapeutic effects.

(MD01097)

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### Chinese Medicine Research and Further Development

✍ LEUNG Ping Chung • FUNG Kwok Pui (Biochemistry) • SUNG Jao Yiu Joseph (Dept of Medicine & Therapeutics) • HAINES Christopher John (Dept of Obstetrics & Gynaecology) • SUNG Yn Tz Rita (Paediatrics) • WOO Kam Sang (Dept of Medicine & Therapeutics) • CHE Chun Tao (School of Chinese Medicine) • CHAU F T\* • TSIM Karl W K\* • FONG W F\*

□ 1 November 2001

❖ UGC Area of Excellence

While western medicine has advanced very rapidly, it has failed to treat all illnesses with equal effectiveness. In areas such as viral infection, chronic disorder, degenerative disease, allergy and preventive therapy, its efficacy is surpassed by that of Chinese medicine. The five priority projects under the AoE programme of the “Chinese Medicine Research and Further Development”, as follows, were chosen in these areas where western medicine has no optimal solution:

- (1) Treatment of Chronic Hepatitis B Virus Infection with Phyllanthus Compound
- (2) Treatment of Common Female Ailments with Danggui Buxue Tang
- (3) Treatment of Diabetic Foot Ulcer with Huangqi Preparation
- (4) Treatment of Childhood Asthma with Dongchong Xiacao Preparation
- (5) Danshen and Gegen Preparation as Cardiovascular Tonic

The uniqueness of this AoE project is the adoption of the efficacy-driven approach for doing Chinese medicine research. The research findings will not only provide more scientific evidence for the efficacy of Chinese medicine, but can also affirm its role as alternative or complementary therapy in the international arena. The AoE will also provide important references and set models for Chinese medicine research, its integration with western medicines and the development of nutraceuticals as well as herbal drugs.

(MD01714)

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### Low Intensity Pulsed Ultrasound for Accelerating Bone-tendon Junction Repair

✍ QIN Ling • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • LENG Yang\* • WONG Wan Nar Margaret

□ 1 December 2001

❖ Research Grants Council (Earmarked Grants)

Many trauma surgeries and reconstructive surgeries involve re-establishment of a bone-tendon junction, such as repair of patella fractures. Due to difficulties in reconstructing the fracture fragments, partial patellectomy has become the clinical routine whereby the smaller bony fragment is removed and the patellar tendon is reattached directly onto the remaining patella for surgical fixation, without preservation of the junctional fibrocartilage zone between the patellar tendon and patella. Unfortunately, such direct bone-tendon repair requires prolonged immobilization, hospitalization, and subsequently a longer period of rehabilitation due to slow and poor regeneration of the transitional fibrocartilage zone resulting in a weak knee as found by the investigators both in clinical observation and experimental studies.

Biophysical intervention using low intensity pulsed ultrasound (LIPU) has demonstrated certain effectiveness in accelerating fracture healing, delayed union, non-union, and soft tissue repair process, possibly by stimulating some endogenous biological growth factors. This investigation will employ the established partial patellectomy model in rabbits to study the effect of LIUP on accelerating bone-tendon junction repair with earlier restoration of the junctional fibrocartilage zone. The results to be obtained will help us to modify clinical treatment protocols which may lead to an earlier repair and

active rehabilitation and reduction of the associated complications. The results will also improve our understanding on the potential mechanisms and role of LIPU in reconstructive surgeries involving bone-tendon junction repair. The potential beneficial effects of LIPU in accelerating direct bone-tendon healing in our patial pectomy model can also be gearlized to other regions involving direct bone to tendon junction repair.

(MD01098)

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**The Effect of Glucocorticoid on Human Tendon Explant: The Link with Tendon Rupture**

✉ WONG Wan Nar Margaret • FU Sai Chuen Bruma\* • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • CHAN Kai Ming

☐ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Glucocorticoid injections are used in a wide spectrum of soft tissue disorders and inflammatory conditions. The potent anti-inflammatory action often gives rapid clinical response. There are a number of reports on spontaneous tendon ruptures with previous glucocorticoid injection in the literature. However, an association or cause-effect relationship has never been established. Previous *in vitro* and *in vivo* studies using animals to evaluate the relationship of local steroid injection with tendon damages were non-conclusive, and the validity of extrapolating animal study result to human is doubtful. The effect of glucocorticoid on tendon remains unrevealed. As there is yet no replacement for local steroid injection therapy, the practice will continue in indicated cases, though with trepidation. A clarification of its effect is needed to allow practice with evidence-based medicine.

Our group has studies the effect of dexamethasone (a glucocorticoid) on human tendon fibroblast cultures. We have demonstrated cytotoxic and cytostatic effects, and also suppressed 35-sulphur uptake, indicating decreased proteoglycan synthesis. The cell culture system lacks the extracellular matrix and three-dimensional structure of normal tendons, which affect the response to stimuli. As the eventual link is to tendon rupture, which is related to the extracellular matrix integrity, this cannot be studied in the cell culture system. We propose to further

investigate the link between glucocorticoid and eventual tendon ruptures using human tendon explant tissue culture, which has the advantage of controlled *in vitro* experiment, yet maintaining the three dimensional structure of tendons and the presence of extracellular matrix.

The study will examine the effect of a commonly used glucocorticoids (dexamethasone) in human tendon explant culture. Assessment parameters include cell viability, extracellular matrix metabolism and regulation enzyme, collagen cross link.

The result of this study will clarify the link between glucocorticoid injections and spontaneous tendon ruptures. With the identification of the cellular and matrix disturbance, the possible mechanism of action may be identified. Evidence based recommendations on the proper use of local steroid may then be devised. The findings also form basis for future studies to search for ways to allow the continuous use of this useful therapeutic regime, while limiting its adverse effects.

(MD01921)

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

<u>Edition</u>	<u>Title/Investigators</u>
2000-01	Low Intensity Pulsed Ultrasound Retained Change of Bone Mineral Content of Complex Tibial Fractures (MD00354) ✉ CHAN Chun Wai* • LEUNG Kwok Sui • TSUI Hon For • LEE Wing Sze
2000-01	Low Intensity Pulsed Ultrasound Enhanced Bone Mineral Content of Tibial Lengthening (MD00579) ✉ CHAN Chun Wai* • LEUNG Kwok Sui • CHENG Chun Yiu Jack • NG Kin Wah Bobby • LEE Wing Sze • HUNG Wing Yin Vivian
1999-00	The Application of Verbascoside, A Purified Extract of Chinese Medicine on Recovery of Muscle Injury after Immobilization (CU99344) ✉ CHAN Kai Ming • FUNG Kwok Pui (Biochemistry) • QIN Ling • LEE

- Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • LI Jingxian (Dept of Sports Science & Physical Education)
- 1998-99 Low Volumetric Bone Mineral Density in Adolescent Idiopathic Scoliosis (MD98136)  
 ✎ CHENG Chun Yiu Jack • QIN Ling • GUO Xia • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • NG S W Edmond\*
- 1999-00 The Application of Verbascoside, a Purified Extract of Chinese Medicine on Recovery of Muscle Injury After Immobilization (MD99049)  
 ✎ CHAN Kai Ming • FUNG Kwok Pui (Biochemistry) • QIN Ling • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • LI Jingxian (Dept of Sports Science & Physical Education)
- 1999-00 A New Approach to the Treatment of Skeletal Muscle Injury – Isolation and Cloning of a New Myogenic Factor (MD99082)  
 ✎ CHAN Kai Ming • LI Ming (Dept of Medicine & Therapeutics) • TIOLLAIS Pierre\* • WU Yuan Fei\*
- 1999-00 Osteoporosis in Adolescent Idiopathic Scoliosis - A Study of the Genetic Markers, Bone Mineral Turnover and Their Correlation with Severity and Progression of the Spinal Deformity (CU99336)  
 ✎ CHENG Chun Yiu Jack • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • QIN Ling • GUO Xia
- 1999-00 Nutrition & Physical Activity as Possible Factors Affecting Bone Mineral Status in Adolescent Idiopathic Scoliosis (AIS) – Cross-sectional & Case-control Studies (MD99018)  
 ✎ CHENG Chun Yiu Jack • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research) • HO CHAN Suzanne (Dept of Community and Family Medicine) • GUO Xia
- 2000-01 A Study of the Potential of Total Flavone Extract From Chinese Medicine *Hippophae Rhamnoides* in Promoting Tendon Healing (MD20069)  
 ✎ CHAN Kai Ming • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) • LI Jingxian (Dept of Sports Science & Physical Education) • FUNG Kwok Pui (Biochemistry) • GAO Jin\*
- 2000-01 Re-defining the MRI Reference Level for Cerebellar Tonsil - A Study of 225 Adolescents - Normal vs Idiopathic Scoliosis (MD00378)  
 ✎ CHAU Wai Wang • CHENG Chun Yiu Jack • GUO Xia • CHAN Y. L.\*
- 2000-01 An Unintentional Child Injury Surveillance Study in Hong Kong (MD99504)  
 ✎ CHENG Chun Yiu Jack • Chan C.C.\* • CHOW C. B.\* • LUI P. K.\* • WONG Tze Wai (Dept of Community and Family Medicine)
- 2000-01 "Subacute Synovitis of the Hip in Children" A distinct Entity? - A follow up Study of 84 Cases (MD99384)  
 ✎ CHENG Chun Yiu Jack • YUNG Shu Hang Patrick • NG Kin Wah Bobby • LAM Tsz Ping
- 2000-01 The Implications of Preoperative Somatosensory Evoked Potential (SSEP) in Adolescent Idiopathic Scoliosis Patients (MD00430)  
 ✎ CHAU Wai Wang • FU Lap Kun • GUO Xia • CHENG Chun Yiu Jack
- 2000-01 To Purchase Wheelchair Accessories, Computer Access Equipment and Communication Devices for a Pilot Project to Set Up a Library of Assistive

- Technology in the Seating Clinic, Prince of Wales Hospital (MD20002)  
 ✎ CHENG Chun Yiu Jack • FUNG Kwai Yau • MAK Arthur\*
- 2000-01 Can Exogenous Vascular Endothelial Growth Factor (VEGF) Enhance Angiogenesis and Osteogenesis in Posterior Spinal Fusion? (CU00140)  
 ✎ CHENG Chun Yiu Jack • CHOW Pak Ham Patricia (Dept of Anatomy) • GUO Xia • LEE Simon K. M.\* • TABATA Yasuhiko\*
- 2000-01 Virtual Reality (VR) Based Systems for Training on Endoscopic Surgery and Diagnostic Ultrasound Procedures (EE20028)  
 ✎ CHENG Chun Yiu Jack • HENG Pheng Ann (Dept of Computer Science and Engineering) • CHAN Kai Ming • CHUNG Chi Kit Ronald (Dept of Auto. & Computer-Aided Engin.) • CHUNG Sheung Chee Sydney (Dept of Surgery) • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Kwong Sak (Dept of Computer Science and Engineering) • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • TSUI Hung Tat (Dept of Electronic Engineering) • WONG Tien Tsin (Dept of Computer Science and Engineering) • XU Yangsheng (Dept of Auto. & Computer-Aided Engin.) • YIM Ping Chuen Anthony (Dept of Surgery) • Shi Peng Cheng\* • Tso Shiu Kit\*
- 1999-00 Repair of Large Peripheral Nerve Defects with Artificial Nerve Grafts Composing of Cultured Schwann Cells (MD99110)  
 ✎ HUNG Leung Kim • KWONG Wing Hang (Dept of Anatomy) • WU Hay Tong • LUI Kong Kei Walter#
- 2000-01 Electromotive Drug Delivery to Bone by the Pulsed Short-circuit Pulsed Direct Current Mode Iontophoresis (MD00695)
- ✎ HUNG Leung Kim • CHAN Chiu Yeung Raphael (Dept of Microbiology) • LIN Ge (Dept of Pharmacology) • ZHANG Yuanting (Dept of Electronic Engineering)
- 2000-01 Towards Understanding the Molecular Events of Histogenesis and Biological Behaviour of Giant Cell Tumour of Bone - The Significance of Urokinase Type Plasminogen Activating System and Osteoclast Regulatory Factors (CU00142)  
 ✎ KUMTA Shekhar Madhukar • CHOW Tsun Cheung Louis (Dept of Anatomical & Cellular Pathology) • LEE Simon K. M.\* • LEUNG Ping Chung • ZHENG Ming Hao\*
- 2000-01 Anti-angiogenic and Antiresorptive Actions of Bisphosphonates and COX-2 Inhibitors on Osteosarcoma Cells (Surrogate Osteoblasts) (MD00642)  
 ✎ KUMTA Shekhar Madhukar • LUI Po Yee Pauline# • FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) • CHEUNG Wing Hoi
- 2000-01 Monteggia Fracture in Children - A Review of 30 cases (MD00535)  
 ✎ LAM Tsz Ping • Ma RF\* • NG Kin Wah Bobby • CHENG Chun Yiu Jack
- 2000-01 Anterior Spinal Fusion With Halm-Zielke Instrumentation System in Adolescent Idiopathic Scoliosis (MD00788)  
 ✎ LAM Tsz Ping • NG Kin Wah Bobby • CHENG Chun Yiu Jack • Ma RF\*
- 2000-01 Calcium Intakes in Patients With Adolescent Idiopathic Scoliosis (AIS) (MD00838)  
 ✎ LEE Tak Keung Warren • CHEUNG Siu King • LAM See Way Sylvia# • LEE Ching Shun Christine\* • CHAU Wai Wang • CHENG Chun Yiu Jack



- 1998-99 A Biomechanical and Histomorphometrical Study for the Improvement of Implant Fixation on Osteoporotic Bone with Ovariectomised Female Goats (CU98270)  
 ✎ LEUNG Kwok Sui • CHOW Hung Kay, Daniel\* • Anthony Edward JAMES (Laboratory Animal Services Centre) • QIN Ling • CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)
- 1999-00 The Effect of Non-invasive Low Intensity Pulsed Ultrasound on the Consolidation of Osseous Tissue after Callotasis - The Biological Basis and Its Potential Clinical Application (CU99257)  
 ✎ LEUNG Kwok Sui • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • FUNG Kwok Pui (Biochemistry) • CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)
- 2000-01 The Biological Mechanism of Neo-osteogenesis with Callotasis - A Study of the Effect of External Mechanical Stimulation on Biological System and Its Potential in Clinical Modulation (MD00652)  
 ✎ LEUNG Kwok Sui • FUNG Kwok Pui (Biochemistry) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • LUI Po Yee Pauline# • CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)
- 2000-01 Reconstruction of Damaged Physis with 3-D Chondrocytes Pellet Culture (MD20039)  
 ✎ LEUNG Kwok Sui • LUI Po Yee Pauline# • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • CHEUNG Wing Hoi
- 1999-00 Prevention of Osteoporotic Fractures among the "High Risk" Groups of Postmenopausal Women (MD99001)  
 ✎ LEUNG Ping Chung • QIN Ling • AU Sze Ki (School of Public Health)
- 2000-01 Development and Clinical Trials of Compound Yun Zhi (Jiang Su) and Danshen (He Nan) Products (MD20043)  
 ✎ LEUNG Ping Chung • FUNG Kwok Pui (Biochemistry) • LAM Wai Kei Christopher (Dept of Chemical Pathology)
- 2000-01 Associated Osteoporosis of the Host Bone in Tibial Lengthening (MD00633)  
 ✎ NG Kin Wah Bobby • HUNG Wing Yin Vivian • CHENG Chun Yiu Jack
- 1999-00 A New Approach to Rehabilitation of the Musculo-skeletal System after Immobilization – To Study the Combined Use of Muscle Electrical Stimulation and Functional Remobilization with Progressive Treadmill Running in a Rabbit Model (MD99051)  
 ✎ QIN Ling • MAK Arthur\* • CHAN Kai Ming • ROLF Christer# • CHAN Pui Barbara# • ZHANG Yuanting (Dept of Electronic Engineering)
- 2000-01 Muscle-bone Biological Interaction in Adolescent Idiopathic Scoliosis (MD20051)  
 ✎ QIN Ling • CHENG Chun Yiu Jack • Schonau E\*
- 2000-01 Application of Low Intensity Pulsed Ultrasound for Bone-tendon Junction Repair (MD00844)  
 ✎ QIN Ling • WONG Wan Nar Margaret • LEE Kwong Man, Simon\* • LEUNG Kwok Sui
- 2000-01 Treatment of "Floating Elbow" in children (MD00960)  
 ✎ TANG Ning • NG Kin Wah Bobby • CHENG Chun Yiu Jack
- 2000-01 Bacterial Adherence to Gentamicin-PMMA Beads (MD20030)  
 ✎ WONG Wan Nar Margaret • Mamie HUI (Dept of Microbiology)

- 2000-01 Bio-engineered Chondrocyte Pellet as Interposition Material for Acceleration of Bone-tendon Junction Healing and Restoration of Junctional Fibrocartilage Zone (MD00373)  
✉ WONG Wan Nar Margaret • QIN Ling • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)
- Ceramic and Collagen Sponge (MD98751)  
✉ YEUNG Hiu Yan • LEE Kwong Man, Simon\* • CHEUNG Wing Hoi • LAW Lai Pang (Institute of Chinese Medicine) • TABATA Yasuhiko\* • CHENG Chun Yiu Jack
- 2000-01 Culture of Rabbit Chondrocytes Released from Rib Cage on Calcium Phosphate

## RESEARCH OUTPUTS AND PUBLICATIONS

- <P006472> **Dept of Hand Surgery, Huashan Hospital, HUNG Leung Kim, Dept of Hand Surgery, Huashan Hospital, KWONG Wing Hang and LEUNG Ping Chung.** "The Optimal Time to Perform Distal Nerve Anastomosis in Contralateral C7neurotization for Total Brachial Palsy - An Experimental Study". *Hong Kong Journal of Orthopaedic Surgery* vol.4 no.2, pp.102-107. Hong Kong SAR, 2000.10.
- <P008302> **KUMTA Shekhar Madhukar; LEUNG Ping Chung; PANOZZO A. and FONG S. L. .** "Repair of Muscle and Musculotendinous Junction Injuries with an Autogenous Fascial Patch". *Arch Orthop Trauma Surg* 120, pp.198-200. USA: Springer - Verlag, 2000.
- <P008986> **梁秉中、華山醫院、WANG W.S.、熊良儉及華山醫院.** <不同時間段的預變性神經段分子生物學變化> 《中華手外科雜誌》 vol.16 no.3, pp.172-174. 中國: 中華手外科雜誌, 2000.09.
- <P009805> **CHENG Chun Yiu Jack, ZHANG X D, Qu S.X., FAN Hong Song and GUO Xia.** "The Effect of Calcium Phosphate Ceramics on Morphology and Proliferati of Osteoblast in vitro". *13th International Symposium in Ceramics in Medicine* Bologna, Italy, 2000.11.22.
- <P009888> **KUMTA Shekhar Madhukar; LEUNG Ping Chung; GRIFFITH James Francis; CHOW Tsun Cheung Louis and KEW Jacqueline.** "Vascularised Bone Grafting for Fibrous Dysplasia of the Upper Limb". *The Journal of Bone and Joint Surgery* vol.82B no.3, pp.409-412. British Editorial Society of Bone and Joint Surgery, 2000.04.
- <P012419> **CHAN C., Charles, LUIS P.K., Ben, CHOW C.B., CHENG Chun Yiu Jack, WONG Tze Wai, CHAN Kevin and CHUI Fung Ming Sandra.** "Validating Narrative Data on Residential Child Injury". *Journal of Safety Research* vol.32, pp.377-389. USA: National Safety Council and Elsevier Science Ltd, 2001.
- <P012727> **CHAN W.S.; HUI S.C. and WONG H.S.S.** "Relationship Between Body Mass Index and Body Fat in Chinese Children". *Medicine and Science in Sports and Exercise* ed. by PANDOLF B., KENT. vol.33 no.5(supplement), p.1370(S244). USA: American College of Sports Medicine, 2001.05.

- <P012729> **CHAN Wan-Sze and HUI Sai-Chuen.** "Evaluation of Three Physical Activity Questionnaires in Predicting Cardiovascular Fitness of Chinese Children". *Innovation and Application of Physical Education and Sports Science in the New Millennium - An Asia-Pacific Perspective* pp.493-500. Hong Kong Institute of Education, 2001.
- <P013098> **CHOY W.Y.; AU S.K.; HUNG V.W.Y.; QIN L. and CHAN K.M.** "Comparison of Bone Mineral Density and Muscle Strength in Postmenopausal Women with or Without Habitual Exercise". *Abstracts of the International Conference on Tai Chi Chuan* p.63. Hong Kong: The Chinese University of Hong Kong, 2001.12.
- <P015625> **CHAN Kai Ming, LI Jingxian, LI C S, LINEUR G U, QIN Ling and LEE Kwong Man Simon.** "Effect of Verbascoide on Attenuating Oxidative Stress Resulted from Immbilization and Remobilisation in Skeletal Muscle or Rabbits". *The 21st Hong Kong Orthopaedic Association Annual Congress* p.S70. Hong Kong SAR: Hong Kong Orthopaedic Association, 2001.11.
- <P016031> **CHENG Chun Yiu Jack; NG Kin Wah Bobby and HUNG Wing Yin Vivian.** "Associated Osteoporosis of the Host Bone in Tibial Lengthening". *Hong Kong Journal of Orthopaedic Surgery* The 21st Hong Kong Orthopaedic Association Annual Congress vol.5, p.S60. Hong Kong SAR: Hong Kong Orthopaedic Association, 2001.11.
- <P016081> **LEE Tak Keung Warren, CHEUNG Siu King and CHENG Chun Yiu Jack.** "Bone Mineral Density (BMD) and Calcium Intake in Patients with Adolescent Idiopathic Scoliosis". *The Hong Kong Paediatric Society and Hong Kong Paediatric Nurses Association* pp.4. Hong Kong SAR: The Hong Kong Paediatric Society, 2001.10.13.
- <P016172> **ZHENG Ming Hao, KUMTA Shekhar Madhukar, HUANG Lin, CHENG Yuen Yee and CHOW Tsun Cheung Louis.** "Expression of Receptor Activator of NF-kB Ligand in Chondroblastoma - Possible Involvement in Tumour Cell-induced Osteolytic Bone Destruction". *The 21st Hong Kong Orthopaedic Association Annual Congress* Dr. WC Wu, Editor-in-Chief, c/o Dept. of O&T, PYNEH S74. Hong Kong SAR: Lippincott Williams & Wilkins Asia Ltd, 2001.11.10.
- <P016251> **YEUNG Hiu Yan, LAW Lai Pang, LEE Kwong Man, Simon, GUO Xia, CHOW Pak Ham Patricia, CHENG Chun Yiu Jack and TABATA Y.** "The Effect of Vascular Endothelial Growth Factor Combined with Different Biomaterial in a Posterior Spinal Fusion Model (O6)". *Proceeding of 5th Asian Symposium on Biomedical Materials* p.104. Hong Kong SAR: The Hong Kong University of Science and Technology, 2001.12.
- <P016352> **WONG Chin Hong; L. Chow; C.H. Yen; HO Pak Cheong; YIP CL and HUNG Leung Kim.** "Uncommon Hand Tumours". *Hand Surgery* vol.6 no.1, pp.67-80. Hong Kong SAR: World Scientific Publishing Company, 2001.07.
- <P016357> **CHIU Kwok Hing; SHEN Wan Yiu; TSUI Hon For and LAW Sheung Wai.** "Primary Cemented Exeter Total Hip Replacement in Chinese Patients - Results of 10-year follow-up". *Hong Kong Journal of Orthopaedic Surgery* vol.5 no.1, pp.2-10. Hong Kong SAR, 2001.
- <P016383> **YEUNG Hiu Yan; LEE Kwong Man, Simon; LAW Lai Pang; CHENG Chun Yiu Jack; CHEUNG WH and TABATA Y.** "Rabbit Chondrocytes Culture on Hydroxyapatite/Tricalcium Phosphate Ceramic and Collagen Sponge - a Preliminary Report". *Hong Kong Journal of Orthopaedic Surgery* The 21st Hong Kong Orthopaedic Association Annual Congress vol.5, p.S20. Hong Kong SAR: Hong Kong Orthopaedic Association, 2001.11.

- <P016433> **LEE Tak Keung Warren, Jiang Ji, Hu Pei, HUANG Xiaolin and CHENG Chun Yiu Jack.** "Use of Stable Calcium Isotopes (42CA & 44CA) in Evaluation of Calcium Absorption in Beijing Adolescents with Low Vitamin D Status". Paper presented in the 1st International Conference on Bone and Mineral Research p.86. Beijing, China, 2001.09.
- <P016466> **CHAU Wai Wang; CHENG Chun Yiu Jack; CHAN Yu Leung and GUO Xia.** "Redefining the Magnetic Resonance Imaging Reference Level for Cerebellar Tonsil - A Study of 225 Adolescents Comparing Normal Individuals and Patients with Idiopathic Scoliosis". *Hong Kong Journal of Orthopaedic Surgery* The 21st Hong Kong Orthopaedic Association Annual Congress vol.5, p.S57. Hong Kong SAR: Hong Kong Orthopaedic Association, 2001.11.
- <P016522> **YEUNG Hiu Yan, LEE Kwong Man, Simon, LAW Lai Pang, CHENG Chun Yiu Jack, TABATA Y and CHEUNG Wing Hoi.** "Culture of Rabbit Chondrocytes Released from Rib Cage on Calcium Phosphate Ceramic and Collagen Sponge (P11)". *Proceeding of 5th Asian Symposium on Biomedical Materials* p.123. Hong Kong SAR: The Hong Kong University of Science and Technology, 2001.12.
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- <P016676> **ZHAO Xin, HUNG Leung Kim, Gao Meng Zhang and Jie Lao.** "Applied Anatomy of the Axillary Nerve for Selective Neurotization of the Deltoid Muscle". *Clinical Orthopaedics and Related Research* no.390, pp.244-251. USA: Lippincott Williams & Wilkins, Inc., 2001.
- <P016695> **KUMTA Shekhar Madhukar; ZHU QS; LEE Kwong Man Simon; GRIFFITH James Francis; CHOW LTC and LEUNG Ping Chung.** "Clinical Significance of P-glycoprotein Immunohistochemistry and Doxorubicin Binding Assay in Patients with Osteosarcoma". *International Orthopaedics* vol.25, pp.279-282. USA: Springer - Verlag, 2001.06.29.
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- <P016788> **WONG Kwok Chuen and LEUNG Kwok Sui.** "Case Report - Management of Supracondylar Femur Fracture in a Patient with Congenital Antithrombin III Deficiency". *Hong Kong Journal of Orthopaedic Surgery* vol.5 no.2, pp.125-128. Hong Kong SAR: Hong Kong College of Orthopaedic Surgeons, 2001.
- <P016791> **LEE Tak Keung Warren; JIANG J; HU P; HU Xiao Peng; ROBERTS CK David and CHENG Chun Yiu Jack.** "An Inverse Association Between Calcium Absorption and Plasma 25-Hydroxyvitamin D3 Of Adolescents in North China". *5th Annual Nutrition Symposium, Centre of Nutritional Studies* p.14. Hong Kong SAR: School of Public Health, The Chinese University of Hong Kong, 2001.11.10.
- <P016803> **CHAN Kai Ming, LI Linchuan and FU Sai Chuen Bruma.** "Effects of Shaji Total Flavone Extract in Early Stages of Healing Patellar Tendons". *The 21st Hong Kong Orthopaedic Association Annual Congress* p.S71. Hong Kong SAR: Hong Kong Orthopaedic Association, 2001.11.
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- <P016852> **KO Chi Kuen, LAW Sheung Wai and CHIU Kwok Hing.** "Enhanced Soft Tissue Repair Using Locking Loop Stitch after Posterior Approach for Hip Hemiarthroplasty". *The Journal of Arthroplasty 2001* vol.16 no.2, pp.207-211. 2001.
- <P017021> **LEUNG Ping Chung.** "Review Of Osteoporosis Surgery". *Proceedings of the 1st International Conference on Bone and Mineral Research* p.2. Beijing, China, 2001.09.15.
- <P017074> **CHENG Chun Yiu Jack, NG Kin Wah Bobby and HUNG Wing Yin Vivian.** "Callotasis Mineralisation in Achondroplasia Tibial Lengthening - An Individualised Treatment Process". *Proceeding of The 2nd Congress of International Federation of Paediatric Orthopa* p.222. Sendai, Japan, 2001.11.
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## RESEARCH PROJECTS

### Effects of Oxygen-induced Lung Damage on Megakaryocytopoiesis in Neonates Receiving Mechanical Ventilation

✉ FOK Tai Fai • LI Kwai Har Karen • YANG Mo

☐ 1 April 2002

❖ CUHK Research Committee Funding (Direct Grants)

Oxygen toxicity is an important cause of lung injury in preterm infants receiving mechanical ventilation. Thrombocytopenia (low blood platelet counts) is another common complication of these infants. The underlying cause of thrombocytopenia has not been identified. The lung has recently been identified as a location of megakaryocyte (MK) fragmentation and platelet release. We hypothesize that oxygen toxicity induces the activation and reduces the release of platelets from the lungs, leading to thrombocytopenia and a feedback mechanism of increased thrombopoietin (TPO) levels in the circulation. In a previous study, we established a neonatal rat model of hyperoxic lung damage and showed that these animals had low circulating platelets, increased consumption and reduced release of platelets from their lungs when compared to those of control animals. In this project, we aimed to verify our hypothesis in human neonates who have been subjected to mechanical ventilations with a high concentration of oxygen for the treatment of respiratory distress syndrome (RDS). To establish that platelet haemostasis is affected by oxygen-induced lung damage, we shall study serial levels of blood platelets, MK cells and the platelet activation status (P-selectin and CD63 expression) in the pre- and post-pulmonary circulation. These parameters will be compared with baseline levels before the neonate has sustained lung injury. Plasma TPO will be quantified by ELISA assays. The association of this MK-promoting cytokine with oxygen toxicity has not been reported. The activation of the TPO feedback mechanism signifies the physiological importance of hyperoxic lung damage on megakaryocytopoiesis. This study attempts to investigate the relationship between oxygen-induced lung damage and thrombocytopenia, and the possible effects of hyperoxia on cellular events that regulate platelet synthesis. The

information obtained may provide the basis for a more rational management of thrombocytopenia in newborns with lung diseases.

(MD01554)

### The Assessment of Disease Severity of Atopic Dermatitis in Chinese Children Using Clinical Scores and Laboratory Markers

✉ HON Kam Lun • LEUNG Ting Fan • LAM Wai Kei Christopher (Dept of Chemical Pathology) • WONG Chun Kwok (Dept of Chemical Pathology) • MA Kwok Chiu\*

☐ 1 December 2001

❖ CUHK Research Committee Funding (Direct Grants)

Atopic dermatitis (AD) is a common and distressing relapsing inflammatory skin disease associated with inhalant and food allergies. As the clinical judgement of AD is often difficult, it is important for clinicians to have reliable means of assessing disease severity in order to follow the natural history and the usefulness of pharmacological and non-pharmacological treatment. The purposes of this study are:

- (1) To evaluate the usefulness of serum levels of inflammatory markers and cytokines in assessing the disease severity of AD in Chinese children; and
- (2) To validate a Chinese questionnaire for assessing AD severity; and
- (3) To characterize the spectrum of sensitization to food allergens in childhood AD in Hong Kong.

This cross-sectional and observational study will recruit ethnic Chinese children with AD and age-matched control subjects from the hospital outpatient clinic. Atopic dermatitis is diagnosed according to criteria proposed by Hanifin, and the disease severity of AD is evaluated clinically according to the SCORAD index as described by the European Task Force on Atopic Dermatitis. In addition, the Chinese version of a self-administered, published questionnaire for assessing disease severity of AD will be formulated and validated in Chinese children. Sensitization to common food allergens in our Chinese AD patients will be measured using the widely accepted method of fluorescent enzyme immunoassay. Outcome measures in this study include clinical indicators (e.g. severity scores, topical steroid use) and laboratory markers (e.g. cytokines and inflammatory markers).

(MD01484)

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**Characterization of Immunologic Profiles Associated with Hepatitis B Virus Immunoprophylaxis Following Allogeneic Haematopoietic Stem Cell Transplantation**

✉ LEUNG Ting Fan • CHAN Kay Sheung Paul (Dept of Microbiology) • LI Chi Kong\*

☐ 1 November 2001

❖ CUHK Research Committee Funding (Direct Grants)

Haematopoietic stem cell transplantation (HSCT) is performed annually in over 30,000 patients worldwide for a range of malignancies and haematological disorders. With the use of myeloablative conditioning agents, HBV-positive transplant recipients will be severely immunosuppressed immediately after HSCT that enhances HBV replication. This may result in hepatocellular damage or even liver failure. There are currently no effective means to control HBV reactivation after HSCT. Previous studies found that infusion of stem cells collected from HBV-immune donors resulted in the clearance of hepatitis B surface antigenaemia in seropositive recipients. In this project, we conduct a longitudinal cohort study to test the adoptive transfer of HBV-specific cellular and humoral immunity following immunization of HSCT donors with HBV vaccine. We will monitor functions of peripheral blood mononuclear cells as well as HBV-specific antibody production in transplant recipients for 12 months post-transplant. Lastly, we postulate that the adoptive transfer of HBV-specific immunity can also augment the anamnestic immune responses of recipients to post-transplant HBV immunization. We will study the differences in protective antibody responses following HBV re-vaccination at one year following HSCT, in recipients who receive stem cells from HBV-immune or naïve donors.

(MD01630)

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**Thrombospondin-1: Antileukemia Effects and Mechanism of Apoptosis**

✉ LI Kwai Har Karen • LI Chi Kong • CHIK Ki Wai • YANG Mo

☐ 1 September 2001

❖ CUHK Research Committee Funding (Direct Grants)

Thrombospondin-1 (TSP-1) is a platelet granule protein and a naturally occurring anti-angiogenic agent that acts on endothelial cells via its receptor CD36. In experimental models, TSP-1 is known to inhibit the proliferation of solid tumours by inducing apoptosis of the microvascular system surrounding the tumour. In addition to the expression on endothelial cells, our laboratory and others have identified CD36 on some megakaryocytic and myeloid leukemia cells. Our hypothesis is that TSP-1 could be an apoptotic agent that selectively kill leukemia cells which express CD36. Since the CD36 receptor is not expressed on early hematopoietic stem and progenitor cells, the toxicity of TSP-1 treatment on these normal cells in the bone marrow might be spared. In this study, we plan to (1) enumerate the expression of CD36 on megakaryocytic (CHRF-288-11, Meg-01) and myelocytic (HL-60) leukemia cell lines; (2) investigate effects of TSP-1 on the induction of apoptosis in these cells by the expression of the early apoptotic marker Annexin V and the occurrence of DNA fragmentation; (3) study the apoptotic mechanism via the signal transduction proteins caspase-3, bcl-2 and bax and (4) investigate the regulation of this pathway by CD36 blockers and hematopoietic growth factors. This novel approach of TSP-1, if proven to be effective and specific for inducing apoptosis of leukemia cells expressing CD36, could be used as an adjunct to cytotoxic/radiotherapy treatments in eradicating these cells.

(MD01598)

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**"A Multicentre, Randomised, Double Blind, Controlled Study of Two Corticosteroid Regimens for Treatment of Systemic Hypotension in Preterm Infants"**

✉ NG Pak Cheung • CHOW Chun Bong\* • FOK Tai Fai • LAM Wai Kei Christopher (Dept of Chemical Pathology)

☐ 1 December 2001

❖ Research Grants Council (Earmarked Grants)

Low blood pressure or hypotension is a common complication of prematurely born babies. If hypotension persists for a prolonged period, it may

have detrimental effects on body organ systems including the brain, heart, kidney and gut. Traditionally, fluid replacement with colloid (5% albumin) or crystalloid (0.9% NaCl) and vasoactive drugs (dopamine, dobutamine, adrenaline) are used for supporting the blood pressure of preterm babies. However, it has been increasingly apparent that some babies may be refractory to the above treatment or requiring very high doses of vasoactive drugs for maintaining an adequate blood pressure. Cortisol, a steroid hormone produced by the adrenal glands, is known to play an important role in the regulation of blood pressure. In recent years, various research teams (including our own at the Prince of Wales Hospital) have discovered that some premature babies have transient enzyme deficiency in the hypothalamic-pituitary-adrenal (HPA) hormone axis. Hence, it would seem logical to prescribe corticosteroid for replenishing the circulating steroid level of the body. Our experience suggested that only some babies (50%) with severe hypotension responded to low dose hydrocortisone, but most of the non-responders (80%) responded promptly to high dose dexamethasone, a more potent steroid preparation.

In view of the above findings, we propose to carry out a multicentre (4 centres) study by randomly allocating hypotensive babies to receive either low dose hydrocortisone, high dose dexamethasone or placebo (0.9% NaCl) in order to evaluate the efficacy of steroid treatment, and to compare the effectiveness of the two different steroid drug regimens for the treatment of hypotension in premature infants. The results will have a significant impact and will greatly influence the choice of drug being used for management of hypotension in this category of infants, as it would seem logical to replace the missing or inadequate amount of hormone in the blood. Moreover, this study will also help in determining the appropriate corticosteroid regimen so that the proper drug dosage can be prescribed for achieving the desired therapeutic effect. Adverse effects of the drug will also be investigated and closely monitored in the study.

(MD01104)

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#### Thyroid Volumes in Chinese Children

✉ WONG Wing Kin Gary • LAM Wai Kei Christopher (Dept of Chemical Pathology) •

AHUJA Anil Tejbhan (Dept of Diagnostic Radiology & Organ Imaging)

☐ 1 November 2001

❖ CUHK Research Committee Funding (Direct Grants)

The enlargement of thyroid gland or goitre is a common problem in children and adolescents. Iodine deficiency remains the most common cause of goitre and preventable mental retardation worldwide. Even mild iodine deficiency results in subtle impairment of mental ability and iodine deficient communities are typically lower in intellectual ability, work output, and income. The social and economic consequences of iodine deficiency are substantial. Hence, accurate assessment of prevalence of goitre and monitoring of iodine nutrition are of paramount importance in any given population. A most appropriate subgroup in the population for surveys is schoolchildren because their thyroids reflect recent effects of iodine nutrition.

In the past, goiter was usually determined by thyroid palpation. Recent studies have confirmed that palpation is inaccurate especially when the thyroid enlargement is mild. The current gold standard of thyroid volume assessment is by ultrasound examination. The World Health Organization (WHO) standard for thyroid volumes were derived from studies of European children and has been shown to be less applicable for several other ethnic groups. The WHO standard tends to underestimate the prevalence of goitre particularly in borderline iodine deficient areas. Iodine deficiency and endemic goitre are still prevalent in many regions of Mainland China. Without proper reference norms for thyroid volume, accurate interpretation of goiter cannot be obtained. Our previous studies have confirmed that children in Hong Kong have a low prevalence of goitre by palpation and that iodine intake is adequate as reflected in their urinary iodine concentrations. Therefore, a study of normal thyroid volume in children is feasible in Hong Kong. This study proposes to establish the norms for thyroid volume among Hong Kong's Chinese adolescents aged 10 to 15 years and to compare the obtained standard with the WHO standard of normal thyroid volume in children. A representative sample of 1050 children will be recruited for thyroid ultrasound examination. Their urinary iodine concentration will be measured to confirm the adequacy of iodine intake. The results will provide a valuable reference

standard and enable further comparative studies of thyroid volume of Chinese children from different regions of Mainland China.  
(MD01520)

**The Direct Role of the Pro-inflammatory Cytokine IL-1  $\beta$  on Megakaryocytopoiesis: the Signal Transduction Response and Stimulation of Cytokine Response**

✉ YUEN Man Pan Patrick • LI Kwai Har Karen • FOK Tai Fai • YANG Mo

☐ 1 September 2001

❖ CUHK Research Committee Funding (Direct Grants)

Interleukin-1 $\beta$  (IL-1 $\beta$ ), a highly pro-inflammatory cytokine, induces thrombocytosis (high platelet counts) in mice. The effect was suggested to be indirect and mediated by accessory cells such as macrophages, lymphocytes and stromal cells via the secretion of IL-6. In a recent study, we established that IL-1 $\beta$  stimulated murine and human megakaryocyte progenitor cell growth. Our hypothesis is that IL-1 $\beta$  exerts direct stimulatory effects on megakaryocytic cells via its receptors to activate signal transduction and the synthesis of growth and inflammation promoting factors. Our experimental approach is (1) to determine the signal transduction mechanism of IL-1 $\beta$  on megakaryocytopoiesis by the expression of transcription factors GATA-1, NF-E2, c-fos and c-jun; (2) to investigate the effect of IL-1 $\beta$  on the synthesis of growth and inflammatory promoting cytokine thrombopoietin (TPO) (3) to demonstrate the direct role of IL-1 $\beta$  via its receptors through the use of IL-1 receptor antagonists in these functional assays. The direct involvement of IL-1 $\beta$  in the megakaryocytic lineage is a new concept. If proven, it would have significant implications on the functions of IL-1 $\beta$  and provide explanations for the clinical phenomenon of thrombocytosis during inflammatory conditions. IL-1 $\beta$  could also be used for the expansion of megakaryocytic progenitor cells *ex vivo*, a technique being developed for reducing tumor cell contamination and other morbidity such as thrombocytopenia associated with blood/bone marrow stem cell transplantation.  
(MD01778)

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

<u>Edition</u>	<u>Title/Investigators</u>
2000-01	Quantitative Polymerase Chain Reaction Analysis of Chimerism After Allogeneic Bone Marrow Transplantation (MD00739) ✉ CHIK Ki Wai
2000-01	A Randomised, Double-blind, Double-dummy, Parallel-group, Multicentre Study to Compare the Effect on Growth Measured by Stadiometry of Fluticasone Propionate (100 $\mu$ g bd) Administered via Diskus <sup>®</sup> with Budesonide (200 $\mu$ g bd) Administered via Turbuhaler <sup>®</sup> in Prepubescent Children (MD99458) ✉ FOK Tai Fai • LEUNG Ting Fan
2000-01	A Cross-sectional, Single-centre Study on the Levels & Sources of Mercury, Cadmium & Lead in a Hong Kong Mother-infant Cohort (MD20001) ✉ FOK Tai Fai • LAM Wai Kei Christopher (Dept of Chemical Pathology) • YIP Shing Kai Alexander (Dept of Obstetrics & Gynaecology) • NG Pak Cheung • LEUNG Peter Ho Yin* • HJELM Nils Magnus*
1999-00	Study of Varicella-zoster Virus Immunization in Paediatric Haematopoietic Stem Cell Transplantation (MD99087) ✉ LEUNG Ting Fan • CHAN Kay Sheung Paul (Dept of Microbiology) • LI Chi Kong*
2000-01	A Multicenter, Double-blind, Placebo-controlled, Randomized, Parallel-group, Study to Determine the Efficacy of Montelukast in the Prevention of Exacerbations in Asthmatic Patients Aged 2-to-5 Years (MD00738) ✉ LEUNG Ting Fan • LI Man Chim Albert Martin • WAN Helene

- 2000-01 Evaluation of Chemokines and Eosinophil Functions in Neonates and Their Clinical Relevance to Neonatal Respiratory Diseases (MD00895)  
 ✍ LEUNG Ting Fan • NG Pak Cheung • LI Kwai Har Karen • TAM Wing Hung (Dept of Obstetrics & Gynaecology)
- 2000-01 A Randomized, Placebo-controlled and Crossover Clinical Trial of an Elemental Milk Formula in the Treatment of Atopic Dermatitis in Chinese Children (MD20058)  
 ✍ LEUNG Ting Fan • LAM Wai Kei Christopher (Dept of Chemical Pathology)
- 1998-99 Human Stem Cell Technology: *ex vivo* Expansion of Cord Blood Stem/Progenitor Cells and Applications (MD98070)  
 ✍ LI Kwai Har Karen • HUANG POON Wai Sin Dolly (Hong Kong Cancer Institute) • TSANG Kam Sze Kent (Dept of Anatomical & Cellular Pathology)\*
- 2000-01 The Direct Role and Mechanism of the Pro-inflammatory Cytokine IL-1 $\beta$  on Megakaryocytopoiesis: Expression of IL-1 Receptors and the Signal Transduction Response (MD00978)  
 ✍ LI Kwai Har Karen • YANG Mo
- 1998-99 WHO/GSTF Maternity Advice Study (MD98123)  
 ✍ NELSON Edmund Anthony Severn • COWAN S.\* • MANGIATERRA V.\* • CAFFERATA M.\*
- 2000-01 A Hospital-based Study on Disease Burden and Health Costs of Rotavirus Associated Diarrhoea in Hong Kong (MD00598)  
 ✍ NELSON Edmund Anthony Severn • TAM Siu Lun John (Dept of
- Microbiology) • FOK Tai Fai • CHAN Kay Sheung Paul (Dept of Microbiology) • POON K H\* • NG C H\* • IP K S\* • YU Ly Mee Ashley (Centre for Clin. Trials & Epidemiological Research)
- 1999-00 Is Hypotension in Preterm Very Low Birth Weight Infants Due to Hypothalamic-pituitary Adrenal Insufficiency? (MD99055)  
 ✍ NG Pak Cheung • LAM Wai Kei Christopher (Dept of Chemical Pathology) • FOK Tai Fai
- 2000-01 The Effect of Continuous versus Pulsed Maternal Corticosteroid Treatment on Neonatal Pituitary-adrenal Function (MD00593)  
 ✍ NG Pak Cheung • LAM Wai Kei Christopher (Dept of Chemical Pathology) • FOK Tai Fai
- 2000-01 A Randomized Controlled Trial of Strength Training Exercise and Diet in the Management of Obesity in Children (CU00060)  
 ✍ SUNG Yn Tz Rita • CHANG Ka Yin Sandy\* • LAU Edith Ming Chu (Dept of Community and Family Medicine) • NELSON Edmund Anthony Severn • SO Chi Hung Raymond\*
- 2000-01 Effects of Oxygen Toxicity on Megakaryocytopoiesis and Thrombopoietin Production in Neonates - A Rat Model (CU00137)  
 ✍ YUEN Man Pan Patrick • FOK Tai Fai • LEE Simon K. M.\* • LI Kwai Har Karen • YANG Mo

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see also <P012174>, <P012264>, <P012290>, <P012346>, <P012364>, <P012365>, <P012466>, <P012607>, <P012728>, <P012730>, <P012764>, <P012832>, <P013202>, <P013279>, <P013329>, <P016495>, <P016818>, <P017695>, <P019025>, <P020343>, <P021141>, <P021373>, <P021421>, <P026181>, <P026236>, <P026572>, <P026868>, <P027151>, <P02762>, <P028196>

## RESEARCH PROJECTS

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### **The Mechanisms Responsible for the Exaggerated Excitatory Effect of Acetylcholine in the Pulmonary Artery of Spontaneously Hypertensive Rats**

✉ KWAN Yiu Wa • GURNEY A. M.\*

☐ 1 November 2001

❖ Research Grants Council (Earmarked Grants)

The adult pulmonary circulation is a low-resistance, low-pressure system in which the correct distribution of flow is crucial to the body's oxygen requirements. Pulmonary hypertension is a rare blood vessel disorder of the lung, in which the pressure in the pulmonary artery (PA) rises above the normal level. This impedes oxygen delivery to the blood and may become life threatening. An imbalance may exist in the vasoconstricting and vasodilating mediators involved in the control of pulmonary vascular tone.

Acetylcholine (ACh) produces a well-documented endothelium-dependent dilation of pulmonary vessels, but in some circumstances it has an excitatory / contractile effect. The mechanisms of the latter action are relatively unknown. So far, five subtypes of muscarinic receptor ( $M_1$  to  $M_5$ ) have been cloned, but the type(s) of receptor responsible for the contractile effect of ACh on the PA has not been resolved. In our preliminary study, we have successfully demonstrated that the  $M_3$  muscarinic receptors are responsible for the ACh-elicited PA contraction in normotensive Wistar-Kyoto (WKY) rats. We further demonstrated that  $M_3$  receptors mediate ACh-induced contraction of PA in Spontaneously Hypertensive rats (SHR), which provide a general model of hypertension, but interestingly this effect was markedly enhanced (~2-fold), compared to WKY rats.

In this study, we will delineate the intracellular signal transduction pathways and the type(s) of ion channels responsible for elevating the cytoplasmic  $Ca^{2+}$  concentration and promoting contraction of pulmonary artery smooth muscle in SHR and WKY rats. The effects of specific modulators of second messenger pathways (e.g. phospholipase C, protein kinase C) and various ion channels will be examined on both the cytoplasmic  $Ca^{2+}$  concentration and the contractile response to ACh. Results obtained from this study will provide important information for a

better understanding of the pathophysiology of pulmonary hypertension and assist future drug development. Most of the currently available vasodilating drugs are poor dilators of hypertensive pulmonary vessels and also lack pulmonary selectivity. There is therefore a need for new, pulmonary-selective dilator drugs.

(MD01107)

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### **Investigation of the Mechanisms and Significance of Altered Neurogenic Responses in Arthritic Rat Knee Joints**

✉ LAM Fu Yuen

☐ 1 October 2001

❖ CUHK Research Committee Funding (Direct Grants)

Arthritis is a disease of uncertain etiology that manifests itself as a chronic inflammatory disorder in synovial joints. Much evidence is now available to support a role of the peripheral nervous system in this disease. Studies on animal arthritis models suggest that blood vessels of normal and arthritic rat knees respond differently to neurogenic stimuli, such that electrical nerve stimulation elicits marked vasoconstriction in the normal rat knee, but it has no effect in acute and chronically inflamed knees. Moreover, the sensory neurotransmitter substance P produces transient vasodilatation in the normal rat knee; this effect is more prominent and sustained in the acutely inflamed knee but it is absent in the chronically inflamed knee. The significance of these altered neurogenic responses in relation to the pathogenesis of arthritis is unknown.

This proposal aims to elucidate the mechanisms that underlie the changes in neurogenic effects in arthritic rat knees and to clarify the role of the nervous system in the development of chronic joint inflammation. Ultimately, these findings will be used to evaluate the potential of developing anti-arthritic therapy based on modulation of neurogenic activities in the joint.

(MD01988)

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### **Development of TCM-based Products with Known Active Ingredients and Verified Oral Absorbability**

✉ LIN Ge • JONES Robert Leslie • CHOW Hee Lum Albert (School of Pharmacy) • TAM Yun

K\* • SEMPLE Hugh A\* • LI Xing Fang\* • DAMARAJU Vijayalakshmi\*

□ 1 January 2002

- ❖ Kinetana Hong Kong Herbal Pharmaceuticals Ltd. • University-Industry Collaboration Prog.: Matching Grant for Joint Research, ITF, Innovation & Tech. Commission

This project is a two and a half-year collaborative venture between Kinetana Hong Kong Herbal Pharmaceuticals Ltd. (Kinetana) and The Chinese University of Hong Kong (CUHK). The proposed project is to develop a Traditional Chinese Medicine (TCM)-based modern pharmaceutical product with known active ingredients and verified oral absorbability by using modern scientific technologies.

In this project, our objectives are:

- (1) to validate Kinetana's proprietary method for isolating active ingredients from TCM herb;
- (2) using this validated method and other modern scientific technologies to develop a novel TCM-based oral preformulation with known active ingredients and verified absorbability.

The project will provide a novel and modernized approach for the development of TCM products with international pharmaceutical standard. The developed new approach will bring Hong Kong into international repute for the modernisation of TCM products. The project will also provide our first generation of modernized TCM preformulation, which will be ready for further clinical trials and development of the final product for Hong Kong residents along with the economic benefits to Hong Kong of a newly founded industry.

(MD01857)

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**Investigation of Johnson and Johnson Pharmaceutical Research and Development Compounds to Inhibit Both the Acute and Delayed Phases of Cisplatin-Induced Emesis in a Ferret Model.**

✉ RUDD John Anthony

□ 1 April 2002

- ❖ Johnson & Johnson Pharmaceutical Research & Development

The discovery of the anti-emetic action of the 5-HT<sub>3</sub> receptor antagonists lead to the most successful

therapy for the treatment of chemotherapy- and radiation induced sickness in the cancer patient. A Worldwide use of ondansetron and other agents established firstly their highly effective control of 'acute emesis' (i.e. that occurring during the first 24 h), and secondly, revealed that 'delayed emesis' (i.e. that occurring after the first day of treatment) was less effectively managed. The project will investigate the anti-emetic potential of novel compounds supplied by Johnson & Johnson Pharmaceutical Research & Development to antagonize cisplatin-induced acute and delayed emesis in a ferret model.

(MD01607)

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**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>
1998-99	Cellular Mechanisms Involved in the Excitatory Actions of Prostanoid EP <sub>3</sub> -and IP-Receptor Agonists (BL98001) ✉ JONES Robert Leslie • GURNEY A. M.* • KWAN Yiu Wa • KENNEDY C.* • SNEDDON P.*
2000-01	Mapping Signal Transduction Networks by Multidisciplinary Approach (BL99452) ✉ JONES Robert Leslie • WISE Helen • HUANG Yu (Dept of Physiology) • IP Y Nancy* • WONG Yung-hou* • TSIM Karl W. K.* • BARNARD Eric A* • POON Y C Randy* • SUCHER Nikolaus*
2000-01	Investigation of the Mechanisms Underlying the Contractile Action of Prostanoid EP <sub>3</sub> -receptor Agonists on Vascular Smooth Muscle (MD00779) ✉ JONES Robert Leslie • KWAN Yiu Wa • GURNEY A. M.*
1999-00	Role of Sensory Neuropeptides in Chronic Arthritis (MD99112) ✉ LAM Fu Yuen
2000-01	Investigation of the Mechanisms and Significance of Altered Neurogenic

	Responses in Arthritic Rat Knee Joints (MD00464) ✉ LAM Fu Yuen • CHEW CHENG Siew Boon (Dept of Physiology)		Cisplatin- and Motion-Induced Emesis (CU98049) ✉ RUDD John Anthony • YEUNG Hok Keung John
2000-01	The Roles of Mast Cells in the Pathogenesis of Aspirin Sensitive Asthma (CU00064) ✉ LAU Hang Yung Alaster • LEUNG Po Sing (Dept of Physiology) • NAGAKURA Toshikazu* • OBATA Toru* • SAITO Hirohisa* • WU Young Yuen Adrian*	2000-01	Identification of Brain Areas Involved in Emesis Control in the Ferret (CU00066) ✉ RUDD John Anthony • YEW Tai Wai David (Dept of Anatomy)
2000-01	Effects of Cannabinoid Receptor Directed Ligands on Mast Cells (MD00482) ✉ LAU Hang Yung Alaster	2000-01	Characterization of the Role of Vanilloid Receptors in Emesis and Penile Grooming in <i>Suncus murinus</i> (MD00413) ✉ RUDD John Anthony
1998-99	Investigation into the Mechanism of Action of Corticosteroids to Antagonise	1999-00	An Investigation into the Multiple Coupling Capacity of Prostacyclin Receptors (CU99253) ✉ WISE Helen • WONG Yung Hou*

## RESEARCH OUTPUTS AND PUBLICATIONS

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see also <P019633>, <P019784>, <P019950>, <P020330>, <P027020>, <P027842>



## RESEARCH PROJECTS

### Quality Enhancement of Purapharm's Yun Zhi (*Coriolus Versicolor*) Preparation Through Modification of the Associated Extraction Protocol

- ✉ CHOW Hee Lum Albert • CHU Ka Wing#
- 15 September 2001
- ❖ PuraPharm Research Corp. Ltd.

Yun Zhi (*Coriolus Versicolor*) is a traditional Chinese medicine commonly used for the prophylaxis and treatment of certain infections and cancers. Aqueous extracts obtained from *Coriolus Versicolor* (CV) have been extensively shown to display a wide array of immunological activities both preclinically and clinically. These findings have sparked off a surge of commercial interest in developing oral CV preparations with proven efficacy and safety.

The aim of the present project is to enhance the beneficial immunomodulatory effects of PuraPharm's Yun Zhi preparation through optimization of the existing extraction process for the product. The immunological activity of the modified CV preparation will be evaluated using established *in-vitro* and *ex-vivo* animal models. In addition, the immuno-restorative effect of the CV extract will be investigated in immunocompromised animals. The potential acute and subchronic toxicity of the extract will also be evaluated.

(MD01841)

### Development of a Ganoderma (Lingzhi) and Coriolus (Yunzhi) Formula as an Anti-cancer Agent

- ✉ LAU Bik San Clara • ZUO Zhong • CHOW Sing Sum Moses • FUNG Kwok Pui (Biochemistry) • LEUNG Kwok Nam (Biochemistry) • LIN Ge (Dept of Pharmacology) • Anthony Edward JAMES (Laboratory Animal Services Centre) • SHAW Pang Chui (Biochemistry) • John Anthony BUSWELL (Dept of Biology) • LIEBERMAN Ron\*
- 1 April 2002
- ❖ University-Industry Collaboration Prog.: Matching Grant for Joint Research, ITF,

Innovation & Tech. Commission • Vita Green Health Products Co Ltd

The aim of the project is to develop a suitable formulation containing Lingzhi and/or Yunzhi which has previously been demonstrated in different isolated studies to possess useful anti-cancer effect. In this study, five different Lingzhi and Yunzhi related formulae will be screened for anti-cancer activity in a uniform manner so that the most potent formula will be identified and further developed to be suitable for application of an Investigational New Drug (IND) in USA. The study will be conducted in 5 stages, carried out at CUHK. The project team involves various members of different expertise to contribute towards the project.

(MD01301)

### Direct Medical Cost for a Cohort of Chinese Patients with Chronic Hepatitis B and Its Complications in Hong Kong

- ✉ LEE Kwing Chin Kenneth • KWONG Kai Sun Sunny (Dept of Economics) • CHAN Yan Keung Thomas (Dept of Medicine & Therapeutics) • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research) • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • WONG Ian C K\*
- 28 February 2002
- ❖ Bristol-Myers Squibb, Pharmaceutical Research Institute

Hong Kong, with a Chinese population exceeding 95%, is known to be an endemic area for hepatitis B virus infection. Health Authority records show that currently more than 700,000 persons in Hong Kong are hepatitis B carriers. The actual and potential costs of chronic hepatitis B treatment and care are therefore substantial.

The primary objective of the present study is to estimate the direct medical costs in the treatment and care of patients with chronic hepatitis B, including such complications as cirrhosis and hepatocarcinoma.

(MD01434)

### Absorption of Active Components from Hawthorn and Green Tea - *in vitro* and *in vivo* Relationship

- ✉ ZUO Zhong • CHOW Sing Sum Moses
- 1 October 2001

❖ Research Grants Council (Earmarked Grants)

Currently, few data is available on the characteristics, mechanisms and convenient study methods for the systemic absorption of the herbal products after they are taken as either "natural substance" or as extracts. In this study, Hawthorn and Green Tea, which are the most widely used herbs containing flavonoids, are chosen to investigate the intestinal absorption of their active flavonoids components. The *in vitro* Caco-2 monolayer model plus the intestinal perfusion model will be used to study the absorption and transport mechanism of each active component. In addition, the *in vivo* pharmacokinetic studies (i.e. absorption) of Hawthorn and Green Tea on rats will be performed and compared. Knowing both the *in vitro* transport mechanism and the *in vivo* pharmacokinetics involved will help the development of Hawthorn / Green Tea as well as flavonoids as a more effective and safer medicine and may lead to the establishment of a high throughput absorption method for all herbs in the future. The proposed project will have obvious implications on the scientific development of herbs or traditional Chinese medicine, since the systemic absorption is the prerequisite for systemic action.  
(MD01122)

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

Edition      Title/Investigators

1998-99      Controlled Production of Spray-dried Drug Microparticles for Pulmonary Delivery (CU98244)  
 ✍ CHOW Hee Lum Albert • LIN Ge (Dept of Pharmacology) • CHAN Chak Keung\*

1998-99      Establishment of a Certified Drug Evaluation Unit for Assessing the Quality of Oral Generic Drugs in Hong Kong (MD98071)  
 ✍ CHOW Sing Sum Moses • CHOW Hee Lum Albert • HO Yee Ping • Brian TOMLINSON (Dept of Medicine & Therapeutics) • LEE Kwing Chin Kenneth

2000-01      Establishment of a University Based Drug Development Centre for Anticancer and Cerebro/Cardio-vascular Drugs (MD20024)  
 ✍ CHOW Sing Sum Moses • HO Walter K. K. (Biochemistry) • JONES Robert Leslie (Dept of Pharmacology) • HO Yee Ping • LAU Bik San Clara • LIN Ge (Dept of Pharmacology) • Anthony Edward JAMES (Laboratory Animal Services Centre) • CHOW Hee Lum Albert

1999-00      Project on Effect of Isoflavones on Bone Density in Chinese Early Postmenopausal Women (MD99143)  
 ✍ HO Suk San Susan • HO Yee Ping • CHOW Hee Lum Albert • HO CHAN Suzanne (Dept of Community and Family Medicine)

2000-01      "The Effect of Orlistat and Rosiglitazone on Insulin Action in a Group of Chinese Patients Affected by the Metabolic Syndrome - A Randomized, Single-blinded and Placebo-controlled Study" (CU00069)  
 ✍ LEE Kwing Chin Kenneth • CHAN Chung Ngor Juliana (Dept of Medicine & Therapeutics) • Brian TOMLINSON (Dept of Medicine & Therapeutics) • YOU Hoi Sze Joyce

2000-01      Pharmacoeconomic Analysis of Tolterodine Comparing with Oxybutynin for the Treatment of Overactive Bladder (MD20029)  
 ✍ YOU Hoi Sze Joyce • LEE Kwing Chin Kenneth • LEUNG Ho Yin Peter (Dept of Obstetrics & Gynaecology) • YIP Shing Kai Alexander (Dept of Obstetrics & Gynaecology)

2000-01      A Study to Compare the Economic Impacts Between Celecoxib and Conventional NSAIDs with or without Preventive Treatment on Gastrointestinal Adverse Events, in the Outpatient Treatment of Osteoarthritis and

- Rheumatoid Arthritis, from the Perspective of a Public Health Care Organization in Hong Kong (MD20019)  
 2000-01 *In vitro* Intestinal Absorption and *in vivo* Pharmacokinetics Evaluation of Baicalein and Baicalin (MD00566)
- ✉ YOU Hoi Sze Joyce • LEE Kwing Chin Kenneth • CHAN Ka Leung Francis (Dept of Medicine & Therapeutics) • HO Suk San Susan • CHAN Yan Keung Thomas (Dept of Medicine & Therapeutics)  
 ✉ ZUO Zhong • LIN Ge (Dept of Pharmacology)

## RESEARCH OUTPUTS AND PUBLICATIONS

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- <P004262> **CHU K.W. Kevin and CHOW H.L. Albert.** "Impact of Carbohydrate Constituents on Moisture Sorption of Herbal Extracts". *Pharmaceutical Research* vol.17 no.9, pp.1133-1137. 2000.09.
- <P011782> **CHEN Xiao, ZUO Zhong, CHOW Hee Lum Albert and CHOW Sing Sum Moses.** "Low Bioavailability of Quercetin in Rats: Contributions by the Gut and Liver". *Abstracts of American Association of Pharmaceutical Scientists 2001 Annual meeting* vol.3 no.3(Supplement), p.1363. Denver, Colorado, USA, 2001.10.
- <P012217> **PENG Changgeng; CHOW H.L., Albert and CHAN Chak K.** "Hygroscopic Study of Glucose, Citric Acid, and Sorbitol Using an Electrodynamic Balance: Comparison with UNIFAC Predictions". *Aerosol Science and Technology* vol.35, pp.753-758. Taylor and Francis Inc., Philadelphia, 2001.09.
- <P012220> **CHOW M.S.S.; YIN Q.P.; TOMLINSON B. and CHOW A.H.L.** "Comparison of Two Pharmacokinetic Models to Describe the Double-Peak Absorption Profiles of Ranitidine". *Clinical Pharmacology and Therapeutics* vol.69 no.2, p.23. USA: Mosby Inc., St. Louis, USA, 2001.02.
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- <P013015> **YOU Hoi Sze Joyce, LEE Man Wai, POON Tsz Lok, LEE Kwing Chin Kenneth, HO Suk San Susan, John Elsby SANDERSON, Timothy Hudson RAINER and SUNG Joseph Jao Yiu.** "Cost-Effectiveness Analysis of a Chest Pain Unit - A Restructured Approach in Risk Stratification of Chest Pain". *Value in Health; (International Society for Pharmacoeconomics and Outcomes Research Fourth Annual European Congress)* p.498. Cannes, France: Blackwell Science Ltd, 2001.11.12.
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- <P013020> **CHUI Winsome W. S., HO Mandy M. T., HO Suk San Susan and CHIU C.C. Harry.** "A Survey of Physicians' and Nurses' Expectations on Hospital-Based Drug Information Services". *Hong Kong Pharmacy Conference 2001: Health Care Reform, the Role of Pharmacists* Hong Kong: Pharmaceutical Society of Hong Kong, 2001.10.
- <P013057> **CHEN X.; ZUO Z.; CHOW A.H.L.; YIN O.Q.P. and CHOW M.S.S.** "The Bioavailability of Quercetin in the Solution of Hydroxypropyl-Beta-Cyclodextrin in Rats". *Abstracts, EUFFPS (European Federation for Pharmaceutical Sciences) World Conference on Drug Absorption and Drug Delivery* pp.84-85. Copenhagen, Denmark: European Federation for Pharmaceutical Sciences, 2001.06.
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- <P013224> **BLESKE B.E.; SONG J.; CHOW M.S.S.; KLUGER J. and WHITE C.M.** "Hematologic and Chemical Changes Observed During and after Cardiac Arrest in a Canine Model - A Pilot Study". *Pharmacotherapy* vol.21 no.10I, pp.1187-1191. 2001.
- <P013225> **CHOW S.S. Moses; TOMLINSON Brian and YIN Q.P. Ophelia.** "In vivo Bioequivalence and in vitro Dissolution Studies of Gemfibrozil Capsules". *BABE-R01-009* 2001.
- <P013228> **CHOW Sing Sum Moses and WHITE C. Michael.** "Gardiac Arrhythmias". *Applied Therapeutics - The Clinical Use of Drugs* 7th ed., Chapter 18, pp.1-36. Mary Anne Koda-Kimble & Lloyd Yee YoungLippinco, 2001.

- <P013230> **HO S.S. Susan.** "Risedronate for Osteoporosis". *Medical Progress* vol.28 no.11, pp.43-48. 2001.
- <P013231> **CHOW Sing Sum Moses.** "Drug Development for International Marketing". *Collaborative Projects on Education and Research (Dec 2001-Jan 2002)* Hangzhou: Hong Kong Government Printer, 2001.
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see also <P012241>, <P012299>, <P012636>, <P012643>, <P012644>, <P012656>, <P012971>, <P013355>, <P013363>, <P016087>, <P018495>, <P019380>, <P019784>, <P020143>, <P020144>, <P020150>, <P021140>, <P021163>, <P021367>, <P021403>, <P02650>, <P026677>, <P02694>, <P02762>, <P027716>



## RESEARCH PROJECTS

### Epithelial Cell Biology and Functional Genomics

✉ CHAN Hsiao Chang • CHEW CHENG Siew Boon • CHOW Pak Ham Patricia (Dept of Anatomy) • Ronald Ray FISCUS • LEUNG Po Sing • WONG Patrick Yee Ding

☐ 1 July 2001

❖ CUHK Strategic Research Program

The epithelium plays an important role in maintaining the normal functions of various organs and glands. Defective epithelial function has been found responsible for a variety of diseases. The program aims to promote research in the field of epithelial cell biology with an emphasis on functional genomics. Multidisciplinary collaborations will be encouraged with special interest in signal transduction mechanisms underlying various epithelial functions and diseases in different organ tissues. 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 and hope to maintain a leading role in epithelial cell biology and related functional genomic research.

(MD01001)

### Investigation Into Mechanisms of Cerebral Vasodilator Effects of *Ligustrum Purpurascens* Extract and Purified Phenylethanoids in Normotensive and Stroke-Prone Spontaneously Hypertensive Rats

✉ HUANG Yu • CHEN Zhen Yu (Biochemistry) • YAO Xiaoqiang

☐ 1 January 2002

❖ CUHK Research Committee Funding (Direct Grants)

Nest to drinking green tea kudingcha (*Ligustrum purpurascens*, 苦丁茶) is the most popular drink in southern China, and has become one of the most commercial beverages in that region and now also in Hong Kong. We have previously isolated five phenylethanoid glycosides, which are abundant in dry leaves of *L. purpurascens*, and showed that *L. purpurascens* extract and one major component, acetoside relax isolated small cerebral (brain) and

coronary (heart) arteries. However, the mechanisms by which the vasodilatation in the resistance arteries occurs have never been fully investigated. Acetoside also possesses anti-proliferative and antioxidant activities. It is, therefore, possible that drinking kudingcha just like drinking green tea (beneficial effects of polyphenols) may have a long-term beneficial impact in terms of prevention and treatment of cardiovascular disorders such as hypertension, vasospasm and stroke. Therefore, the principle objective of this proposal is to investigate the possible long-term anti-hypertensive effects of chronic consumption of kudingcha. As a model, we will use stroke-prone spontaneously hypertensive rats that reproduce many characteristics of essential hypertension in humans. Changes in vascular functions in intact animals *in vivo* and responses of isolated brain blood vessels *in vitro* will be examined by comparing controls and *L. purpurascens* extract-fed rats and comparing normotensive and hypertensive rats. This proposal will employ a combination of approaches, including intact artery force measurement and blood pressure measurement in whole animals in order to investigate the mechanisms of vasodilator actions of *L. purpurascens* extract, individual phenylethanoids, and other responsible components in small brain blood vessels from rats.

(MD01620)

### Mechanisms of Arterial Smooth Muscle Relaxation by the Novel Calcium Antagonist Cilnidipine and Metabolites of Cytochrome P450

✉ HUANG Yu • GOLLASCH Maik\* • TSANG Suk Ying

☐ 1 January 2002

❖ Germany/Hong Kong Joint Research Scheme

Dihydropyridine calcium antagonists block L-type calcium channels targeting the pore-forming  $\alpha_1$  channel subunit. They are widely used to treat arterial hypertension and angina pectoris in humans. Recently nifedipine and possibly other short-acting 1<sup>st</sup> generation calcium channel blockers have been found to increase mortality in patients with coronary artery disease. The mechanism of this fatal side effect is unknown but may involve the interaction with second messenger molecules in smooth muscle cells and/or endothelium regulating arterial tone. However, there might be strong differences between

“classical” and novel calcium antagonists in blocking protein kinase C and targeting cytochrome P450 in endothelial cells. Due to little information available on calcium antagonists, calcium signaling, protein kinase C activity and BK channel regulation in small arteries and based on our experience with working on the pharmacology and electrophysiology of ion channels in arterial smooth muscle, we will choose isolated cells from rat small, resistance-sized arteries to study the role of L-type channels, protein kinase C and BK channels in relaxation of small arteries by “classical” and novel calcium antagonists. We will specifically examine the following hypotheses: (1) The novel dihydropyridine calcium channel antagonist cilnidipine is an extremely slow-acting channel blocker that induces a channel state-dependent block of complex, multi-subunit vascular L-type calcium channels in small, resistance-sized arteries. (2) Activation of protein kinase C does not regulate arterial L-type calcium channels in small, resistance-sized arteries. (3) Novel dihydropyridine L-type calcium channel antagonists (e.g., cilnidipine) inhibit the sustained contractile phase of small, resistance-sized arteries by reducing calcium influx through L-type channels but not by inhibiting protein kinase C. (4) Novel dihydropyridine L-type calcium channel antagonists (e.g., cilnidipine) release endothelial cytochrome P450 metabolites (i.e., epoxyeicosatetraenoic acids) to induce endothelium-dependent relaxation of small, resistance-sized arteries by activating smooth muscle BK channels. (5) Epoxyeicosatetraenoic acids are novel potent activators of the vascular BK channel and are possible candidates for endothelium-derived relaxing factor (EDRF). (MD01679)

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**Regulation of Ion Transport in Rat and Human Colonic Epithelia: Cellular Actions of Major Flavonoids Derived from Scutellariae Radix**

- ✉ KO Wing Hung
- ☐ 1 September 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Scutellariae Radix has been frequently used as a component of several Kampo medicines (Chinese herbal medicines) for centuries. Pharmacological activity of Scutellariae Radix has been shown to be anti-inflammatory, anti-pyretic, anti-allergic, as well

as anti-tumor. Our pilot studies indicate that baicalein, the major flavonoid derived from Scutellariae Radix, *stimulated* and *potentiated* chloride secretion across rat and human colonic epithelia, respectively. Therefore, the physiological basis of the therapeutic effect of Scutellariae Radix on colonic electrolyte transport has not been reported and the mechanism of action is still unclear. The purpose of the present proposal is to investigate whether baicalein, the major flavonoid derived from Scutellariae Radix cause chloride secretion in rat and human colonic epithelia and examine the mechanism of this response using microspectrofluorimetric and electrophysiological approaches. Experiments will also be conducted using a “combined approach”, that allow measurement of two important parameters, namely fluorescent signals and transepithelial ion transport simultaneously in a polarized epithelium. The information obtained from this study will give us a better understanding of the cellular mechanisms of baicalein with respect to its specific effect(s) on intracellular signaling events and electrolyte transport in rat and human colonic epithelia. This may further enhance the understanding of the therapeutic mechanisms of Scutellariae Radix, which may lead to clinical applications. (MD01621)

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**Molecular Biology of the Touch Corpuscle: Merkel Cell-Neurite Complex**

- ✉ LEUNG Man Sing • WONG Chun Cheung
- ☐ 1 September 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Molecular biological techniques will be used to study genes expression in Merkel cells (MC) especially the possible candidates of neurotransmitters being synthesized 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. The Merkel cells from vibrissal sinus hair of the rat are used for this study. Flow cytometric technique is used to isolate pure Merkel cells labeled with quinacrine. 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, calcium

sensing receptor, etc. are used for the Real Time PCR. The relative abundance of mRNAs for different candidates is determined. The sequence of the PCR products is analyzed by an automatic sequencer to confirm the correct DNA products. Though Merkel cell neuroendocrine carcinoma is not common but attracts attention due to its aggressiveness and similarity to the small cell carcinoma of the lung, in this study the expression of programmed cell death related genes such as Bcl-2, Bax, Caspase 1,3, etc are studied in normal rats. In order to further elucidate the function of Merkel cells as a touch receptor, the expression of the mentioned genes in this study are determined to see their involvement in the reduction in responsiveness of Merkel cell-neurite complex to mechanical stimulation in degenerative skin conditions such as vitamin A deficiency.  
(MD01770)

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**Activation of Pancreatic Renin-angiotensin System: Its Role in the Regulation of Reactive Oxygen Species and Apoptosis in Pancreas**

- ✉ LEUNG Po Sing • IP Siu Po (School of Chinese Medicine)
- ☐ 20 December 2001
- ❖ Research Grants Council (Earmarked Grants)

Previous studies have provided solid evidence for the existence of a pancreatic reninangiotensin system (RAS), which could play a paracrine/autocrine role in the regulation of exocrine/endocrine functions of the pancreas. Such a pancreatic RAS has been recently demonstrated to be markedly activated by experimental rat models of chronic hypoxia and acute pancreatitis. Interestingly, the upregulation of RAS was believed to provide a potential mechanism for inflammatory cellular responses and inflammatory cell death by apoptosis, probably via the involvement of free radicals in various cell types, leading to the pathogenesis of tissue damage/injury. Accordingly, the association between the activation of pancreatic RAS by chronic hypoxia and by acute pancreatitis in the pancreas may be inextricably linked to free radicals and apoptosis, which may in turn lead to possible pathophysiology of the pancreas. In the present proposal, the effects of chronic hypoxia and acute pancreatitis on the induction of reactive oxygen species (ROS) and apoptosis will be first addressed in the pancreas. The association between the activation of pancreatic RAS and its role in the

regulation of ROS and apoptotic cell death in the pancreas will then be elucidated. The results of the present study should not only provide a link between hypoxia-induced injury and acute pancreatitis but also a potential importance of the activation of local RAS in the regulation of pancreatic injury. The significance of activation of pancreatic RAS by chronic hypoxia and acute pancreatitis and its role in the induction of ROS and apoptotic cell death in the pancreas may have pathophysiological relevance to the pancreas.  
(MD01116)

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**Apoptotic DNA Fragmentation in Uterine Epithelial Cells: Cellular Mechanisms and Quantification by Capillary Electrophoresis with Laser-induced Fluorescence**

- ✉ Ronald Ray FISCUS • CHAN Hsiao Chang • CHEW CHENG Siew Boon
- ☐ 1 September 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Apoptotic cell death of uterine epithelial cells is thought to play an important role in onset of menstruation and successful implantation of an embryo during early pregnancy. Abnormal apoptosis in these cells can result in dysmenorrhea and infertility. In addition, decreased rate of epithelial apoptosis likely contributes to endometriosis. The cellular mechanisms regulating apoptosis in uterine epithelial cells are not clearly understood. Recently, our laboratory has developed a quantitative ultrasensitive technique for measuring DNA fragmentation in apoptotic neural cells using capillary electrophoresis with laser-induced fluorescence detection (CE-LIF). The proposed project will utilize this novel CE-LIF technology to elucidate cellular mechanisms regulating apoptotic DNA fragmentation in uterine epithelial cells. The objectives are: 1) to establish the ultrasensitive CE-LIF technique for measuring apoptotic DNA fragmentation in uterine epithelial cells, and 2) to determine the role of cGMP/protein kinase G (PKG) pathway in estrogen-, progesterone- and nitric oxide (NO)-induced inhibition of apoptotic DNA fragmentation in uterine epithelial cells. Involvement of NO synthase (NOS) expression in the anti-apoptotic actions of estrogen/progesterone and the pro-apoptotic actions (via toxic levels of NO) of

inflammatory cytokines will be determined using uterine epithelial cells isolated from control and NOS-knockout mice. The resulting data will provide valuable new information about cellular mechanisms of epithelial apoptosis and the use of the novel CE-LIF technology.  
(MD01386)

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**The Role of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) in Spermatogenesis**

- ✉ WONG Patrick Yee Ding
- 1 September 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

In our laboratory we have explored the role of a membrane protein, the *cystic fibrosis transmembrane conductance regulator*, *CFTR* in male reproduction. This protein has been shown to have a widespread effect on human reproduction. Although *CFTR* is also expressed by other exocrine glands, the male reproductive tissues appear to be most highly dependent on *CFTR* for normal functions and are therefore most vulnerable to mild *CFTR* mutations. In the epididymis, *CFTR* functions as a camp-activated chloride channels which play a central role in the formation of the fluid inside the epididymis. Interference with this protein should lead to disruption of the epididymal microenvironment and secondarily to a decrease of sperm quality. Recently, we have accumulated evidence that the germ cells, notably the round and elongated spermatids also express *CFTR*. Although the exact functions of germ cell *CFTR* remains obscure, we speculate that it plays a role in eliciting cell volume decrease during spermatogenesis by studying the coexpression of *CFTR* and aquaporin-7 in germ cells using RT-PCR, immunoblotting, immunohistochemical techniques and to study their functions by coexpressing germ cell *CFTR* and aquaporin (*AQP-7*) in *Xenopus* Oocytes. We believe that such studies will shed light on the role of *CFTR* in the male reproduction. The long term goal of the project is to investigate the feasibility of blocking transformation of spermatids into spermatozoa through intervention of *CFTR* function as a novel method of male contraception.  
(MD01670)

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**The Regulation of Store-operated  $Ca^{2+}$  Influx by Vesicle Fusion and Protein Kinase G**

- ✉ YAO Xiaoqiang • KWAN Hiu Yee
- 1 October 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Store-operated  $Ca^{2+}$  influx is the predominant  $Ca^{2+}$  influx pathway in vascular endothelial cells.  $Ca^{2+}$  influx in endothelial cells triggers the release of vasoactive compounds such as nitric oxide, endothelium-derived hyperpolarizing factor (EDHF), and  $PGI_2$ , and thus regulating vascular tone and blood pressure. Our previous studies have demonstrated that the activity of this channel is down-regulated by cellular messenger cGMP via a protein kinase G-dependent pathway in vascular endothelial cells. On the other hand, a recent important discovery suggests that activation of store-operated  $Ca^{2+}$  influx in neurons may depend on exocytosis of membrane channels or regulatory molecules. In this proposal, we plan to examine the importance of exocytosis in the activation of store-operated  $Ca^{2+}$  influx in vascular endothelial cells and we will also examine the possible interplays between exocytosis and cGMP in regulating store-operated  $Ca^{2+}$  influx in vascular endothelial cells. This study will help to elucidate the underlying mechanism for the regulation of store-operated Ca influx in vascular endothelial cells.  
(MD01429)

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**Role of Vesicle Fusion and Protein Kinase G in Regulating Store-operated Calcium Influx**

- ✉ YAO Xiaoqiang • VILLAZ Michel\*
- 1 January 2002
- ❖ France/Hong Kong Joint Research Scheme

Store-operated  $Ca^{2+}$  influx is the predominant  $Ca^{2+}$  influx pathway in vascular endothelial cells. Changes in endothelial  $Ca^{2+}$  levels alter vascular tone and blood pressure. Store-operated Ca entry may be regulated by several cytoplasmic factors such as small molecular weight G proteins, tyrosine kinase, and tyrosine phosphatase. Our previous studies have demonstrated that cGMP, via a protein kinase G-dependent pathway, may also regulate store-operated  $Ca^{2+}$  influx in vascular endothelial cells. On the other hand, a recent important

discovery suggests that activation of store-operated  $Ca^{2+}$  influx in neurons may depend on exocytosis of membrane channels or regulatory molecules. In this study, we plan to examine the role of exocytosis in the store-operated  $Ca^{2+}$  influx in vascular endothelial cells and we will also examine the possible interplays between exocytosis and cGMP in regulating store-operated  $Ca^{2+}$  influx in vascular endothelial cells. This study will help to elucidate the underlying mechanism for the regulation of store-operated Ca influx in vascular endothelial cells. (MD01340)

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

Edition      Title/Investigators

1998-99      Research in Epithelial Cell Biology (MD98084)

✉ CHAN Hsiao Chang • CHEW CHENG Siew Boon • Ronald Ray FISCUS • LEUNG Po Sing • WONG Patrick Yee Ding • YAO Xiaoqiang

1999-00      Innovation Development of Chinese Medicine-based Health Care Products for Women of All Ages (MD99127)

✉ CHAN Hsiao Chang • BUT Pui Hay Paul (Dept of Biology) • Li K Y\*

2000-01      "Functional Studies of a Novel Epididymis-specific Gene, Bin-1b: Role in Epididymal Host Defense and Male Fertility" (CU00070)

✉ CHAN Hsiao Chang • CHEN Xu\* • ZHANG Yong Lian\*

2000-01      International Symposium on Cell Signal - from Diseases to Drug Discovery (MD00818)

✉ CHAN Hsiao Chang • WANG Jun (Biochemistry) • Ronald Ray FISCUS • CHEW CHENG Siew Boon • LEUNG Po Sing • YAO Xiaoqiang • WAYE Mary Miu Yee (Biochemistry)

1998-99      Physiological Role of Membrane Potential in Regulation of Resistance Arterial Tone (MD98008)

✉ HUANG Yu • CHAN Leung Franky (Dept of Anatomy) • NELSON Mark T.\* • GOLLASCH Maik\*

2000-01      Investigation into Mechanisms of Vascular Action of Purified Neferine from *Nelumbo nucifera Gaertn* in Rat and Mouse Arteries (MD20025)

✉ HUANG Yu • CHAN Wood Yee (Dept of Anatomy) • CHEN Zhenyu (Biochemistry) • KO Wing Hung • YAO Xiaoqiang • YEW Tai Wai David (Dept of Anatomy) • TSANG Suk Ying

2000-01      Studies on the Cellular and Ionic Mechanisms Involved in Estrogen-induced Beneficial Effects on Coronary Artery (MD00545)

✉ HUANG Yu • YAO Xiaoqiang

2000-01      Role of Protein Kinase C in Relaxation of Arterial Smooth Muscle by "Classical" and Novel Calcium Antagonists (MD20048)

✉ HUANG Yu • GOLLASCH Maik\*

2000-01      Simultaneous Measurement of Bioelectric and Fluorescent Signals in Intact Epithelial Tissue (MD20049)

✉ KO Wing Hung • Jens LEIPZIGER\*

2000-01      Association between Pancreatic Angiotensin System and Pancreatic Blood Flow and Ductal Secretion: The Significance of Changes by Chronic Hypoxia in the Rat Pancreas (CU00075)

✉ LEUNG Po Sing • FUNG Man Lung\* • NOBILING Rainer\*

2000-01      Changes of Angiotensin Converting Enzyme Activity and Expression in Experimentally Induced Pancreatitis from the Rat Pancreas (MD00688)

✉ LEUNG Po Sing

2000-01      Changes in the Expression of Renin-angiotensin System in Patients

- with Idiopathic Dilated Cardiomyopathy:  
A Activation of the Transcription Factor  
NF $\kappa$ B (MD20050)  
✉ LEUNG Po Sing • Gerd Wallukat\*
- 2000-01 Regulated Expression and Function of  
Pancreatic Renin-angiotensin System: Its  
Significance in Transplanted Pancreatic  
Islets (MD20057)  
✉ LEUNG Po Sing • Carlsson  
Per-Ola\*
- 2000-01 Calcitonin Gene-related Peptide (CGRP)  
and Nitric Oxide Interactions in Blood  
Vessels: Cellular Mechanisms of Growth  
Inhibition and Protection Against  
Vascular Complications of Diabetes  
Mellitus (MD00772)  
✉ Ronald Ray FISCUS • CHEW  
CHENG Siew Boon • HAN Chide\*  
• WANG Xian\*
- 2000-01 Trichosanthin as an Antiviral Agent -  
Mechanism of Action (MD00577)  
✉ TAM Michael S C
- 1999-00 The Role of Cyclooxygenase in  
Epididymal Functions and Male Fertility  
(CU99293)  
✉ WONG Patrick Yee Ding • LEE  
Will M.\*
- 1999-00 To Investigate the Feasibility of Blocking  
Epididymal Anion Channels as a Novel  
Method for Male Fertility Regulation  
(MD99014)
- ✉ WONG Patrick Yee Ding
- 1999-00 Isolation and Characterization of An  
Endothelial Cyclic Nucleotide-gated  
Cation Channel (CNG) (CU99259)  
✉ YAO Xiaoqiang • HUANG Yu
- 2000-01 Regulation of CNGI Channel Expression  
by a Natural Antisense Gene (MD00583)  
✉ YAO Xiaoqiang • KWAN Hiu Yee
- 2000-01 Nucleotide Modulation of Non-selective  
Cation Channels in Vascular Endothelial  
Cells (MD00479)  
✉ YAO Xiaoqiang • GARLAND  
Christopher\*
- 2000-01 Protein Kinase G-sensitive Ca $^{2+}$  Influx  
in Endothelial Cells and Its Role in  
Vasoregulation (CU00079)  
✉ YAO Xiaoqiang • HUANG Yu •  
YEW Tai Wai David (Dept of  
Anatomy)
- 2000-01 Analysis of GABAergic  
Neurotransmission in Rat Globus  
Pallidus: Correlation of  
Electrophysiology with Ultrastructural  
Immunocytochemistry (CU00080)  
✉ YUNG Wing Ho • BOLAM John  
Paul\* • YUNG Kin Lam Ken\*

## RESEARCH OUTPUTS AND PUBLICATIONS

- <P006065> **LIU C.Q., WANG X. F., YU Mei Kuen, LEUNG Ka Man, CHAN Hsiao Chang, YIP Chung Yin and KO Wing Hung.** "Involvement of Na $^{+}$ -HCO $_{3}^{-}$  Cotransporter in Mediating Cyclic Adenosine 3', 5'-Monphosphate-Dependent HCO $_{3}^{-}$  Secretion by Mouse Endometrial Epithelium". *Biology of Reproduction* vol.66, pp.1846-1852. 2000.
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## RESEARCH PROJECTS

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### **"Life Clinic", 3-Tier Coordinated Service Model, Joint Project on Prevention of Elderly Suicide**

- ✉ CHIU Fung Kum Helen • LAM Chiu Wa
- ☐ 1 November 2001
- ❖ Hong Kong Council of Social Services

The project will establish a Life clinic for 3 years in Li Ka Shing Psychiatric Clinic and a 3-tier co-ordinated service model for elderly suicide prevention in Hong Kong. There will be a clinic run by a psychiatrist to treat elderly with suicidal risk, as well as training GPs, volunteers and counselors to detect elderly with suicide risk. (MD01324)

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### **Association Between Pro-inflammatory Genotypes and Alzheimer's Disease in Chinese**

- ✉ LAM Chiu Wa • TANG Leung Sang Nelson (Dept of Chemical Pathology)
- ☐ 1 November 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Alzheimer's disease (AD) is the most prevalent degenerative disorder of the brain. It is characterized by progressive deterioration in memory and intellectual abilities. Although formally documented a century ago, pathological mechanism of the neurodegeneration and potential curative treatment are still under active research. Recent research findings have found widespread brain-specific inflammation in the brains of patients with AD. The inflammatory hypothesis is recently considered as one of the primary process leading to progressive neuronal death.

The hereditary predisposition of AD suggested that constitutional factors are important determinants for the development of the disorder. As brain inflammation is an important modulating factor of disease progression, it is likely that individuals with pro-inflammation genotypes are conferred particular susceptibility for brain inflammation, thus are at risk of developing AD. The present project aims to identify the association between polymorphisms of genes with pro-inflammatory properties and AD in

Chinese. Genes that are known to play significant roles in the inflammatory process including interleukin-1A, interleukin-1B, interleukin-1RN, tissue necrotic factor  $\alpha$  would be examined with known polymorphisms in Chinese patients with AD. Genotypes of age-matched healthy controls would be compared for risk of developing AD. (MD01538)

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### **Antenatal Depression among Hong Kong Chinese Women**

- ✉ LEE Tak Shing Dominic • CHUNG Kwok Hung Tony (Dept of Obstetrics & Gynaecology) • YIP Shing Kai Alexander (Dept of Obstetrics & Gynaecology)
- ☐ 16 September 2001
- ❖ Research Grants Council (Earmarked Grants)

Postnatal depression has captured the attention of researchers, clinicians and lay public, but comparatively little is known about depression during pregnancy. This is partly related to the fact that pregnancy was regarded as a period relatively protected from psychiatric morbidity. Research in the past two decades, however, suggests that antenatal depression is probably as common, and as damaging, as postnatal depression. Epidemiological studies in western societies show that depressive episodes occur in 10 to 20% of pregnant women. Furthermore, longitudinal studies have demonstrated that antenatal depression is one of the most powerful determinants of postnatal depression. Several studies have also indicated that antenatal psychological distress can adversely affect maternal and foetal well being. For these reasons, there is a growing awareness that antenatal depression deserves more attention from researchers. The investigators propose to examine the rates and risk factors of antenatal depression among 1000 consecutive Hong Kong Chinese women who present for antenatal booking at a university affiliated public hospital. The participants will be followed through the pregnancy, completing depression rating scales at baseline, mid and late pregnancy. In addition, putative risk factors will be assessed and collated. To establish the rates of antenatal depression, a random sub-sample of 150 of the participants will be interviewed by a psychiatrist using standard diagnostic interview. These findings will inform us as to how many Hong Kong women are affected by



antenatal depression and what psychosocial factors put local women at risk of depression in pregnancy. (MD01120)

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**A Mutli-centre Efficacy Trial of Naltrexone Maintenance Therapy in Hong Kong**

✉ LEE Tak Shing Dominic • CHEUNG Kin Leung Ben • LEUNG Shun Pun\* • WONG Chi Keung\* • CHAN Ronald\* • LAM Ming

☐ 1 June 2002

❖ Beat Drugs Fund Association

There is growing evidence that naltrexone maintenance therapy will be useful in preventing relapse among recently detoxified opiate addicts. The Review of Methadone Treatment Programme by the Hong Kong SAR Government has recommended that naltrexone should be considered as a drug to assist relapse prevention. This study aims to examine the efficacy of naltrexone maintenance therapy among 150 recently detoxified opiate addicts in Hong Kong. Participants will be recruited at substance abuse clinics, methadone clinics, and NGO treatment agencies, and received 6 months naltrexone maintenance under supervision. Rehabilitative counseling will also be provided during the naltrexone maintenance. Upon completion of the maintenance therapy, the participants will be followed up for 6 months. Efficacy of the therapy will be examined in terms of treatment retention rate, drug free days, abstinent rate, and days to relapse. The cost and policy implications of implementing naltrexone maintenance programme in Hong Kong will also be examined.

This study will provide empirical data that help inform future policy on naltrexone maintenance programme. (MD01462)

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**Poststroke Dementia in Hong Kong: A Pilot Study**

✉ TANG Wai Kwong • CHAN Sau Man Sandra • UNGVARI Gabor Sandor • CHIU Fung Kum Helen • SZE Kai Hoi Frank\* • WOO Jean (Dept of Medicine & Therapeutics)

☐ 15 November 2001

❖ CUHK Research Committee Funding (Direct Grants)

Both dementia and stroke are major health problems in Hong Kong. Stroke is a frequent cause of dementia. There are only a handful of studies published on poststroke dementia (PSDE) and none of them has involved Chinese populations. There is a lack of consensus concerning the diagnostic criteria, prevalence and risk factors of PSDE.

The aim of the present study is (1) to compare three commonly applied sets of criteria for diagnosing PSDE in Chinese stroke patients, (2) to approximate the prevalence of PSDE in local stroke patients, (3) to determine the optimal cut-off point for the Mini Mental State Examination in screening PSDE and (4) to determine the clinical correlates of PSDE.

Four hundred stroke patients consecutively admitted to the medical wards of Prince of Wales Hospital will be identified as subjects of the investigation. Subjects will be interviewed by a psychiatrist 3 months after their stroke. The presence of previous and current dementia will be diagnosed according to the Information Questionnaire on Cognitive Decline in the Elderly and Diagnostic and Statistical Manual-Fourth Edition (DSM-IV), respectively. Three different sets of criteria for vascular dementia – (1) DSM-IV, (2) ‘National Institute of Neurological Disorders and Stroke-Association / Internationale pour la Recherche et l’Enseignement en Neurosciences’, and (3) ‘Stroke-related dementia’ – will be simultaneously applied to the whole sample and the prevalence of PSDE determined by each sets of criteria compared. In addition, demographic, clinical and radiological data of all subjects with and without dementia will be collected and compared.

(MD01380)

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**Psychological Morbidity in Burn-injured Patients in Hong Kong Chinese - A Prospective Follow-up**

✉ WING Yun Kwok • HO Wai Sun\* • KAM Irene\* • YING SY\*

☐ 1 November 2001

❖ CUHK Research Committee Funding (Direct Grants)

With the advancement of resuscitation and acute management, the survival rates for burn-injured patients have greatly improved. This means that more patients with disfigurements, contractures and functional disability will need long-term and intensive rehabilitation. The limited available western data suggested that nearly two third of burns

patients may have suffered from various degree of under-recognized and under-treated psychological morbidities. Moreover, the few longitudinal follow-up studies suggested that these psychological morbidities tended to persist and even increase in a proportion of patients, especially for depression and post-traumatic stress disorders. Locally, there is an alarming dearth of any data on this very important aspect of psychological well being of burn-injured patients. The recent major catastrophes with a number of burns casualties in Hong Kong have attracted a great deal of public attention on the need of better burns care for the patients, for both acute and long-term care. Thus, we aim to determine the prevalence and risk factors of psychological morbidity in a longitudinal cohort of burn-injured adult patients from an university burns unit will be recruit and assessed at 2 weeks, 6-months and 12-months interval. All patients will be assessed with a semi-structured clinical interview and a list of psychometric assessments for detecting the psychological morbidity and psychosocial functioning, both at syndromal and sub-syndromal level. It is hypothesized that a high percentage of hidden psychological morbidity may lead to appropriate medical treatment, facilitate the rehabilitation of patients and future health care planning. The identified risk factors may help to develop relevant psychological intervention that may ameliorate or prevent the occurrence of psychosocial complications of burn injuries in the world's literature. Although the acute physical pain and wound may heal, the lifelong scars and psychological trauma may remain.  
(MD01663)

● CHAN W F\* ● YU K K\* ● PAN P C\* ● POON T K\* ● LAW Daphne\* ● WONG Elsie\* ● NG Janna Ng\* ● TSANG Maria\* ● LEE Kar Mut\* ● AU YEUNG Wing On\*

2000-01 A Study of the Neurobiological Correlates of Behavioural and Psychological Symptoms in Alzheimer's Disease (CU00082)  
✉ LAM Chiu Wa ● CHIU Fung Kum Helen ● TANG Leung Sang Nelson (Dept of Chemical Pathology) ● Garcia Barcelo Maria Mercedes\*

2000-01 Attitudes toward and Cultural Meanings of Suicide in Contemporary Chinese Society (CU00380)  
✉ LEE Sing ● Arthur Kleinman\* ● Michael Phillips\*

2000-01 Mental Health Service Users' Experience of Discrimination in Hong Kong (MD20032)  
✉ LEE Sing ● Chiu Marcus\* ● Ching Chi Kong\*

1999-00 The Outcome of Postnatal Depression among Chinese Women in Hong Kong (CU99294)  
✉ LEE Tak Shing Dominic ● YIP Shing Kai Alexander (Dept of Obstetrics & Gynaecology) ● CHUNG Kwok Hung Tony (Dept of Obstetrics & Gynaecology)

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

Edition      Title/Investigators

1999-00 Consultancy Study on Pilot Projects on Day Care Centre for Demented Elderly and Dementia Unit for the Elderly in Residential Care Homes for the Elderly (MD99071)  
✉ CHIU Fung Kum Helen ● LAM Chiu Wa ● WOO Jean (Dept of Medicine & Therapeutics) ● LUM Christopher\* ● LI S. W.\* ● AU S Y\*

1999-00 Development of a Local Drug Abuse Treatment Outcomes Measure (MD99119)  
✉ LEE Tak Shing Dominic

2000-01 Charcoal Burning Suicide in Hong Kong (MD20036)  
✉ LEE Tak Shing Dominic ● CHAN Sau Man Sandra ● CHUNG Wai Sau Dicky ● Chan Po Man Kathy\* ● Yip Siu Fai Paul\*

2000-01 Prospective Memory in Patients with Schizophrenia and Its Relationship with Retrospective Memory, Executive

Functions, and Daily-life Adjustment  
(CU00330)

✉ UNGVARI Gabor Sandor • AU  
Wing Cheong\* • CHU Man Keung\*

• TANG Wai Kwong • SHUM H K  
David\*

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- <P02623> **WING Yun-Kwok; LI Hiu-Yeung Raymond; LAM Ching-Wan; HO Kwok-Wah Crover; FONG Yuk-Yat Samson and LEUNG Tony.** "The Prevalence of Narcolepsy Among Chinese in Hong Kong". *Annals of Neurology* vol.51, pp.578-584. Wiley-Liss Inc., 2002.05.
- <P02624> **ZHANG Yalin; YOUNG Derson; LEE Sing; LI Lingjiang; ZHANG Honggen; XIAO Zeping; HAO Wei; FENG Yongmin; ZHOU Hongxiang and CHANG F. Doris.** "Chinese Taoist Cognitive Psychotherapy in the Treatment of Generalized Anxiety Disorder in Contemporary China". *Transcultural Psychiatry* vol.39, pp.115-129. Canada, 2002.03.
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- <P02626> **LEE Sing and KLEINMAN Arthur.** "Psychiatry in its Political and Professional Contexts: A Response to Robin Munro". *The Journal of the American Academy of Psychiatry and the Law* vol.30, pp.120-125. USA, 2002.

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- <P02965> **CHIU H.; UNGVARI G.S.; YIU G.C.; YIP K.C.; NG F.S. and TANG W.K.** "Prescription Pattern for Chinese Schizophrenic Patients". *The International Journal of Neuropsychopharmacology XXIII CINP Congress* vol.5 no.Supplment 1, p.S182. Montreal, Canada: CINP, 2002.06.
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## RESEARCH PROJECTS

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### Apoptosis in Infiltrating Mononuclear Cells of Colorectal Cancer is a Novel Mechanism for Tumor Escape

- ✉ CHEN Gong George • LEE Fung Yee Janet
- ☐ 31 October 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Others and our studies have demonstrated that colon cancer cells continue to proliferate rather than become apoptotic despite showing an increase in proapoptotic molecules such as Fas and Fas ligand (FasL). The mechanism responsible for is unclear, though Fas or tumor counterattack several has been proposed as a possible mechanism of resistance against apoptosis in colorectal cancer cells. However, this theory has recently been challenged, as colon cancer monolayers fail to inhibit the growth of Fas-expressing lymphoid cells. The immune system plays an important role in the regulation of malignancies in humans. Stimulation of immune system has been considered as a factor responsible for spontaneous tumor regression, whereas suppression of immune system many contribute to the induction of tumor. The number of tumor infiltrating mononuclear cells in resected tumor specimens negatively correlates with the size of tumor but positively with survival in various malignancies such as melanoma, lung cancer and colon cancer. Mononuclear cells are known to express apoptotic molecules other than Fas and FasL, such as Bcl-2, Bax and caspases. However, the roles of these non-Fas/FasL apoptotic molecules in infiltrating mononuclear cells of human colorectal cancer have not yet been studies. The aim of the present study is to examine apoptotic pathway in infiltrating mononuclear cells of colorectal cancer, and to test whether there is a novel mechanism contributing to the growth of human colorectal cancer. This study will set a foundation for more dedicated experiments in this direction. Finding out why colon cancer grow uncontrollably is important for the development of an effective therapy towards this disease whose incidence has steadily increased in areas where a comfortable life style becomes available.

(MD01624)

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### Isolation and Characterisation of the Nitrite Reductase Gene of *Helicobacter Pylori* and Its Role in Gastric Carcinogenesis

- ✉ CHUNG Sheung Chee Sydney • CHAN Chiu Yeung Raphael (Dept of Microbiology) • CHENG Fun Bun Augustine (Dept of Microbiology) • LEUNG Wai Keung (Dept of Medicine & Therapeutics) • LING Kin Wah Thomas (Dept of Microbiology) • NG Enders Kwok-wai • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics)
- ☐ 1 November 2001
- ❖ Research Grants Council (Earmarked Grants)

Gastric cancer is the second most common cause of cancer-related death in the world. It is also the leading cause of cancer mortality in China. While chronic *Helicobacter pylori* infection is undoubtedly an important causative agent of stomach cancer, the exact pathogenic mechanism remains obscure. *H. pylori* has been shown to exhibit nitrosating activity *in vitro* and increased endogenous nitrosating activity has been reported in subjects with *H. pylori* infection. Recently, we have demonstrated that *H. pylori* isolated from patients with gastric cancer express significantly higher levels of nitrosating activity than those collected from patients with duodenal ulcer or non-ulcer dyspepsia. However, little is known about the nitrosating enzyme system of *H. pylori*. This research project aims to isolate the gene encoding the denitrifying enzyme of *H. pylori* and to assess its relation to various gastroduodenal diseases. The results of this study will yield important information concerning the mechanism of gastric carcinogenesis related to *H. pylori* infection, and it may have profound implication in the prevention of the malignancy in the future.

(MD01126)

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### Biological Effects of Laser Energy on Post-Burn Keloid Fibroblast Cells

- ✉ David Andrew Ross BURD
- ☐ 1 January 2002
- ❖ CUHK Research Committee Funding (Direct Grants)

In the proposed study we look at clinically relevant model of abnormal tissue, post-burn scar tissue. We focus on the behavior of the fibroblast, which is the most abundant cell type in dermal connective tissue including scar tissue. There is a spectrum of dermal matrix organization and cellular behavior that again ranges from normal to frankly malignant. Although fibrosarcoma is extremely rare both cutaneous burns and exposure to radiation are recognized aetiological factors. The malignant transformation typically occurring years after the precipitation event (Wheedon, 1992).

Laser Energy

↓

Normal Skin Normal Scar Hypertrophic Scar ?←  
Keloid Scar → ? Fibrosarcoma

→

Increasing abnormality

In this study we focus on the effects of laser energy on cultured fibroblasts from normal skin and post-burn keloid scar tissue. The effects of two lasers used therapeutically are compared: the pulsed dye laser with a wavelength of 585nm and the Nd:YAG laser with a wavelength of 532nm.

While we are looking for evidence of a shift to the RIGHT again we are also particularly concerned to explore ways of normalizing (shifting to the LEFT) cellular behavior with laser intervention.

(MD01802)

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### The Interaction between Endothelium and Smooth Muscle/Cardiac Myocytes During Heart Surgery and Clinical Significance

✉ HE Guo Wei

☐ 1 September 2001

❖ Research Grants Council (Earmarked Grants)

Normal coronary function plays a key role in myocardial perfusion. The endothelium secretes endothelium-derived relaxing factors (EDRFs) to maintain the normal function of the coronary circulation. Endothelium-derived nitric oxide [NO] and a chemically unidentified endothelium-derived hyperpolarizing factor [EDHF] are the major regulators for the coronary flow. During open heart surgery, the heart is arrested and ischemia-reperfusion injury is the main cause of subsequent alteration of the heart function. Our previous work demonstrated that hyperkalemic cardioplegia or organ preservation solution reduce the

EDHF-mediated relaxation and membrane hyperpolarization in coronary arteries and that this function may be restored by hyperpolarizing cardioplegia using potassium channel openers. However, little is known about (1) what the correlation between the mechanical and electrophysiological activities is during this period; (2) what effect of NO on the electrophysiological changes of the smooth muscle cell is; (3) what the interaction between NO and EDHF on the above activities; (4) whether there is a direct electrophysiological communication between the endothelium and the cardiac myocytes; and (5) whether the linked activities may be restored by pharmacological agents such as hyperpolarizing cardioplegia. We propose this study to answer the above questions. The study will be conducted in isolated coronary arteries and myocardium from pig hearts in organ chambers and myographs. Direct measurement of NO and the membrane potential in a single cell will be performed. The results will be partially confirmed in the *in vivo* pig model. The results derived from these studies will provide important knowledge to develop new methods to protect the heart in order to prevent and treat perioperative cardiovascular complications in heart surgery including heart transplantation. (MD01127)

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### Activation of NF- $\kappa$ B and NF-IL6, the Common Pathway Towards Angiogenesis of Hepatitis-B-Related Hepatocellular Carcinoma

✉ LAI Bo San Paul • CHEN Gong George • LAU Wan Yee Joseph

☐ 1 January 2002

❖ CUHK Research Committee Funding (Direct Grants)

Angiogenesis is a process of generating new blood vessels. Increasing amount of evidence indicates that progressive growth of solid tumors including hepatocellular carcinoma (HCC) is dependent on angiogenesis. The mechanism leading to angiogenesis in HCC is not fully known. Chronic infection with hepatitis B virus (HBV) is a well-known causative element in the development of HCC and about 90% of HCC is associated with HBV infection. Interleukin 8, cyclooxygenase 2 (COX-2), inducible nitric oxide synthase (iNOS), vascular endothelial growth factor (VEGF) and peroxisome

proliferator-activated receptor gamma (PPAR $\gamma$ ) are important mediators related to HBV infection and tumor angiogenesis. By analysis of gene promoter regions of these elements, we have found that they contain either one of the two important transcription factors, NF- $\kappa$ B or NF-IL6. We further noted that these two transcription factors can be affected by HBV. Therefore, we believe that NF- $\kappa$ B and NF-IL6 are two critical regulators that control angiogenesis in HBV-positive HCC. The present study is to investigate the interaction between HBV and NF- $\kappa$ B/NF-IL6 and to find out how this interaction contributes to the expression of angiogenic or angiostatic molecules and thus the growth of HCC.  
(MD01511)

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**Expression of Double-stranded RNA-activated Protein Kinase in Hepacellular Carcinoma with Hepatitis B Virus Infection**

- ✉ LAU Wan Yee Joseph • CHEN Gong George
- 1 March 2002
- ❖ CUHK Research Committee Funding (Direct Grants)

Despite the existence of efficient vaccines, an estimated 10-20% of population in Southeast Asia including Hong Kong is hepatitis B virus (HBV) carrier. With such a high incidence and the fact that 90% of hepatocellular carcinoma (HCC) in Asia is associated with HBV, HBV infection is considered as a major health problem in Southeast Asia. HBx, a major component of HBV, plays a central role in HBV infection by transactivating critical molecules, and it also contributes to the development of HCC. Double-stranded RNA-activated protein kinase (PKR) is considered as a tumor suppressor because the expression of dominant negative mutants of PKR causes malignant transformation. Inhibition of PKR function is related to persistent infection of some viruses including hepatitis C virus (HCV), and it is believed to be the main mechanism that hepatitis viruses resist interferon (INF) therapy. The virus may evolve various devices to downregulate PKR and therefore, to overcome the host defense mechanism against viral replication. Our preliminary data showed that PKR is significantly lower in HBx-expressed human hepatoma cells than in HBx-negative hepatoma cells. Therefore, we hypothesize that HBx is a molecule responsible for

the reduction of PKR in HBV infection and that a decreased level of PKR contributes to persistent HBV infection, which eventually leads to the development of HBV-related HCC. This research project is thus designed to investigate the expression of PKR in HCC and to analyze how PKR expression is related to HBV infection.  
(MD01468)

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**A Randomized, Third-party-blind, Multicenter Study to Assess the Efficacy, Safety, and Cost-effectiveness of Intravenous Sulbactam/Ampicillin Compared with Cefuroxime Plus Metronidazole Combination for the Prophylaxis of Infection in Subjects (including those with colorectal cancer) Following Colorectal Surgery**

- ✉ LEUNG Ka Lau • LEE Fung Yee Janet • NG Siu Man Simon
- 1 June 2002
- ❖ Pfizer Corporation Hong Kong Limited

A randomized, Third-Party-Blind, Multicenter Study to Assess the Efficacy, Safety, and Cost-Effectiveness of Intravenous Sulbactam / Ampicillin Compared with Cefuroxime Plus Metronidazole Combination for the Prophylaxis of infection in Subjects (Including Those With Colorectal Cancer) Following Colorectal Surgery.  
(MD01354)

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**Which Traumatic Intracerebral Haematoma should be Surgically Evacuated? An Autoregulation and Neurochemical Monitoring Study**

- ✉ POON Wai Sang • CHAN Matthew Tak Vai (Dept of Anaesthesia & Intensive Care) • GIN Tony (Dept of Anaesthesia & Intensive Care) • LAM Wai Man Wynn (Dept of Diagnostic Radiology & Organ Imaging) • NG CP\* • LAM Joseph MK\*
- 1 October 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Intracerebral haematoma are common in patients with severe head injuries. Traditionally, surgical evacuation of these lesions is determined by the



patient's clinical status, size of the haematoma and intracranial pressure (ICP). However, the prediction for non-operative management is incorrect in significant number of cases, resulting in unfavourable outcome. We hypothesize that the addition of cerebral haemodynamic and neurochemical monitoring in the peri-lesional brain will result in a more accurate evaluation for the necessity and timing of surgery.

We propose a prospective study of 10 moderate-to-severe head-injured patients with intracerebral haematoma that do not require immediate surgical evacuation. Continuous monitoring of ICP, blood flow velocity, pulsatility index (PI) and its autoregulatory response of both middle cerebral arteries (MCA) using transcranial Doppler ultrasonography (TCD), peri-lesional measurements of extracellular concentrations of glucose, lactate, glycerol, glutamate and pyruvate (by intracerebral microdialysis), intracerebral pH, oxygen ( $PO_2$ ), carbon dioxide ( $PCO_2$ ) tension and temperature (using a combined fiberoptic and Clark electrode sensor) will be instituted for 7-10 days. Regional cerebral blood flow (CBF) will also be measured on day 1, 3 and 5 using stable xenon enhanced computed tomography (Xe/CT). The intracerebral haematoma will be removed if there is clinical deterioration and/or ICP > 30 mmHg occurs. Monitoring will be continued during and after surgery, until the patient is discharged from the intensive care unit (ICU).

This is the first systematic study of traumatic intracerebral haematoma to examine the hypothesis that autoregulation tests and neurochemical monitoring can predict the need for surgery earlier than the conventional indications (i.e. clinical deterioration and/or elevated ICP).

(MD01947)

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### **Epidemiological Study of Primary Nocturnal Enuresis (Bed-Wetting) in Young Adults in Hong Kong**

✉ YEUNG Chung Kwong • LAU Tak Fai Joseph  
(Centre for Clin. Trials & Epidemiological Research)

☐ 1 September 2001

❖ Health Care & Promotion Fund, Hospital Authority

Traditionally, urinary incontinence has been regarded as normal for young children before the age of 4-5 years in most Chinese families, and primary nocturnal enuresis (PNE), or bedwetting, had hardly received any attention from parents and even medical practitioners as a condition that warranted any investigation or treatment. However, a recent large epidemiological study comprising of 16,512 school children aged 5-19 years revealed that PNE in Hong Kong was, very contrary to our existing belief, just as prevalent as in other western countries. At age 5 years, 16.2% children had PNE (20.5% males, 11.0% females), and at age 8 and 19 years, 6.3% and 1.5% children had PNE respectively. This highlights the fact that the problem of bed-wetting has all along been grossly underestimated and neglected in Hong Kong. Of note, the prevalence of PNE remained rather static with no further significant drop after the age of 11-12, with around 2% of both adolescent boys and girls remaining enuretic. More importantly, the reduction in overall prevalence of PNE with advancing age was seen mainly among those with mild symptoms (wets less than 3 nights per week), as compared to those with more frequent bedwetting. At age 5, only 14% of enuretic children had wetting 7 nights per week, as compared to 37% at age 19 ( $p < 0.05$ ). This indicated that the previous notion that PNE will get better and spontaneously resolve with growing age probably applies largely to those with mild enuretic symptoms only. As the age advances, those with severe symptoms would very likely have persistent problems into adult life. Furthermore, studies in our unit have shown that bladder dysfunctions are very common among enuretic patients with refractory symptoms. Specific therapies targeted at the underlying problems have now enabled us to achieve a very high cure rate even in patients with refractory symptoms. Studies from our units as well as from other workers have also shown that enuretic children had significantly more behavioral and psychological problems and worse self-esteem compared with normal controls. These adverse effects showed marked reversal to normal after successful cure. As many frequent bedwetters tend to have persistent enuretic symptoms into adult life, and a large proportion of these may have bladder dysfunctions that would require treatment per se, detailed epidemiological data of bed-wetting in adults in Hong Kong is urgently needed. We propose to study the prevalence of PNE in young adults aged 16-40 by individual

phone-interview, and to identify possible adverse effects on the socioeconomic and psychological status of affected individuals.

(MD01708)

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**Primary Nocturnal Enuresis in Young Adults in Hong Kong: An Epidemiological, Hormonal Cystometric and Somnographic Study**

✉ YEUNG Chung Kwong • Charles Andrew VAN HASSELT • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research)

☐ 1 September 2001

❖ CUHK Research Committee Funding (Direct Grants)

Primary nocturnal enuresis (PNE), or bed-wetting, is a very common problem in western countries. A recent large epidemiological study of PNE in Hong Kong comprising of 14,755 school children aged 5-19 years revealed that at age 7, 9.8% of boys and 8.3% of girls still has bed-wetting. Of note, the proportion of frequent bed-wetters progressively increased with increasing age. At age 5, only 12% of enuretic children wets very night, compared with 33% at age 19 ( $p < 0.01$ ). Studies in our unit have also shown that bladder dysfunctions and sleep disturbances are very common among enuretic children with persistent symptoms. Specific therapy targeted at the underlying disturbances has now enabled us to achieve a very high cure rate even in these patients. Furthermore, our studies have shown that enuretic children had significantly more behavioral and psychological problems and worse self-esteem compared with normal controls. These adverse effects showed marked reversal to normal after successful cure. As our pilot experience showed many frequent bed-wetters tend to have persistent enuretic symptoms into adult life, and a large proportion of these may have bladder dysfunctions that needs treatment per se, detailed epidemiological and pathophysiological studies of bed-wetting in adults is urgently needed. We propose to study the prevalence of PNE in young adults aged 16-40 by individual phone-interview. In addition, we will evaluate the abnormal physiological characteristic in local enuretic adults with urodynamic and sleep polysomnogram studies, bladder ultrasound and assays of diurnal / nocturnal rhythm of antidiuretic hormone (ADH) secretion. The findings may help us to identify

different treatment subgroups and have very important implications to our future management strategy for PNE in adults.

(MD01812)

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**Children's Continence Care Centre**

✉ YEUNG Chung Kwong • Wendy Fiona BOWER • Sit K Y Frances\* • YEW Siu Yin\*

☐ 1 June 2002

❖ S K Yee Medical Foundation

There is currently no other established service in Hong Kong or China, and indeed most parts of Asia, to which children with the debilitating medical problem or either urinary or faecal incontinence can go for speedy and efficient help in becoming clean and dry. For children suffering the embarrassment of wet or smelly clothing, attempts to hide the problem are difficult and alienating. Poor bladder or bowel control is a hidden problem that is rarely discussed and tragically society persists in shaming affected individuals and their families. There is limited access to help since knowledge among doctors is inadequate, only in recent days have families been offered more than the hope that children will grow out of the symptoms.

This project will directly benefit physical space will be bladder or bowel problems, since it will provide a defined center for the investigation and management of their unique disorders. A specific physical space will be dedicated, rather than shared with other services, and staffed by specialists and experts in the field. Since the service will be offered at Prince of Wales Hospital, it will be financially accessible to all families of children suffering from incontinence. The service provided will be co-ordinated and streamlined for optimal administrative efficacy, whilst the medical management will be scientifically scrutinized and updated as new initiatives are reported in the literature.

*Aims:*

- (1) To develop a comprehensive facility and care service for children who suffer with the devastating problem of bladder or bowel dysfunction.
- (2) To prevent secondary psychological, behavioural, socialisation and self-esteem problems that are frequently a result of elimination disorders.
- (3) To prevent the serious and often life-threatening sequelae of unidentified and unmanaged urinary tract dysfunction.

(4) To educate the public towards realizing that continence difficulties in children are a medical problem rather than a phenomenon that will disappear as a child becomes older.

(5) To educate health care providers in the identification of incontinence in children and facilitate appropriate explanation to families of the known causes and treatments.

(6) To establish an effective assessment and intervention service model for children with bladder and bowel problems and to facilitate the expansion of this model to China and across Asia.

(7) To actively evaluate intervention strategies and regularly contribute to international academic discussion and publication with research in the arena of children's continence care.

Currently the multidisciplinary team at Prince of Wales Hospital diagnoses and manages children with continence difficulties through four different clinics (spina bifida service one session per month; bedwetting review service one session each fortnight; intervention for bowel and daytime urinary problems one session each fortnight; and a weekly one day urotherapy service for children with control problems during the day). Each clinic has rapidly expanded and it is now crucial that a new center with dedicated space be established for the co-ordination, integration and cross-referral from the different services. The Children's Continence Care Centre will be an holistic and unique service in Hong Kong. Staff will bring a multidisciplinary perspective, local and international skills and experience, and a proven contribution to the care of children with continence problems. Children with both bladder and bowel problems will attend the center as a one stop facilitate for comprehensive diagnostic procedures and for all forms of conservative intervention. It is envisaged that such a dedicated resource will facilitate a dramatic increase in service provision. It may be expected that waiting lists for help would be cut appreciably, however in this emerging area of children's medicine it is likely that the current demand reflects only a portion of the real problem. (MD01896)

**A Phase III, Randomized, Double Blind, Multicenter and Multinational Study to Determine the Efficacy and Safety of Tolterodine Prolonged Release Capsules in Children 5 to 10 Years of Age with Symptoms of Urge Urinary Incontinence, Suggestive of Detrusor Instability**

✉ YEUNG Chung Kwong • Shit Kam Yee Frances\* • Sihoe, Deary Yin Jennifer\*

□ 12 June 2002

❖ Pharmacia Singapore Pte. Ltd.

Tolterodine is a muscarinic receptor antagonist that increases bladder capacity by diminishing unstable detrusor contractions. Previous studies have demonstrated that it is safe and effective for treating detrusor instability in adults. Bladder instability is also a significant problem in children aged 5 years and above. In a previous placebo-controlled trial in children 5-10 years of age, all subjects with urge urinary incontinence were enrolled with a urinary frequency of >2 micturitions/24 hours. The greatest efficacy was noted among children who did not demonstrate an infrequent micturition pattern, those patients with  $\geq 6$  micturitions per day.

The clinical pharmacology of tolterodine has been studied in children 11 to 15 years of age (PR) and in children 5 to 10 years of age (IR). The present study is intended to provide further efficacy and safety data of tolterodine PR capsules (2mg qd) in the same age group, 5 to 10 years, but including also those children with a mean micturition frequency of  $\geq 6$  micturitions per 24 hours.

(MD01597)

**"Homocysteine, Oxidant Stress and Vein Graft Failure: Interactions with Diabetes and Hypercholesterolaemia and Novel Approaches to Therapy Using Gene Transfer in a Porcine Model"**

✉ YIM Ping Chuen Anthony • ARIFI Ahmed A\* • HE Guo Wei • JEREMY Jamie\* • NEWBY Andrew C\* • WAN Song

□ 31 December 2001

❖ Research Grants Council (Earmarked Grants)

A modest elevation of plasma homocysteine (HC) concentrations (from 7 to 14.5  $\mu$ moles / L) is an established risk factor for the development of cardiovascular disease and vein graft failure following arterial reconstructive surgery. The exact mechanisms underlying these established relationships are poorly understood. However, we found that copper markedly augments the generation of superoxide ( $O_2^-$ ) from HC.  $O_2^-$  negates nitric

oxide (NO) bioactivity via the formation of peroxynitrite [ONOO] (NO+O<sub>2</sub>-> ONOO). In turn, impaired NO formation has been implicated in graft failure following CABG bypass due to: 1) increased thrombotic episodes and 2) increased vascular smooth muscle cell proliferation. In diabetes mellitus and hypercholesterolaemia (both major risk factors for vein graft failure), HC and copper levels are elevated. In turn, we found that in diabetic and hypercholesterolaemic animal models, HC and copper markedly impaired NO formation through the potentiation of vascular O<sub>2</sub>- formation. Therefore, we have postulated that: 1) in patients undergoing arterial reconstructive surgery, HC constitutes a risk factor through the generation of O<sub>2</sub>- and 2) patients with other risk factors such as diabetes mellitus and hypercholesterolaemia are at greater risk of vein graft failure through potentiation of oxidant stress by HC and copper. In order to explore this postulate further, we propose to investigate vein graft thickening in pigs rendered: 1) homocysteinaemic by supplementation of the diet with methionine, 2) hypercholesterolaemic with a lipid rich diet and 3) diabetic with alloxan. We will determine the interactions of these risk factors on vein graft pathology, i.e. diabetic + homocysteinaemia and hypercholesterolaemia + homocysteinaemia on vein graft disease. (MD01133)

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

<u>Edition</u>	<u>Title/Investigators</u>
2000-01	Impact of Continuous Ventilation on Pulmonary Injury After Cardiopulmonary Bypass (MD00456) ✉ ARIFI Ahmed A* • NG Sze Hang Calvin • HO Ming Hei Anthony (Dept of Anaesthesia & Intensive Care) • WAN Song • YIM Ping Chuen Anthony
2000-01	A Multi-centered Randomized Controlled Trial Comparing Standard Oesophagectomy Versus Primary Chemo-irradiation without Surgery as the Treatment for Squamous Oesophageal Cancer (CU00084)

	✉ CHAN Chi Wai Angus • CHUNG Sheung Chee Sydney • James Francis GRIFFITH (Dept of Diagnostic Radiology & Organ Imaging) • KWOK Po Yin Samuel • LEONG Heng Tat • LEUNG Sing Fai (Dept of Clinical Oncology) • ONG Lina Lilian • LI Ka Wah Michael
2000-01	A Functional and Molecular Study of Mitochondria in the Progress of Carcinogenesis of Urinary Bladder Tumours In Rats (MD00894) ✉ CHAN Siu Foon Peter • CHAN Leung Franky (Dept of Anatomy)
2000-01	Kupffer Cells Kill Tumor Cells by Generating Inducible Nitric Oxide synthase (MD00339) ✉ CHEN Gong George • LAI Bo San Paul
2000-01	Altered Expression and Mutations of the HBV Transactivator X Gene in Hepatocellular Carcinoma and Liver Cirrhosis (MD00305) ✉ CHUI Ka Keung Albert • CHEN Gong George • LAU Wan Yee Joseph
1998-99	Helicobacter Pylori Infection and Intra-gastric N-nitrosation in Gastric Carcinogenesis (CU98218) ✉ CHUNG Sheung Chee Sydney • NG Enders K. W.* • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • LING Kin Wah Thomas (Dept of Microbiology) • CHAN Chi Wai Angus • LAU Yun Wong James
2000-01	A Randomized Trial on the Need for Cholecystectomy in Elderly Patients After Endoscopic Sphincterotomy for Bile Duct Stones (MD00455) ✉ CHUNG Sheung Chee Sydney • LAU Yun Wong James • CHAN Chi Wai Angus • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) •

- LAU Wan Yee Joseph • NG Enders Kwok-wai
- 1998-99 Development of a Cantonese Basic Speech Perception Test for Hearing-Impaired Children and Children with Minimal Language Ability – Establishing Validity and Reliability (AL98028)  
 ✍ Charles Andrew VAN HASSELT • TONG Chi Fai Michael • LEE Y.S. Kathy\* • CHIU S. N.\* • WONG K.C. Terence\*
- 2000-01 A Study of the Biological Effects of 532nm Laser on Human Post-burn Keloid Fibroblast Cells with Particular Reference to the Effect on Malignant Potential (MD00824)  
 ✍ David Andrew Ross BURD • HO Wai Sun • POON Kwok Man
- 1999-00 Protection of Coronary Endothelium-smooth Muscle Function During Cardiac Surgery (CU99246)  
 ✍ HE Guo Wei
- 1997-98 Prospective Study on the Relationship of Central Venous Pressure and Blood Loss During Hepatectomy (MD96217)  
 ✍ LAI Bo San Paul • CHUI Po Tong (Dept of Anaesthesia & Intensive Care) • LEOW Chon Kar# • LAU Wan Yee Joseph
- 1998-99 The Bioenergetic Basis of Liver Regeneration Following Partial Hepatectomy in Man - A <sup>31</sup>P Magnetic Resonance Spectroscopy Study (CU98214)  
 ✍ LAU Wan Yee Joseph • Darren Vivian MANN • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • HJELM Nils Magnus (Dept of Chemical Pathology)# • LAM Wai Man Wynn timer (Dept of Diagnostic Radiology & Organ Imaging)
- 1997-98 The Comparative Impact of Videoconsultation on Neurosurgical Health Services (MD97095)  
 ✍ POON Wai Sang • KWOK Po Yin Samuel • JACOBS Philip\*
- 2000-01 Non-invasive Assessment of Patients with Thalamic Brain Haemorrhage for Surgical Indications: A Study with Continuous Compliance Monitoring (CM) and Transcranial Doppler Ultrasonography (TCD) (MD00487)  
 ✍ POON Wai Sang • CHAN Matthew Tak Vai (Dept of Anaesthesia & Intensive Care) • LAM Ming Kuen Joseph • BUCKLEY Thomas Anthony (Dept of Anaesthesia & Intensive Care) • LAM Wai Man Wynn timer (Dept of Diagnostic Radiology & Organ Imaging)
- 2000-01 A Systematic Review of the Effectiveness of Ofloxacin Otic Solution for the Treatment of Suppurative Otitis Media (MD20013)  
 ✍ TONG Chi Fai Michael • Generoso T Abes\* • Noel L Espallardo\*
- 2000-01 Long-term Safety, Tolerability and Clinical Efficacy of Tolterodine Prolonged Release Capsules in Children 5-15 Years of Age. A Phase III Open-label, Multinational 12-month Study (MD00637)  
 ✍ YEUNG Chung Kwong • SIHOE Dart Yin Jennifer\* • SHIT Kam Yee\*
- 1995-96 Video Assisted Thoracic Surgery (MD92192)  
 ✍ YIM Ping Chuen Anthony
- 1999-00 Investigating the Mechanism of the Beneficial Effect of External Stenting of Saphenous Vein Bypass Graft in Preventing Late Graft Failure with Emphasis on the Role of the Adventitia (CU99310)  
 ✍ YIM Ping Chuen Anthony • IZZAT Mohammad Bashar# • WAN Song

- 1999-00 Novel Strategies for the Treatment of Vein Graft Failure: Investigation Using a Pig Model (MD99089) ✉ YIM Ping Chuen Anthony • ARIFI Ahmed A\* • JEREMY Jamie\* • WAN Song  
✉ YIM Ping Chuen Anthony • WAN Song\* • JEREMY Jamie\*
- 2000-01 Novel Strategies for the Treatment of Vein Graft Failure: Investigations Using a Porcine Model (CU00091)

## RESEARCH OUTPUTS AND PUBLICATIONS

- <P004240> **LEE F.Y.J.; LAI P.B.S.; NG S.M. and LAU W.Y.** "Minimally Invasive Surgery for Symptomatic Hepatic Cysts". *HPB* vol.2 no.4, pp.417-419. UK, 2000.
- <P004242> **GADSDON P.; YIM A.; WAN S.; NEWBY A.C.; ANGELINI G.D. and JEREMY J.Y.** "Nitrated Tyrosine in Porcine Stented and Unstented Vein Grafts". *Abstracts of the International Symposium on Atherosclerosis* vol.151, p.108. 2000.06.27.
- <P004243> **TONG C.F., Michael; YUE Virgil and HASSELT C. Andrew Van.** "The Use of Pre-Operative Antibiotics for Tympanoplasty - A Randomized Controlled Study". *Proceedings of 6th International Conference on Cholesteatoma & Ear Surgery* ed. by MAGNAN Jacques, CHAYS Andre. pp.389-392. France: Label Production, 2000.
- <P004279> **KE C.; POON W.S.; NG H.K.; TANG N.L.S.; CHAN Y.; WANG J.Y. and HSIANG J.N.K.** "The Impact of Acute Hyponatraemia on Severe Traumatic Brain Injury in Rats". *Acta Neurochirurgica (Wien)* vol.76, pp.405-408. 2000.
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- <P011465> **COCKS R.A.** "Developing New Standards within CNST". *NHSLA Review* vol.21, p.11. UK, 2001.
- <P011607> **Charles Andrew VAN HASSELT, WOO Kong Sang John and TONG Chi Fai Michael.** "Nasopharyngeal Pathologies: Diagnosis, Documentation and Treatment". *American Academy of Otolaryngology - Head and Neck Surgery Bulletin* vol.20 no.4, p.103. USA, 2001.08.
- <P011751> **LAM P.K., TO Wai Hei Edward, YEN Siu Ching Rita and LAU H. C. H..** "The *in vitro* Invasion Effect of Retinoic Acid and Interferon-alpha of Squamous Carcinoma Cancer Cell Lines of Head and Neck Cancer". *Abstracts of the 4th European Workshop on Basic Biology of Head and Neck Cancer* (4th-6th October 2001). Amsterdam, The Netherlands, 2001.
- <P011784> **ZOU Wei, YANG Qin, YIM Ping Chuen Anthony and HE Guo Wei.** "Epoxyeicosatrienoic Acids (EET11,12) May Partially Restore Endothelium-Derived Hyperpolarizing Factor-Mediated Function in Coronary Micro-arteries". *Annals of Thoracic Surgery* vol.72, pp.1970-1976. 2001.

- <P011792> **POON W.S.** "Invited Commentary 'Extradural Haematoma - A Five-Year Audit as a Tertiary Trauma Centre in Hong Kong". *Asian Journal of Surgery* vol.24 no.3, pp.305-309. Hong Kong, 2001.07.
- <P011802> **LAU W.Y., Joseph.** "Laparoscopic Cholecystectomy for Gallstone Pancreatitis". *Asian Journal of Surgery* vol.24, p.S102. Hong Kong: Springer, 2001.11.
- <P011803> **LAU W.Y., Joseph.** "Management of Recurrent Hepatocellular Carcinoma". *Asian Journal of Surgery* vol.24, p.S88. Hong Kong: Springer, 2001.11.
- <P011826> **MOK S.W. Johnny; PAK Wai, Martin; CHAN K.F.; CHOW, John and VAN HASSELT C.A.** "Unusual T- and T/NK- Cell Non-Hodgkin's Lymphoma of the Larynx: A Diagnostic Challenge for Clinicians and Pathologists". *Head and Neck* vol.23, pp.625-628. USA: John Wiley & Sons, Inc., 2001.08.
- <P011852> **NG Siu Man Simon, LAI Bo San Paul, LEE Fung Yee Janet and LAU Wan Yee Joseph.** "Soft-Tissue Case 41 Bouveret's Syndrome". *Canadian Journal of Surgery* vol.44 no.5, pp.364-365. Canada, 2001.10.
- <P011856> **TO E.W.H.; PANG P.C.W.; CHAN D.T.M. and LAM J.M.K.** "Subcranial Anterior Skull Base Dural Repair with Galeal Frontalis Flap". *British Journal of Plastic Surgery* vol.54 no.5, pp.457-460. UK, 2001.07.
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- <P011871> **TO E.W.H.; TSANG W.M.; YIU F. and CHAN M.** "A Missing Throat Pack". *Anaesthesia* vol.56, pp.383-384. UK: Blackwell Science Ltd, 2001.08.
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- <P011901> **TO W.H. Edward; PANG C.W. Peter and KU K.M. Peter.** "Use of an Extended Glabellar Fascial-Cutaneous Flap for Reconstruction of the Nasopharynx". *Plastic and Reconstructive Surgery* vol.108, pp.151-153. USA, 2001.07.
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## RESEARCH PROJECTS

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### **Cost-effectiveness Analysis of Oral Paracetamol, Diclofenac and Indomethacin for the Treating Pain After Soft Tissue Limb Injuries: A Randomized, Controlled Trial**

✉ MAN Shin Yan • WOO Wing Keung • Timothy Hudson RAINER • Robert Anthony COCKS (Dept of Surgery) • LAM Kwok Wai (Centre for Clin. Trials & Epidemiological Research) • JACOBS Philip\* • NG Ying Chu\*

□ 24 September 2001

❖ CUHK Departmental Funding

*Background:* Non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol are commonly used oral analgesics in emergency departments (ED) not only in Hong Kong but throughout the world. Every year, much money is spent prescribing analgesics for soft tissue injuries, and some of this is spent on expensive NSAIDs. Studies have shown that there is little difference in analgesic effect among NSAIDs prescribed orally despite differences in cost although there may be differences in adverse effects. There are no large-scale, prospective, randomized studies comparing paracetamol with NSAIDs in the management of soft tissue injury. As paracetamol is cheaper than most NSAIDs, may be as effective in the management of pain and possibly with fewer adverse effects, a large-scale, randomized, controlled trial study is needed to answer questions of relative analgesic efficacy, safety and cost-effectiveness.

*Objective:* To compare the efficacy, safety and cost between oral diclofenac, ibuprofen and paracetamol in pain control in soft tissue injuries in an ED. Design: Prospective, randomized, controlled study.

*Participants:* 750 subjects having sustained isolated soft tissue ankle injury without fracture presenting to the ED of Prince of Wales Hospital.

*Main Outcome measures:* Pain relief, adverse effects and overall cost effect.

(MD01438)

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### **Role of Plasma DNA and Other Markers in the Prediction and Development of Post-traumatic Complications 1224/1202**

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□ 1 November 2001

❖ CUHK Research Committee Funding (Direct Grants)

Injury is the leading cause of death from infancy until middle age in many geographical regions including Hong Kong, and represents an important public health problem requiring further research. The incidence of multiple organ dysfunction syndrome (MODS) after major trauma ranges from 11 to 25%, and the mortality ranges from 50 to 100%. Many anti-inflammatory agents currently exist which could improve mortality and morbidity after trauma but difficulties in identifying which patients are at high-risk of developing MODS mean that their efficacy at an early stage have not been studied. The early identification of high-risk patients using prediction rules would make it possible to study old and new interventions in the prevention of MODS.

We have recently shown that plasma DNA levels increase early after injury and may predict post-traumatic organ failure. Preliminary data suggest that DNA and other predictors of post-traumatic MODS may be combined to give highly accurate prediction rules. In this project we propose to validate prediction models and to study the underlying mechanisms resulting in circulating DNA abnormalities in trauma. We aim:

(1) to prospectively validate our prediction rule in a large trauma population;

(2) to investigate temporal relationships between plasma DNA, the time from injury and the development of post-traumatic complications;

Data from these studies will allow the identification of patients at high-risk of developing post-traumatic organ failure and permit studies of interventions that may prevent the development of lethal complications. Biologically, our understanding of the parameters governing the production and clearance of plasma DNA will also be enhanced.

(MD01839)

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

Edition      Title/Investigators

- 1999-00 A Cost-effectiveness Analysis of the Treatment of Pain Following Limb Injury in an Emergency Department: A Comparison Between Intravenous Ketorolac Tromethamine & Morphine Sulphate (MD99095) Epidemiological Research) • JACOBS Philip\* • NG Ying Chu\*
- ✉ Timothy Hudson RAINER • Robert Anthony COCKS (Dept of Surgery) • CHEUNG Nai Kwong • LAM Kwok Wai (Centre for Clin. Trials &

## RESEARCH OUTPUTS AND PUBLICATIONS

- <P012810> **CHAN S.S.W.; YUEN E.H.Y.; KEW J.; CHEUNG W.L. and COCKS R.A.** "Community-Acquired Pneumonia-Implementation of a Prediction Rule to Guide Selection of Patients for Outpatient Treatment". *European Journal of Emergency Medicine* vol.8 no.4, pp.279-286. Lippincott Williams & Wilkins, 2001.
- <P012910> **TSOI L.C.H.** "A Randomised Controlled Trial on Health Promotion Program for Re-injury Prevention in Young Children Treated in Emergency Department". *Hong Kong Journal of and Emergency Medicine* vol.8 no.3, pp.127-134. Hong Kong: HKCEM & HKSEMS, 2001.07.
- <P012911> **CHAN Jimmy.** "Hospital Authority HAZMAT Incident Contingency Plan". *Abstracts, Asian Emergency Care and Defence Medicine Exhibition and Conference* p.14. Singapore: PSA Exhibitions, 2001.09.
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- <P012919> **CHAN J.T.S.** "What Will be the Percentage Drop in Attendance of Accident & Emergency Department After Implementation of Charges?". *Hong Kong Journal of Emergency Medicine* vol.8 no.4, pp.241-246. Hong Kong: HKCEM & HKSEMS, 2001.10.
- <P012920> **YEUNG Richard.** "Emergency Department HazMat Decontamination Contingency Plan". *Abstracts, Asian Emergency Care and Defence Medicine Exhibition and Conference* p.56. Singapore: PSA Exhibitions, 2001.09.
- <P012921> **MEYER Alastair Dmcr; BERNARD Stephen; SMITH Karen L.; MCNEIL John J. and CAMERON Peter A.** "Asystolic Cardiac Arrest in Melbourne, Australia". *Emergency Medicine* vol.13, pp.186-189. Australia: Blackwell Publishing, 2001.
- <P012925> **PEETERS Anna; SMITH Karen; CAMERON Peter and MCNEIL John.** "Predicted Impact on Victoria's Ambulance Services of a New Major Trauma System". *ANZ Journal of Surgery* vol.71, pp.747-752. Australia, 2001.
- <P012937> **RAINER Timothy H.; NG H.L. Margaret; LAM Y.L. Nicole; CHAN Y.F. Tina and COCKS Robert A.** "Role of Monocyte L-selectin in the Development of Post-traumatic Organ Failure". *Resuscitation* vol.51 no.2, pp.139-149. Ireland: Elsevier Science Ireland Ltd, 2001.11.
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- <P012939> **Timothy Hudson RAINER, James Francis GRIFFITH, LAM E., LAM Kwok Wai and METREWELI Constantine.** "Role for Ultrasound in the Clinical Management of Chest Injury". *Emergency Medicine Journal* p.279. UK: BMJ Publishing Group/FAEM, 2001.12.
- <P013122> **SULTANA Ronald V.; ZALSTEIN Salomon; CAMERON Peter and CAMPBELL Donald.** "Dipstick Urinalysis and the Accuracy of the Clinical Diagnosis of Urinary Tract Infection". *The Journal of Emergency Medicine* vol.20, pp.13-19. 2001.
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- <P013330> **RAINER H. Timothy; LO Y.M. Dennis; CHAN Y.S. Lisa; LAM Y.L. Nicole; LIT C.W. Lydia and COCKS A. Robert.** "Derivation of a Prediction Rule for Posttraumatic Organ Failure Using Plasma DNA and Other Variables". *Annals of the New York Academy of Sciences* vol.945, pp.211-220. USA, 2001.



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- <P02667> **CHAN Siu Wa Stewart.** "Efforts to Help Develop Emergency Medicine in Rural Sichuan: a Brief Report". *Hong Kong Journal of Emergency Medicine* vol.9 no.2, pp.110-112. HKCEM & HKSEMS, 2002.04.
- <P02668> **YUEN E.** "S1QT3 Syndrome and Bronchogenic Carcinoma". *Abstracts, Emergency Medicine Journal* vol.19 no.Supp1, p.A33. UK: BMJ Publishing Group, 2002.05.
- <P02669> **YUEN E.** "Dettol Poisoning Causing Severe Central Nervous System Depression". *Abstracts, Emergency Medicine Journal* vol.19 no.Supp1, p.A32. UK: BMJ Publishing Group, 2002.05.
- <P02670> **TANG S.Y.H.; LAU H.L. and CHAN J.T.S.** "The Effectiveness of Catheter Aspiration in the Treatment of Spontaneous Pneumothorax". *Hong Kong Journal of Emergency Medicine* vol.9 no.1, pp.18-22. Hong Kong: HKCEM & HKSEMS, 2002.01.
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- <P02676> **CAMERON P.A.** "Rule Out Coronary Syndrome". *Abstracts, Emergency Medicine Journal* vol.19 no.Supp1, p.A7. UK: BMJ Publishing Group, 2002.05.
- <P02677> **TAYLOR David McD, WOLFE Rory and Peter Alistair CAMERON.** "Complaints from Emergency Department Patients Largely Result from Treatment and Communication Problems". *Emergency Medicine* vol.14, pp.43-49. Australia: Blackwell Publishing, 2002.
- <P02690> **CAMERON P.A.** "Strategies for ACEM in the New Millennium PA Cameron". *Abstracts, Emergency Medicine* vol.14 no.1, p.A2. Australia, 2002.03.
- <P02691> **李寶珠 及 陳德勝.** <生化武器淨化程序>. 《第九次全國急診醫學學術會暨首屆兩岸四地急診醫學研討會論文集.》《「宜蘭研究」第二屆國際學術研討會論文集》中國, 廣州: 中華醫學會急診醫學分會, 2002.06.
- <P02816> **YEUNG R.S.D.; CHAN J.T.S. and HO S.T.** "Prehospital Response to Hazmat Incidents". *Hong Kong Journal of Emergency Medicine* vol.9 no.2, pp.90-94. Hong Kong: HKCEM & HKSEMS, 2002.04.
- <P02817> **YUEN E.** "'Taro' (Plant) Poisoning: The Imminent Risk of Upper Airway Obstruction". *Abstracts, Emergency Medicine Journal* vol.19 no.Supp1, p.A33. UK: BMJ Publishing Group, 2002.05.
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- <P02997> **KNOTT C. Jonathan; BALDEY C.R. Andrew; GRIGG E. Leeanne; CAMERON A. Peter; LICHTENSTEIN Melr and BETTER Nathan.** "Impact of Acute Chest Pain Tc-99m Sestamibi Myocardial Perfusion Imaging on Clinical Management". *Journal of Nuclear Cardiology* vol.9 no.3, pp.257-262. 2002.

see also <P012645>, <P013015>, <P02815>

## RESEARCH OUTPUTS AND PUBLICATIONS

- <P011762> **LI Wen; TSE Y. John; JAMES E. Anthony; LAM Lik-Wang; YIP Chi-Kwan; CHAN Man-Po and CHUNG S.C. Sydney.** "Delivery and Scavenging System for Small Animal Inhalational Anesthesia". *Journal of Surgical Research* vol.99, pp.175-178. USA: Academic Press, 2001.08.
- <P013378> **SHI Y.L.; JAMES A.E.; BENZIE I.F.F. and BUSWELL J.A.** "Anti-Genotoxic Properties of Mushroom-Derived Components". *Abstracts of the Third International Conference on Natural Antioxidants and Anticarcinogens in Nutrition, Health and Disease* p.59. Helsinki, Finland: Kupio University, 2001.
- <P013379> **SHI Y.L.; JAMES A.E.; BENZIE I.F.F. and BUSWELL J.A.** "Genoprotective Properties of Mushrooms". *Proceedings of the Asian International Mycological Congress* p.82. Karaj, Iran: Botanical Journal of Iran, 2001.
- <P021435> **SHI Y.; JAMES A.E.; BENZIE I.F.F. and BUSWELL J.A.** "Genoprotective Effects of Selected Mushroom Species". *Proceedings of the 4th International Conference on Mushroom Biology and Mushroom Products* pp.357-365. Cuernavaca, Mexico: Universidad Autonoma Del Estado De Morelos, 2002.

**see also** <P011969>, <P012299>, <P012473>, <P012474>, <P012485>, <P013311>, <P013384>, <P016231>, <P017570>, <P018495>, <P020223>, <P02436>, <P02519>

## RESEARCH PROJECTS

### Understanding Adolescent Project 4

- ✉ LAU Tak Fai Joseph • LEUNG Kit Sang • LAU Man Chun Mason
- ☐ 1 September 2001
- ❖ Education Department, Hong Kong SAR Government

The project aims to develop an instrument for early identification of primary school children who are potential at-risk of developing psychological or social problems in the future. The early detection tool will be incorporated with an universal preventive program which will be offered to all students in the participating schools and an intensive program will be offered to students screened positive by this tool. The study covers about 70 primary schools in the territory. It is founded on a similar tool and program developed by the Centre (the Hong Kong Student Information Form) for secondary school students. The screening-prevention packages has the potential of a territory-wide application, as witnessed by the similar program developed for secondary school children. (ED01367)

### Evaluation of the Primary Preventive Programs of the Understanding the Adolescent Project (UAP) in Secondary Schools

- ✉ LAU Tak Fai Joseph • LEUNG Kit Sang • LAU Man Chun Mason
- ☐ 1 November 2001
- ❖ Social Welfare Department, HKSAR Government

The objective of the study is to evaluate the effectiveness of the primary preventive programmes in helping students to build up resilience in terms of competence, sense of belongingness and optimism, as well as in bringing about positive changes in the relevant external systems of the students. Besides, attempts will be made to summarize experience from the evaluation study with a view to drawing up recommendations on improvement of the preventive programmes.

The CCTER will randomly select a sample of 20 schools from the pool of 150 secondary participating in the UAP 2001/02 school year. In case the initially drawn schools refuse to participate in the study, random replacement will be made. Form one students of the sampled schools who have joined the primary preventive programmes together with their parents, teachers, school principals and school social/ youth workers will be the subjects for the evaluation. (ED01748)

### 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>
1998-99	Evaluation of a Program for Frequent Travellers Crossing the China-Hong Kong Border (MD98147) ✉ LAU Tak Fai Joseph • SIAH Poh Chua#
1999-00	Emotional Education for Primary School Students (ED99058) ✉ LAU Tak Fai Joseph • CHAN Kam Kuen#
1999-00	Behavioural Surveillance of the Sexually-related Behaviours of the Chinese Female General Population in Hong Kong (SS99005) ✉ LAU Tak Fai Joseph • SIAH Poh Chua# • BROW Tin*
2000-01	Step Beyond Limits: Learning Effective Multiple Intelligence (ED00961) ✉ LAU Tak Fai Joseph • LEUNG Kit Sang • WONG Wing Sze (Dept of Psychiatry)#
2000-01	The 2000 Survey of Drug Use among Students (MD20035) ✉ LAU Tak Fai Joseph • CHAN Kam Kuen# • WONG Chung Kwong • WONG Wing Sze (Dept of Psychiatry)# • LAU Man Chun Mason • Choi Yuen Wan*
2000-01	The Hong Kong Men Who Have Sex with Men Study – A Study of

Behavioural Surveillance, Bisexual Behaviours and Need Assessment (SS20006)

✉ LAU Tak Fai Joseph • SIAH Poh Chua#

Kong and to Improve the Acceptance of PLWA among Secondary Students (SS20014)

✉ LAU Tak Fai Joseph • TSUI Hi Yi

2000-01 The Development of an Instrument to Measure Discrimination Toward People Living with HIV/AIDS (PLWA) in Hong

## RESEARCH OUTPUTS AND PUBLICATIONS

<P012001> **LAU T.F. Joseph and WONG S. Wing.** "HIV Antibody Testing Among the Hong Kong Mainland Chinese Cross-Border Sex Networking Population in Hong Kong". *International Journal of STD & AIDS* vol.12, pp.595-601. 2001.09.

<P012173> **JUNG M.Y.; CHAN M.S.; CHOW S.F.; CHAN Y.T.; LEUNG P.F.; LEUNG M.F.E.; LAU F.Y.; MAN C.W. and LAU J.** "Estimating Geriatric Patient's Body Weight Using the Knee Height Caliper in Hong Kong". Paper presented in the 9th Annual Congress of Gerontology-Into the New Millennium: Vision for Total Care of Older Persons, organized by Hong Kong Association of Gerontology. Hong Kong, 2001.11.24.

<P020154> **LAU J.T.F.; TSUI H.Y.; SIAH P.C. and ZHANG K.L.** "A Study on Female Sex Workers in Southern China (Shenzhen): HIV-Related Knowledge, Condom Use and STD History". *AIDS Care* vol.14 no.2, pp.219-233. Taylor & Francis Ltd, 2002.04.

<P020315> **LAU J.T.F. and WONG W.S.** "HIV Antibody Testing Among Male Commercial Sex Networkers, Men Who Have Sex with Men and the Lower-Risk Male General Population in Hong Kong". *AIDS Care* vol.14 no.1, pp.55-61. Taylor & Francis Ltd., 2002.

<P022152> 刁鑑興、鄭道城、劉德輝、王慶生、鍾山、曾仁山、楊健、范瑞強、劉青及阮偉雄。〈性病患者有關性病和愛滋病健康知識水平情況分析〉。Southern China Journal of Dermato-Venereology. 第9卷 第2期, 頁148-150. 中國, 2002.06.

<P029475> **LAU Tak Fai Joseph; THOMAS Joe and LIN C K.** "HIV-related Behaviours among Voluntary Blood Donors in Hong Kong". *AIDS Care* vol.14 no.4, pp.481-492. Taylor & Francis Ltd., 2002.

**see also** <P011020>, <P011848>, <P011971>, <P012012>, <P012117>, <P012118>, <P012121>, <P012122>, <P012125>, <P012336>, <P012380>, <P012938>, <P012939>, <P013111>, <P013205>, <P013316>, <P020036>, <P020075>, <P020094>, <P020156>, <P020274>, <P021122>, <P021246>, <P021260>, <P021346>, <P021347>, <P021388>, <P021404>, <P02482>, <P02504>, <P02514>, <P02516>, <P02532>, <P026668>, <P027029>, <P027151>, <P02751>, <P027658>, <P02801>, <P02802>, <P02815>, <P02818>, <P028517>, <P028575>, <P028798>

## RESEARCH PROJECTS

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### Molecular Mechanism of Somatic Hypermutation and Its Potential Clinical Application

- ✉ CHUI Yiu Loon • CHING Kar Keung
- 1 January 2002
  - ❖ CUHK Research Committee Funding (Direct Grants)

The part of the immunoglobulin (Ig) genes, V(D)J, that encodes the antigen-binding region of antibodies mutate very fast after cells that produce them (B cells) are activated by antigens. This phenomenon, known as somatic hypermutation, increases the binding affinity of antibodies over the course of activation, and thereby improves the quality of the immune response. In this proposal, we seek to explore the possibility of harnessing this powerful endogenous mutation system to treat diseases, which are difficult to cure. Evidence is gathering to indicate that the somatic hypermutation system is not so tightly regulated to the exclusive operation on the Ig genes. Hypermutation to a battery of non-Ig possible outcome of hypermutation to non-Ig self proteins is the induction of autoimmunity. On the other hand, immune reaction against the hypermutated gene products could lead to an immune attack of the cancer cells or cells infected by the pathogens expressing that mutated gene. Thus, the powerful ongoing mutagenic activity of the somatic hypermutation system may be used to produce internal vaccines against cancers and retroviral infections. We propose a transgenic system choosing a widely expressed endogenous gene, a mutant of which is a tumor-associated antigen, to explore the possibility of generating an immune response against the tumor through the working of the hypermutation system, and to investigate whether autoimmunity could also be generated. (MD01659)

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### Crystallization of a Carrier-Specific Antibody

- ✉ LIM Pak Leong

- 1 December 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Antibodies are extremely useful reagents for the diagnosis and treatment of diseases, and as probes in biological investigations. They owe this to their exquisite specificity. Although we now know fairly well the structural basis for the specificity of many antibodies, precise and high-resolution information is still lacking on how some antibodies bind to or discriminate against antigens. An area of specificity that is not well addressed is carrier specificity. Carrier-specific antibodies are often overlooked but are important in immune responses. We have previously described such an antibody based on serological analysis. We will presently examine the 3-D structure of this antibody to understand the structural correlates of the fine specificity. In addition, we will also similarly examine a single-chain Fv derivative of this antibody that we made recently but which has lost the carrier specificity. (MD01325)

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

<u>Edition</u>	<u>Title/Investigators</u>
2000-01	Identification of the DNA Sequence Element That Regulates the Strand Bias in Somatic Hypermutation of Immunoglobulin Genes (MD00465) ✉ CHUI Yiu Loon • CHING Kar Keung

## RESEARCH OUTPUTS AND PUBLICATIONS

- <P012775> **WUN Hau-Ling; LEUNG Tze-Ming Danny; WONG Kong-Chiu; CHUI Yiu-Loon and LIM Pak-Leong.** "Molecular Mimicry: Anti-DNA Antibodies May Arise Inadvertently as a Response to Antibodies Generated to Microorganisms". *International Immunology* vol.13, pp.1099-1107. USA: The Japanese Society for Immunology, 2001.09.13.
- <P013120> **CHING Kar Keung Arthur; LI Pik Shan; LI Qing; CHAN Chung Lap Ben; CHAN Yeuk Hon John; LIM Leung Pak; PANG Chung Sean Jesse and CHUI Yiu Loon.** "Expression of Human BRE in Multiple Isoforms". *Biochemical and Biophysical Research Communications* vol.288, pp.535-545. USA: Academic Press, 2001.11.02.

## RESEARCH OUTPUTS AND PUBLICATIONS

<P012269> 布士律、伍韻垣、秦嶸. <科研基金要素及科研基金申請准則>. 《體育生物醫學基礎研究與進展》 秦嶸,胡聲宇,陳啟明編. 第 1 版, 頁 10-31. 中國北京: 人民體育出版社, 2001.04.

see also <P012227>, <P014471>



## RESEARCH OUTPUTS AND PUBLICATIONS

<P029155> **LEE Woon Chu Polly; WOO Jean; LAU Edith Ming Chu; LAU CS; KWOK Chi Yui Timothy; CHIU P; LAM D; CHAN Kai Ming and CHAN Shiu Yee Cynthia.** "Health-Related Quality of Life of Patients with Osteoarthritis in Hong Kong". *Quality of Life-from Concepts to applications* China: Guangdong Branch of the Chinese Medical Association, 2002.01.10.

see also <P028603>

