

RESEARCH PROJECTS

Cardiovascular and Respiratory Effects of Laparoscopic Surgery in Children

✉ AUN Sui Tee Cindy • KARMAKAR Manoj Kumar • CHAN Simon Kin Cheong • CHUNG Chi Keung • TAM Yuk Ho

☐ 1 August 2000

❖ CUHK Departmental Funding

A retrospective study to analyse the cardiovascular and respiration parameters collected during laparoscopic surgery in children. The aim is to determine the factors that influence the changes in respiratory effects and haemodynamics in paediatric laparoscopic procedures. The data collected in the computer will be downloaded for analysis. (MD20017)

Evaluation of Two Traditional Chinese Medicine Formulations for the Treatment of the Metabolic Syndrome Regarding Cardiovascular Function and Insulin Sensitivity

✉ CRITCHLEY Lester Augustus Hall • CHAN Chung Ngor Juliana (Dept of Medicine & Therapeutics) • CHAN Yan Keung Thomas (Dept of Medicine & Therapeutics) • CRITCHLEY Julian A J H (Dept of Medicine & Therapeutics)# • DING Baoguo (Dept of Medicine & Therapeutics)# • THOMAS Neil G (Dept of Medicine & Therapeutics) • TOMLINSON Brian (Dept of Medicine & Therapeutics) • WANG Deqing (Dept of Medicine & Therapeutics)# • ZHANG Ye (Dept of Medicine & Therapeutics)#

☐ 4 September 2000

❖ Research Grants Council (Earmarked Grants)

Diabetes, hypertension, dyslipidaemia and obesity, collectively known as metabolic syndrome, have an increasingly high prevalence in Hong Kong and place a high social and financial burden on the community. Two traditional Chinese medicines "Three Essence Capsules" and "Total Flavinoids of Astragalus" are currently being used in Mainland China to treat the circulatory consequences of metabolic syndrome. However, evidence for their efficacy is currently anecdotal. This project sets out, using rigorously controlled placebo-comparison trials, to determine if a scientific basis exists for their clinical use. Using a multiple outcome approach, the researchers will assess the impact of these two medicines on patients with metabolic syndrome. In addition to standard biochemical markers, plasma and urinary catecholamines, cortisol and lipid; the bio-availability and level of antioxidants and insulin sensitivity will

all be measured. Cardiovascular function will be assessed from finger plethysmography blood pressure and impedance cardiac output changes during head up tilting. Psychomotor and cognitive function will also be tested. It is envisaged that a combination of traditional Chinese and conventional medicine will improve the prognosis of patients with metabolic syndrome and this project will provide a scientific basis.

(CU00134)

Evaluation of a New Impedance Cardiograph Using an Aortic Flowmeter in Dogs

✉ 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)# • JAMES Anthony Edward (Laboratory Animal Services Centre)

☐ 1 March 2001

❖ CUHK Research Committee Funding (Direct Grants)

This project aims to validate a new impedance cardiograph, the RheoCardioMonitor (RCM). This device measures cardiac output and left ventricular function noninvasively. Validation will be performed in anaesthetised dogs. An ultrasonic flow probe will be used to measure cardiac output and left ventricular function. The probe will be placed on the aorta via a chest incision. The status of the dog's circulation will be adjusted using infusions of stimulant and depressant drugs, thus providing a wide range of flow conditions. Lung oedema will also be induced using toxin. Twenty dogs will be needed and destroyed at the conclusion of each experiment. The project will take 12 months to complete.

The researchers hope to show that the impedance method accurately reflects changes in cardiac output and that the RCM reliably monitors left ventricular function. The effects of lung injury and pulmonary fluid on the performance of the RCM will also be investigated.

It is intended that this work will lead to establishing the RCM as a noninvasive and very cost effective bedside monitor of heart function which will have considerable beneficial clinical implications. No machine currently fills this role as the only available options are highly invasive.

(MD00816)

Pressure in Paediatric Tracheal Tube Cuffs

✉ HO Ming Hei Anthony • AUN Sui Tee Cindy

☐ 1 July 2000

❖ CUHK Departmental Funding

Cuffed paediatric tracheal tubes are becoming more popular because they minimize gas leak, the risk of aspiration, and the need for tube changes. Cuff pressure increases during anaesthesia if nitrous oxide is used. Excessive cuff pressure can lead to tracheal mucosal ischemia and necrosis. The researchers wish to document in this prospective study the time course and magnitude of cuff pressure increase in tracheal cuff used in children.
(MD20011)

Correlation Between Intraocular and Intracranial Pressure in Patients with Raised Intracranial Pressure

✉ HO Ming Hei Anthony • JOYNT Gavin Matthew • RAMSAY Sarah Jane • CHUNG David Chi Wai • POON Wai Sang (Dept of Surgery)

☐ 1 August 2000

❖ CUHK Departmental Funding

A non-invasive technique of assessing the intracranial pressure of patients with intracranial pathology would greatly assist patients caring for these patients. The researchers wish to study whether intraocular pressure correlates with intracranial pressure. Using a tonopen, they are studying intensive care patients who have had intracranial pressure monitors inserted for monitoring. The researchers will try to establish if they correlate, and if there is any time lag between them.
(MD20010)

Heat Stroke in Hong Kong

✉ HO Ming Hei Anthony • KARMAKAR Manoj Kumar • CHUNG David Chi Wai

☐ 1 September 2000

❖ CUHK Departmental Funding

Heat stroke is not uncommon in Hong Kong. It involves potentially debilitating and even fatal multisystem derangement typically requiring intensive care management. This project involves a comprehensive review of charts of patients with heat stroke at four of Hong Kong's major hospitals in recent years. The researchers will compare their findings with other published series and see if there are important lessons to be learned.
(MD20009)

The Effect of Intravenous Colloid Preload on Vasopressor Requirement and Hypotension During Spinal Anaesthesia for Caesarean Section

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

☐ 1 July 2000

❖ CUHK Departmental Funding

Hypotension is the most common adverse effect of spinal anaesthesia, our standard aesthetic technique for Caesarean section, and can have detrimental effects on both mother and fetus. Intravenous fluid preload is often given before induction of spinal anaesthesia to reduce the incidence and severity of hypotension, followed by titration of vasopressor drugs. However, the effectiveness of intravenous preload has been questioned recently. In particular, the use of crystalloid preload has been abandoned in some centres. It has previously been suggested that preload using colloids may be more effective than crystalloids, but few data are available evaluating colloid against no preload. Therefore, the researchers designed a randomized, double-blind study to assess the effect of intravenous infusion of gelofusin solution on the incidence of hypotension and the vasopressor requirement when given before spinal anaesthesia in healthy non-labouring women having elective or semi-elective Caesarean section.
(MD20008)

Development of Effective Strategies to Reduce the Incidence of Hypotension During Spinal Anaesthesia for Caesarean Section

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

☐ 1 November 2000

❖ CUHK Research Committee Funding (Direct Grants)

Spinal anaesthesia is now the commonest anaesthetic technique for elective Caesarean section. However, spinal anaesthesia causes rapid and extensive sympathetic block and as a consequence of this, a common serious adverse effect is hypotension. This can have detrimental effects on both mother and neonate and therefore the development of effective strategies to prevent and manage hypotension is important. Previous work has focussed on the use of intravenous fluid preload and use of vasopressor drugs, but results have been inconclusive and hypotension still occurs in up to 85% of cases. The researchers have previously investigated the efficacy of intravenous ephedrine by intravenous bolus to prevent hypotension. As a continuation of this work, they propose to perform two further related randomized double-blind studies: firstly to determine the efficacy of intravenous crystalloid preload and secondly to compare the relative efficacy of the vasopressor drugs ephedrine and metaraminol. Specific clinical measurements that the researchers will compare include maternal haemodynamic changes, uteroplacental blood flow measured by Doppler velocimetry, and neonatal outcome assessed clinically and biochemically. The overall objective

of this study will be to develop effective strategies that can be recommended to prevent hypotension associated with spinal anaesthesia for Caesarean section, and thus reduce the morbidity associated with this common procedure.
(MD00860)

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

Edition Title/Investigators

1999-00 Comparison of Respiratory Effects of Sevoflurane & Halothane in Children (MD99074)
 ✍ AUN Sui Tee Cindy • KARMAKAR Manoj Kumar • TAM Yuk Ho • CHAN Simon Kin Cheong

1998-99 Plasma Lignocaine Level Following Topical Anesthesia of the Airway by the Aspiration (MD98160)
 ✍ CHUNG David Chi Wai • HO Ming Hei Anthony • WOODWARD David Keith#

1999-00 Plasma Lignocaine Level Following Topical Anaesthesia Applies to the Airway By the Aspiration Techniques (MD99130)
 ✍ CHUNG David Chi Wai • HO Ming Hei Anthony • TAY Beng Aik

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

1999-00 Incidental Heparin Exposure and Development of Heparin Induced Thrombocytopenia (MD97187)
 ✍ HO Ming Hei Anthony

1999-00 Predicting the Post-cardiopulmonary Bypass Coagulation Function (MD98167)
 ✍ HO Ming Hei Anthony • LEE Anna

1999-00 Regional Anaesthesia for Cardiac Surgery (MD99081)
 ✍ HO Ming Hei Anthony • KARMAKAR Manoj Kumar • JOYNT Gavin Matthew • CHUNG David Chi Wai • YIM Ping Chuen Anthony (Dept of Surgery) • NG Siu Keung • ARIFI Ahmed A (Dept of Surgery)*

1999-00 Bilateral Thoracic Paravertebral Block for Patients Undergoing Coronary Artery Bypass Grafting – A Randomised Controlled Trial (MD99096)
 ✍ HO Ming Hei Anthony • KARMAKAR Manoj Kumar • NG Siu Keung • CHUNG David Chi Wai • ELAREFI Ahmed Abdalla (Dept of Surgery) • YIM Ping Chuen Anthony (Dept of Surgery) • JOYNT Gavin Matthew

1999-00 The Preventive and Resuscitative Role of Lung Isolation in Systemic Air Embolism After Lung Trauma (MD99134)
 ✍ HO Ming Hei Anthony • GIN Tony • CHUNG David Chi Wai

1999-00 Use of Heliox in Peripheral Airway Obstruction – A Systemic Review (MD99135)
 ✍ HO Ming Hei Anthony • LEE Anna • KARMAKAR Manoj Kumar • CHUNG David Chi Wai

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 Ropivacaine as an Intrathecal Agent, PII – The Effects of Baricith (MD99073)
 ✍ KHAW Kim Sun • CRITCHLEY Lester Augustus Hall • NGAN KEE Warwick Dean

1998-99 Determination of the Influence of Inspired Oxygen Concentration on Maternal and Neonatal Outcome During General Anaesthesia for Caesarean Section (MD98092)
 ✍ NGAN KEE Warwick Dean • KHAW Kim Sun • MA Kwok Chiu (Dept of Paediatrics) • LEE Bee Beng

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 • LAU Tze Kin (Dept of Obstetrics & Gynaecology)
- ✍ NGAN KEE Warwick Dean • LEE Bee Beng • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • KHAW Kim Sun
- 1999-00 Assesment of the Efficacy of Intravenous Crystalloid Preload for the Prevention of Hypotension During Rapid Extension of Epidural Block for Caesarean Section in Labouring Patients (MD99078)
 ✍ NGAN KEE Warwick Dean • KHAW Kim Sun • LEE Bee Beng
- 1999-00 Ultrasound Guided Peripheral Nerve Block (MD99132)
 ✍ TAY Beng Aik • GRIFFITH James Francis (Dept of Diagnostic Radiology & Organ Imaging) • HO Ming Hei Anthony • CHUNG David Chi Wai • WONG Wan Nar Margaret (Dept of Orthopaedics & Traumatology)
- 1999-00 Randomized Double-blind Comparison of Obstetric Outcome After Epidural Labour Analgesia Using Ropivacaine or Bupivacaine (MD99116)

RESEARCH OUTPUTS AND PUBLICATIONS

- <P996080> **GIN Tony.** "Nitrous Oxide - Time to Stop Laughing". Paper presented in the 4th Annual Scientific Meeting in Anaesthesiology 1999.11.07.
- <P996132> **GIN Tony.** "Balanced Anaesthesia". Paper presented in the 2nd Congress of the Asian and Oceanic Society for Intravenous Anaesthesia Australia, 1999.10.
- <P996199> **GIN Tony; JOYNT Gavin Matthew; LIPMAN J and GOMERSALL Charles David.** "Protein Binding of Ceftriaxone in the Critically Ill". Paper presented in the 24th Australian & New Zealand Annual Scientific Meeting on Intensive Care & 6th Australian & New Zealand Paediatric & Neonatal Intensive Care Conference New Zealand, 1999.10.
- <P998138> **AUN Sui Tee Cindy.** "Family Medicine And Anaesthesia". *Hong Kong Practitioner* 21 3, pp. 97-99. Hong Kong: The Hong Kong College of Family Physicians, 1999.03.
- <P998301> **GIN Tony.** "Clinical Pharmacokinetics". Paper presented in the 4th Annual Scientific Meeting in Anaesthesiology 1999.11.
- <P999590> **GIN Tony.** "Development of Examination and Assessment System in Hong Kong". *Ten Years and Beyond. The Hong Kong College of Anaesthesiologists (1989-1999)* pp.83-7. 1999.11.
- <P001253> **Ho, A.M.H. and J.D. Wells.** "Sudden Hemiplegia after a Motorcycle Accident". *Postgraduate Medical Journal* vol.76 no.897, p.431, 442-444. UK, 2000.07.
- <P001849> **TAM Y.H. and LI Xiaoshuang .** "Computer Monitor Program - A Window Based Program to Display and Collect Medical Equipment Signals". 2000.07.
- <P002125> **Morley, A.P.; D.C. Chung; A.S.Y. Wong; T.G. Short.** "The Sedative and Electroencephalographic Effects of Regional Anaesthesia". *Anaesthesia* vol.55, pp.864-869. UK, 2000.09.
- <P006092> **ZHANG Ye; CRITCHLEY Lester Augustus Hall and CRITCHLEY Julian A J H.** "A Stimulated Model of Tilting for Analysing Continuous Haemodynamic Data Series". *Proceeding of the IEEE/EMBS Asia-Pacific Conference on Biomedical Engineering* pp.350-351. Hangzhou, China: The World Trade Centre Zhejiang, 2000.09.

- <P006256> **GIN Tony.** "Nausea and Vomiting". *Textbook of Obstetric Anesthesia* ed. by Birnbach DJ, Gatt SP and Datta S. pp.687-692. Churchill Livingstone, 2000.05.
- <P006582> **NGAN KEE Warwick Dean.** "Anaesthesia for High Risk Parturients". Paper presented in the Annual Scientific Meeting in Anaesthesiology, organized by Hong Kong College of Anaesthesiologists and Society of Anaesthetists of Hong Kong Hong Kong SAR: Hong Kong College of Anaesthesiologists and Society of Anaesthetists of Hong Kon, 2000.09.09.
- <P006629> **LEE Bee Beng and LAI Chit Ying.** 《減輕產痛方法之簡介》· A Brief Introduction to Pain Relief in Labour 香港特別行政區: Dept of Anaesthesia & Obstetrics & Gynaecology, 2000.10.
- <P006734> **CHAN Matthew Tak Vai; NG Stephanie; LEUNG Clarence; LAM Joseph M. K.; POON Wai Sang and GIN Tony.** "Re-Defining the Ischemic Threshold for Jugular Venous Oxygen Saturation - A Microdialysis Study in Patients with Severe Head Injury". *Journal of Neurosurgical Anesthesiology* vol.12 no.4, p.386. USA, 2000.10.
- <P006776> **NGAN KEE Warwick Dean.** "Debate: All Thoracic Epidurals Should be Performed Awake". *Annual Scientific Meeting in Anaesthesiology* Hong Kong: Hong Kong College of Anaesthesiologists and Society of Anaesthetists of Hong Kong 2000.09.09.
- <P006786> **NG Siu Keung.** "Transoesophageal Echocardiography and Anaesthesiologists". *Annual Scientific Meeting in Anaesthesiology (Perioperative Medicine in the New Millennium)* p.19. Hong Kong SAR: The Hong Kong Anaesthesiologists, The Society of Anaesthetists of Hong Kong, 2000.09.
- <P006792> **JOYNT Gavin Matthew.** "Tonometry as a Monitoring Tool - Less Than Ideal?". *Critical Care and Shock* vol.3 no.4, S19T1, p.28. Indonesia: Western Pacific Association of Critical Care Medicine 11th Congress, 2000.11.
- <P006803> **CHAN Matthew T. V.; Chui PT; TAM Yuk Ho and GIN Tony.** "Prospective Validation of the Context Sensitive Half Times for Propofol". *Anesthesiology* vol.93 no.3A, p.A518. 2000.09.
- <P006996> **JOYNT Gavin Matthew.** "Management of Peri-Operative Myocardial Infarction". *Critical Care and Shock* vol.3 no.4, S9T3, p.18. Indonesia: Western Pacific Association of Critical Care Medicine 11th Congress, 2000.11.
- <P007062> **HO Ming Hei Anthony; CHUNG David Chi Wai; TAY Beng A; YU LM and YEO Patricia.** "Diluted Venous Blood Appears Arterial: Implications for Central Venous Cannulation". *Anesth Analg* vol.91 no.6, pp.1356-1357. USA, 2000.12.
- <P007242> **OH Teik; PAECH Michael; THIRLWELL-JONES Jeannette and GIN Tony.** "So You Want to be an Author? Correct Use of Statistics". Paper presented in the ASA 59th National Scientific Congress 2000.10.04.
- <P007338> **NGAN KEE Warwick Dean; CRITCHLEY Lester Augustus Hall and CHUNG David Chi Wai.** "A Survey of Student Opinion of Undergraduate Teaching in Anaesthesia and Intensive Care". *Continuing Education Committee of Anaesthetist of New Zealand* New Zealand, 2000.11.16.
- <P007485> **HO Ming Hei Anthony and HEWITT G.** "Warning Devices for Prevention of Dental Injury During Laryngoscopy". *Journal of Clinical Monitoring and Computing* vol.16 no.4, pp.269-272. The Netherlands, 2000.10.
- <P007523> **JOYNT Gavin Matthew.** "Intra-Abdominal Hypertension". *Critical Care and Shock* vol.3 no.4, S3T4, p.12. Indonesia: Western Pacific Association of Critical Care Medicine 11th Congress, 2000.11.
- <P007673> **WOODWARD David Keith; LEUNG Tai Shing; TSE WML; LAW Wai Kee and NGAN KEE Warwick Dean.** "Peribular Anaesthesia with 1% Ropivacaine and Hyaluronidase 300 IU ml-1: Comparison with 0.5% Bupivacaine/2% Lidocaine and Hyaluronidase 50 IU ml-1". *British Journal of Anaesthesia* vol.85 no.4, pp.618-620. UK, 2000.10.

- <P007682> **GIN Tony.** "Monitoring Depth of Anaesthesia". *New Zealand Society of Anaesthetists ASM* 2000.11.16.
- <P007814> **MORLEY Andrew Peter; DERRICK J. and CHUNG David Chi Wai.** "Epidural Blockade and Intraoperative Isoflurane Requirements". *Anaesthesia and Intensive Care* vol.28 no.5, p.579. Australia: Australian and New Zealand College of Anaesthetists, 2000.10.
- <P007945> **GIN Tony.** "Maternal Mortality and Anesthesia: A World-Wide Perspective: Asia / Oceania". Paper presented in the 12th World Congress of Anaesthesiologists 407B at P47. Canada, 2000.06.04.
- <P007954> **李美明、Lai Chit Ying.** 〈剖腹取嬰手術及其麻醉法之簡介〉 · A Brief Introduction to Caesarean Section and Its Anaesthetic Techniques 香港特別行政區: Dept of Anaesthesia & Dept of Obstetrics & Gynaecology, 2000.10.
- <P007980> **GIN Tony.** "5-HT3 Antagonists - Are They A Waste of Time?". *ASA 59th National Scientific Congress* 2000.10.01.
- <P007989> **GIN Tony.** "Future of IV Anaesthesia". *Proceedings of the Annual Scientific Meeting in Anaesthesiology (Perioperative Medicine in the New Millennium)* p.33. Hong Kong SAR: The Hong Kong of Anaesthesiologist, The Society of Anaesthetists of Hong Kong, 2000.09.
- <P008073> **ZHANG Ye; CRITCHLEY Lester Augustus Hall; CRITCHLEY Julian A J H; CHAN W. B.; TOMLINSON B and CHAN Chung Ngor Juliana.** "Different Haemodynamic Responses of Diabetics with Autonomic Neuropathy and Other Metabolic Syndrome Patients to Head-up Tilting". *2nd HK Diabetes & Cardiovascular Risk Factors East Meets West Symposium* p.40. Department of Medicine & Therapeutics, CUHK, 2000.10.01.
- <P008077> **BUCKLEY Thomas Anthony.** "Quality of Life in Long-Term Intensive Care Unit Survivors". *Critical Care and Shock* vol.3 no.4, S31T3, p.40. Indonesia: Western Pacific Association of Critical Care Medicine 11th Congress, 2000.11.
- <P008083> **LEE Bee Beng and LAI Chit Ying.** 《分娩止痛法簡介》 · A Brief Introduction to Pain Relief in Labour Hong Kong: Dept of Anaesthesia & Dept of Obstetrics & Gynaecology, 2000.10.
- <P008124> **NGAN KEE Warwick Dean; KHAW Kim Sun; WONG E.L.Y.; LIU Yat Wa Justina and LEE B. B.** "Randomized Double-blind Investigation of Ropivacaine + Adrenaline as an Epidural Test Dose in Parturients". *European Society of Regional Anesthesia 19th Annual Conference* Roma, Italy, 2000.09.21.
- <P008328> **HO Ming Hei Anthony.** "Absent CO2 Detection after Tracheal Intubation Due to Sampling Line Obstruction". *Journal of Clinical Monitoring and Computing* vol.16 no., p.229. The Netherlands, 2000.
- <P008515> **KARMAKAR Manoj Kumar; AUN Sui Tee Cindy; WONG E.L.Y.; WONG Sum Yee April; CHAN Simon and YEUNG Chung Kwong.** "System Absorption of Ropivacaine and Bupivacaine Following Caudal Epidural Administration in Children". *European Society of Regional Anaesthesia 19th Annual Conference* p.271. Rome, Italy, 2000.09.
- <P008920> **JOYNT Gavin Matthew; GOMERSALL Charles David; LEE Anna; BUCKLEY TA and TAN P.** "Factors Associated with Triage Decisions for Admission to Intensive Care". *European Society of Intensive Care Medicine (13th Annual Congress)* vol.26 no.S3, p.S323. Germany: Intensive Care Medicine, 2000.10.
- <P008934> **GIN Tony.** "Clinical Pharmacokinetics". *Proceedings of the Annual Scientific Meeting in Anaesthesiology (Perioperative Medicine in the New Millennium)* p.17. The Hong Kong Anaesthesiologists, The Society of Anaesthetists of Hong Kong, 2000.09.

- <P008947> **DERRICK J.** "Advances in Clinical Measurement". *Proceedings of the Annual Scientific Meeting in Anaesthesiology* (Perioperative Medicine in the New Millennium) p.15. The Hong Kong Anaesthesiologists, The Society of Anaesthetists of Hong Kong, 2000.09.
- <P009012> **BUCKLEY Thomas Anthony.** "Limitation of Life Support in the Critically Ill: The Asian Perspective". *Critical Care and Shock* vol.3 no.4, S28T4, p.37. Indonesia: Western Pacific Association of Critical Care Medicine 11th Congress, 2000.11.
- <P009029> **CRITCHLEY Lester Augustus Hall.** "Intramuscular Metaraminol During Spinal Anaesthesia". *Anaesthesia and Intensive Care* vol.28 no.5, p.574. Australia: ANZCA ASM May 2000, 2000.10.
- <P009256> **HO Ming Hei Anthony; LEE Sumin; TAY Beng A and CHUNG David Chi Wai.** "Lung Isolation for the Prevention of Air Embolism in Penetrating Lung Trauma. A Case Report". *Canadian Journal of Anaesthesia* vol.47 no.12, pp.1256-1258. Canada, 2000.12.
- <P009293> **MYLES Paul S and GIN Tony.** "Statistical Methods for Anaesthesia and Intensive Care". *Butterworth* pp.1-147. UK, 2000.09.
- <P009376> **AUN Sui Tee Cindy.** "Anaesthesia for Paediatric Emergencies". *Abstracts of the Annual Scientific Meeting in Anaesthesiology* Perioperative Medicine in the New Millennium p.24. Hong Kong SAR: The Hong Kong Anaesthesiologists, The Society of Anaesthetists of Hong Kong, 2000.09.
- <P009578> **JOYNT Gavin Matthew.** "Perioperative Haemodynamic Goals". *Annual Scientific Meeting in Anaesthesiology* (Perioperative Medicine in the New Millennium) p.30. The Hong Kong Anaesthesiologists, The Society of Anaesthetists of Hong Kong, 2000.09.
- <P009691> **LEE B. B. & LAI Chit Ying.** 《剖腹分娩手術前教育手冊》· A brief introduction to Caesarean section and its anaesthetic techniques 香港特別行政區: Dept of Anaesthesia & Dept of Obstetrics & Gynaecology, 2000.10.
- <P009739> **CHEE Yee Eot; CHAN Matthew Tak Vai; AUN Sui Tee Cindy and GIN Tony.** "Age Dependent Changes in the Dose-Response Relation of Ci-satracurium During Propofol Anesthesia". *Anesthesiology* vol.93 no.3A, p.A-1007. USA, 2000.09.
- <P009808> **MORLEY Andrew Peter; DERRICK J.; MAINLAND Phoebe; LEE B. B. and SHORT Timothy Gordon.** "Closed Loop Control of Anaesthesia: An Assessment of the Bispectral Index as the Target of Control". *Anaesthesia* vol.55, pp.953-959. UK, 2000.10.
- <P009903> **BUCKLEY Thomas Anthony.** "Organization of In-Hospital Cardiopulmonary Resuscitation". *Critical Care and Shock* vol.3 no.4, S13T2, p.22. 2000.11.
- <P011732> **LEUNG Wilson YS; CRITCHLEY Lester A.H.; THOMAS Neil G.; CHAN Y.K. Thomas; CHAN C.N. Juliana; TOMLINSON Brian and CRITCHLEY Julian A.J.H.** "The Cyclooxygenase (COX)-2-Specific Inhibitor, Rofecoxib, for the Treatment of Arthritis and Pain". *Medical Progress* vol.28, pp.43-47. 2001.01.
- <P016006> **GIN Tony; CHAN Matthew Tak Vai and CHUNG Chi Keung.** "Suppression of Spinal Motoneuron (H-Reflex) Predicts Surgical Immobility Better Than EEG During Sevoflurane Anaesthesia". *Minerva Anestesiologica* vol.67 supplement S. 1, N. 5, pp.148-149. Italy: 11th European Congress of Anaesthesiology (CENSA), 2001.06.
- <P016015> **GOMERSALL Charles David; JOYNT Gavin Matthew; TAN P Y; RAMSAY Sarah Jane; BUCKLEY Thomas Anthony and LAM Siu Wai Charlotte.** "ICU Nursing Workload is Not Related to Hospital Survival". *Critical Care* (Congress Center, Abstracts of Posters) vol.5 no.S1, P253, S119-20. 21st International Symposium on Intensive Care and Emergency Medicine, 2001.03.20.
- <P016035> **NGAN KEE Warwick Dean.** "Presentation Skills". *ANZCA & HKCA CSM 2001* ANZCA & HKCA, 2001.05.06.

- <P016106> **RAMSAY Sarah Jane; GOMERSALL Charles David; JOYNT Gavin Matthew; BUCKLEY Thomas Anthony and LAM Siu Wai Charlotte.** "Comparison of Prediction of Hospital Mortality by ICU Medical Staff and Referring Parent Team Doctors". *Critical Care* (Congress Center, Abstract of Posters) vol.5 no.S1, P230, S108. 21st International Symposium on Intensive Care and Emergency Medicine, 2001.03.20.
- <P016198> **KARMAKAR Manoj Kumar; CHUI Po Tong; JOYNT Gavin Matthew and HO Ming Hei Anthony.** "Thoracic Paravertebral Block for Management of Pain Associated with Multiple Fractured Ribs in Patients with Concomitant Lumbar Spinal Trauma". *Regional Anesthesia and Pain Medicine* vol.26 no.2, pp.169-172. USA, 2001.04.
- <P016289> **CHUNG David Chi Wai; HO Ming Hei Anthony and TAY Beng Aik.** "Apnea-Volume Warning During Normal Ventilation of the Lungs: An Unusual Leak in the Narkomed 4 Anesthesia System". *Journal of Clinical Anesthesia* vol.13, pp.40-43. USA, 2001.02.
- <P016368> **GIN Tony.** "Anaesthetic Depth". *Combined Scientific Meeting* p.A34. ANZCA & HKCA, 2001.05.
- <P016410> **LAM Desmond and CHUI Po Tong.** "A Prospective Evaluation of a Microcoagulation Analyser". *Combined Scientific Meeting* p.A14. ANZCA & HKCA, 2001.05.
- <P016435> **KARMAKAR Manoj Kumar.** "Lymphatic Drainage of the Thoracic Paravertebral Space". *British Journal of Anaesthesia* vol.86 no.3, pp.453-454. UK, 2001.03.
- <P016703> **CHAN Simon Kin Cheong.** "Paediatric Post-Operative Pain - Who to Assess?". *Combined Scientific Meeting* p.V.65. ANZCA & HKCA, 2001.05.
- <P016718> **CHENG C.** "Current Status of Organ Donation in Hong Kong". *Combined Scientific Meeting* p.A41. ANZCA & HKCA, 2001.05.
- <P017082> **JOYNT Gavin Matthew; LEE Anna; HO Oi Man; WONG E.L.Y. and Charles David GOMERSALL.** "Limitation of Life-Support Therapy in Critically Ill Patients: Family Response and Attitudes". *Critical Care* (Congress Center, Abstracts of Posters) vol.5 no.S1, P255, S120. 21st International Symposium on Intensive Care and Emergency Medicine, 2001.03.20.
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- <P017536> **DERRICK J.; HO Ming Hei Anthony and DERRICK GH.** "A Quantitative Analysis of Inspired Oxygen Concentration During an Anaesthetic Machine Oxygen Supply Failure". *Combined Scientific Meeting* p.A64. ANZCA & HKCA, 2001.05.
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- <P018340> **LEE Anna.** "The Cochrane Collaboration and Evidence-Based Anaesthesia Practice". *Combined Scientific Meeting* p.A52. ANZCA & HKCA, 2001.05.
- <P018409> **HO Ming Hei Anthony; WONG Wendy; LING Elizabeth; CHUNG David Chi Wai and TAY Beng A.** "Airway Difficulties Caused by Improperly Applied Cricoid Pressure". *Proceedings of the Journal of Emergency Medicine* vol.20 no.1, pp.29-31. USA, 2001.01.
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- <P019130> **LEE Anna; NGAN KEE Warwick Dean and GIN Tony.** "Vasopressors in the Management of Hypotension during Spinal Anaesthesia for Caesarean Section: A Meta-Analysis". *Combined Scientific Meeting* p.A91. ANZCA & HKCA, 2001.05.
- <P019222> **HO Ming Hei Anthony.** "Regional Techniques for Pump Cases: Risks, Benefits & Choices". *Combined Scientific Meeting* p.A100. ANZCA & HKCA, 2001.05.
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see also <P000297>, <P002382>, <P003988>, <P009047>, <P010212>, <P010611>, <P010612>, <P011458>, <P011733>

RESEARCH PROJECTS

The Long Arm of Chromosome 6 and Non-hodgkin's Lymphomas

- ✉ CHAN Wing Yee • LIU Yong • LEI Ieng Kit Kenny (Dept of Clinical Oncology)
- ☐ 1 November 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

It is now generally accepted that cancer development and progression is associated with accumulation of genetic alterations in the tumor cells. Carcinogenesis is the consequence of either oncogene activation or loss of function of tumor suppressor genes (TSG). According to Knudson's hypothesis, two hits are required to inactivate TSG. Frequently, one of these hits involves chromosomal deletion of one of the two alleles. Searches for regions of minimal deletions (RMD), by loss of heterozygosity (LOH) study, using polymorphic markers distributed along the length of chromosomes, TSG are localized to certain segments. Although Non-Hodgkin's lymphoma (NHL) is a common cancer with high mortality, very little is known regarding its carcinogenesis, especially in regard to TSG. Previous cytogenetic studies of many subtypes of NHL have identified common regions of deletion in the long arm chromosome 6. It has been postulated that several TSG important in the development of these tumors are likely to be present within the deleted segments. Comparative genomic hybridization (CGH) overcomes the technical limitation of karyotyping, enables large number of cases to be screened for losses of chromosomal regions. The deletions can then be further confirmed by fluorescence in-situ hybridization (using specific regional probes) and defined with LOH study. After localizing the RMD, the regions can be sequenced for identification of hidden TSG. The researchers propose to study the suspected chromosomal deletions using a combination of recently established, reproducible techniques in interphase cytogenetics and molecular genetics. The aim is to identify the hidden tumor suppressor genes in a stepwise manner. (MD00858)

Characterization of a Primary Gastric Choriocarcinoma

- ✉ CHAN Wing Yee
- ☐ 1 November 2000
- ❖ United College Lee Hysan Endowment Research Grant, CUHK

Primary gastric choriocarcinoma is extremely rare, accounting for less than 0.5% of gastric cancers world-wide. Only three cell-lines of gastric

choriocarcinoma have been reported in the literature. From a primary gastric choriocarcinoma resected from a patient in December, 1999, the researchers have successfully cultured and established a cell-line. They analyzed the original tumor by comparative genomic hybridization (CGH), fluorescence in-situ hybridization (FISH) (1), single strand conformation polymorphism (SSCP) and immunohistochemistry. The tumor genome showed trisomy 12 and polysomy 17, normal p53 gene and overexpressed *cerbB2* oncogene. It has cytoplasmic human chorionic gonadotrophin (hCG) and placental lactogen (hPL). The researchers need to monitor the changes and establish the steady state characteristics of the cell-line before it can be reported in an international journal. As established cell-line is an important asset in scientific research, forming the starting point for numerous functional and genetic studies of the tumors *in vitro*. (MD00952)

Evaluation and Characterization of a New Composite Biocompatible Skin Graft Incorporated on the Neodermis of Integra in Experimental Burn Wounds

- ✉ LIEW Choong Tsek • CHAN Sun Yin Eric (Dept of Surgery)# • LAM Ping Kuen (Dept of Surgery) • LI Hiu Ming
- ☐ 1 August 2000
- ❖ Research Grants Council (Earmarked Grants)

Early wound coverage is essential for the treatment of burn. Because of the lack of dermis in full thickness burn wound, the autologous epidermal autograft (CEA) "take" rate is often unpredictable. Integra™, a bilayer artificial skin has been documented as a biocompatible acellular dermal replacement in full-thickness burn wounds in many burn centers. By 14 - 19 days post grafting of the Integra, there is full vascularization of the neodermis in the Integra. Then an ultra-thin split thickness skin graft is harvested from a donor site of the patient to cover the neodermis immediately after the outer layer of silicone membrane is removed from the Integra. Research effort has been focused on grafting the CEA onto the neodermis of Integra. If successful, this technique will eliminate multiple operative stages of skin harvesting which is associated with pain and scarring. In recent meeting for burn injuries, the difficulty with the conventionally cultured graft anchoring onto the neodermis of Integra was addressed.

A new composite CEA was recently developed in the researchers' laboratory which involves the cultivation of autologous keratinocytes on a hyaluronate-derived membrane (Laserskin™) pre-seeded with dermal fibroblasts. The combination of this composite CEA with Integra has been successfully applied to the surgical wounds of three patients who underwent

reconstructive surgery. Since the pathophysiology of the healing process of burn wound is quite different from that of clean surgical wounds, the incorporation junction between the cultured graft and the neodermis will be evaluated and characterized by light and electron microscopies and immunohistochemistry in experimental burn wounds of animals. (CU00153)

Comprehensive Study of Nasopharyngeal Carcinoma Genome

✉ LO Kwok Wai • HUANG POON Wai Sin Dolly (Dept of Clinical Oncology) • PANG Chung Sean Jesse • TEO Man Lung Peter (Dept of Clinical Oncology) • TO Ka Fai

□ 1 September 2000

❖ Research Grants Council (Earmarked Grants)

Nasopharyngeal carcinoma (NPC) is rare in most parts of the world, but prevalent in Hong Kong and Southern China. Although this disease poses a serious health problem in our population, we have yet to understand the underlying genetic alterations that lead to the development and progression of NPC. In this proposal, the researchers aim to search intensively for genetic alterations in NPC tumorigenesis by localizing tumor suppressor loci and potentially identifying specific genes associated with NPC tumorigenesis. Two comprehensive and complementary approaches, high-resolution allelotyping and methylation-specific restriction fingerprinting (MSRF), will be used to screen for chromosomal deletion and hypermethylated CpG islands throughout the entire NPC genome. The high-resolution allelotyping will identify chromosomal regions that may harbor tumor suppressor genes associated with NPC tumorigenesis. Further detailed deletion mapping will localize precisely the tumor suppressor loci and allow us to test known tumor suppressor genes, for inactivation, in these regions. By methylation-sensitive restriction fingerprinting, the researchers will identify common hypermethylated CpG islands in the NPC samples and isolate novel or known cancer-related genes whose expression are repressed by DNA methylation. The identified genetic and epigenetic abnormalities will be correlated with disease status, response to treatment, and tumor behavior. The results of these studies will contribute to a much better understanding of the molecular pathogenesis of NPC. It will also provide the basis for the development of more effective diagnostic and treatment strategies for this common malignancy affecting our population. (CU00154)

Genetic Mechanism of Malignant Progression in Low-grade Astrocytomas

✉ PANG Chung Sean Jesse • NG Ho Keung

□ 1 November 2000

❖ CUHK Research Committee Funding (Direct Grants)

The natural history of low-grade (WHO grade II) astrocytoma is not well understood. Some patients with low-grade astrocytomas may survive for many years, whereas others experience a malignant transformation to high-grade tumors resulting in a short survival time. No biological marker has yet been identified that would indicate patients who are at risk for malignant transformation of low-grade astrocytoma. Previous genetic studies from the researchers' group and others' on paired recurrent astrocytomas, in which low-grade astrocytomas showed progression to high-grade tumors, have demonstrated that these low-grade tumors already accumulated genetic aberrations characteristic of the high-grade gliomas. These results strongly indicate that genetic alterations precede phenotypic transformation and histopathology alone is insufficient to predict tumor behavior. In this study, the researchers propose to study the genetic mechanism underlying the malignant progression in low-grade astrocytomas. They intend to perform a genome-wide survey for genetic abnormalities on paired recurrent astrocytomas and on low-grade astrocytomas that show no relapse. Comparison of genetic profiles between these two groups of tumors will unveil the major genetic events that contribute to the malignant transformation of low-grade astrocytomas. Such analysis will aid in understanding the genetic mechanism leading to malignant gliomas as well as identifying biomarkers that are predictive for an aggressive clinical course in the low-grade astrocytomas. (MD00421)

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

<u>Edition</u>	<u>Title/Investigators</u>
1997-98	Gastric Cancers and Helicobacter Pylori - A Combined Study by Interphase Cytogenetics, Comparative Genomic Hybridization and Molecular Genetic Analysis (Including Microsatellite Analysis) (CU97624) ✉ CHAN Wing Yee • LO Kwok Wai • LEE Chuen Kwun Joseph (School of Chinese Medicine) • WONG Nathalie (Dept of Clinical Oncology)
1996-97	Cervical Screening Programme (MD96223) ✉ CHANG Alexander Russell

- 1999-00 Evaluation of Clonality and Genetic Progression in Metachronous Bilateral Breast Cancers (MD99097)
✉ CHANG Alexander Russell • LO Kwok Wai • NG Ho Keung
- 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)
- 1997-98 A Comparative Investigation of Telomerase Activity in Human Liver with Hepatocellular Carcinoma, Chronic Viral B Hepatitis, Cirrhosis, and Normal Liver (CU97677)
✉ LIEW Choong Tsek • LAU Wan Yee Joseph (Dept of Surgery) • LEE Chuen Kwun Joseph (School of Chinese Medicine)
- 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 The Study of Genetic Alterations of the PTEN/MMAC/Gene in Multiple Myeloma and Its Relation to Plasmacytoma Development (MD99067)
- 1997-98 Studies on the Molecular Genetics of CNS Tumors (CU97671)
✉ NG Ho Keung • HUANG POON Wai Sin Dolly (Dept of Clinical Oncology) • LAM Yeng Po Paula# • LO Kwok Wai • PANG Chung Sean Jesse • POON Wai Sang (Dept of Surgery)
- 1999-00 Follow-up Study on Genetic Events Regulating Telomerase Activity in Gliomas (MD99022)
✉ NG Ho Keung • PANG Chung Sean Jesse
- 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 (Dept of Clinical Oncology) • POON Wai Sang (Dept of Surgery)
- 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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- <P002559> **Ng, H.K.; Cheng J.; Cheung C.K.; Sung J.; Su M.; Xu X.H. and Chung S.S.C.** "Tele-Clinicopathologic Conferences via Satellite Link". *APAMI-MIC 2000 Conference (Asia Pacific Association for Medical Informatics Hong Kong Society of Medical Informatics) IT & Health in the 21st Century* p.86. Hong Kong, 2000.09.
- <P002790> **TSANG K.S.; LI Karen.; HUANG D.P.; WONG A.P.; LEUNG Y.; LAU T.T.; CHANG A.M.Z.; LI C.K.; FOK T.F. and YUEN P.M.P.** "A Simple Processing Procedure in a Semi-Closed System for the Clinical Banking of Umbilical Cord Blood". Paper presented in the Symposium on Umbilical Cord Blood: From the Bench to the Bedside, organized by the Department of Paediatrics, The Chinese University of Hong Kong, Prince of Wales Hospital and Hong Kong Medical Technology Association. vol.5. Hong Kong, 2000.11.25.

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RESEARCH PROJECTS

An Expression and Functional Study of a Prostatic Secretory Protein of 94 Amino Acids in Normal and Neoplastic Rat Prostate Glands

✉ CHAN Leung Franky

☐ 1 October 2000

❖ Research Grants Council (Earmarked Grants)

The prostatic secretory protein of 94 amino acids (PSP94) is one of the major proteins secreted by the human prostate gland, in addition to prostatic acid phosphatase (PAP) and prostate-specific antigen (PSA). This protein was originally isolated from human seminal plasma and shown later to be secreted in large amount by the prostate gland. It is a small, non-glycosylated protein, containing 10 cysteine residues and has a molecular weight of 10.7 kDa. Recently, there has been much research interest in this protein because of its potential clinical use as a diagnostic marker for prostate cancer. Its serum and urine levels are elevated in patients with prostate cancer. Moreover, its expression pattern in neoplastic prostates is correlated with different histological grades of tumors as are two other established tumor markers, PSA and PAP. This suggests that PSP94 could be useful as a marker to monitor the progression of prostate cancer during and after therapy. Recently, similar homologous proteins of PSP94 have been identified, and their cDNAs and genes have been cloned in other mammalian species including primates, pigs and rodents. However, its exact biological functions and hormonal regulation are still unclear despite its isolation in 1984. The main difficulty is that its homologous protein or gene has not been identified in experimental animals such as rat and mouse. Recently, however, its cDNA and gene have been cloned in mouse and rat prostate glands by us as well as others. The identification of its homologous protein in rat and mouse offers us an opportunity to study in-depth its gene expression and hormonal regulation in normal prostate and in animal models of prostate cancer. The researchers propose to study the expression of PSP94 and its hormonal regulation in normal, castrated and hormone-treated rat prostates. For comparison, two well-studied rat prostate-specific secretory proteins, probasin and seminal vesicle secretion II will also be studied in parallel with PSP94. Moreover, the expression pattern of PSP94 and its alternatively spliced transcript in premalignant and neoplastic prostates will be analyzed in three rat models of prostate cancer, including Noble rat model, two Dunning prostatic tumors and an androgen-independent Noble rat prostatic tumor. Once the spliced transcript is cloned and characterized, the researchers will generate polyclonal antibody by recombinant fusion protein technique. The antibody generated will be

used to study the protein expression of the putative spliced PSP94 isoform in the tumor tissues. The researchers will also attempt to explore the biological functions of PSP94 in reproduction by investigating whether it could behave as a sperm-coating protein, IgG-binding protein or protease inhibitor. It is expected that this study will provide more important information on the regulation of synthesis of PSP94 and elucidate its biological functions in the prostate gland.
(CU00131)

The Roles of Chondroitin Sulfate Proteoglycans on Axon Growth at the Mouse Chiasm

✉ CHAN Sun On

☐ 1 November 2000

❖ Research Grants Council (Earmarked Grants)

In the optic chiasm, retinal axons undergo several changes in fiber arrangements that are essential for the formation of normal connections in the visual relays. The developmental mechanisms that control such changes in axon order at the chiasm are the focuses of this research. The roles of one family of extracellular matrix molecules, chondroitin sulfate (CS) proteoglycans (PGs), which have been implicated in the regulation of axonal growth in both central and peripheral nervous systems, will be investigated as mediators of axon patterning in the mouse chiasm. The proteoglycans compose of a core protein that is linked to a variety of glycosaminoglycan chains. Expression patterns of CS-PGs will be investigated in the chiasm of mouse embryos at different stages of pathway development using immunocytochemistry for the CS glycosaminoglycans and for the core proteins. The functions of the CS moieties and the core proteins of the PGs to axon routing at the chiasm will be studied in a slice culture of the mouse retinofugal pathway by either enzymatic removal of the CS moieties, or blocking the functional domains of the core proteins using specific antibodies. The changes in partial decussation pattern, age-related order and segregation of retinal axons from dorsal and ventral retina in the chiasm will be determined. The distributions of cell adhesion molecules LI, NCAM and N-cadherin, which are known to interact with CS-PGs, will be determined in the mouse chiasm. Results of these experiments will provide important information on mechanisms that guide axons in decision regions of a neural pathway in the central nervous system of mammals.
(CU00132)

Therapeutic Effects of Pien Tze Huang Without Natural Musk on Hepatitis

✉ CHAN Wood Yee • YEW Tai Wai David •
KWONG Wing Hang • LEE Ka Ho Kenneth

- 1 November 2000
- ❖ University-Industry Collaboration Prog.: Matching Grant for Joint Research, ITF, Innovation & Tech. Commission • Zhang Long Industrial Co Ltd.

Hong Kong is one of the cities at high risk of hepatitis. However, medications capable of dependably eliminating hepatitis are still absent. In collaboration with the Faculty of Medicine of the Chinese University of Hong Kong, Zhang Long Industrial Company proposes to embark on this study to determine the therapeutic effects of a traditional Chinese medicine, Zhang Zhou Pien Tze Huang, on hepatitis through different types of animal experiments. Pien Tze Huang has been used as a folk medicine for hundreds of years in China for its remarkable therapeutic effects on various kinds of liver diseases. One of the major components of Pien Tze Huang is musk, which is a unique secretion from the endangered animal male musk deer. In compliance with the international agreements, musk will soon be banned for use as a Chinese medicine or for trading. In this study, the therapeutic effects of Pien Tze Huang containing a synthetic musk, which was successfully developed by the Health Ministry of China, will also be assessed to gauge the possibility of replacing the natural with synthetic musk in Pien Tze Huang and in other traditional Chinese medicines. (MD20021)

Role of BRE, a New Modulator of TNF- α Action, in Skeletal Muscle Proliferation and Differentiation

- ✉ LEE Ka Ho Kenneth
- 1 January 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Tumour necrosis factor (TNF- α) has been implicated in muscle atrophy. Patients with cancer and AIDS lose a great deal of their body weight through the loss of skeletal muscles. An elevated level of TNF- α is often found in the serum of these patients. Muscle wasting is now recognized as one of the contributory factors that causes death amongst cancer patients. In this project, the researchers will first establish the effects of TNF- α on satellite cells obtained from adult skeletal muscles. The actions of this cytokine on myogenic cell proliferation, differentiation and cell death will be studied. Before TNF- α can exert its effect, it must first bind to its receptor TNFR1 and this in turn activates the NF- κ B transduction pathway. The activation of NF- κ B triggers a cascade of gene transcriptional activities that play an important role in muscle development and physiology. The researchers want to determine whether they can use a gene, that they have previously cloned, called BRE to

modulate the actions of TNF- α in satellite cells. BRE can bind to the juxtamembrane domain of TNFR1 and block NF- κ B activation by TNF- α . The researchers will establish the physiological function of BRE by over-and under-expressing this gene in satellite cells, and examine its effect on cell proliferation, differentiation and cell death. They will also over-express BRE in the presence of TNF- α to determine whether they can reverse the actions of TNF- α on muscle cells. (MD00801)

Cloning, Sequencing and Biological Characterization of an Immunomodulatory Fungal Protein

- ✉ LIU Wing Keung Ken • NG Tzi Bun (Biochemistry)
- 1 October 2000
- ❖ Research Grants Council (Earmarked Grants)

Mushrooms are very popular in both western and oriental cuisines. The white button mushroom is the most common one in the western market, but more varieties are available in Asian countries, such as Japan and China. Mushroom has been considered a type of health food in these countries, partly because of its high nutritive values and partly because of the belief of its medicinal activities. In addition to an immunomodulatory polysaccharopeptide, the researchers have also isolated a novel protein designated as VVL from the straw mushroom, *Volvariella volvacea*. This protein has a molecular mass of 30 kDa and it possesses potent proliferative and immunostimulatory activities towards mouse lymphocytes, it is thus considered as a member of the fungal immunomodulatory proteins (FIPs). The mechanism underlying these activities is not clear and the protein deserves detailed chemical and biological characterization. The project is planned to clone the gene encoding this protein for use in studies on its molecular structure and functional domains. It is also anticipated that through a study of the biological activities of VVL to gain an insight into the molecular mechanism of lymphocyte activation. (CU00125)

A Study to Determine Whether Hyperglycemia is Responsible for Increased Susceptibility to Vitamin A Embryopathy in Diabetic Pregnancy

- ✉ SHUM Sau Wun Alisa
- 1 February 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

It is well documented that babies of diabetic mothers have a higher incidence of congenital anomalies than those of non-diabetic mothers. The increased

prevalence is thought to arise from the teratogenic effect of the maternal diabetic milieu on the developing embryo. Little attention has been paid to determine if there is any interaction between the maternal diabetic milieu and environmental factors, such as drugs or food taken during early pregnancy. Recently, by using a mouse model, the researchers have found that embryos of diabetic mice are much more susceptible to develop caudal regression syndrome and cleft palate when maternally exposed to vitamin A, indicating that the maternal diabetic milieu can indeed interact with environmental factors to increase the risk of malformations in the offspring. However, many serum factors are altered in the maternal diabetic milieu, it is unclear which factor is involved in affecting the embryo's susceptibility to vitamin A. The aim of this project is test whether elevated glucose can be responsible for the increased susceptibility to vitamin A embryopathy.

The specific objectives to be achieved are:

(1) To determine if *reducing* the blood glucose level in *diabetic* mice will abolish the increased susceptibility of their embryos to vitamin A-induced anomalies,

(2) To determine if *elevating* the blood glucose level in *non-diabetic* mice will increase the susceptibility of their embryos to vitamin A-induced anomalies.

(MD00359)

Genes and Heroin Addiction in the Chinese Population: Association Studies on Receptor Gene

✉ 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*

☐ 4 January 1999

❖ CUHK Departmental Funding

Heroin is highly addictive with 75-85% of reported drug abuse cases shown to abuse heroin in Hong Kong in the last 5 years. Heroin-dependence represents a significant and growing health and social problem in Hong Kong in terms of treatment and social costs. Both environmental and genetic factors have been shown to play a role in the risk of developing heroin addiction. A recent study on the conjoint abuse of drugs in over three thousand male twin pairs showed that heroin had a larger genetic influence than marijuana, stimulants or psychedelic drugs. Genetic linkage and association studies showed a linkage of a number of receptor genes of the brain reward pathway with alcoholism and other addictive behaviors like smoking and pathological gambling. The present study therefore aims to examine the genetic contribution of a list of target genes related to (1) receptors that heroin binds to in the brain, (2) the receptors in the reward pathway of addiction, and (3) sensation or novelty seeking,

which may predispose individuals to drug seeking behaviour and to a variety of drug abuse disorders. This therefore poses new challenges for the development of treatment and prevention strategies. Since ethnicity plays an important role in the differences observed in gene frequencies, Hong Kong is in a unique position in which a uniform, well-controlled Chinese population of heroin addicts can be used for such a study and for the identification of new genetic variants.

(MD98904)

Analysis of Gene Expression fo MPTP-treated Mice Using DNA Microarray Technology

✉ STADLIN Alfreda • CHAN Pui*

☐ 1 July 2000

❖ CUHK Mainline Research Scheme

It is well established that the neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) when administered to non-human primates and mice produces the depletion of striatal dopamine and cell loss in the substantianigra (SN) similar to that observed in idiopathic Parkinson's Disease (PD) [Langston et al. (1984) Brain Res 292:390-394]. This model has been widely used to study the etiology of PD over the last 15 years. In an effort to discover the genes that may be involved in the progression of the disease process, the present study aims to use DNA microarray technology to identify the gene products expressed during the degeneration of the striatum and SN after MPTP treatment. Adult C57BL/6 mice will receive four intraperitoneal injections of 20mg/kg MPTP at a 2-hour interval between injections. Animals will be sacrificed at 1, 3, 7 days and 2 months after treatment. Control animals will receive saline injection. Total RNA from the striatum and SN will be isolated and hybridized onto DNA microarrays containing over 1000 different genes (Mergen, USA). Using a microarray of over 1000 genes, potential genes that are down or up regulated during the degenerative process will be identified. Furthermore, animals will be examined at 2 months after injury to ascertain whether there is any regenerative capability afforded to the damaged brain regions. The genes of interest will then be amplified by PCR, sequenced and northern blot analysis performed to confirm differences in gene expression between the control and the MPTP-treated groups.

The identification of the genes that are differentially expressed in the degenerative process of Parkinson's disease is important for understanding the molecular basis of this neurological disorder. DNA microarray technology represents a powerful new tool that will enable the rapid identification of genes associated with the degenerative and regenerative process of PD. This will assist in defining possible targets for therapeutic intervention as well as for the

identification of gene markers for early diagnosis for PD.
(MD20026)

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

Edition Title/Investigators

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 Role of *Bcl-2* in Neural Tube Defects Using Normal and Mutant Mouse Embryos (MD99023)
 ✉ CHAN Wood Yee • COPP A. J.*

1998-99 The Influence of Mature Astrocytes on the Survival and Regeneration of Adult Retinal Ganglion Cells (CU98265)
 ✉ CHO Yu Pang Eric

1999-00 A Study on the Ability of Sertoli Cells to Promote Regeneration of Retinal Ganglion Cells (MD99098)
 ✉ CHO Yu Pang Eric

1998-99 Ampullary Gland, Ventral prostate and Embryo Implantation (CU98030)
 ✉ CHOW Pak Ham Patricia • O Wai Sum*

1999-00 Effect of Male Accessory Sex Gland Secretions on the Oxidative Stress, Functional Competence and Genomic Integrity of Hamster Spermatozoa (MD98170)
 ✉ CHOW Pak Ham Patricia • O wai Sum*

1999-00 Histological and Morphological Effects of Tadenan on the Response of the Rabbit Bladder to Partial Outlet Obstruction (MD99013)
 ✉ CHOW Pak Ham Patricia • LEVIN R* • GOSLING John Arthur*

1999-00 Effects of Ribosome-inactivating Proteins on Motor and Ganglionic Neurons (BL97043)
 ✉ KWONG Wing Hang

1998-99 Role of Fibroblast Growth Factor Isoforms in the Development of the Mammalian Limb Musculature (CU98273)
 ✉ LEE Ka Ho Kenneth • PAULIN Denise*

1999-00 Systemic Application of Curcumin, an NF κ B Inhibitor, to Enhance Skeletal Muscle Healing Following Traumatic Injury (MD99099)
 ✉ LEE Ka Ho Kenneth

1999-00 Cloning and Sequencing of an Immunomodulatory Protein (MD99024)
 ✉ LIU Wing Keung Ken • NG Tzi Bun (Biochemistry)

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.*

1998-99 An Experimental Study to Determine the Role of Sonic Hedgehog (Shh) in Controlling Neuronal Differentiation in the Neural Tube (MD98007)
 ✉ SHUM Sau Wun Alisa • ROELINK Henk*

1999-00 A Study of the Pathogenetic Mechanism of Renal Agenesis (CU99283)
 ✉ SHUM Sau Wun Alisa • WOOLF Adrian S.*

1996-97 The Effects of Prenatal Heroin Exposure on Postnatal Brain Development and Behavior in Rats (CU96615)
 ✉ STADLIN Alfreda • ALI Syed F.*

1998-99 MPTP-Induced Neurotoxicity in Metallothionein-I, II Knock Out Mice (MD98095)
 ✉ STADLIN Alfreda

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)
 ✉ YEY Tai Wai David • CHAN Wood Yee • POON W.F.Paul*

RESEARCH OUTPUTS AND PUBLICATIONS

- <P994675> **WANG Z.H.; DING M.X.; JIN M.L.; CHEW-CHENG S.B.; CHEW E.C.; LI H.K. and NG C.C.** "Expression of Nuclear Matrix Associated BCL-2 and Bax Proteins in Egfr-Antisense Transfected and Untransfected Glioblastoma Cell Lines". Paper presented in the 8th International Symposium of Society of Chinese Bioscientists in America (SCBA). Hong Kong, 1999.08.
- <P994676> **邱殷慶、王子慧、金梅林、丁明孝、邱鄭秀文.** <以核基質蛋白為腫瘤細胞之特異性標記>. 《第四屆海峽兩岸顯微學學術研討會》 頁 88-89. 中國烏魯木齊, 1999.
- <P996702> **LI Zegui; CAI Wenqin and CHAN Wood Yee.** 〈神經管發生與編程性細胞死亡〉 · Progress of Anatomical Sciences vol.5 no.3, pp.222-226. Chongqing, China, 1999.
- <P998757> **LI Zegui; CAI Wenqin and CHAN Wood Yee.** "Morphogenetic Events and Molecular Mechanism During Neurulation". ACTA Academiae Medicinae Militaris Tertiae vol.21 no.8, pp.613-616. China, 1999.08.
- <P001111> **CHAN Billy W.H.; LEUNG Yun-Chung and SHUM Alisa S.W. .** "A Role of Glutamic Acid Decarboxylase in the Pathogenesis of Retinoic Acid-Induced Caudal Agenesis". *Poster Abstracts of Santa Cruz 2000 Developmental Biology Conference* p.134. Santa Cruz, USA, 2000.07.
- <P001112> **Tse Herman, K.W.; Adrian S. Woolf; Aschwin Menke; Nicholas D. Hastie and Alisa S.W. Shum.** "Retinoic Acid Induces Down-Regulation of WTI and Leads to Renal Agenesis". *Poster Abstracts of Santa Cruz 2000 Developmental Biology Conference* p.175. Santa Cruz, USA, 2000.07.
- <P001759> **Wang, Z.H.; D. Yu; H.K. Li; C.C. Ng; P.F. Chen; S.B. Cheng and E.C. Chew.** "Alterations of Nuclear Matrix Protein Patterns of Tumor Cells after Arsenic Treatment". *Paper presented in the International Kunming Symposium on Microscopy, organized by Chinese Electron Microscopic Society* ed. by Chinese Electron Microscopy Society. Kunming, China, 2000.07.
- <P001832> **Ko, G.T.; Cockram C.S.; Critchley J.A.; Lau M.S. and Chan J.C.** "No Relationship Between Antibodies to GAD and Microangiopathic Complications in Young Chinese Diabetic Patients". *Diabetes Care* vol.23, pp.1045-1046. 2000.07.
- <P002171> **Jin M.L.; J.Y.H. Chan; P. Zhang; Z.H. Wang; H.K. Li; C.C. Ng; P.F. Chen; S.B. Cheng Chew and E.C. Chew.** "Altered Nuclear Matrix Protein Profiles in Etoposide Treated HL-60 Cells". Paper presented in the X11 EUREM (European Congress on Electron Microscopy), organized by Czechoslovak Society for Electron Microscopy. Brno, Czech Republic, 2000.07.
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see also <P002238>, <P002253>, <P007912>, <P009378>, <P010245>, <P010618>, <P011695>, <P019039>, <P019737>

RESEARCH PROJECTS

Studies on Growth Hormone Secretagogue Receptors in Fish

- ✉ CHENG Hon Ki Christopher
- 1 January 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Growth hormone (GH) plays a crucial role in regulating body growth. Understanding the mechanisms underlying the neuroendocrine regulation of growth is important for the farming of fish and other vertebrate species. Using seabream as a model, this study will investigate the tissue expression of receptors for growth hormone secretagogues (GHS) in fish. Attempts to clone the cDNA for the GHS receptor (GHSR) in seabream has been met with initial success and efforts would be made to obtain the full-length sequence. Functional expression of the cloned receptor in eukaryotic cell lines would be performed as a means of studying its biological activity. Recently, novel and orally active GHS analogs have been developed for stimulation of GH secretion in mammals. The elucidation of the molecular structure and physiological functions of GHSR in seabream would shed light on the regulation of GH secretion in fish species. (BL00654)

Development of Compound Formulation Products of GMP Standard Consisting Danshen from Zhongjiang, Sichuan and Sanqi from Wenshan, Yunnan

- ✉ FUNG Kwok Pui
- 1 September 2000
- ❖ New World BioSciences Co. Ltd. • University-Industry Collaboration Prog.: Matching Grant for Joint Research, ITF, Innovation & Tech. Commission

A consortium comprises New World China Enterprises Projects Limited, Institute of Chinese Medicine (ICM) of The Chinese University of Hong Kong (CUHK), and Hong Kong Institute of Biotechnology (HKIB) will develop quality indices guidelines and methodologies for the products of Danshen [丹 参] and Sanqi [三 七] . Formulations of the products will be developed for the prevention and/or treatment of ischemic heart diseases. The objectives are to produce several batches of effective and safe Danshen and Sanqi products for this project. The deliverables of this project will be a reliable and practical quality indices system for the products of Danshen and Sanqi, formulations of Danshen and Sanqi products, safety

and efficacy data of these products and protocols. The success of this project can help the company to evaluate the possible establishment of Danshen and Sanqi products production line and quality control laboratory. The safety and biological data obtained in this project will be valuable for designing clinical trials so that the products can be ultimately registered as a medicine globally. These outcomes will inevitably strengthen the development of Chinese medicine in Hong Kong. (MD20033)

Isolation and Characterization of Novel Lectins From Chinese Medicinal Materials and Legumes

- ✉ NG Tzi Bun • WANG Hexiang*
- 15 October 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Lectins are a class of intensively studied proteins that have important implications and applications in research and medicine. They exhibit a spectrum of important biological activities comprising antitumor, immunomodulatory antiviral, antibacterial, antifungal and anti-insect activities. The intent of this study research is to isolate and characterize novel lectins from Chinese medicinal materials such as Smilax glabra and Dendrobium species and edible materials including Castanea mollissima, Capsicum frutescens, Colocasia esculenta, Phaseolus vulgaris. (MD00483)

Characterization of Differentially Expressed Genes during Terminal Differentiation of Cardiomyocytes

- ✉ TSUI Kwok Wing • FUNG Kwok Pui • LEE Cheuk Yu • WAYE Mary Miu Yee
- 1 November 2000
- ❖ Research Grants Council (Earmarked Grants)

In 1998, heart diseases were the second leading causes of death in Hong Kong. These diseases affect mainly elderly people and will continue to dominate as Hong Kong's population ages. Among heart diseases, myocardial infarction is a leading cause of mortality because cardiomyocytes do not regenerate after birth, and they respond to mitotic signals by cell hypertrophy rather than by cell hyperplasia once they have terminally differentiated. Currently, the exact mechanism of terminal differentiation in cardiomyocytes remains largely unknown. In an attempt to better understand the mechanism, the researchers recently embarked on the isolation of genes that are differentially expressed in the neonatal rat heart. After screening two gene libraries by colony hybridization, over 200 putative differentially expressed clones have been isolated. This pool of

genes should contain many important factors involved in the molecular mechanism of the rat myocardial terminal differentiation. In this project, the researchers propose to characterize the putative differentially expressed genes and study their relationship with the growth and differentiation of the heart. The elucidation of the functional roles of these genes in the regeneration of the myocardium is prerequisite for developing new effective therapies for cardiovascular injury or diseases. (CU00116)

Inhibitory Effects of Antifungal Proteins on HIV Enzymes

- ✉ WAN Chi Cheong David • NG Tzi Bun
- ☐ 15 April 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Antifungal proteins have been isolated from a variety of species. Some of the antifungal proteins also possess antibacterial activity. Preliminary experiments in the researchers' laboratory have revealed that antifungal proteins may exhibit an inhibitory activity against HIV-1 reverse transcriptase. The present investigation therefore aims at examining the possible inhibitory activity of various antifungal proteins toward HIV-1 enzymes in a more thorough study.

A variety of antifungal proteins will be isolated from seeds of leguminous plants including French bean, cowpea, field bean, mung bean, peanut and red kidney bean. They will be assayed for ability to inhibit human immunodeficiency virus type 1 (HIV-1) reverse transcriptase, protease and integrase, enzymes essential to the life cycle of HIV-1. (BL00637)

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>
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)
1999-00	Studies on Fish Prolactin (BL99017) ✉ CHENG Hon Ki Christopher
1997-98	Oligonucleotide Combinatorial Library: Application in Diagnostic and Therapeutic Drug Development (BL97005)

	✉ CHEUNG Wing Tai • HO Walter K. K. (Biochemistry) • WAN Chi Cheong David
1998-99	Biochemical Characterisation of Mas Oncoprotein and its Interactions with RAMP (BL98030) ✉ CHEUNG Wing Tai • POYNER David*
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*
1997-98	Low Density Lipoprotein as Carrier for Targeted Delivery of Antitumoral Drugs (CU97309) ✉ FUNG Kwok Pui
1998-99	Glucose Transporter as an Anti-tumour Target (CU98148) ✉ FUNG Kwok Pui • LEE Cheuk Yu
1999-00	Examination of the Feasibility of Using Novel Antioxidants Isolated From Traditional Chinese Medicine and Other Natural Sources as Anti-tumour Agents: Studies of Their Mechanism, Multidrug Resistance Counteraction and Cardioprotection (MD99025) ✉ FUNG Kwok Pui
1998-99	The Role of Growth Factor Signalling and c-Jun Expression in the Anti-tumour Effect of Natural Polysaccharides (CU98141) ✉ KWOK Tim Tak • CHOY Yuen Min (Biochemistry)
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
1999-00	Chemopreventive and Hormone-replacement Therapeutic Evaluations on Some Dietary Phytoestrogens (MD99100) ✉ LEUNG Lai Kwok
1999-00	Determining the Chemopreventive Potential of Tea Phytochemicals (BL99028) ✉ LEUNG Lai Kwok

- 1997-98 Natural Products with Anti-Human Immunodeficiency Virus Activity (CU97688)
 ✉ NG Tzi Bun • WAN Chi Cheong David • FONG Wing Ping (Biochemistry) • Yeung Hin Wing*
- 1997-98 Sequence Analysis of the SLIM1(FHL1) Gene (BL97017)
 ✉ WAYE Mary Miu Yee • BENTLEY David R.* • ROSS Mark*
- 1998-99 Isolation and Characterization of Ribosome - Inactivating Proteins with Novel Features (CU98331)
 ✉ NG Tzi Bun
- 1998-99 Establishment of a Catalogue of Genes Expressed in Human Liver Cancer and Mental Diseases (MD98069)
 ✉ WAYE Mary Miu Yee • LEE Cheuk Yu • FUNG Kwok Pui • TSUI Kwok Wing • JOHNSON Philip James (Dept of Clinical Oncology) • LIEW Choong Tsek (Dept of Anatomical & Cellular Pathology) • XUE Hong* • SMITH Michael* • LING Victor*
- 1998-99 Characterization of the Human 14-3-3 Epsilon Protein (MD98032)
 ✉ TSUI Kwok Wing
- 1998-99 Study on the Expression of LIM-Domain Proteins in Human and Animal Myocardial Tissues (BL98034)
 ✉ WAYE Mary Miu Yee • ZIMMERMANN Rene* • Andreas KAMPMANN*
- 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
- 1999-00 Cell Cycle Control: Regulation of CDC25B Phosphatases by Calmodulin and CaM Kinase (BL99008)
 ✉ TSUI Kwok Wing • WAYE Mary Miu Yee • DUCOMMUN Bernard*
- 1999-00 Structural and Functional Studies of Human 14-3-3 Epsilon Protein (MD99027)
 ✉ WAYE Mary Miu Yee • LEE Cheuk Yu • FUNG Kwok Pui • TSUI Kwok Wing
- 1998-99 The Role of Pre-synaptic Motor Neuron Acetylcholinesterase in Neuromuscular Synaptogenesis (CU98140)

RESEARCH OUTPUTS AND PUBLICATIONS

- <P994738> **LEUNG L.K. and WANG T.T.Y.** "Paradoxical Regulation of Bcl-2 Family Proteins by 17 Beta-Oestradiol in Human Breast Cancer Cells MCF-7". *British Journal of Cancer* vol.81 no.3, pp.387-392. Britain, 1999.10.
- <P002100> **Su, Ya-Lun; Lai Kwok Leung; Yu-Rong Bi; Yu Huang and Zhen-Yu Chen.** "Antioxidant Activity of Flavonoids Isolated from *Scutellaria Rehderiana*". *Journal of the American Oil Chemists' Society* vol.77 no.8, pp.807-812. USA, 2000.08.03.
- <P002410> **Yang, Lin; Lai Kwok Leung; Yu Huang and Zhen-Yu Chen.** "Oxidative Stability of Conjugated Linoleic Acid Isomers". *Journal of Agricultural and Food Chemistry* vol.48 no.8, pp.3072-3076. USA, 2000.08.03.
- <P002449> **Chim, Stephen S.; Kwok-Pui Fung; Mary M.Y. Waye; Cheuk-Yu Lee and Stephen K.W. Tsui.** "Expression of Replication Factor C 40-kDa Subunit is Down-Regulated During Neonatal Development in Rat Ventricular Myocardium". *Journal of Cellular Biochemistry* vol.78, pp.533-540. 2000.
- <P002450> **Cheng, Shuk Han; Wing Lam; Agnes S.K. Lee; Kwok Pui Fung; Rudolf S.S. Wu and Wang Fun Fong.** "Low-Level Doxorubicin Resistance in Benzo[a]Pyrene-Treated KB-3-1 Cells is

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- <P002451> **Chan, Judy Yuet-Wa; Andrew Chi-Yuen Chu and Kwok-Pui Fung.** "Inhibition of P-Glycoprotein Expression and Reversal of Drug Resistance of Human Hepatoma HepG2 Cells by Multidrug Resistance Gene(mdr1) Antisense RNA". *Life Sciences* vol.67 suppl.2000, pp.2117-2124. 2000.
- <P002452> **Wu, Tai-Wing; Ling-Hua Zeng; Jun Wu and Kwok-Pui Fung.** "MCI-186: Further Histochemical and Biochemical Evidence of Neuroprotection". *Life Sciences* vol.67 suppl.2000, pp.2387-2392. 2000.
- <P002537> **Wan, David C.C.; Roy C.Y. Choi; Nina L. Siow and Karl W.K. Tsim.** "The Promoter of Human Acetylcholinesterase is Activated by a Cyclic Adenosine 3',5'-Monophosphate-Dependent Pathway in Cultured Ng108-15 Neuroblastoma Cells". *Neuroscience Letters* vol.288, pp.81-85. USA, 2000.
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- <P002542> **Yuen, W.F.; K.P. Fung; C.Y. Lee; Y.M. Choy; S.K. Kong; Samuel Ko and T.T. Kwok.** "Hyperthermia and Tumour Necrosis Factor- α Induced Apoptosis via Mitochondrial Damage". *Life Sciences* vol.67, pp.725-732. 2000.
- <P002705> **LIU Meizheng; YU Biao; WU Xiangyang; HUI Yongzheng and FUNG Kwok Pui.** "Synthesis of (25*R*)-Ruscogenin-1-Y1 β -D-Xylopyranosyl-(1 \rightarrow 3)-[β -D-Glucopyranosyl-(1 \rightarrow 2)]- β -D-Fucopyranoside". *Carbohydrate Research* vol.329, pp.745-754. 2000.
- <P003367> **YEUNG Chi Hang Thomas; YANG Lin; HUANG Yu; WANG Jun and CHEN Zhen-Yu.** "Dietary Conjugated Linoleic Acid Mixture Affects the Activity of Intestinal Acyl Coenzyme A: Cholesterol Acyltransferase in Hamsters". *British Journal of Nutrition* vol.84, pp.935-941. UK, 2000.12.
- <P003414> **SUEN Y.K.; FUNG K.P.; CHOY Y.M.; LEE C.Y.; CHAN C.W. and KONG S.K.** "Concanavalin A Induced Apoptosis in Murine Macrophage PU5-1.8 Cells Through Clustering of Mitochondria and Release of Cytochrome C". *Apoptosis* vol.5, pp.369-377. The Netherlands, 2000.10.
- <P003979> **LAM T.L.; LAM M.L.; AU T.K.; IP D.T.M.; NG T.B.; FONG W.P. and WAN D.C.C.** "A Comparison of Human Immunodeficiency Virus Type-1 Protease Inhibition Activities by the Aqueous and Methanol Extracts of Chinese Medicinal Herbs". *Life Sciences* vol.67, pp.2889-2896. 2000.
- <P003980> **AU T.K.; COLLINS R.A.; LAM T.L.; NG T.B.; FONG W.P. and WAN D.C.C.** "The Plant Ribosome Inactivating Proteins Luffin and Saporin are Potent Inhibitors of HIV-1 Integrase". *FEBS Letters* vol.471, pp.169-172. 2000.
- <P003981> **ZHANG X.; TSIM K.W.K.; CHOI R. and WAN D.C.C.** "Overexpression of Mitogen-Activated Protein Kinase Kinase Kinase (MEKK) Upregulates Acetylcholinesterase Promoter Activity in NG108-15 Cells". Paper presented in FAONS Symposium 2000 and the 20th Scientific Meeting of the Hong Kong Society of Neurosciences. Hong Kong, 2000.12.
- <P003982> **ZHANG X.; TSIM K.W.K. and WAN D.C.C.** "Characterization of a Polyclonal Antibody Against Chick P2Y1 Receptor". Paper presented in FAONS Symposium 2000 and the 20th Scientific Meeting of the Hong Kong Society of Neurosciences. Hong Kong, 2000.12.

- <P003983> **IP A.L.F. and WAN D.C.C.** "Cloning and Characterization of Endothelin Converting Enzyme Type-2 from Rat Brain". Paper presented in FAONS Symposium 2000 and the 20th Scientific Meeting of the Hong Kong Society of Neurosciences. Abstracts no.8P28. Hong Kong, 2000.12.
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- <P003994> **CHENG Man and CHEUNG Wing-Tai.** "Angiotensin and Endothelin-I -Potentiated Field-Stimulated Smooth Muscle Contraction in Prostatic Rat Vas Deferens Are Mediated by Different Cellular Mechanisms". FAONS Symposium 2000 & the 20th Annual Meeting of Hong Kong Society of Neurosciences Hong Kong, 2000.12.
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RESEARCH PROJECTS

Intracellular Signal Transduction for Tumor Necrosis Factor- α -induced Eotaxin Synthesis of Human Eosinophils in Allergic Inflammation

- ✉ LAM Wai Kei Christopher • WONG Chun Kwok
- ☐ 1 November 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Eosinophils are the principal effector cells of late-phase inflammation in allergic diseases. Severe tissue damage occurs as eosinophils release cytotoxic granular proteins including eosinophilic cationic protein, major basic protein and eosinophil protein X. A potent eosinophil-specific chemoattractant, eotaxin, has recently been shown to be crucial for the induction of allergic inflammation and pathogenesis of asthma. Eotaxin generated at allergic inflammatory sites promotes eosinophil accumulation to cause tissue damage.

This project aims to utilize our established (1) human blood eosinophil culture and (2) mitogen-activated protein kinases (MAPK) assay techniques to elucidate the roles of different signal transduction regulators including MAPK and NF- κ B for TNF- α -induced eotaxin synthesis in eosinophils. It will study: (1) effect of TNF- α on intracellular MAPK (ERK, JNK, p38 MAPK), NF- κ B in human peripheral blood eosinophils. (2) Relationship between the activation of MAPK and NF- κ B and eotaxin synthesis and release in eosinophils. (3) Effect of specific inhibitors of MAPK and NF- κ B on eotaxin and CCR3 gene transcription and synthesis. Elucidation of the crucial signal transduction mechanisms that control the eotaxin synthesis and eosinophil recruitment to tissues is fundamental to understanding of allergic inflammatory disease and will provide a rationale for design of drug therapy. (MD00783)

Molecular Analysis of Cell-free RNA in the Plasma of Pregnant Women

- ✉ LO Yuk Ming Dennis • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Tse Ngong (Dept of Obstetrics & Gynaecology)
- ☐ 4 October 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Recently, there has been much interest in the use of plasma DNA for molecular analysis. This project aims to take this field onto the next logical step, namely, the extension of plasma nucleic acid analysis to RNA. The researchers plan to look for the

existence of circulating fetal RNA in the plasma of pregnant women using reverse transcriptase polymerase chain reaction (RT-PCR). The demonstration of fetal RNA in maternal plasma will be a world-first which will open up a new field of investigation. Thus, the detection of fetal RNA would potentially allow one to monitor the gene expression pattern of an unborn fetus non-invasively, just by analysing the mother's blood. Apart from its biological interest, this project would also have many diagnostic and commercial implications. (MD00848)

Enhanced Expression of a Novel Gene BRE That May Modulate Steroid Metabolism in Adrenal Gland and Testis

- ✉ PANESAR Nirmal Singh • CHAN John Y H*
- ☐ 1 April 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Genes that modulate the action of hormones, cytokines and stress responses play a critical role in the homeostasis, survival, growth and differentiation of cells. Many of these biological response modifiers are responsible for the various pathological conditions including inflammation, infection, cachexia, aging, genetic disorders and cancer. The researchers have previously identified a new gene BRE that is responsive to DNA damage and retinoic acid. BRE gene was found to interact with the tumor necrosis factor- α receptor-1 (TNFR1) and modulates the activation of the transcriptional factor NF- κ B induced by TNF- α . Using Dot-blot and Northern blotting and immunohistochemistry, BRE was found to express strongly in adrenal cortex and medulla, testis and pancreas while low expression was found in the thyroid, thymus, small intestine and stomach. BRE also expressed strongly in the zona glomerulosa of the adrenal cortex, which synthesizes and secretes TNF and the mineralocorticoid hormones. It also expressed highly in the glial cells of the brain, the round spermatids and the androgen-producing Leydig cells of the testis. However, BRE expression was down-regulated in adrenal adenoma and pheochromocytoma while its expression was enhanced in abnormal adrenal-tissues of rats chronically treated with nitrate or nitrite. These data, taken together, indicate that the expression of BRE is apparently associated with TNF production and/or the regulation of endocrine functions. BRE may play an important role in the regulation of endocrine synthesis and action including the cytokine-endocrine interaction of the adrenal gland, testis and brain.

The researchers proposed to (1) determine the expression of BRE in androgen-producing Leydig cells treated with hCG or TNF; (2) transfect the sense- or antisense-BRE into Leydig cells treated with hCG, and to determine if the production of

androgen is altered; (3) analyze the expression of BRE in adrenal glands of rats after dexamethosone treatment to suppress ACTH production, and in testis of rats treated with androgen to suppress the action of gonadotropins.
(MD00669)

Genetic Susceptibility for Hepatocellular Carcinoma in Chronic Hepatitis B Carriers: A Study of Genetic Polymorphisms in CYP1A1, GST-M1, IL-1 β and IL-1RN Genes

✉ TANG Leung Sang Nelson • LAI Bo San Paul (Dept of Surgery) • CHAN Ka Leung Francis (Dept of Medicine & Therapeutics)

☐ 1 November 2000

❖ CUHK Research Committee Funding (Direct Grants)

This project studies the genetic risk factors for hepatocellular carcinoma (HCC). HBV is an important risk factor in pathogenesis of HCC, however only a small proportion of all chronic HBV carriers develop HCC. There are reports on the genetic predisposition to HCC in patients carrying particular polymorphisms of P450 1A1 and glutathione S-transferase (GST) genes. These genes encode for enzymes, which play an important role in metabolism of carcinogens.

The researchers proposed to carry out a case-control study to determine the association of genotypes in five candidate genes (*CYP1A1*, *GST-M1*, *PPAR α* , *IL-1 β* and *IL-1RN*) and risk of HCC. HCC patients will form the case group and sex- and age-matched chronic HBV carrier without HCC will be the controls.

GSTM1 and *CYP1A1* are genes involved carcinogen metabolism. Peroxisome proliferator activated receptor α (*PPAR α*), which encodes for a transcription factor controlling expression of cell proliferation genes, plays a key role in the rodent model of peroxisome proliferator induced HCC. Interleukin-1 β (IL-1 β) and interleukin 1 receptor antagonist (IL-1RN) modulates the immune response to pathogens. Genotypes of IL-1 β and IL-1RN have been associated with development of cirrhosis.

Polymorphisms of *GST-M1*, *CYP1A1*, *IL-1 β* and *IL-1RN* genes will be studied. The researchers would identify novel polymorphisms in *PPAR α* gene, which has not been explored, and then determine their frequency in their patients groups.

The role of *PPAR- α* , IL-1 β and IL-1RN in development of HCC in human will be documented for the first time in this study. It will enhance the understanding of pathogenesis and genetic predisposition for HCC. In the long run, it may provide a foundation for new means of chemoprevention.

(MD00880)

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	Non-invasive Prenatal Screening of β -thalassaemia by Molecular Analysis of Maternal Plasma (MD99101) ✉ CHIU Wai Kwun Rossa • LO Yuk Ming Dennis • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Tse Ngong (Dept of Obstetrics & Gynaecology)
1999-00	Mitochondrial Genome in Wolff-Parkinson-White Syndrome (MD99028) ✉ LAM Ching Wan • SANDERSON John Elsby (Dept of Medicine & Therapeutics) • WONG Lee-Jun C* • FONG Win Hon*
1998-99	Novel Analyte Assay in Experimental and Human Cataract (MD98089) ✉ LAM Wai Kei Christopher • PETERS T J*
1999-00	Signal Transduction for Dexamethasone-Induced Apoptosis of Human Eosinophils in Allergic Inflammation (MD99029) ✉ LAM Wai Kei Christopher • WONG Chun Kwok • HJELM Nils Magnus#
1998-99	Evaluation of Molecular Markers for Solid Organ Rejection (MD98034) ✉ LO Yuk Ming Dennis • HJELM Nils Magnus# • PANG Chi Pui Calvin (Dept of Ophthalmology and Visual Sciences) • YEUNG Chung Kwong (Dept of Surgery) • CHAN Albert Yan Wo* • TONG Kwok Lung*
1998-99	Non-Invasive Prenatal Diagnosis (MD98115C) ✉ LO Yuk Ming Dennis
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# • JOHNSON Philip James (Dept of Clinical Oncology)

1998-99 Genetic Predisposition to Breast Cancer in Chinese: Study of Mutations and Genotypes of BRCA1, Estrogen Receptor and Estradiol 17 Betadehydrogenase II Genes (MD98096)

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RESEARCH PROJECTS

Biweekly Irinotecan (CPT-11), 5-Fluorouracil (5-FU) and Folinic Acid (FA) in Unresectable Liver Metastases from Colorectal Cancer: A Phase II Study

✉ CHAN Anthony Tak Cheung • MOK Shu Kam Tony • LEUNG Wai Tong Thomas • YEO Winnie • JOHNSON Philip James • LAI Bo San Paul (Dept of Surgery) • CHUI Ka Keung Albert (Dept of Surgery) • LAU Wan Yee Joseph (Dept of Surgery) • Hui Edwin P*

☐ 1 September 2000

❖ Aventis Pharma Ltd.

The objectives of this study are to study the response rate of a biweekly CPT-11 and 5FU/FA regimen in unresectable liver metastases from colorectal origin, to assess the safe profile in patients receiving this regimen, and to assess the percentage of patients with resectable liver metastases after 4,8 and 12 cycles of this regimen.

Patients with histologically proven adenocarcinoma of the colon or rectum and unresectable liver metastases without detectable extrahepatic tumour will be screened for the study. A complete patient history will be taken at study entry. Physical examination, chest X-ray, CT scan of abdomen and pelvis and haematology, biochemistry, urinalysis will be part of the initial baseline assessment. During the Treatment period physical examination, evaluation of tumor by imaging, haematology, biochemistry urinalysis, and CEA will be performed at regular intervals. Patients who fulfil all the eligibility criteria and have given written informed consent will receive CPT-11 180mg/m² by 1/2 hour infusion on day one, 5FU 400mg/m² IV bolus then 600mg/m² by 22 hours infusion on days one and two, and FA 200mg/m² by 1/2 hour infusion on days one and two. (MD20018)

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)

✉ CHAN Anthony Tak Cheung • MOK Shu Kam Tony • YEO Winnie • LEUNG Wai Tong Thomas • JOHNSON Philip James • LEE Chi Yan Conrad

☐ 15 February 2001

❖ Merck (Singapore) Pte. Ltd.

This multicenter, open-label, uncontrolled phase II study with one dose level will enrol up to 60 patients with recurrent/metastatic undifferentiated

nasopharyngeal carcinoma who failed a platinum based chemotherapeutic regimen without Cetuximab. (MD00719)

A Randomized, Open-label, Multicenter Phase III Study of 5-Fu/Leucovorin with or without Concomitant SU5416 in Patients with Metastatic Colorectal Cancer

✉ CHAN Anthony Tak Cheung • MOK Shu Kam Tony • YEO Winnie • LEUNG Wai Tong Thomas • JOHNSON Philip James • HO Wing Ming

☐ 5 March 2001

❖ Pharmacia Hong Kong Limited

This is a randomized, open-label, controlled, multicenter, international Phase III study in which 710 patients with metastatic colorectal cancer will be randomized to be treated with either 5-FU/LV therapy alone or 5-FU/LV therapy co-administered with SU5416, an angiogenesis inhibitor. (MD20065)

Adenocarcinoma of the Lung in Hong Kong Chinese Females: A Genome Investigation for Underlying Genetic Alterations

✉ JOHNSON Philip James • TSAO Ming Sound* • WONG Nathalie • YIM Ping Chuen Anthony (Dept of Surgery)

☐ 1 October 2000

❖ Research Grants Council (Earmarked Grants)

Lung cancer is the leading cause of cancer-related death in Hong Kong. Whilst in men this is clearly associated with cigarette smoking, there is also a high, and rising, incidence of lung cancer in young, non-smoking women that cannot, to date, be linked to any specific environmental factors. The majority of such cases are adenocarcinomas and indeed the incidence of this type of lung cancer in Chinese women (32.6/100,000) is amongst the highest in the world. Although some genetic abnormalities of lung cancers in Chinese patients have been identified, the presence of aberrations specific to adenocarcinoma has received little attention. In the present proposal, the researchers aim to undertake the first systematic investigation into the genomic alterations in non-smoking adenocarcinoma of the lung in Chinese females by the two recently developed molecular cytogenetics techniques, *Comparative Genomic Hybridization* (CGH) and *Spectral Karyotyping* (SKY). CGH enables the identification of regions of DNA sequence gains and losses in the entire tumour genome, while SKY elucidates chromosomal rearrangements. The combined application of these two techniques is expected to offer a comprehensive picture of the genomic abnormalities and permit

comparison with analogous studies that will be undertaken on Chinese and Western smokers with lung cancer. The researchers hope thereby to identify chromosomal regions of interest that are specific for adenocarcinoma of the lung in young Chinese non-smoking women.

(CU00112)

Identification of Metastasis-related Genes in a Human Lung Cancer Cell Line Using Representational Difference Analysis and cDNA Array Technology

✉ JOHNSON Philip James • ZHONG Sheng • Zheng Jie* • LIU Cuiling*

☐ 1 December 2000

❖ CUHK Research Committee Funding (Direct Grants)

Lung cancer is a significant cause of death in Hong Kong and effective treatment (surgical resection) is limited by the presence of overt or occult metastases that are present at the time of diagnosis. The molecular events involved in metastatic lung cancer cells remain unclear. The researchers have isolated two cell lines, PGBE1 and PGLH7, which were derived from the primary and metastatic lesions of a patient with large cell carcinoma. These two lines have different metastatic properties and can therefore offer a unique opportunity in understanding the molecular events responsible for metastasis. The researchers plan to combine representational difference analysis (RDA) and the recently developed cDNA arrays technique to study altered gene expression profiles in the two lines. If identification of the altered gene expression profile in PGLH7 and PGBE1 by RDA and cDNA array is successful, novel genes responsible for metastases will be identified. This information may provide insights into the mechanism of lung cancer and development of anti-metastasis therapy.

(MD00741)

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

✉ JOHNSON Philip James • MOLASIOTIS Alexandros (The Nethersole School of Nursing)# • ZEE Chung Ying Benny • Mak So Shan* • Chan Eunice*

☐ 18 December 2000

❖ Health Services Research Fund, Hospital Authority

NPC is a highly malignant but potentially curable cancer that is widely prevalent in Hong Kong. The

primary treatment is radiation therapy. Although effective this treatment produces desquamation wounds that can adversely affect the quality of life of the patients involved. This project, which is a prospective randomized trial involving 60 patients, aims to assess which of 2 types of dressing (gentian violet, the conventional approach, and a non-adherent dressing), is most effective. The outcome measures include wound-healing time, incidence of infection and patient acceptability.

(BL20009)

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

✉ LEI Ieng Kit Kenny • LEUNG Wai Tong Thomas • HUI Pun

☐ 7 November 2000

❖ Roche Hong Kong Limited

Interferon alpha-2a (IFN) is a therapy that has been proven to improve survival in patients with Philadelphia chromosome positive chronic phase chronic myeloid leukaemia (CML). However, the use of conventional IFN therapy is associated with side effects that may lead to interruption or discontinuation of treatment. This will adversely affect the ability to achieve a complete cytogenetic response and benefit on survival. For these reasons, agents that are potentially active against CML with less toxicity but better tolerability are currently being investigated. This study is a randomized open-label, parallel arm, multi-centre study that has been designed to evaluate the efficacy, safety, tolerability, impact on quality of life, pharmacokinetic and pharmacodynamic profiles, and immunogenicity of pegylated form IFN alpha-2a (PEG-IFN) as compared to conventional IFN. The rationale behind is that PEG-IFN used in a once weekly regimen may reduce the toxicity, improve the tolerability, and hence enhance patient compliance and outcome. After a 4-week screening period, all eligible patients with Philadelphia chromosome positive CML will be randomized to receive subcutaneous injections of either PEG-IFN 450 µg once weekly, or Roferon-A (interferon alpha-2a) 9 MIU once daily for a period of 12 months, or until evidence of progressive disease. Patients who exhibit complete haematologic response or cytogenetic response within the first 12 months treatment period may continue therapy for a maximum of 4 additional years. All patients will be followed for survival analysis for at least 8 years regardless of treatment outcome.

(MD20042)

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)

✉ LEI Ieng Kit Kenny • LEUNG Wai Tong Thomas • HUI Pun

□ 17 April 2001

❖ Pharmacia & Upjohn Asia Limited

Aggressive non-Hodgkin's lymphoma (NHL) is a common malignancy. Despite high response rate to current chemotherapy regimens, only 30-50% of the cases are cured. Most cases develop refractory disease or recurrence and require further intensive chemotherapy. DHAP is one of the most commonly employed salvage chemotherapy regimen for patients with refractory or relapsed NHL. However, this regimen is associated with significant thrombocytopenia that may lead to major bleeding and often requires platelet transfusion. Frequent platelet transfusion is also associated with infection risk, transfusion reactions, and alloimmunization. Thrombopoietin (TPO) is a naturally occurring glycosylated peptide which stimulates growth and differentiation of bone marrow stem cells to megakaryocyte and ultimately increases the production platelets. The use of synthetic recombinant human TPO (rhTPO) has been shown to increase platelet counts in both pre-clinical and clinical studies. Therefore, the administration of rhTPO in patients undergoing chemotherapy may increase the platelet and reduce the risk of thrombocytopenia. In the present project the researchers evaluate the effectiveness of intravenous rhTPO as primary prophylaxis in reducing the proportion of patients requiring platelet transfusion during salvage DHAP therapy for relapsed or refractory aggressive lymphomas. This study is a phase III randomized, double-blind, placebo-controlled trial. All patients undergoing repeated cycles of DHAP chemotherapy are randomized to receive either intravenous rhTPO 1.2 mcg/kg or placebo on D-5, D-3, D-1, D1, D3, D5 during chemotherapy. Following the completion of initiate 2 cycles of DHAP, patients in both rhTPO or placebo arms will be considered to participate in the extension of 4 additional cycles of DHAP. For all eligible patients, all patients will receive rhTPO 1.2 mcg/kg on the same dosing schedule as during the initial cycles. Comparison will be performed between rhTPO and placebo groups on the number of transfusions, incidence of associated transfusion reactions, platelet recovery time, adverse events and survival.

(MD20067)

Neoadjuvant Systemic Chemotherapy for Operable Hepatocellular Carcinoma

✉ LEUNG Wai Tong Thomas • JOHNSON Philip James • LAU Wan Yee Joseph (Dept of Surgery) • LIEW Choong Tsek (Dept of Anatomical & Cellular Pathology) • ZEE Benny*

□ 1 October 2000

❖ CUHK Research Committee Funding (Direct Grants)

Hepatocellular carcinoma (HCC), also known as primary liver cancer, is a common disease worldwide especially in Hong Kong. The major obstacles in curing HCC are due to the fact that most patients present at an inoperable stage and there is also high recurrence rate after successful surgical resection. The overall cure rate of all HCC in different stages so far is only about 5%. There are 2 approaches to alleviate the dismal outlook of the disease. First is to develop effective non-surgical treatment for patients with inoperable disease, either to eradicate or to convert inoperable to operable disease by shrinking the tumour. Secondly, for the operable stage disease, to use non-surgical treatment before (neoadjuvant) or after (treatment) surgery to control microscopic disease which in turn, reduce recurrence rate and improve survival. The researchers' centre had discovered an effective combination chemotherapy using a 4 drug regimen called "PIAF" (cisplatin, alpha-interferon, doxorubicin and 5-fluorouracil) for inoperable HCC. PIAF can by itself cause complete pathological remission for relatively large and symptomatic HCC. Twenty percent of inoperable disease can be made operable after PIAF treatment. In this proposed study, the researchers are taking another step ahead in using the PIAF regimen as a neoadjuvant treatment for operable HCC. They hypothesize that PIAF given before surgery can downsize tumour and treat microscopic metastases which in turn reduces post-operative recurrence rate and prolongs survival. The researchers further hypothesize that pathological assessment of tumour response after chemotherapy is an important prognostic factor for survival. A direct potential benefit from this study is to establish the theoretical basis of an effective multi-modality treatment with respect to response rate so that they can further test this neoadjuvant treatment in a phase III setting with respect to overall survival. This study would also provide us with pathological information of tumour tissue after chemotherapy in order to develop strategy of using tumour marker such as alpha-fetoprotein as part of a new response criteria in addition to conventional radiological assessment such as CT scan or ultrasound. The development of this new response criteria would enhance the sensitivity and specificity of future screening of new drugs in phase II setting for HCC.

(MD00994)

A Phase I/II Open Label Study of T138067-sodium in Patients with Advanced Surgically Unresectable Hepatocellular Carcinoma

✉ LEUNG Wai Tong Thomas • MOK Shu Kam Tony • JOHNSON Philip James

□ 8 March 2001

❖ Tularik Inc.

Hepatocellular carcinoma is a common cancer and cure for advanced unresectable stage disease is rare. The cancer is generally resistant to most cancer drugs. T138067-sodium is a novel compound developed by Tularik Inc, which has shown both *in-vitro* and *in-vivo* anti-tumour activity. The present study aims to delineate activity of T138067-sodium in hepatocellular carcinoma as well as toxicity after treatment. (MD20061)

A Double-blind Placebo-control Randomized Study of the Efficacy of Chinese Herbal Medicine in Reduction of Cytotoxic Chemotherapy-induced Toxicity

✉ MOK Shu Kam Tony • JOHNSON Philip James • YEO Winnie • ZEE Chung Ying Benny

□ 1 October 2000

❖ Research Grants Council (Earmarked Grants)

Chinese Herbal Medicine (CHM) is widely practiced throughout Hong Kong and China. The government of Hong Kong intends to integrate CHM into the health care system (China has endorsed a dual system since 1958) and develop Hong Kong as the international trading and manufacturing center for CHM. Although regulatory bodies in United States and European Union have established rigorous criteria for the testing and introduction of new therapeutic agents, fundamental differences in philosophy between CHM and Western medicine have made direct application of Western research methodology difficult. However, if CHM is to achieve broad international acceptance, application of Western research methodology to TCM is essential. The aim of this study is to determine whether CHM may reduce incidence of hematological or non-hematological toxicity induced by systemic chemotherapy. Such claim, as frequently made by Chinese herbalists and patients, is based on limited laboratory data on immunomodulatory effects of CHM, and there is no clinical evidence to confirm or dispute this claim. The researchers will adopt a study design of double-blind controlled randomized study. Eligible patients are assessed by a licensed CHM practitioner before an independent research assistant randomizes the patient to either an active treatment arm (combination of single herb extract packages, as

per prescription by the TCM practitioner) or a placebo arm (nonspecific herbs in package). The researchers shall evaluate endpoints including hematological toxicity, non-hematological toxicity, quality of life, dose-density and treatment compliance. (CU00109)

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

✉ MOK Shu Kam Tony • CHAN Anthony Tak Cheung

□ 1 December 2000

❖ AstraZeneca Hong Kong Limited

Patient with advanced lung cancer will be randomized to receive chemotherapy (gemcitabine plus cisplatin) and a novel tyrosine kinase inhibitor (ZD1839) versus chemotherapy plus placebo. The primary endpoint is survival as the novel drug is intended to slow progression of disease. (MD20046)

Phase I/II Study of a Paented Labyrinthin Peptide Base Vaccine in Patients with Advance Stage Labyrinthin Expressing Cancer

✉ MOK Shu Kam Tony

□ 1 April 2001

❖ ImmvaRx, Inc.

This is the first human study using the labyrinthin peptide, an antigen commonly found in adenocarcinoma, as a tumor vaccine. The researchers shall test the vaccine on 7 patients using zero-conversion and toxicity as endpoints. If feasible, the treatment will be offered to another 20 patients. (MD20064)

Investigation of the Cellular Factors Associated with the Resistance of Hepatocellular Carcinoma to Combination Chemotherapy, PIAF

✉ MOK Shu Kam Tony • LEUNG Wai Tong Thomas • POON Chuen Wai • LIEW Choong Tsek (Dept of Anatomical & Cellular Pathology)

□ 1 June 2001

❖ CUHK Research Committee Funding (Direct Grants)

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide. It is the second most cancer in Hong Kong, with an age-standardized

incidence rate of 47 per 100,000. Surgical resection is the only treatment for HCC that consistently offers the hope of cure. However, only 9-27% of patients are suitable for resection. Recently the researchers' Phase II study have investigated the response rate, toxicity, and the effect on survival of the combination of cisplatin, doxorubicin, 5-fluorouracil, and α -interferon (PIAF) in 50 patients with advanced unresectable hepatocellular carcinoma. The PIAF regimen was able to convert nearly 20% of inoperable lesions to operable. Therefore the induction chemotherapy with PIAF can significantly increase the overall operability rate of HCC. Although PIAF is active in inoperable hepatocellular carcinoma, it has considerable hematological toxicity. Therefore it is important to identify the subgroup that can be benefited from the PIAF treatment. This helps to prevent the non-responsive subgroup from the unnecessary exposure to the hematological toxicity. On the one hand, the effect of interferon must be achieved by binding to its receptor. On the other hand, overexpression of P-glycoprotein, EGFR, HER2, p53, p73 have shown in certain HCC subgroups, and these cellular factors have been associated with chemotherapy resistance and/or poor patient survival in different cancers. Therefore this project aims to investigate retrospectively the effect of expression patterns of interferon receptor, P-glycoprotein, p53, p75, EGFR and cerbB2 on the resistance to the PIAF treatment among patients with inoperable hepatocellular carcinoma. The successful identification of the tissue proteins associated with resistance can help to select the responsive group for administrating the treatment to prevent unnecessary toxicity to the non-responsive patients. Moreover, the understanding of why some HCC are non-responsive to the PIAF may help us to develop other potential regimens for the non-responsive subgroup. (MD00625)

Lamivudine for Prevention of HBV Reactivation in HBsAg Seropositive Patients Undergoing Cytotoxic Chemotherapy

- ✉ YEO Winnie • JOHNSON Philip James • 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)
- ☐ 15 September 2000
- ❖ Glaxo Wellcome China Limited

Cancer patients who are chronic carriers of hepatitis B virus infection have a higher incidence of developing hepatic complications during cytotoxic chemotherapy, and this has mainly been attributed to hepatitis B virus reactivation. In this study, patients who are chronic carriers of hepatitis B virus infection are commenced with antiviral therapy lamivudine

after consent, prior to the cytotoxic chemotherapy to assess if such therapy can reduce the incidence of hepatitis B virus reactivation during chemotherapy. (MD20031)

A Phase I/II Study of Weekly Paclitaxel, UFT and Leucovorin in Patients with Metastatic Breast Cancer

- ✉ YEO Winnie • MOK Shu Kam Tony • CHAN Anthony Tak Cheung • LAM Kwok Chi
- ☐ 1 December 2000
- ❖ Cancer Therapeutics Research Group

This is a study using combination chemotherapy Taxol, UFT and leucovorin as first line treatment for patients with metastasis breast cancer. The first phase of the study is a Phase I dose finding study; the second phase is a Phase II study. The study is conducted under the Clinical Trialist Research Group, members of which include Chinese University of Hong Kong, John Hopkins's Singapore, National University of Singapore and the Sydney Cancer Centre in Australia. (MD00480)

Definition and Measurement of Methylation Index (MI) in Hepatocellular Carcinoma Tissues and Their Corresponding Non-tumor Tissues

- ✉ YEO Winnie • JOHNSON Philip James • ZHONG Sheng
- ☐ 4 December 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

DNA methylation has important regulatory effects on gene expression, especially when involving CpG-rich areas known as CpG islands, located in the promoter regions of many genes. Aberrant methylation has been associated with chromosomal DNA instability and silence of tumor suppressor genes in various tumors. However, due to lack of effective mean to assess overall methylation status, including assessment of both genome-wide hypomethylation and CpG island hypermethylation density in one assay, a specific tumor methylation status has not been applicable in practice. The availability of such information may be useful as a factor for tumor staging and prognosis. Methylation Index (MI), as suggested in this study will give a measurable means to assess gene expression in the tumor, and can be used to correlate with the tumor staging and prognosis. Hepatocellular carcinoma (HCC) is one of the most common malignancies in Hong Kong and is the second major cause of cancer death locally. In this study, the researchers propose to apply the new cytosine extension method for the measurement of Methylation Index in HCC. If it is proven applicable

in HCC, there will be a great potential for its application in other types of tumor. (MD00568)

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

- ✉ YEO Winnie
- ☐ 20 December 2000
- ❖ International Collaborative Cancer Group

To compare the sequential administration of exemestane with administration of further tamoxifen until 5 years in Postmenopausal women with operable breast cancer who have already received 2-3 years of adjuvant tamoxifen, in terms of disease-free survival (DFS) and overall survival (OS). (MD00331)

A Phase II Study of Herceptin Monotherapy Administrated 3 weekly in Women with HER 2 Overexpression/amplification in Metastatic Breast Cancer

- ✉ YEO Winnie • MOK Shu Kam Tony • LAM Kwok Chi
- ☐ 1 January 2001
- ❖ Roche Hong Kong Limited

A Phase II Study using 3- weekly Herceptin monotherapy as a first line therapy in women with HER 2 overexpression/amplification in Metastatic Breast Cancer (MD20044)

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

Edition Title/Investigators

1998-99 Molecular Characterization of Differentially Expressed Genes in Nasopharyngeal Carcinoma (CU98284)
 ✉ HUANG POON Wai Sin Dolly • CHUI Yiu Loon (Clinical Immunology Unit) • TSAO George* • VAN HASSELT Charles Andrew (Dept of Surgery) • TO Ka Fai (Dept of Anatomical & Cellular Pathology) • PANG Chung Sean Jesse (Dept of Anatomical & Cellular Pathology) • LO Kwok Wai (Dept of Anatomical & Cellular Pathology)

1999-00 Comprehensive Study of Nasopharyngeal Carcinoma Genome by High-resolution Allelotyping (MD99021)
 ✉ HUANG POON Wai Sin Dolly • LO Kwok Wai (Dept of Anatomical & Cellular Pathology) • TEO Man Lung Peter • TO Ka Fai (Dept of Anatomical & Cellular Pathology)

1998-99 Specific Inactivation of a Suppressor Gene PML in Small Cell Lung Cancer (CU98280)
 ✉ JOHNSON Philip James • YIM Ping Chuen Anthony (Dept of Surgery) • CHAN Yeuk Hon John#

1999-00 Gene Expression Profile Analysis of Human Prostate Cancer Cell Lines with or without Metastatic Feature (MD99102)
 ✉ JOHNSON Philip James • ZHONG Sheng

1999-00 A Comprehensive Cytogenetic Characterization on Nasopharyngeal Carcinoma Cell Lines and Xenografts by Spectral Karyotyping and Comparative Genomic Hybridization (MD99103)
 ✉ LEUNG Sing Fai • WONG Nathalie

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 or 776C85/5-Fluorouracil Versus Intravenous 5-Fluorouracil Plus Leucovorin as First-time Therapy in Patients with Advanced Colorectal Cancer (Protocol No.FUMB3002) (MD97178C)
 ✉ LEUNG Wai Tong Thomas • JOHNSON Philip James • CHAN Anthony Tak Cheung • YEO Winnie

1999-00 A Comprehensive Genome Analysis on Hepatocellular Carcinoma by Spectral Karyotyping and Comparative Genomic Hybridization (MD99032)
 ✉ LEUNG Wai Tong Thomas • WONG Nathalie • JOHNSON Philip James

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
- 1999-00 An Open-Label Randomized Controlled Phase 2 Study of Herceptin in Combination with Chemotherapy in Patients with HER-2 Over-expression Amplification in Advanced and Metastatic Non-Small-Cell Lung Cancer (MD99016)
 ✎ MOK Shu Kam Tony • CHAN Anthony Tak Cheung • LEUNG Wai Tong Thomas
- 1999-00 An Open-Label, Multicenter, Randomized, Phase III Comparator Study of Oral Topotecan versus Intravenous Topotecan for Second-Line Therapy in Patients with SCLC Who Have Relapsed Greater than or Equal to 90 Days After Completion of First-Line Therapy (MD99019)
 ✎ MOK Shu Kam Tony • LEUNG Wai Tong Thomas • CHAN Anthony Tak Cheung
- 1999-00 Investigation of Beta-Galactoside Alpha2, 6-sialyltransferase Activity and Its Regulation in Hepatocellular Carcinoma (MD99033)
 ✎ MOK Shu Kam Tony • JOHNSON Philip James • LAI Bo San Paul (Dept of Surgery) • POON Chuen Wai
- 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 Adjuvant Tamoxifen - Longer Against Short (ATLAS) (MD96216)
 ✎ YEO Winnie • KWAN W. H.* • LEUNG C. M.*
- 1997-98 A Randomized Open-Label Phase III Study of a 28-Day Oral Regimen of 776C85/5-Fluorouracil Versus Intravenous 5-Fluorouracil Plus Leucovorin as First Line Therapy in Patients with Advanced Colorectal Cancer (MD97166)
 ✎ YEO Winnie • JOHNSON Philip James • LEUNG Wai Tong Thomas
- 1997-98 Randomized Trial of Tamoxifen versus Placebo for the Treatment of Inoperable Hepatocellular Carcinoma (MD97169)
 ✎ YEO Winnie • JOHNSON Philip James • LEUNG Wai Tong Thomas
- 1999-00 A Multicentre Phase III Trial of Taxotere and Doxorubicin vs. 5-Fluorouracil, Doxorubicin & Cyclophosphamide in Patients with Unresectable Locally Advanced Breast Cancer (MD99144)
 ✎ YEO Winnie

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RESEARCH PROJECTS

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

- ✉ CHAN Shiu Yee Cynthia • WUN Yuk Tsan Kyran Patrick • DICKINSON James Arthur
- ☐ 1 April 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

This project aims to study the baseline communication skills (COSK) of primary care physicians in Hong Kong and whether their COSK shows significant improvement after a 9 month Diploma Course in family Medicine. The design is a before and after study of the 80 enrollees in the 2000-2001 course. Candidates will have direct observation of their COSK by independent assessor rating of videotaped interview with simulated patients and in objective structured clinical examinations. Knowing the existing strength and weakness of local general practitioners (GPs) will enable trainers to design better teaching programmes to improve our local GPs' COSK and thus improve patient care for the community. This validated method can then be further developed for teaching the larger class of undergraduate medical students. (MD00831)

Preventive Guidelines for Primary Care

- ✉ DICKINSON James Arthur
- ☐ 1 November 1999
- ❖ The Hong Kong College of Family Physicians

Preventive medicine is an important part of the role of primary care doctors. The number of possible personal preventive activities is increasing as technology develops, and new techniques are produced. However, activities undertaken in the name of prevention (especially screening) can do harm as well as good, so careful assessment of the activities, the appropriate ways to undertake them, the right population, and interval is needed to decide how they should best be used. Many are put into practice proper assessment. Both doctors and patients are hopeful that prevention is effective, and largely unaware of the caveats that must be observed to ensure that the net effect is positive.

This project will critically analyse preventive medicine recommendations, and summarize them with focus on the needs of Hong Kong, for the information of both doctors and the people of Hong Kong. (MD99453)

Comprehensive School Health Education Programme: Implementing the Concept of Health-promoting Schools to Enhance Quality Education

- ✉ LEE Albert • LEE Shiu Hung • TSANG Kwong Ka • TO Cho Yee
- ☐ 1 September 2000
- ❖ Quality Education Fund, HKSAR Government

Background: Health is vital to the achievement of quality education. The Healthy Schools Program (QEF 1998/1808) launched by the Chinese University of Hong Kong, together the three School Councils place particular emphasis on training and education, networking, community partnership, research and information dissemination. The programme also covered comprehensive school health surveillance on over 26,000 school children providing important data for future health education curriculum. The WHO has recommended a health-promoting school programme under which all members of the school community work together to enable healthy physical, emotional, and intellectual development of students.

Objectives: It is aimed to develop teacher training programme in health education, and also include other key objectives: establishing a district based task force in health education, school health research, publications, health education curriculum enrichment, and consultancy services in health education and promotion.

Targets and expected number of beneficiaries: Students, parents and teachers will all be benefited. For phase one, it is expected to train another 240 school health educators, i.e., from September 1,2000 to June 30,2003. It is also planned to train another 480 school health educators by 2007 during the 2nd and 3rd phases so half of the schools in H.K. will be beneficiaries, i.e., about 500,000 students and their parents. This project will continue to maintain a Youth Risk Behaviour Surveillance System for planning of youth health programmes. (MD20016)

New Initiatives for School Based Management to Promote Healthy Educational Environments: The Hong Kong Healthy Schools Award Scheme

- ✉ LEE Albert • LEE Shiu Hung • TO Cho Yee
- ☐ 1 April 2001
- ❖ Quality Education Fund, HKSAR Government

Background: School Based Management (SBM) is a major component of our reform in education. Its implementation involves all the six segments of a school's community: the headmasters, teachers, supporting staff, parents, students and others. Health promoting school, proposed and promulgated by the

World Health Organization (WHO), is a major domain in SBM to improve the school's physical and social environment, its curriculum, teaching and learning methods, and the personal and social development of students.

Objectives of the Scheme: (1) To promote educational achievements, physical and mental health; cumulating in an improvement to the quality of living of staff and students. (2) To promote staff development, parental education, involvement of whole school community, and linkage with different stakeholders so as to improve the health and well-being of the pupils, parents, staff, and the community at large.

Targets and Expected Number of Beneficiaries: 50 schools will participate in the Scheme at initial stage (2001-2) needs to give due attention to every minor detail in order to set up a good prototype to be replicable in other schools. Then another 50 schools will enroll at later stage (2002-4). 100 schools with over 80,000 pupils, 3,000 school staff, 80,000 families and numerous community organizations will benefit. Once established, the Scheme would then be used and replicated in other schools as Quality Education Programme since the training kits and procedures, and the protocols have been well developed. The scheme would enable those trained school health educators to apply and sustain their skills.

Methodology: The Award Scheme covers six key areas: the school health policy, the school physical environment, the school social environment, community relationships, personal health skills and health services; each with a number of components and benchmarks to be achieved. These will include staff development, parental education as well as healthy youth development. The project team will meet with the coordinating group of the school to help planning of health education and promotion strategies and activities, and support them in implementing their action plans. Training workshops and seminars would also be provided. Then project team will visit each school frequently to monitor the progress. The school must have achieved a required number of points to qualify for different levels of award.

(MD00896)

Utilization of Neuro-cognitive Science for the Improvement of Language Education in Hong Kong

✉ 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 (Institute of Chinese Studies (General)) • 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*

□ 1 September 2000

❖ Quality Education Fund, HKSAR Government

This project represents a concerted effort of a highly organised team of educators, teachers, scientists, doctors, psychologists, applied linguists, and engineers, who possess relevant expertise and are committed to the improvement of language education in Hong Kong. They are volunteers and will train a group of young university graduates to become competent researchers and leaders.

Members of the project understand fully that language is a process of the brain, and effective language learning (both mother tongue and foreign language) cannot be achieved without going through the right paths to the right areas of the brain. In the past decade, knowledge about the brain and its many functions has increased greatly and has been used productively in clinical settings. Yet few attempts have been made to use neuro-cognitive science for the enhancement of education in Hong Kong. The present project proposes to exploit this readily available scientific "gold-mine" for Hong Kong's language education.

The project will initially focus on three topics:

- (1) What do neuroscience and cognitive science data indicate as the best time for children to begin systematic learning of their native language and second languages, respectively?
 - (2) What are the approaches to acquiring proficiency in the first and second languages in different instructional media settings that appear to yield the best (qualitatively and quantitatively) results?
 - (3) What practical guidelines on effective language teaching/learning can be scientifically developed for policy makers, teachers, learners, and curriculum designers?
- (MD20022)

Provision of Service for Continuation Study of the Short-term Effects of Air Pollution on Morbidity in Hong Kong

✉ WONG Tze Wai • WUN Yuk Tsan Kyran Patrick • YU Tak Sun Ignatius • TAM Wai San Wilson

□ 1 February 2001

❖ Environmental Protection Department, HKSAR Government

To explore the association between air pollution and respiratory diseases in the community, a time series study is conducted to collect daily GP consultations for respiratory diseases among a network of GPs (general practitioners) and to correlate this with daily variations in air pollution concentrations. The study, initiated in January 2001, will be continued for one year, so as to improve the power of the study. Risk estimates of respiratory morbidities per unit increase in air pollutant concentrations will be calculated from Poisson regression models. A significant, positive association will be useful in assessing the population sick of illnesses posed by air pollution and the public health benefit of air pollution control. (MD20053)

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	Preventive Medicine Activities by Hong Kong Doctors (MD99007) ✍ DICKINSON James Arthur • CHAN Shiu Yee Cynthia • TANG Shao Fen Joyce
1999-00	Cholesterol Management in Primary Care in Hong Kong (MD99120) ✍ DICKINSON James Arthur • WUN Yuk Tsan Kyran Patrick
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 (School of Public Health) • CHEN Zhenyu (Biochemistry)
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)
1998-99	Work-Related Factors and Risk of Incident Low Back Pain in Hong Kong Nurses – A Cohort Study (MD98078) ✍ LAU Edith Ming Chu • LEUNG Arran* • CHAN Eric* • WONG C. M.* • LAM Dicky*
1998-99	Manual Handling and Low Back Pain among Nursing Home Staff in Hong Kong (MD98114C) ✍ LAU Edith Ming Chu • LEUNG Ping Chung (Dept of Orthopaedics & Traumatology) • WONG Louisa* • LEUNG Arran* • CHAN Wai Sing*
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
1998-99	(MD98068) ✍ LEE Shiu Hung • LEE Albert • TO Cho Yee
1989-90	Characterization of i P (BP88019) ✍ MARK Kai Keung
1999-00	The Study of the Short Term Effects of Air Pollution on Morbidity of the General Population and the Associated Cost of Illness (MD99125) ✍ 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*

1999-00 A Study on the Neurobehavioural Effects of Occupational Exposure to Organic Solvents Among Printing Workers in Hong Kong (MD99034)

RESEARCH OUTPUTS AND PUBLICATIONS

- <P991411> **Lee, S.H.** "Speech at the National Seminar 1999- 'Combating Drug Abuse in the 21st Century'". *Speech at National Seminar 1999* Singapore: National Council Against Drug Abuse, Singapore, 1999.04.17.
- <P997060> 李紹鴻. 編. 〈香港的醫療及基層健康服務〉. 《家庭醫學》第1期. 香港特別行政區: 中文大學出版社, 2000.
- <P000278> **Dickinson, James A. and Y. T. Wun.** "Complications of Hepatitis B in Southern Chinese People". *AUDGP 2000 - An International Conference on Primary Care* p.82. Bournemouth, UK: AUDGP, 2000.07.
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RESEARCH PROJECTS

Turbo Spectroscopic Imaging Evaluation of Dose-response Relationship in Irradiated Normal Brain Tissue after Arteriovenous Malformation Radiosurgery

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

□ 1 October 2000

❖ Research Grants Council (Earmarked Grants)

Stereotactic radiosurgery is a non-invasive alternative to surgical removal of a broad spectrum of intracranial lesions. It is an established method in the treatment of arteriovenous malformations, especially for deep lesions with complicated surgical access, in patients at high risk for, or unwilling to undergo neurosurgery. The principle of radiosurgery is to deliver in a single session a therapeutic dose of radiation to a target lesion whilst minimizing the irradiation to surrounding normal brain tissue by the use of arc and collimator arrangement. The surrounding tissue is irradiated invariably in different dose contents. Radiation induced complications, which can be disabling or even fatal, may ensue. While the clinical use of radiosurgery is increasingly rapidly, the radiobiology of high dose, single fraction irradiation remains poorly understood. The dose-response behaviour has not been adequately defined. Clinical assessment and conventional CT or MRI imaging have limitations as response assessment endpoints. The provision of a precise, objective, and quantifiable endpoint, as can be achieved with brain metabolite study on spectroscopic imaging, is of value in treatment planning as well as in furthering the understanding of radiosurgery induced changes. The researchers therefore propose to investigate the dose-response relationship in irradiated normal brain tissue by spectroscopic imaging in patients undergoing linear accelerator radiosurgery for malformation. (CU00104)

Are Western Skeletal Age Standards Applicable to Hong Kong Chinese?

✉ GRIFFITH James Francis • CHENG Chun Yiu Jack (Dept of Orthopaedics & Traumatology)

□ 1 January 2001

❖ Health Services Research Fund, Hospital Authority

Objective: To test the hypothesis that the skeletal age standards currently in use are not applicable to Hong Kong (HK) Children.

Subject: 2000 hand wrists radiographs of normal subjects of differing age groups attending Accident and Emergency with suspected wrists/hand fracture.

Intervention: Assign two skeletal ages using two established reference scoring systems (Twenty bone Tanner and Whitehouse method and Greulich and Pyle method) for the radiographs of each normal subject. Record subject's chronological age and gender.

Main outcome measures: Compare assigned skeletal ages with subject's chronological age and assess difference for each age subgroup and gender.

Results: Define the appropriate level of adjustment for each age subgroup gender for the present skeletal age standards (TW2 and Greulich and Pyle) in order to apply to present day HK children. Produce appropriate HK standards.

Conclusion: Western skeletal age standards may need re-adjustment for the local population. Such re-adjustment can influence predication of adult height, diagnosis and treatment of hormonal diseases and the timing of orthopaedic and dental procedures in the skeletally immature.

(MD20014)

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*

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RESEARCH PROJECTS

Establishment of a Catalogue of Chinese-specific Genetic Markers for Obesity, Diabetes and Diabetic Kidney Disease

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

☐ 1 August 2000

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The project aims to establish a catalogue of Chinese-specific genetic markers implicated in the development of obesity, diabetes and diabetic kidney disease which are relevant to Hong Kong Chinese. This will be done by identifying mutations and polymorphisms in known candidate genes and genome-wide search for novel diabetes-related gene loci in unaffected and affected sibling pairs. Identification of these genetic markers unique to Chinese will be used for further development into microchips for diagnostic purposes and new pharmaceutical agents. This project will benefit the 0.5 million of diabetic subjects in Hong Kong, many of them remain undiagnosed. These benefits can be extended to the 18 million diabetic subjects in Mainland China.
(MD20020)

Effects of COX-2 Inhibition on Ulcer Healing and Prevention of Recurrent Ulcer Hemorrhage in High-risk NSAID Users

✉ CHAN Ka Leung Francis • SUNG Joseph Jao Yiu

☐ 1 January 2001

❖ CUHK Research Committee Funding (Direct Grants)

Nonsteroidal anti-inflammatory drug (NSAID) is one of the most important causes of peptic ulcer bleeding in Hong Kong. The therapeutic and adverse effects of NSAIDs are mediated by inhibition of the enzyme cyclooxygenase (COX). The recent discovery of the two isoforms of COX (COX-1 and COX-2) has led to the development of a new class of NSAID - COX-2 specific inhibitors. These drugs offer the prospect of effective anti-inflammatory control (inhibition of COX-2) with minimal gastrointestinal side effects (inhibition of COX-1). Previously the researchers have shown that prophylactic acid suppressive therapy using proton-pump inhibitor (PPI) can

markedly reduce recurrent ulcer bleeding in high-risk NSAID users. Whether COX-2 specific inhibitors can achieve similar therapeutic advantage in high-risk subjects remains to be verified.

The current proposal aims to investigate whether COX-2 specific inhibitor alone can reduce recurrent ulcer bleeding in high-risk patients. Chronic NSAID users with a past history of ulcer bleeding will be randomized to receive conventional NSAID plus PPI or COX-2 specific inhibitor plus placebo. The primary endpoint is the cumulative incidence of recurrent ulcer bleeding at 6 months. The results of these studies will be an important guide to formulate strategies for ulcer prevention in high-risk NSAID users.

(MD00881)

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

✉ CHOW Chun Chung Francis • COCKRAM Clive Stewart • CHAN W. B.*

☐ 1 August 2000

❖ Novo Nordisk Health Care (Asia Pacific) Pte Ltd

This is a randomised, double-blind, 2-period, cross-over, multicentre, multinational trial. After screening and obtaining informed consent, the subjects will be randomised to the first treatment period of 12 weeks (0 w) receiving either biphasic insulin aspart 30 (BIAsp 30) or biphasic human insulin 30/70 (BHI 30/70)-Period I. At the final visit of period I (12 w) the subject will change trial product, from BIAsp 30 to BHI 30/70 or visa versa and start the second treatment period of 12 weeks - Period II. Trial product will be discontinued at the end of period II (24 w), and the subjects will be offered treatment at the discretion of the Investigator.

Primary Objective:

To compare the long-term glycaemic control of BIAsp 30 and BHI 30/70 in Type 2 diabetics by HbA_{1c} assessment after 12 weeks of treatment.

Secondary Objectives:

- (1) To compare BIAsp 30 and BHI 30/70 with respect to incidence of hypoglycaemic episodes (over-all and nocturnal) during 12 weeks of treatment.
- (2) To compare BIAsp 30 and BHI 30/70 with respect to immediate glycaemic control as assessed by 8-point glucose profiles after 12 weeks of treatment.
- (3) To compare BIAsp 30 and BHI 30/70 with respect to the Treatment Satisfaction as assessed by the subject after 12 weeks of treatment.

- (4) To compare the economic implications of the two treatments as assessed by resource utilisation measures after 12 weeks of treatment.
(MD20012)

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)

- ✉ CHOW Chun Chung Francis • COCKRAM Clive Stewart • Ozaki R*
□ 1 February 2001
❖ Merck Sharp & Dohme (Asia) Ltd

Study objective: To compare the antihypertensive efficacy of losartan 50 mg + hydrochlorothiazide (HCTZ) 12.5 mg versus losartan 50 mg titrated as needed to losartan 100 mg in lowering mean trough sitting diastolic blood pressure (SiDBP) to goal (< 90 mm Hg) after 4 weeks of first-line double-blind therapy in patients with severe hypertension (confirmed trough SiDBP \geq 110 mm Hg).

Study design and duration: This is a prospective, double-blind, randomized, losartan-controlled, clinical study to evaluate the antihypertensive efficacy and safety of regimens of losartan + HCTZ combination therapy (losartan 50 mg + HCTZ 12.5 mg \rightarrow losartan 100 mg + HCTZ 25 mg) versus losartan monotherapy (Losartan 50 mg \rightarrow losartan 100 mg \rightarrow losartan 150 mg) in patients with severe hypertension (SiDBP \geq 110 mm Hg). The study design includes a baseline/washout period and 6 weeks of double-blind therapy. Patients will be titrated as necessary at 2-week intervals based upon their blood pressure.
(MD20059)

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

- ✉ HUI Shu Cheong David • CHENG Gregory
□ 1 September 2000
❖ Research Grants Council (Earmarked Grants)

Obstructive sleep apnoea syndrome (OSA) is a common disorder affecting 2 to 4% of the middle-aged adults. Repetitive episodes of obstructive respiratory events cause sleep fragmentation and, in more severe cases, respiratory failure. Excessive daytime sleepiness is a major consequence of OSA and results from fragmented sleep and micro-arousals associated with obstructive respiratory events. Community based studies have pointed towards an association between OSA and systemic hypertension,

independent of age and body mass index, with a higher incidence of stroke and acute myocardial infarction in patients with snoring and OSA. The mechanism for this linkage is not fully determined but surges in sympathetic nerve activity are seen at the end of each apnoeic episode accompanied by large rises in systemic arterial blood pressure. The increased levels of muscle sympathetic nerve activity are diminished by nasal continuous positive airway pressure (CPAP) therapy. Catecholamines play an important role in platelet activation and aggregation and the links between cardiovascular events and OSA may involve increased platelet activation and aggregation during sleep. This study aims to assess the degree of platelet activation, fibrinolysis, activities of the sympathetic nervous system and the renal kallikrein-kinin system before and after nasal CPAP treatment in the OSA patients.
(CU00147)

Clinical Evaluation of A Ben-chair Monitoring System in Rehabilitation ‘Wards for the Elderly

- ✉ KWOK Chi Yui Timothy • WOO Jean • TSUI Hung Tat (Dept of Electronic Engineering)
□ 1 October 2000
❖ S K Yee Medical Foundation

Elderly people in hospitals and old age homes are at risk of falls and fractures. In the attempt to prevent falls, nursing staff in hospitals or old age homes often resort to physical restraints which can lead to increased confusion, agitation and physical dependency.

Electronic systems monitoring pressure sensors placed in beds and chairs can act as alarms to alert nursing staff about the movement of elderly patients at risk of falls. It is envisaged that these devices can reduce the need for physical restraints and prevent falls at the same time. However the acceptance of these device by nursing staff has not been evaluated in Hong Kong. Moreover the effectiveness of such monitoring systems in improving clinical outcomes in elderly patients has not been evaluated. The researchers therefore propose to perform a randomised-controlled trial to examine the clinical effectiveness of a bed-chair monitoring system in two rehabilitation wards for the elderly.

A bed-chair monitoring system capable of activating a visual or auditory alarm when the monitored patient leaves his/her bed or chair will be installed in two rehabilitation wards. 180 patients who can sit out but at risk of falls are randomised into monitoring and control groups. The subjects are reviewed daily until discharge. The primary end point is no restraint for twenty-four hours. Secondary end-points are full continence, AMT, mobility score, falls, length of stay and old age home placement.
(MD20023)

Quality of Life and Handicap of Stroke Survivors in Hong Kong

✉ 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*

☐ 1 May 2001

❖ Health Services Research Fund, Hospital Authority

Objective: To investigate the determinants of handicap and quality of life (QOL) in stroke survivors, and to identify risk factors for deteriorating handicap and QOL in the longer term.

Design: Cohort study

Subject: 300 consecutive patients with first disabling stroke discharged from hospital

Method: Demographic characteristics, stroke severity, pre-morbid Rankin score were recorded within two days of stroke. All subjects are followed-up at three, six and twelve months at their residence.

At follow-up, subjects are interviewed to obtain Barthel index, Instrumental activity of daily living (IADL), London handicap scale (LHS), the Hong Kong Chinese version WHO QOL questionnaire (short form) and Geriatric depression scale. Physical exercise habit is enquired by a questionnaire. Psychological status of caregiver is assessed by General health questionnaire.

Data analysis: The association of measured variables with LHS and QOL scores are examined by stepwise multiple regression. The differences in LHS and QOL scores between the three follow-up assessments are examined by Student Paired to test. Risk factors of deterioration in LHS and QOL are examined by stepwise multiple logistic regression. The associations between LHS and QOL and between IADL and QOL over the one-year period are assessed by path analysis and the multilevel approach. (MD20055)

Trefoil Peptides, Cyclooxygenase-2 & Gastric Carcinogenesis

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

☐ 1 April 2001

❖ CUHK Research Committee Funding (Direct Grants)

Although gastric cancer is still the leading cause of cancer mortality in China, the gastric carcinogenesis mechanism remains unknown. This study examines the role of trefoil peptides (TFF) and cyclooxygenase-2 (COX-2) in the development of gastric cancer. Trefoil peptide family domain peptides are synthesized and secreted by mucus-secreting cells of the intestine that play a pivotal role

in maintaining the mucosa integrity and repair mechanism. COX-2 is an inducible enzyme responsible for the conversion of arachidonic acid to prostaglandins. Interestingly, both TFF and COX-2 have been linked to the carcinogenesis process. As yet, their interactions and significance in gastric carcinogenesis remains largely unknown. The results from these experiments will bring new insight into the role of different forms of trefoil peptides, and their potential interactions with COX-2, in different stages of gastric carcinogenesis. With the availability of potential therapeutic agents that can modulate these two factors, this result may ultimately translate into clinical applications for the chemoprevention of gastric cancer.

(MD00526)

Elucidation of the Production and Action Mechanisms of Novel Proinflammatory Cytokines IL-17 and IL-18 in Systemic Lupus Erythematosus

✉ LI Kwok Ming Edmund • LAM Wai Kei Christopher (Dept of Chemical Pathology) • WONG Chun Kwok (Dept of Chemical Pathology)

☐ 1 November 2000

❖ CUHK Research Committee Funding (Direct Grants)

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by the activation of T and polyclonal B lymphocytes, production of autoantibodies, and formation of immune complexes causing tissue and organ damages. Abnormal T helper (Th) cell cytokine response has been shown to be involved in the pathogenesis of autoimmune diseases. However, Th cytokine response in SLE has been found to be very complex and their production mechanism requires further investigation.

Two novel proinflammatory cytokines interleukin (IL)-17 and IL-18 have recently been identified and shown to be important for the activation of natural killer cells (NK) and cytotoxic T lymphocytes (CTL) for Th1 response. We have found and published that plasma levels of IL-17 and IL-18 are significantly elevated and the elevation of plasma IL-18 concentration is correlated with disease activity in SLE patients. However, the *in vitro* production mechanisms of IL-17 and 18 in SLE have not yet been elucidated. In the present project, the *in vitro* production of IL-17 and 18 from whole blood cells upon activation by T cell and monocyte mitogens will be investigated and the expression of IL-17 and 18 receptors and Fas ligand on target cells, NK and CTL will also be studied. Results would be useful to further elucidate the production and action mechanisms and pathogenic role of these novel proinflammatory cytokines in SLE, thereby providing a biochemical basis for these cytokines to serve as the

markers for SLE disease activity and efficacy of treatment.
(MD00306)

Purification of a Novel Muscle Healing Protein That Enhances Muscle Repair and Regeneration

✉ LI Ming • CHAN Kai Ming (Dept of Orthopaedics & Traumatology) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)

□ 1 January 2001

❖ CUHK Research Committee Funding (Direct Grants)

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

In their previous studies, the researchers identified and partially purified a protein fraction, probably containing muscle healing protein, ranging from 35-50 kDa from rat muscle extract that enhanced the proliferation and differentiation of cultured myoblast (C2C12) and promoted skeletal muscle repair and regeneration in rat model. In this 35-50 kDa fraction, it contained about 15 different proteins confirmed by SDS-PAGE. N-terminal sequencing data of this fraction in conjunction with functional testing in myoblast culture system have excluded 5 abundant proteins, and further Heparin affinity chromatography has excluded another 4 proteins from being the candidate of the unknown muscle healing protein(s). Currently the myogenic fraction with about 6 proteins are under investigation

In this study, the researchers will further isolate this novel muscle healing protein. The function of the purified muscle healing protein will be studied using their established their model. There is far-reaching clinical application in providing a new approach for the treatment of skeletal muscle injuries. With the local injection of exogenous muscle healing protein, it will significantly increase the local concentration to such a level that the satellite cells, previously quiescent, could be triggered to proliferate and fuse with previously injured muscle fibers during the repair process or completely replace them by forming new myotubes.

(MD00386)

Relationships of Peroxisomal Proliferator Activated Receptor- γ Gene Polymorphisms with Insulin Resistance and Obesity in Chinese Patients with Type 2 Diabetes Mellitus

✉ NG Chor Yin • CHAN Chung Ngor Juliana • COCKRAM Clive Stewart • CRITCHLEY Julian A J H#

□ 1 June 2001

❖ CUHK Research Committee Funding (Direct Grants)

Insulin resistance with coexisting obesity, is a characteristic feature of Type 2 diabetes and other components of the metabolic syndrome. Peroxisomal proliferator activated receptor- γ (PPAR γ) is a nuclear receptor that plays an important role in adipocyte differentiation, as well as lipid and glucose homeostasis. It also counter-regulates the expression of leptin and tumor necrosis factor- α , markers for obesity which are secreted from adipocytes.

Recent studies in Caucasians have identified a missense and a silent polymorphisms of the PPAR γ gene, Pro12Ala and codon 447 C \rightarrow T, to be associated with either an altered risk for Type 2 diabetes or other cardiovascular diseases, as well as indices for obesity and insulin resistance, including body mass index and leptin levels.

In view of the important physiological role of PPAR γ in the regulation of glucose and lipid homeostasis, as well as the benefits of thiazolidinediones (e.g. rosiglitazone) in improving insulin sensitivity in diabetic patients, the researchers aim to investigate the association of gene polymorphisms in PPAR γ with insulin resistance and obesity in Type 2 diabetes. Five hundred Type 2 diabetic patients with a duration of disease \leq 5 years and 200 healthy control subjects will be recruited for association study. In addition, insulin resistance and obesity indices will be compared between the carriers of different genotypes. In an ongoing preliminary study, the association of PPAR γ polymorphism with the efficacy of rosiglitazone treatment in 45 patients followed up for 6 months will be examined.

No such data have been reported in Chinese diabetic patients. This study will assist the risk stratification of diabetes and allow individualisation of treatment for patients with different genetic susceptibilities.
(MD00615)

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

✉ SANDERSON John Elsby • TOMLINSON Brian • FUNG Wing Hong • CHIU Chun Wai Roman • Chan Kin Yin*

□ 1 December 2000

❖ Merck Sharp & Dohme (Asia) Ltd

The primary object of this study is to compare the effect of a Losartan/Hydrochlorothiazide combination with Amlodipine plus Hydrochlorothiazide for the treatment of isolated systolic hypertension (systolic blood pressure 160-200 mmHg and diastolic blood pressure > 65 and < 90 mmHg). This is an international Collaborative randomized double blind study. Isolated systolic hypertension is common in the elderly and occurs in approximately 15% of people > 60 years but it is not yet clear what is the best treatment and if the newer angiotension II receptor antagonists are more effective with fewer side-effects.
(MD20037)

Omapatrilat versus Enalapril Randomized Trial of Utility in Reducing Events (OVERTURE)

✉ SANDERSON John Elsby • YEUNG Leata Y.C.* • CHAN Kit Wan Skiva

☐ 1 May 2001

❖ Bristol-Myers Squibb Pharmaceuticals

Omapatrilat is a highly selective, competitive inhibitor of both the angiotensin-converting enzyme (ACE) and of neutral endopeptidase, and thus would be expected to produce hemodynamic, neurohormonal and prognostic effects greater than that expected from ACE inhibition alone. The superiority of omapatrilat over ACE inhibition has been demonstrated in experimental studies and in intermediate-term clinical trials in subjects with heart failure, and thus would be expected to be confirmed in a long-term, large-scale trial designed to evaluate the effect of omapatrilat on major clinical events.

The objectives of this study are to determine in subjects with heart failure whether omapatrilat is superior to enalapril in prolonging survival, delaying the progression of heart failure (as reflected by a decrease in the need for hospitalization for heart failure), and improving symptoms and clinical status. In addition, the study will evaluate the safety and tolerability of omapatrilat therapy in subjects with chronic heart failure.

This is a multicenter, randomized, double-blind, and active-controlled, parallel groups study with an average follow-up >23 months.
(MD20068)

Identification and Isolation of a Chinese Herbal Medicine that Could Enhance Cardiac Muscle Revascularization and Healing Following Heart Muscle Infarction

✉ SANDERSON John Elsby • LI Ming

☐ 1 June 2001

❖ CUHK Research Committee Funding (Direct Grants)

Cardiac muscle healing following infarction is slow and incomplete and the fibrous replacement of the damaged cardiac muscle is inevitable. To date, there is no effective therapeutic treatment for cardiac muscle infarction. In their previous studies, the researchers screened and identified a compound collection of a Chinese herbal medicine (CCHM) that could significantly enhance myogenic cell proliferation and differentiation in cell culture and significantly promote revascularization and muscle healing in rat skeletal muscles. In this study, the researchers propose to investigate the ability of this CCHM to promote cardiac muscle revascularization and healing following cardiac muscle infarction in animal models. Coronary artery ligation of rat heart will be used to induce muscle damage. This CCHM or placebo will be injected to the relevant site of the cardiac muscle 7 days before the coronary artery ligation or right after the ligation. The healing processes of infarcted cardiac muscle including revascularization, infarction size and severity of the affected heart will be evaluated by performing histology studies, immunohistologic investigations with PCNA and anti-angiogenetic factors, such as VEGF, PDGF and bFGF immunostainings at the time points of 3, 7 and 14 days after coronary artery ligation.

(MD00667)

Eradication of H. Pylori in Gastro-esophageal Reflux Disease: A Clinical and Pathophysiological Study

✉ SUNG Joseph Jao Yiu • WU Che Yuen Justin • CHAN Ka Leung Francis

☐ 1 January 2001

❖ CUHK Research Committee Funding (Direct Grants)

With the decline in prevalence of HP infection in the last few decades, however, an alarming increase in incidence of esophageal cancers related to gastroesophageal reflux disease (GERD) was noticed in the West. GERD was not a common disease in Chinese but recent data suggest a rising trend in Asia. The researchers' previous study showed a strong negative association between HP infection and GERD. The researchers have also found that among patients with GERD, those who are infected by HP (about one-third of them) tend to have milder disease. This evidence supports the notion that HP PROTECTS against GERD. However, the mechanisms of this protective effect of HP are uncertain. The aim of this project is to study the CLINICAL and PHYSIOLOGICAL effects of HP eradication in GERD. Patients with co-existing HP and GERD will be randomized to receive either PPI or anti-HP therapy prior to PPI. Healing of esophageal erosions and relief of GERD symptom are compared between the two groups. In a separate

group of patients with co-existing HP and GERD, esophageal manometry, 24-h ambulatory pH monitoring, antro-duodenal manometry and gastric emptying will be studied before and 6-months after eradication of HP.
(MD00307)

A Randomised, Double-blinded, Placebo-controlled Trial of Lamivudine Treatment in HBeAg Negative Chronic Hepatitis B Patients (in Asia)

✉ SUNG Joseph Jao Yiu • CHAN Lik Yuen • CHAN Ka Leung Francis • LEUNG Wai Yee Nancy • HUI Y.*

☐ 1 February 2001

❖ Glaxo Wellcome China Limited

This is a randomised, double-blind, placebo-controlled, multi-centre trial evaluating the efficacy and safety of 2 years lamivudine therapy versus placebo in the treatment of HBeAg negative patients in Asia with active liver disease.

Evaluable subjects will be randomised on a 2:1 basis to receive either lamivudine 100mg orally once daily or matching placebo. Treatment will be for 24 months. Post-treatment, subjects will be observed for sustained response to lamivudine for a further 6 months.

Approximately 200 evaluable subjects will be recruited (male and female subjects, > 18 years of age with HBeAg negative chronic hepatitis B) from centres in Hong Kong and mainland China and will be seen as out-patients for the duration of the study.

The primary efficacy endpoint is the proportion of patients with complete anti-viral response (normalisation of ALT, ie. <1xULN and disappearance of HBV DNA, ie. <0.5Meq/mL, lower limit of detection) at Month 24. The secondary endpoints include: proportion of patients with partial anti-viral response (normalisation of ALT but still detectable HBV DNA by NAXCOR assay) at Month 24, histological improvement at Month 24, proportion of patients with complete and partial antiviral response post-treatment (at Month 30), HBeAg seroconversion and safety comparisons of clinical adverse events and laboratory abnormalities.
(MD20060)

Correction of Metabolic Acidosis in Continuous Ambulatory Peritoneal Dialysis Patients with Borderline Dialysis Adequacy-effect on Nutritional Status, Systemic Inflammatory Response & Patient Morbidity

✉ SZETO Cheuk Chun • Li Kam Tao Philip*

☐ 1 December 2000

❖ Health Services Research Fund, Hospital Authority

Objective: To study the effect of metabolic acidosis, dialysis adequacy, and systemic inflammatory response in nutritional status and morbidity of patients receiving continuous ambulatory peritoneal dialysis (CAPD).

Design: Randomised prospective control trial.

Setting: Renal unit of a university teaching hospital.

Subjects: End-stage renal failure patients receiving CAPD, with weekly Kt/V 1.6 to 1.9 and metabolic acidosis (plasma bicarbonate < 24 mmol/l).

Interventions: Patients will be randomised to receive either oral sodium bicarbonate 0.9 gm tds or placebo. The study will be double-blinded.

Main outcome measures: Patients will be followed for 1 year. Nutritional parameters including serum albumin, subjective global assessment, normalised protein nitrogen appearance, lean body mass (as assessed by creatinine kinetics) and anthropometry measurements will be monitored. Systemic inflammatory markers such as serum C-reactive protein and IL-1 β will be assayed. Number of days of hospitalisation, episodes of peritonitis, and overall patient survival will be recorded during study period.

Expected result: Nutritional parameters are expected to improve with bicarbonate therapy. The magnitude of improvement in nutrition, as well as patient morbidity, will be compared with placebo.
(MD20027)

Molecular Biology of Hypertension: A Study Investigating Genetic Markers and Possible Underlying Pathogenic Mechanisms of Hypertension in Chinese

✉ TOMLINSON Brian • CHAN Chung Ngor Juliana • THOMAS Neil G

☐ 1 October 2000

❖ Research Grants Council (Earmarked Grants)

Essential or primary hypertension results from an interaction of environmental and genetic factors. It is common in the Hong Kong population, resulting in considerable morbidity and mortality. Several genes associated with hypertension or its underlying pathophysiological mechanisms have been identified recently. The researchers have already examined associations between blood pressure and certain candidate gene polymorphisms, including those for components of the renin-angiotensin system in sibling and population-based studies. During these investigations the researchers have recruited over 200 sibling pairs, over half of which are discordant for hypertension, but larger numbers are required to perform a conclusive sibling pair analysis.

In this project more siblings will be recruited to achieve an adequate number for effective determination of genetic contributions to this complex disorder and this will facilitate more reliable evaluation of the contribution of the genetic polymorphisms which have already been examined in

the earlier cohorts. The researchers will characterise the subjects in terms of obesity, insulin resistance, lifestyle factors, family history and biochemical parameters to provide a well-defined cohort of siblings, with and without hypertension, which will allow the use of the latest genetic techniques to identify susceptibility loci for hypertension and its underlying pathogenic factors in this Chinese population. The results should lead to an improvement in the identification, prevention and treatment of this major disorder.
(CU00095)

Spatial Redistribution of Signaling Molecules Following Insulin Stimulation in Rat Skeletal Muscle Cells

- ✉ TONG Peter Chun Yip • LEE Shao Chin (Dept of Clinical Oncology)
- ☐ 1 June 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

The binding of insulin to its receptor activates cascades of signaling pathways and leads to various metabolic and mitogenic effects in specific target tissues. Redistribution of signaling molecules to specific intracellular compartments may contribute to the specificity of insulin action. The underlying mechanisms for the intracellular traffic of signaling molecules are not well defined. The actin cytoskeleton provides structural support and participates in various cellular functions. The researchers hypothesize that the remodeling of actin filaments by insulin facilitates the delivery of signaling proteins to specific locations for interactions with downstream targets. They propose to use two-dimensional gel electrophoresis to identify proteins in intracellular compartments in rat skeletal muscle cell line, L6 myotubes. Proteins in subcellular fractions of L6 myotubes will be separated by use two-dimensional gel electrophoresis. Movement of proteins between fractions following insulin stimulation will be visualised by the process of subtraction. Specific signaling proteins will be identified by immunoblotting. The participation of the actin cytoskeleton in redistribution of signaling proteins will be assessed by perturbing the microfilaments with chemical agents. Novel proteins involved in the transduction of insulin signal may be identified. The knowledge gained from this study will advance our understanding of insulin action in skeletal muscle.
(MD00720)

Epidemiology of Cardiovascular Problem in Chinese Continuous Ambulatory Peritoneal Dialysis Patients: Prevalence, Severity & Risk Factors

- ✉ WANG Yee Moon Angela • SANDERSON John Elsby • CHAN Kam Wing (Dept of Diagnostic Radiology & Organ Imaging) • LUI Siu Fai
- ☐ 1 July 2000
- ❖ Health Services Research Fund, Hospital Authority

Background: There are currently around 3000 patients receiving dialysis treatment in HK among which 80% are on CAPD and the remaining 20% on hemodialysis (HD). The annual mortality rate in the dialysis population is around 11% and cardiovascular causes accounted for at least 40% of the total mortality. According to recent data from the HK Renal Registry, there is also a significant rising trend in the incidence of cardiovascular deaths in dialysis patients over the years.

Aims: This study aims to determine the prevalence and nature of cardiovascular disease (CVD) in Chinese CAPD patients and to identify risk factors that best predict the CVD outcomes. It will also provide baseline data for future prospective studies and allow international comparisons.

Sample: All CAPD patients (n around 300) from a regional dialysis centre in HK will be studied.

Method: A cross-sectional study design will be used to determine the prevalence, severity and risk factors of coronary artery disease (CAD), congestive cardiac failure (CCF), left ventricular hypertrophy (LVH) and ventricular dysfunction in our CAPD population.

Outcome: This study will provide a better understanding of the prevalence and risk factors for CVD in our local CAPD patients and will help to define future cardiac disease prevention programmes and intervention strategies in this population. The data will also form the basis for further prospective study.

(MD20005)

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

- ✉ WONG Ka Sing Lawrence • FU Yat Pang Michael
- ☐ 1 January 2001
- ❖ Pfizer Corporation

Recent advances in the treatment of migraine headache emphasizes the use of a new class of drugs, the “triptan”. Eletriptan is the latest drug in this class available for clinical use. However, its safety and efficacy have not been investigated in the Asian populations. In this randomized, double-blind, placebo-control trial involving a number of countries in Asian, the efficacy of eletriptan will be tested.

(MD00343)

A Prospective Study of the Long Term Outcome of Patients with Intracranial Arterial Occlusive Disease

- ✉ WONG Ka Sing Lawrence • LAM Wai Man Wynnie (Dept of Diagnostic Radiology & Organ Imaging) • LI Huan • KAY Li Chi Richard
- 1 January 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

In China, stroke kills more than 1.2 million people and disables millions more every year. Recent successes in stroke prevention emphasize specific remedies that target the underlying stroke mechanisms such as carotid stenosis and atrial fibrillation. In Chinese, intracranial large artery occlusive disease is the most common vascular cause of stroke. Data from a previous RGC-funded study on stroke patient showed that the presence and the extent of occlusive vessels are independent predictors of vascular event or death in the 6 months following cerebral ischemia. However, it remains unclear whether these adverse outcomes extend beyond this relatively short period. Furthermore, the relationship of progression of stenosis on transcranial Doppler (TCD) to clinical events remains uncertain. In this study, the researchers aim to extend the follow up period of these 700 patients to 5 years. This study will provide important data on the long term prognosis and progression of intracranial occlusive disease and on the differences in outcome of patients with or without progression on TCD. Such data are indispensable for the planning of future therapeutic study and for the assessment of the impact of intracranial occlusive disease on our population. (MD00869)

Effects of the Ultrasound Contrast Enhancing Agent Levovist on the Detection of Intracranial Arteries and their Stenoses by Transcranial Doppler Ultrasound

- ✉ WONG Ka Sing Lawrence • E. B. RINGELSTEIN* • Tjark Hansberg*
- 1 January 2001
- ❖ Germany/Hong Kong Joint Research Scheme

The investigators in Hong Kong have an established track record in studying the prevalence, determinants and significance of intracranial large artery stenosis in Chinese by TCD. However, the lack of good acoustic window hinders more accurate diagnosis of intracranial stenoses, especially the middle cerebral arteries. The German investigators have an established track record in studying the use of contrast enhancing agent in clinical use. However,

intracranial large artery stenosis is a common disease in Germany. By combining the expertises in both Hong Kong and Germany investigators, the researchers aim to use the start-of-the-art technology in improving the management (especially prevention) of stroke which is estimated by the WHO to cause more than 2 million deaths by 2020 in China. (MD20054)

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

- ✉ WONG Ka Sing Lawrence • HUI Andrew Che Fai • MOK Vincent*
- 1 June 2001
- ❖ Janssen Pharmaceutica

Dementia is a major problem in Hong Kong and stroke is one of the leading causes of dementia. The results of a number of Phase III trials indicate that treatment with galantamine, a reversible cholinesterase inhibitor, can improve cognition. The efficacy of cholinesterase inhibitor for the treatment of vascular dementia have not been confirmed. The safety and efficacy of galantamine will be evaluated in this randomized, double-blind, placebo controlled trial in subjects with Vascular Dementia. After a 30-day, single-blind, placebo run in phase, subjects will be titrated, over a period of 4 weeks, to target doses during the 26-week double-blind period. Safety will be tracked by means of adverse event reports, laboratory parameters, physical exam and ECG. Efficacy will be evaluated by means of the ADAS-cog and other neuropsychological Inventory. Pharmacokinetics of galantamine will be assessed. (MD00553)

Development of the Chinese MNA

- ✉ WOO Jean • KWOK Chi Yui Timothy • HUI E.*
- 2 January 2001
- ❖ Nestec Limited

There is a high prevalence of malnutrition among the elderly in residential care settings. Therefore a simple nutrition screening tool that may be used by any health care worker would be useful in ensuring that this aspect of care is not neglected. Among Caucasians, the Mini-Nutritional Assessment is a well established tool. However it requires adaptation before it can be tried in the Chinese population. This study has the following objectives:

- (1) Develop the Chinese MNA 2000 for the Chinese elderly population in hospitals and nursing homes
- (2) Conduct a feasibility study to pretest the validity and reliability of the Chinese MNA 2000 in order to

determine the modifications necessary before a full-scale study

(3) Conduct a full scale study to test the validity of the Chinese MNA 2000 in order to establish the criteria for elderly Chinese at risk for malnutrition or who are malnourished in order to implement nutritional intervention programs.
(MD20041)

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

✉ WOO Kam Sang • SANDERSON John Elsby • YIP Wai Kwok Gabriel

□ 1 February 1998

❖ The Medicines Company

Background: Acute myocardial infarction (AMI) is an ominous presentation of coronary artery disease with case fatality around 20% in Hong Kong hospitals. Thrombolytic therapy (mainly streptokinase in Hong Kong) in combination with heparin has been a major advance but patients' outcome remained suboptimal (bleeding complications around 10% and 30 days mortality 15%). Hirulog is a novel but more clot-specific antithrombin, with less bleeding complication and higher patency of infarct-related artery in preliminary studies.

Objective of Study: To compare the efficacy and tolerability of Hirulog with heparin as adjunctive therapy with streptokinase in AMI patients.

Methods: AMI patients within 6 hours of symptom onset will be randomized, in open fashion, to take intravenous Hirulog (0.25mg/kg bolus, 0.5mg/kg/hr for 12 hours and 0.25mg/kg/hr for 36 hours) or intravenous weight-adjusted heparin (5000u bolus, 800-1000u/hr infusion x 48 hours) in combination with intravenous streptokinase (1.2 megarmit over 30-60 minutes) starting after administration of Hirulog/heparin bolus. Clinical progress and coagulopathy profiles were monitored with prothrombin time (INR) kept at 2-3 level. A prodromal angina substudy will be performed to evaluate the influence of prodromal angina symptom on clinical outcome and preservation of left ventricular function.

Primary endpoint: 30 days mortality

Secondary endpoint: Bleeding complications

Sub study endpoint: Prevalence of prodromal angina, difference in ST segment changes

Sample Size: World wide 17,000

Hong Kong (PWH) 50

Significance of Study: This project will evaluate the efficacy and tolerability of a novel adjunctive therapy

in combination with SK in treatment of AMI, which if confirmed will benefit AMI patients in Hong Kong (MD97341)

Tolerability and Clinical Application of Platelet Glycoprotein IIb-IIIa Inhibitor (Epiibatide) Therapy in Hong Kong Chinese

✉ WOO Kam Sang • SANDERSON John Elsby • CHAN Wai Man Wilson • TSE Kin Kee • CHAN C K* • CHAN S K*

□ 1 December 2000

❖ Schering-Plough (HK) Ltd.

Background: Acute coronary syndrome (ACS) is a serious manifestation of coronary artery disease. Plaque rupture with platelet aggregation and triggering of coagulation cascade of the coronary artery is the key event in pathogenesis of ACS. Antiplatelet and antithrombin agents have been advocated, including aspirin, ticlopidine, clopidogrel, unfractionated and low-molecular weight heparin and more recently specific platelet receptor glycoprotein IIb-IIIa inhibitors, epiibatide have been found more effective in treatment of ACS and management of PCI when added to standard therapies. Epiibatide has been an approved marketed item in Hong Kong since April 2000. Documentation of the safety and efficacy of glycoprotein IIb-IIIa inhibitor like epiibatide, would be of much clinical relevance.

Objective of Surveillance Programme: To monitor the tolerability of intravenous glycoprotein IIb-IIIa inhibitor (epiibatide) according to standard regimen in ACS and non-urgent PCI in Hong Kong Chinese.

Methods: 20 patients with ACS and 40 patients undergoing percutaneous coronary intervention will be studied. For 20 ACS subjects, patients will be give intravenous bolus of epiibatide 180 µg/Kg as soon as possible following diagnosis, followed by a continuous infusion of epiibatide of 2 µg/Kg/min until hospital discharge or up to 72 hours. For 20 PCI subjects, intravenous epiibatide will be given standard treatment regimen, 180 µg/Kg body weight bolus, immediately followed by 2 µg/Kg/min infusion, a second bolus (180 µg/Kg) 10 min later, and infusion for up to 18-24 hour in PCI. For patients with plasma creatinine between 180-360 µmol/L, a 180 µg/Kg bolus and reduced infusion at 1.0 µg/kg/min infusion will be administered. Bleeding complications, haemetological profiles, units of blood transfusion, blood pressures and heart rate (primary monitor endpoints), as well as recurrence of angina, acute myocardial infarction (including non-Q infarct) and requirement of bailed-out PCI within 30 days (secondary monitor endpoints) will be monitored.
(MD20063)

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

Edition Title/Investigators

1997-98 A Multicentre Study to Examine the Renoprotective Effects of Losartan, an Angiotensin II Antagonist Versus Placebo in Type 2 Diabetic Patients (MD97168)
 ✉ CHAN Chung Ngor Juliana • COCKRAM Clive Stewart • CRITCHLEY Julian A J H#

1998-99 The Effect of Irbesartan on Morbidity and Mortality in Hypertensive Patients with Type II Diabetes and Diabetic Nephropathy (MD98086)
 ✉ CHAN Chung Ngor Juliana • COCKRAM Clive Stewart • CRITCHLEY Julian A J H#

1998-99 Mapping Genes for Young Onset Diabetes, Obesity and Diabetic Nephropathy (MD98116)
 ✉ CHAN Chung Ngor Juliana • CRITCHLEY Julian A J H# • TOMLINSON Brian • CHAN Yan Keung Thomas • COCKRAM Clive Stewart • NG Chor Yin • LEE Shao Chin (Dept of Clinical Oncology) • LEE Suk Kuen • THOMAS Neil G • 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) • COCKRAM Clive Stewart

1999-00 Screening for Mutation/Polymorphisms in Obesity-related Genes, Melanocortin-4 Receptor, Uncoupling Protein 2 and 3 and Tumor Necrosis Factor- α , in Chinese Patients with Early-onset Type 2 Diabetes and a Positive Family History (MD99037)
 ✉ CHAN Chung Ngor Juliana • NG Chor Yin • LEE Shao Chin (Dept of Clinical Oncology) • LEE Suk Kuen • COCKRAM Clive Stewart • 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)

1999-00 Eradication of Helicobacter Pylori Infection for Secondary Prevention of Upper Gastrointestinal Hemorrhage in Patients with Ischemic Heart Disease and Stroke: A Prospective Randomized Study (MD99009)
 ✉ CHAN Ka Leung Francis • SUNG Joseph Jao Yiu • LUK Yiu Wing* • LAI Moon Sing* • LI Ting Ho* • LI Michael Kin Kong*

1999-00 A Randomized, Multi-centre, Double-blind, Parallel-group, Placebo-controlled Trial to Investigate the Safety and Efficacy of Five Doses of DRF2593 in OHA - and/or Diet Treated Patients with Type 2 Diabetes (MD99129)
 ✉ CHOW Chun Chung Francis • COCKRAM Clive Stewart

1997-98 The Effects of an Education Programme on the Compliance with Nasal CPAP in the Treatment of Obstructive Sleep Apnoea (MD97006)
 ✉ HUI Shu Cheong David • LAI Kei Wai Christopher • LEUNG Chung Chuen Roland • CHAN Ka Wing, Joseph*

1998-99 Prevalence of Sleep-Disordered Breathing and the Effects of Nasal Continuous Positive Airway Pressure on Outcome After Ischemic Stroke (MD98102)
 ✉ HUI Shu Cheong David • WONG Ka Sing Lawrence • KAY Li Chi Richard • LUM Chor Ming Christopher • KWOK Chi Yui Timothy • WOO Jean

1999-00 A Randomised, Multi-centre, Double-dummy, Parallel-group Comparison of Seretide RPID (50/100ug strength) Twice Daily with Budesonide BADPI 400 μ g Twice Daily in Adolescents and Adults with Reversible Airways Obstruction (MD99151)
 ✉ HUI Shu Cheong David

1999-00 Nocturnal Nasal Positive Pressure Ventilation Plus Oxygen Therapy versus Oxygen Alone in Severe Stable Chronic

- Obstructive Pulmonary Disease (MD99017)
 1998-99 The 2nd Symphony Trial – Sibrafin Versus Aspirin as Therapy for the Long Term Prevention of Secondary Vascular Events Post Acute Coronary Syndromes (MD98125C)
 1999-00 A Study of Aspirin versus Warfarin for the Prevention of Stroke among Chinese Patients with Nonvalvular Atrial Fibrillation (MD99038)
 1999-00 The Effect of Adrenergic Receptor Blockade on Myocardial Collagen and Ventricular Remodeling in Heart Failure Post Myocardial Infarction (CU99340)
 1998-99 The Efficacy of a Community Nurse Specialist in Preventing Hospital Readmission of Older Patients with Chronic Lung Disease and Cardiac Failure (MD98075)
 1999-00 The Effects of α - and β -adrenoreceptor Stimulation on Collagen Production in Cultured Cardiac Fibroblasts (MD99104)
 1999-00 A Randomized, Stratified, Double-blind, Multicenter Study of the Safety and Efficacy of 52 Weeks Treatment with Adefovir Diproxil and Lamivudine for Patients with Chronic Hepatitis B Who Have Developed Hepatitis B Virus Variants and Evidence of Reduced Therapeutic Response to Lamivudine (NUC20904) (MD99115)
 1998-99 The Effect of Hydroxychloroquine on Serum Lipids, Apolipoproteins and Lipoprotein(a) in Patients with Systemic Lupus Erythematosus (MD98039)
 1998-99 The SYMPHONY Trial: A Phase III, Multicenter, International, Randomized, Double-Blind, Aspirin-Controlled Trial to Evaluate the Efficacy and Safety of Sibrafin (Ro 48-3657), an Oral Platelet Glycoprotein IIb/IIIa Antagonist, as Therapy for the Prevention of Secondary Vascular Events in Patients after an Acute Coronary Syndrome (MD97176C)
 1998-99 The Paragon-B Trial (MD98146)
 1995-96 *Helicobacter pylori*: Mode of Transmission and Carcinogenesis (MD95255)
 1998-99 Does *Helicobacter Pylori* Cause Or Protect Against Gastro-Esophageal Reflux In Asia (CU98260)
 1999-00 A Double-blind Placebo Controlled Clinical End-points of Lamivudine in Patients with Hepatitis B Related Cirrhosis (MD98164)
 1999-00 Gastric Cancer – A Study on Genetic and Bacterial Mechanisms (MD99092)
- 1998-99 HUI Shu Cheong David
 1999-00 SANDERSON John Elsby
 1999-00 KAY Li Chi Richard • SANDERSON John Elsby
 1998-99 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 LEUNG Wai Yee Nancy
 1998-99 LI Kwok Ming Edmund • TOMLINSON Brian • LAM Wai Kei Christopher (Dept of Chemical Pathology) • TAM Lai Shan
 1998-99 SANDERSON John Elsby • CALIFF, Robert*
 1998-99 SANDERSON John Elsby • CHIU C. W.* • TANG Kare Hung* • FUNG Wing Hong*
 1995-96 SUNG Joseph Jao Yiu • CHUNG Sheung Chee Sydney (Dept of Surgery) • TO Ka Fai (Dept of Anatomical & Cellular Pathology) • CHENG Fun Bun Augustine (Dept of Microbiology) • LIN Sar-ren*
 1998-99 SUNG Joseph Jao Yiu • CHUNG Sheung Chee Sydney (Dept of Surgery) • NG Enders K. W. (Dept of Surgery)* • CHAN Ka Leung Francis • WU Che Yuen Justin*
 1999-00 SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • TSANG W. C. Steven* • CHAN L. Y. Henry* • HUI Y.*
 1999-00 SUNG Joseph Jao Yiu • YU Jun • Peter Malferteiner* • Matthias Ebert*

- 1999-00 The Role of Vascular Permeability and Fibrosing factors in Longitudinal Change of Peritoneal Solute Kinetics (MD99039)
 ✉ SZETO Cheuk Chun • LI Kam Tao Philip
- 1998-99 A Multicenter, Double-Blind, Randomized, Parallel, 36-week Dose Escalating Study to Evaluate the Efficacy and Safety of Simvastatin 40 and 80 mg/day Versus Atrovastatin 20, 40 and 80 mg/day in Patients with Hypercholesterolaemia (International) (MD98121C)
 ✉ TOMLINSON Brian
- 1999-00 The Participation of the Actin Cytoskeleton in Insulin-mediated Glucose Uptake in Rat Skeletal Muscle Cells (MD99040)
 ✉ TONG Peter Chun Yip • COCKRAM Clive Stewart • CHAN Chung Ngor Juliana
- 1995-96 Regress of Cerebral Artery Stenosis Study (MD95268)
 ✉ WONG Ka Sing Lawrence • KAY Li Chi Richard • LAM Wai Man Wynn timer (Dept of Diagnostic Radiology & Organ Imaging) • CHAN Yu Leung (Dept of Diagnostic Radiology & Organ Imaging)
- 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
- 1998-99 Clinical Trial for GLYB 3001 in Acute Stroke (MD98145)
 ✉ WONG Ka Sing Lawrence
- 1998-99 Pramipexole: Efficacy, Safety and Tolerability Study in Parkinson's Disease patients, a Multinational Study (MD98085)
 ✉ WONG Ka Sing Lawrence • 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* • TOMLINSON Brian • LAM Wai Man Wynn timer (Dept of Diagnostic Radiology & Organ Imaging) • LAM Wai Kei Christopher (Dept of Chemical Pathology) • KAY Li Chi Richard
- 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*
- 1999-00 Chinese Atherosclerosis in the Aged and Young (Cathay Study) (MD96224)
 ✉ WOO Kam Sang • WOO Jean • SANDERSON John Elsby • CRITCHLEY Julian A J H# • CHENG Gregory • LAM Ching Wan (Dept of Chemical Pathology) • LAU Tak Fai Joseph (School of Public Health)
- 1999-00 A Double-blind, Randomized Study on Valsartan vs Diuretics in Essential Hypertension: The Impact of Antihypertensive Therapy on Arterial Endothelial Function (MD97188)
 ✉ WOO Kam Sang • FUNG Wing Hong • SANDERSON John Elsby • Dr. Chiu R C W*
- 1999-00 Hyperhomocysteinaemia and Arterial Endothelial Dysfunction: An Emerging Strategy for Prevention of Atherosclerosis (CU99282)
 ✉ WOO Kam Sang • WOO Jean • SANDERSON John Elsby • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • FUNG Kwok Pui

(Biochemistry) • LAU Tak Fai
Joseph (School of Public Health)

1999-00 A Multicenter, Randomized, Controlled, Double-blind Trial to Investigate the Clinical Efficacy and Tolerability of Early Treatment with Simvastatin 40mg Daily for 30 Days, Followed by Simvastatin 80mg Daily thereafter in Tirofiban-Treated Acute Coronary

Syndrome Patients Who have been Randomized to Receive Enoxaparin or Unfractionated Heparin in Conjunction with Aspirin. (A to Z study) (MD99072)
≈ WOO Kam Sang • SANDERSON John Elsby • FUNG Wing Hong* • CHAN W M Wilson*

RESEARCH OUTPUTS AND PUBLICATIONS

- <P953680> **SUNG J.Y. Joseph; CHUNG S.C. Sydney and YUNG Man Yee.** "Antibacterial Treatment of Gastric Ulcers". *The New England Journal of Medicine* vol.333, pp.191-192. 1995.
- <P953681> **SUNG J.Y. Joseph and CHUNG S.C. Sydney.** "Omitting Side Holes in Biliary Stents". *Gastrointestinal Endoscopy* vol.41, pp.177-178. USA, 1995.
- <P970290> **Woo, Jean.** "The Quest for Longevity". *Professorial Inaugural Lecture Series 23 (Chinese University Bulletin Supplement 37)* pp.1-7. Hong Kong, 1997.05.
- <P994707> **WOO J. and HO S.** "Determinants of Cardiovascular Disease in the Asian Pacific Region: Protocol for a Collaborative Overview of Cohort Studies". *CVD Prevention* vol.2, pp.281-289. 1999.
- <P994709> **SUNG J.Y. Joseph; SOLLANO D. Jose; CHI Wai Lai; ISMAEL Albert; YUNG Man Yee; TUMALA Isabel and CHUNG S.C. Sydney.** "Long-Term Ciprofloxacin Treatment for the Prevention of Biliary Stent Blockage: A Prospective Randomized Study". *The American Journal of Gastroenterology* vol.94 no.11, pp.3197-3201. USA, 1999.
- <P994737> **LO R.S.K.; OR K.H.; CHOW F.P.; SJE K.H. and WOO J.** "Risk Factors of Developing Pneumonia in Post Stroke Dysphagia". *Cerebrovascular Diseases* ed. by M.G. Hennerici. vol.9, p.136. Karger, 1999.03.
- <P994758> **SOMWAR R.; SWEENEY G.; YAWORSKY K.; RAMAL T.; TONG P.; KHAYAT Z. and KLIP A.** "Regulation of Glucose Transport by Insulin in Muscle and Fat Cells: Translocation and Activation of Glucose Transporters" *Membrane Structure in Disease and Drug Therapy* ed. by G. Zimmer. pp.283-302. New York: Marcel Dekker, Inc., 1999.
- <P000115> **Woo, Jean and Clive Cockram.** "Cost Estimates for Chronic Diseases". *Disease Management and Health Outcomes* vol.8 no.1, pp.29-41. New Zealand, 2000.07.
- <P000443> **Sanderson, John E.** "Heart Failure". *Management of Complex Cardiovascular Problems: The Consultants Approach* pp.57-71. USA, New York: Future Publishing Co. Inc, 2000.12.
- <P001035> **Leung, W.K.; K.F. To; F.K.L. Chan; T.L. Lee; S.C.S. Chung and J.J.Y. Sung.** "Interaction of Helicobacter Pylori Eradication and Non-Steroidal Anti-Inflammatory Drugs on Gastric Epithelial Apoptosis and Proliferation: Implications on Ulcerogenesis". *Alimentary Pharmacology & Therapeutics* vol.14, pp.879-885. 2000.07.
- <P001728> **Wei, Shan; Louis T.C. Chow and John E. Sanderson.** "Effect of Carvedilol in Comparison with Metoprolol on Myocardial Collagen Postinfarction". *Journal of the American College of Cardiology* vol.36 no.1, pp.276-281. USA, 2000.07.

- <P002138> **Sanderson, John E.** "Collagen and Transforming Growth Factor- β in Dilated Cardiomyopathy". *Circulation* vol.102, p.a66. USA, 2000.
- <P002274> **Lee, Yuk Tong; Francis K.L. Chan; Enders K.W. Ng; Vincent K.S. Leung; Kai Bo Law; Man Yee Yung; S.C. Sydney Chung and Joseph J.Y. Sung.** "Endoscopy-Guided Injection of Cyanoacrylate for Bleeding Gastric Varices". *Gastrointestinal Endoscopy* vol.52 no.2, pp.168-174. USA, 2000.08.
- <P002296> **Ng, Maggie C.Y.; Wing-Yee So; June K.Y. Li; Shao C. Lee; Clive S. Cockram; Julian A.J.H. Critchley and Juliana C.N. Chan.** "The β -Cell Glucokinase Gene Promoter G to A Variant Is Associated with Higher Fasting and Postprandial Glucose Levels in Nondiabetic Siblings of Chinese Young-Onset Diabetic Patients". *Diabetes* vol.49 suppl.1, pp.A399-A400. USA, 2000.
- <P002365> **So, Wing Yee; Maggie C.Y. Ng; June K.Y. Li; Chun-Chung Chow; Vincent T.F. Yeung; Gary T.C. Ko; Shao C. Lee; Peter C.Y. Tong; Julian A.J.H. Critchley; Clive S. Cockram and Juliana C.N. Chan.** "Angiotensin Converting Enzyme Polymorphisms (ACE) and Cardiovascular Risk Factors Amongst Siblings of Chinese Young-Onset Diabetic Patients". *Diabetes* vol.49 suppl.1, p.A401. USA, 2000.
- <P002367> **Ng, M.C.Y.; J.K.Y. Li; W.Y. So; G.I. Bell; J.A.J.H. Critchley; C.S. Cockram and J.C.N. Chan.** "Nature or Nurture: An Insightful Illustration from a Chinese Family with Hepatocyte Nuclear Factor-1 α Diabetes (MODY3)". *Diabetologia* pp.816-818. 2000.
- <P002368> **Li, June K.Y.; Cherry K.P. Chiu; Maggie C.Y. Ng; Shao C. Lee; Jonathan C. Levy; Robert C. Turner; Wing-Yee So; Chun-Chung Chow; Vincent T.F. Yeung; Gary T.C. Ko; Julian A.J.H. Critchley; Clive S. Cockram and Juliana C.N. Chan.** "Clustering of Cardiovascular Risk Factors amongst Siblings of Chinese Young-Onset Diabetic Patients". *Diabetes* vol.49 suppl.1, pp.A388-389. USA, 2000.
- <P002430> **Szeto, Cheuk-Chun; Teresa Yuk-Hwa Wong; Ka-Bik Lai; Christopher Wai-Kei Lam; Kar-Neng Lai and Philip Kam-Tao Li.** "Dialysate Hyaluronan Concentration Predicts Survival But Not Peritoneal Sclerosis in Continuous Ambulatory Peritoneal Dialysis". *American Journal of Kidney Diseases* vol.36 no.3, pp.609-614. USA, 2000.09.
- <P002446> **Kwok, T.** "Geriatrics Update". *Journal of the Hong Kong Geriatrics Society* vol.10 no.1, pp.36-58. 2000.
- <P002470> **McCrohon J.A.; Woo Kam S. and Celemajer David S.** "A Comparison of Endothelial Function in Caucasian and Chinese Women before and after the Menopause". *Maturitas* vol.35 suppl.2000, pp.31-37. Ireland, 2000.07.
- <P002633> **SUNG J.Y. Joseph and LAU W. Joseph.** "Gastrointestinal Hemorrhage". *Surgery* pp.2.1-2.12. UK: Harcourt Publishers Limited, 2000.01.
- <P002652> **WOO J.; HO S.C.; YU A.L.M. and LAU J.** "An Estimate of Long-Term Care Needs and Identification of Risk Factors for Institutionalization Among Hong Kong Chinese Aged 70 Years and Over". *Journal of Gerontology: Medical Sciences* vol.55A no.2, pp.M64-M69. USA, 2000.
- <P002708> **NG C.Y. Maggie.** "Heterogeneity of Young-Onset Diabetes in Hong Kong Chinese". *Programme Book of the 2nd HK Diabetes & Cardiovascular Risk Factors East Meets West Symposium* p.14. Hong Kong: Department of Medicine & Therapeutics, CUHK and the Hong Kong Foundation for Research and Development in Diabetes, 2000.
- <P002709> **NG C.Y. Maggie.** "Qualitative and Quantitative Analysis of Mitochondrial DNA in Hong Kong Chinese Patients with Diabetes Mellitus". *The Proceedings of the 2nd Symposium on Molecular Diabetology in Asia* pp.48-49. Seoul, Korea: The Study Group of Molecular Diabetologia in Asia, 2000.12.
- <P002731> **WANG Mei; YIP Gabriel and SANDERSON John E.** "Color M-Mode Mitral Propagation Velocity and Diastolic Dysfunction: Relationship to Diastolic Filling Patterns and LV Systolic

Function". *Journal of the American Society of Echocardiography 11th Annual Scientific Sessions* vol.13, p.470. USA: American Society of Echocardiography, 2000.05.

- <P002773> **THOMAS G. Neil; CRITCHLEY A.J.H. Julian; TOMLINSON Brian; ANDERSON Patricia J.; LEE S.K. Zoe and CHAN C.N. Juliana.** "Obesity, Independent of Insulin Resistance, Is a Major Determinant of Blood Pressure in Normoglycemic Hong Kong Chinese". *Metabolism* vol.49 no.12, pp.1523-1528. 2000.
- <P002775> **KO Gary T.C.; LEE Shao C.; COCKRAM Clive S. and CHAN Juliana C.N.** "Tumor Necrosis Factor-Alpha (TNF α)-308 (G to A) Gene Polymorphism in Chinese Subjects with Type 2 Diabetes". *Diabetes Research and Clinical Practice (Abstract Book Diabetes Federation Congress)* vol.50, p.S96, Abstracts no.418. Mexico City, 2000.
- <P002789> **LEE C.W.; TOMLINSON B.; YEUNG J.H.K.; LIN G. and DAMANI L.A.** "Distribution of the N-Oxidation of Dietary-Derived Trimethylamine in a Male Chinese Population". *Pharmacogenetics* vol.10, pp.829-831. USA, 2000.12.
- <P002826> **KO T.C. Gary; CHAN C.N. Juliana; TSANG W.W. Lynn and COCKRAM Clive S.** "Combined Use of Fasting Plasma Glucose and HbA_{1c} Predicts the Progression to Diabetes in Chinese Subjects". *Diabetes Care* 1st ed. vol.23 no.12, pp.1770-1773. 2000.
- <P002828> **CHAN W.B.; CHOW C.C.; YEUNG V.T.F.; CHAN J.C.N.; SO W.Y. and COCKRAM C.S.** "Effect of Lispro on Glycaemic Control in Chinese Diabetic Patients on Twice Daily Insulin Injection". *Diabetes Research and Clinical Practice (Abstract Book Diabetes Federation Congress)* vol.50 suppl.1, p.S45, Abstracts no.P247. Mexico City, 2000.
- <P002829> **THOMAS G. Neil; CRITCHLEY A.J.H. Julian; TOMLINSON Brian; SANDERSON E. John; COCKRAM Clive S. and CHAN C.N. Juliana.** "The Dopamine D2 Receptor TaqI Gene Polymorphism and Hypertension". *Abstract Book, Diabetes Research and Clinical Practice* vol.50, p.S370-S371, Abstracts no.P1458. Mexico City, 2000.
- <P002830> **CRITCHLEY A.J.H. Julian; THOMAS G. Neil; TOMLINSON Brian; SANDERSON E. John; COCKRAM Clive S. and CHAN C.N. Juliana.** "Renin-Angiotensin System (RAS) Gene Polymorphisms: An Association of the ACE I/D Polymorphism with Chinese Type 2 Diabetics". *Abstract Book, Diabetes Research and Clinical Practice* vol.50 Suppl.1, p.S371, Abstracts no.P1460. 2000.
- <P002831> **LI J.K.Y.; NG M.C.Y.; LEE S.C.; CHIU C.K.P.; KO G.T.C.; SO W.Y.; CHOW C.C.; TONG P.C.Y.; YEUNG V.T.F.; CRITCHLEY J.A.J.H.; COCKRAM C.S. and CHAN J.C.N.** "First Degree Relatives of Albuminuric, Young-Onset Chinese Type 2 Diabetic Patients Have Impaired Insulin Secretion and Increased Risks of Microalbuminuria". *Diabetes Research and Clinical Practice (Abstract Book Diabetes Federation Congress)* vol.50 suppl.1, p.S399, Abstracts no.P1555. Mexico City, 2000.
- <P002873> **CHAN H.L. Henry; WOO Jean; CHAN W.M. and HJELM Magnus.** "Tele dermatology in Hong Kong: A Cost-Effective Method to Provide Service to the Elderly Patients Living in Institutions". *International Journal of Dermatology* vol.39, pp.774-778. UK, 2000.
- <P002891> **KO T.C. Gary; CHAN C.N. Juliana; CRITCHLEY A.J.H. Julian and COCKRAM S. Clive.** "Cardiovascular Disease in Chinese Type 2 Diabetic Women is Associated with a Prolonged QTc Interval". *International Journal of Cardiology* vol.76, pp.75-80. 2000.
- <P002909> **THOMAS G. Neil; TOMLINSON Brian; CHAN C.N. Juliana; LEE S.K. Zoe; COCKRAM S. Clive and CRITCHLEY A.J.H. Julian.** "An Insulin Receptor Gene Polymorphism is Associated with Diastolic Blood Pressure in Chinese Subjects with Components of the Metabolic Syndrome". *American Journal of Hypertension* vol.13, pp.745-752. 2000.
- <P002910> **THOMAS G. Neil; TOMLINSON Brian and CRITCHLEY A.J.H. Julian.** "Modulation of Blood Pressure and Obesity with the Dopamine D2 Receptor Gene TaqI Polymorphism". *Hypertension* vol.36, pp.177-182. 2000.

- <P002922> **SZE Kai-Hoi; WONG Eric; OR K.H.; LUM C.M. and WOO Jean.** "Factors Predicting Stroke Disability at Discharge: A Study of 793 Chinese". *Arch Phys Med Rehabil* vol.81 no.7, pp.876-880. USA, 2000.07.
- <P002964> **LEE H.Y.; WOO J.; CHEN Z.Y.; LEUNG S.F. and PENG X.H.** "Serum Fatty Acid, Lipid Profile and Dietary Intake of Hong Kong Chinese Omnivores and Vegetarians". *European Journal of Clinical Nutrition* vol.54, pp.768-773. UK, 2000.
- <P002968> **WOO J.** "Relationships Among Diet, Physical Activity and Other Lifestyle Factors and Debilitating Diseases in the Elderly". *European Journal of Clinical Nutrition* vol.54 suppl.3, pp.S143-S147. UK, 2000.
- <P003053> **KWOK Timothy; WOO Jean; HO Suzanne and SHAM Aprille.** "Vegetarianism and Ischemic Heart Disease in Older Chinese Women". *Journal of the American College of Nutrition* vol.19 no.5, pp.622-627. USA, 2000.
- <P003104> **WONG Ka Sing; LI Huan; CHAN Yu Leung; AHUJA Anil; LAM W.M. Wynn; WONG Agatha and KAY Richard.** "Use of Transcranial Doppler Ultrasound to Predict Outcome in Patients with Intracranial Large-Artery Occlusive Disease". *Stroke* vol.31, pp.2641-2647. USA, 2000.
- <P003163> **WANG M.; YIP G.W.K.; HO P.Y. and SANDERSON J.E.** "Is Mitral Flow Propagation Velocity Useful for Assessing Diastolic Function in the Presence of Normal Left Ventricular Systolic Function?". *European Journal of Echocardiography Euroecho* vol.1 suppl.2, Abstracts no.S27. 2000.12.
- <P003164> **YIP G.W.K.; WANG M.; HO P.Y. and SANDERSON J.E.** "Left Ventricular Long Axis in Diastolic Heart Failure - is Left Ventricular Systolic Function Truly Normal?". *European Journal of Echocardiography Euroecho* vol.1, Abstracts no.S60. WB Saunders, UK, 2000.12.
- <P003231> **SO W.Y.; NG M.C.Y.; LEE S.C.; SANKE T.; LEE H.K. and CHAN J.C.N.** "Genetics of Type 2 Diabetes Mellitus". *Hong Kong Medical Journal* vol.6 no.1, pp.69-76. Hong Kong, 2000.03.
- <P003238> **SANDERSON John E.** "Effectiveness of Beta Blockers in Congestive Heart Failure". *Journal of the American Medical Association* vol.16, pp.6-7. USA, 2000.
- <P003251> **WILDER-SMITH E.; CHOW K.M.; KAY R.; IP M. and TEE N.** "Group B Streptococcal Meningitis in Adults: Recent Increase in Southeast Asia". *Australian and New Zealand Journal of Medicine* vol.30 no.4, pp.462-465. Australia, 2000.08.
- <P003266> **WOO Jean.** "Nutrition". *Medicine and Surgery in the Older Person* ed. by W.S. Pang, M.K. Teoh and S.K. Ming. pp.70-76. Singapore: Armour Publishing Pte Ltd., 2000.
- <P003277> **CHAN K.Y. Daniel; HU Gang; TAO Helen; OWENS Daniel; VUN M. Chee; WOO Jean and CHONG Beng Hock.** "A Comparison of Polymorphism in the 3'-Untranslated Region of the Prothrombin Gene between Chinese and Caucasians in Australia". *British Journal of Haematology* vol.111, pp.1253-1255. UK, 2000.
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RESEARCH PROJECTS

Development of a Rapid *in vitro* Drug Susceptibility Test Method for *Mycobacterium Tuberculosis* Using Metabolic Markers

- ✉ CHAN Chiu Yeung Raphael
- ☐ 1 September 2000
- ❖ Research Grants Council (Earmarked Grants)

Tuberculosis, especially those caused by drug resistant and multi-drug resistant isolates of *Mycobacterium tuberculosis*, have become important uprising problems in infectious diseases worldwide. Since *M. tuberculosis* is a slow-growing organism, it would take four and up to eight weeks for the laboratory to recover the pathogen from a clinical specimen, and using the time- and labour-consuming classical methods of routine *in-vitro* drug susceptibility testing would add another two to four weeks before a drug report can be issued to clinicians. Although efforts have been put into rapid culture in shortening the time of colony recovery to 10-14 days, most of the classical methods of drug susceptibility testing, and even some modern methods, require two to four weeks to generate a drug report, which may still cause a delay in treatment. Some modern methods of drug testing can reduce the result reporting time from weeks to days, but these methods either require sophisticated and expensive equipments or have limitations to the drugs being tested. Thus it is necessary to develop a simple and rapid method of *in vitro* drug susceptibility test for *M. tuberculosis*. The present proposal aims at the development of an *in vitro* drug susceptibility testing method by assessing, visually or spectrophotometrically, the inhibition or reduction in the productions of niacin and nitrite in *M. tuberculosis* after exposure to various concentrations of different drugs. It is anticipated that such a test, after optimization of different conditions, would provide *in vitro* drug susceptibility results within one day or even several hours after the pathogens are recovered. Since this test bases on the measurement of the production of metabolic markers which directly reflects growth or no growth of the pathogen, it can be used to assess the effects of a single drug and/or a combination of drugs; and can be applied directly to clinical use because of its simplicity, rapidity and cost-effectiveness. (CU00097)

Viral Load Quantification of Human Papillomavirus: Correction with Staging and Application in Post-treatment Surveillance of Cervical Carcinoma

- ✉ 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
- ☐ 15 October 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Background: Human papillomaviruses (HPVs) are aetiologically associated with cervical neoplasia. While HPV detection is currently applied in cervical cancer screening, the clinical application of HPV test should not be limited to this. Here, the researchers propose to develop an HPV DNA quantification assay based on a novel real-time polymerase chain reaction technique, and to explore the possible clinical applications of HPV DNA load measurement. *Objectives:* (1) To establish the correlation between HPV DNA load in primary tumour tissue and the related lymph nodes with (a) staging, and (b) recurrence rate of cervical carcinoma. (2) To elucidate the temporal correlation between HPV DNA load in plasma with (a) treatment (surgery / radiotherapy / chemotherapy), and (b) recurrence. *Methods:* (1) *Retrospective study* - Paraffin-embedded primary tumour tissues and lymph nodes resected from patients with cervical carcinoma over the last 2 years will be retrieved for HPV detection and quantification. The HPV results will be correlated with their staging at presentation, and subsequent recurrence rates. (2) *Prospective study* - (a) Case group 1 ~ Plasma HPV DNA load will be measured for 50 newly diagnosed cases of invasive cervical carcinoma before, during and after treatment, and at 2-3 months follow-up intervals. The HPV results will be correlated temporally with treatment and subsequent recurrence. (b) Case group 2 ~ 100 patients who are currently at post-treatment follow-up will be measured for plasma HPV DNA loads at 2-3 months intervals, correlated temporally with recurrence. Women with genital HPV infections but without cervical cancer will be recruited as negative controls. (MD00949)

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

- ✉ CHENG Fun Bun Augustine • CHAN Chiu Yeung Raphael • HUI Mamie
- ☐ 1 September 2000
- ❖ Research Grants Council (Earmarked Grants)

The battle against the re-emergence of tuberculosis has been complicated by the emergence of resistant

strains of *Mycobacterium tuberculosis* (MTB), especially the multi-drug resistant ones (MDR-TB), which can be resistant to almost all first-and second-line antituberculous drugs. Since *M. tuberculosis* is a slow-growing organism, two to four weeks are required to obtain results from routine *in vitro* susceptibility testing, resulting in a delay in treatment. Detection of resistance to rifampicin and isoniazid has been of critical importance since they are the key first-line drugs used for the treatment of tuberculosis. As the organisms may be resistant to first-line agents and patients who have liver dysfunction cannot tolerate the hepatotoxic first-line drugs like rifampicin or isoniazid, the detection of resistance to fluoroquinolones, which are used as the key second-line agents, is of paramount importance also. Recent development in molecular biology techniques has allowed not only direct detection of mutations in drug-resistant genes of *rpoB*, *katG*, *inhA*, *ahpC*, *embB*, *pncA* and *gyrA* for the elucidation of resistance to rifampicin, isoniazid, ethambutol, pyrazinamide and fluoroquinolones respectively, but also to correlate different mutations to different levels of drug resistance. The researchers plan to study all the mutation sites of the drug-resistant mutants from a local collection of their clinical isolates of *M. tuberculosis* to sort out the resistance mechanism(s) utilized by this group of pathogens. Results obtained from this study will serve as a pioneer in our future development of different rapid laboratory methods for the detection of drug resistance in *M. Tuberculosis* isolates using modern molecular biology approaches, and will provide us with useful epidemiology data for the combat of this re-emerging disease in Hong Kong. (CU00098)

***In vitro* Antimicrobial Susceptibility of Linezolid**

- ✉ CHENG Fun Bun Augustine • LING Kin Wah Thomas
□ 1 March 2001
❖ Pharmacia Hong Kong Limited

There is an increasing incidence of severe infections caused by multiply drug resistant Gram-positive bacteria. Linezolid, the first oxazolidinone antibiotic, is active against gram-positive bacteria and is bioequivalent oral and intravenous (IV) formulation. Linezolid acts by inhibiting the initiation phase of protein translation through direct interaction with the bacterial ribosome and the 70S ribosomal RNA initiation complex. This unique mode of action results in linezolid susceptibility in organism resistant to other antibacterials. Therefore linezolid would likely be of value in treating infection due to gram-positive organisms such as staphylococci (including methicillin-resistant strains), enterococci (including vancomycin-resistant strains), and pneumococci (including penicillin-resistant strains).

It is proposed to undertake the study in order to ascertain the likely efficacy of linezolid in Hong Kong. (MD00793)

Characterisation and Detection of an Integron Carrying the Newly Described Carbapenemase IMP3 Gene

- ✉ HOUANG Ting Sou Elizabeth • CHU Yiu Wai
□ 1 December 2000
❖ CUHK Research Committee Funding (Direct Grants)

The researchers recently cloned and sequenced the gene *bla_{IMP3}* encoding IMP3, the new enzyme responsible for imipenem resistance in acinetobacters in Hong Kong. Their current work indicates that *bla_{IMP3}* may be associated with integron(s), the transferable genetic elements. This project is for the completion of the sequencing of the integron associated with the *bla_{IMP3}* cassette and for the development of a PCR method for its detection. The PCR method will be evaluated using the researchers' collections of *bla_{IMP3}⁺* and some clonally related *bla_{IMP3}⁻* *Acinetobacter* isolates of different species. The results will shed light on the *in vivo* role of integrons as dispersers of antibiotic resistance at the inter-strain and inter-species level. A part of this project will include the *in vivo* validation of the mathematical modeling on the emergence and spread of imipenem resistance in the Intensive Care Unit (overseas collaborator-Prof. R. Anderson, Oxford, UK). The *bla_{IMP3}* gene and its carrier integron will be used as markers for the spread of resistance. If validated successfully, the mathematical model may be used to formulate timely antibiotic policies to prevent the full scale emergence of resistance. The PCR method for the detection of the carrier integron(s) for *bla_{IMP3}* developed under this project is an important tool to validate mathematical modeling of antibiotic resistance. (MD00815)

Development of a Rapid Diagnostic Method for Invasive Candidiasis by Detection of D/L-arabinitol Using Gas Chromatography / Mass Spectrometry

- ✉ HUI Mamie • CHAN Chiu Yeung Raphael • CHEUNG Siu Wai • CHENG Fun Bun Augustine
□ 1 November 2000
❖ CUHK Research Committee Funding (Direct Grants)

Invasive fungal disease had taken a great toll in the immunocompromised patients, with the various *Candida* species accounting for the majority of the

invasive diseases. Diagnosis based on blood cultures, tissue cultures and/or histopathological evidences are time consuming, technically demanding and of low sensitivity. Moreover, it is often not possible for the already frail patients to undergo invasive diagnostic procedures. Rapid non-culture diagnostic methods had been explored. The researchers' laboratory had developed a rapid identification method for medically important *Candida* by the use of polymerase-chain reaction with single strand conformational polymorphism (PCR-SSCP). Notwithstanding, no single method is ideal. D-arabinitol is a metabolite produced by *Candida* species. In invasive candidiasis, D-arabinitol levels were found to be raised in serum and urine. Its detection can be made possible by the use of gas chromatography with mass-spectrometry (GC-MS). The researchers' proposed: (1) to establish a detection method for D-arabinitol using GC-MS; and (2) to establish the application of this method through the use of simulated serum and urine specimens. The results, coupled with the molecular detection method, will provide the clinicians a diagnostic battery of tests for patient management, as well as leading to further studies on clinical trials, early diagnosis of high risk patient groups and monitoring of patient's response to treatment.

(MD00737)

Mechanisms of Fluoroquinolone-resistance in Salmonellae in Hong Kong

✉ LING Mei Lun Julia

□ 2 October 2000

❖ Research Grants Council (Earmarked Grants)

Fluoroquinolones have been used successfully in the treatment of salmonellosis. However, treatment failures due to development of resistance in salmonellae were soon reported. The most common mechanism of resistance to fluoroquinolones is modification of the target enzyme, DNA gyrase, leading to a reduction in the affinity of the enzyme for fluoroquinolones. Such modification is due to mutations in the *gyrA* gene that codes for subunit A of the enzyme. Other mechanisms include mutations in the *gyrB* gene that codes for subunit B of the enzyme; mutations in the *parC* gene that codes for topoisomerase IV, another target enzyme of fluoroquinolones; and reduced intracellular accumulation of antibiotics because of changes in the bacterial cell envelope. It has also been demonstrated that these resistant strains belonged to one clone that spread among humans and animals. The researchers' previous study showed that 9% of *S. typhimurium* isolated in Hong Kong from 1989 to 1995 had reduced susceptibility to fluoroquinolones. This project aims to use molecular biological techniques to elucidate the resistance mechanisms in all salmonella isolated in 1989 - 2001. The relatedness of resistant

isolates will also be investigated using molecular typing methods developed in their previous study. By understanding the mechanisms of resistance and epidemiology of resistant strains, the researchers will be able to locate the origins and trace the spread of resistance genes and thus to develop strategies for preventing the emergence and spread of resistant bacteria.

(CU00049)

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

✉ TAM Siu Lun John • FOK Tai Fai (Dept of Paediatrics) • CHENG Fun Bun Augustine

□ 15 August 2000

❖ American Home Products, Wyeth Lederle Vaccines

Influenza is an acute viral respiratory illness characterized by abrupt onset of fever, myalgia, non-productive cough, headache, sore throat, nasal congestion, and malaise. In Asia, influenza rates also appear to be highest in young children. In residential kindergartens in Beijing, China, 19% of acute respiratory infections of children aged 6 months to 7 years were confirmed by culture to be attributed to influenza. In community surveillance of children under 5 years with acute lower respiratory infections in Manila, Philippines, and Dhaka, Bangladesh, influenza was confirmed by culture as the probable etiology in 22% and 14%, respectively.

The purpose of this study is to provide a virus isolation service in association with a prospective, randomized, double-blinded, placebo-controlled, multi-centred influenza vaccine trial. The main objective of the trial is to test the efficacy of the live attenuated influenza vaccine against culture-confirmed influenza illness. The vaccine consisted of types A (H1 and H3) & B influenza viruses derived from cold-adapted vaccine strains. It is expected that approximately 3000 subjects will be enrolled at multiple study sites in Asia. Each subject will be required to participate for approximately 24 months (range 22 to 24 months). All subjects will be monitored for respiratory illnesses with culture confirmation for viruses. All nasal swabs collected from children under study during illness are sent to Hong Kong for virus culture and molecular detection of respiratory viruses. A total of 45,000 specimens are expected from the two year follow up of the 3000 subjects.

(MD00369)

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

✉ 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)

☐ 15 August 2000

❖ American Home Products, Wyeth Lederle Vaccines

Influenza is an acute viral respiratory illness characterized by abrupt onset of fever, myalgia, non-productive cough, headache, sore throat, nasal congestion, and malaise. In Asia, influenza rates also appear to be highest in young children. In residential kindergartens in Beijing, China, 19% of acute respiratory infections of children aged 6 months to 7 years were confirmed by culture to be attributed to influenza. In community surveillance of children under 5 years with acute lower respiratory infections in Manila, Philippines, and Dhaka, Bangladesh, influenza was confirmed by culture as the probable etiology in 22% and 14%, respectively.

The purpose of this study is to determine the efficacy of Influenza Virus Vaccine, Trivalent, Types A & B, Live Cold-Adapted (CAIV-T) in a diverse Asian population aged from 6 months to less than 36 months, in tropical and temperate climates, against culture-confirmed influenza illness. In addition, the trial provides the opportunity to investigate the efficacy of CAIV-T over multiple influenza seasons, and to investigate the effect of CAIV-T on acute otitis media. It is expected that approximately 3000 subjects will be enrolled at multiple study sites in Asia. In Hong Kong 300 subjects ages from 6 months to 3 years will be enrolled as part of this multi-centered trial. Each subject will be required to participate for approximately 24 months (range 22 to 24 months). All subjects will be monitored for respiratory illnesses with culture confirmation for viruses. A subset of subjects will be monitored for serum and mucosal antibody response to the different influenza vaccine strains.
(MD00691)

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

Edition Title/Investigators

1998-99	Mechanisms of aminoglycoside/aminocyclitol resistance in mycobacteria (CU98237) ✉ 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
1999-00	Quinolone and Multidrug Resistance in <i>Acinetobacter</i> spp (CU99290) ✉ HOUANG Ting Sou Elizabeth • CHU Yiu Wai • IP Margaret • PIDDOCK L. J. V.*
1999-00	Speciation of Unclassifiable <i>Acinetobacters</i> from Hong Kong (MD99042) ✉ HOUANG Ting Sou Elizabeth • CHU Yiu Wai • DIJKSHOORN Lenie*
1999-00	Mechanisms of Macrolide, Lincosamide, Streptogramin (MLS Group) Resistance in Drug-resistant <i>Streptococcus Pneumoniae</i> and Other <i>Streptococci</i> (CU99331) ✉ IP Margaret • LYON Donald James • CHENG Fun Bun Augustine
1999-00	Effects of Respiratory Pathogens on an <i>in vitro</i> Nasal Ciliated Epithelial Monolayer Cell Culture Model (MD99105) ✉ IP Margaret • LEE Wai Chung (Dept of Surgery) • VAN HASSELT Charles Andrew (Dept of Surgery) • 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
1999-00	Mechanisms of Fluoroquinolone-resistance in <i>Salmonella Typhimurium</i> in Hong Kong (MD99043) ✉ LING Mei Lun Julia

RESEARCH OUTPUTS AND PUBLICATIONS

- <P994637> **IP M.; LYON D.J.; YUNG R.W.H.; HUI M.; CHAN C. and CHENG A.F.B.** "Macrolide, Lincosamide, Streptogramin Resistance in *Streptococcus Pneumoniae*". *Abstracts of the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy* Abstracts no.1223. USA: American Society for Microbiology, 1999.09.
- <P001922> **Chan, Paul K.S.; Ching-Wan Lam; William W.H. Li; May Y.M. Chan; Jo L.K. Cheung and Augustine F. Cheng.** "Human Papillomavirus Type 58 E6 Sequence Variation and Risk for Cervical Cancer: A Preliminary Report". Paper presented in the 18th International Papillomavirus Conference, organized by Spanish Association of Cervical Pathology & Colposcopy. Barcelona, 2000.07.
- <P001923> **Chan, Paul K.S.; Ching-Wan Lam; William W.H. Li; May Y.M. Chan; Jo L.K. Cheung and Augustine F. Cheng.** "Sequence Variation of Human Papillomavirus Type 58 E7 Oncogene in Chinese Women: A Pilot Study". Paper presented in the 18th International Papillomavirus Conference, organized by Spanish Association of Cervical Pathology & Colposcopy. Barcelona, 2000.07.
- <P001924> **Chan, Paul K.S.; Ho-Keung Ng; Jo L.K. Cheung and Augustine F. Cheng.** "Survey for the Presence and Distribution of Human Herpesvirus 8 in Healthy Brain". *Journal of Clinical Microbiology* vol.38 no.7, pp.2772-2773. USA, 2000.07.
- <P002176> **Ip, M.; D.J. Lyon; E.T.S. Houang; T. Leung and A.F.B. Cheng.** "Macrolide Resistance and Distribution of *Erm* and *Mef* Genes Among β -Haemolytic Streptococci in Hong Kong". Paper presented in the 40th Interscience Conference on Antimicrobial Agents and Chemotherapy, organized by American Society for Microbiology. USA, 2000.09.
- <P002549> **Li, W.W.H.; M.Y.M. Chan; D.P.C. Chan and P.K.S. Chan.** "Human Papillomavirus Typing in the Management of Low-Grade Cervical Abnormalities". *Abstracts of the 16th Figo World Congress of Gynecology and Obstetrics* Abstracts no.FC1, p.21,02. Washington, 2000.09.
- <P002578> **CHAN K.S. Paul; NG Ho-Keung; CHEUNG Jo L.K.; NG King-Cheung and CHENG Augustine F.** "Prevalence and Distribution of Human Herpesvirus 7 in Normal Brain". *Journal of Medical Virology* vol.62, pp.345-348. USA, 2000.
- <P002894> **LING T.K.W.; FUNG K.S.C. and CHENG A.F.B.** "The Post-Antibiotic Effect and Bactericidal Kinetics of Quinupristin/Dalfopristin (Synercid)". Paper presented in the 7th Western Pacific Congress on Chemotherapy & Infectious Diseases, organized by International Society of Chemotherapy. Hong Kong, 2000.12.
- <P002895> **LING T.K.W.; XIONG J.H.; YE H.F.; WEI Y.C.; LIU E.Y.M.; CHEN F. and CHENG A.F.B.** "The Antimicrobial Susceptibility Testing of Extended Spectrum Beta-Lactamase Producing Bacteria Isolated from Two Major Areas in South China". Paper presented in the 7th Western Pacific Congress of Chemotherapy & Infectious Diseases, organized by International Society of Chemotherapy. Hong Kong, 2000.12.
- <P002896> **LING T.K.W.; CHEN M.J. and CHENG A.F.B.** "Susceptibility of Common Hospital Pathogens to Piperacillin-Tazobactam Compared with Other Antibiotics: Results of Beijing and Hong Kong Study". Paper presented in the 7th Western Pacific Congress of Chemotherapy & Infectious Diseases, organized by International Society of Chemotherapy. Hong Kong, 2000.12.
- <P003049> **HUI Mamie; IP Margaret; CHAN K.S. Paul; CHIN Miu Ling and CHENG F.B. Augustine.** "Rapid Identification of Medically Important *Candida* to Species Level by Polymerase Chain Reaction and Single-Strand Conformational Polymorphism". *Diagnostic Microbiology and Infectious Disease* vol.38, pp.95-99. USA, 2000.

- <P003253> **LAM Rebecca; LYON Donald J. and CHENG F.B. Augustine.** "Optimal Duration of the Monitoring of the Bact Alert Blood Culture System". Paper presented in the 7th Western Pacific Congress of Chemotherapy & Infectious Diseases, organized by International Society of Chemotherapy. Hong Kong, 2000.12.
- <P003254> **LEUNG W. Joseph; LIU Yan-Lei; CHAN C.Y. Raphael; TANG Yaya; MINA Yvonne; CHENG F. Augustine and SILVA Joseph.** "Early Attachment of Anaerobic Bacteria May Play an Important Role in Biliary Stent Blockage". *Gastrointestinal Endoscopy* vol.52 no.6, pp.725-729. USA, 2000.
- <P003705> **CHIOU C.C.; RIHS B.L.; FELDMAN C.; MORRIS A.; RELLO J.; ORTQVIST A.; BADDOUR L.; SNYDMAN D.R.; IP M.; HUI D.; BLAZES D.L.; KLUGMAN K.P. and YU V.L.** "Pneumococcal Bacteremia: MICs, Serotypes and Clinical Implication". *Abstracts of the 40th Interscience Conference on Antimicrobial Agents and Chemotherapy* Abstracts p.111. Ontario, Canada: American Society for Microbiology, 2000.09.
- <P010151> **CHAN P.K.S.; CHAN D.P.C.; TO K.-F.; YU M.Y.; CHEUNG J.L.K. and CHENG A.F.** "Evaluation of Extraction Methods from Paraffin Wax Embedded Tissues for PCR Amplification of Human and Viral DNA". *Journal of Clinical Pathology* vol.54 no.4, pp.401-403. UK, 2001.
- <P010152> **LEUNG W. Joseph; LIU Yan-Lei; CHEUNG Siu-Wai; CHAN C.Y. Raphael; INCIARDI John F. and CHENG F. Augustine.** "Effect of Antibiotic-Loaded Hydrophilic Stent in the Prevention of Bacterial Adherence: A Study of the Charge, Discharge, and Recharge Concept Using Ciprofloxacin". *Gastrointestinal Endoscopy* vol.53 no.4, pp.431-437. USA, 2001.
- <P010153> **LING M. Julia; KOO C. Irene and CHENG F. Augustine.** "Epidemiological Analysis of *Salmonella Enterica* Serotype Typhimurium from Hong Kong by Ribotyping and Pulsed-Field Gel Electrophoresis". *Scandinavian Journal of Infectious Diseases* vol.33, pp.272-278. Sweden, 2001.
- <P010154> **CHAN K.S. Paul; TAM Wing-Hung; YEO Winnie; CHEUNG L.K. Jo; ZHONG Sheng and CHENG F. Augustine.** "High Carriage Rate of TT Virus in the Cervices of Pregnant Women". *Clinical Infectious Diseases* vol.32, pp.1376-1377. USA, 2001.05.01.
- <P010222> **HUI Mamie; CHEUNG S.W.; CHAN C.Y. and CHENG F.B. Augustine.** "Rapid Identification of *Mycobacterium Tuberculosis* Complex from Bactec 12B Broth Cultures Originating from Non-Respiratory Secretion Specimens: Comparison between Accuprobe and In-House Polymerase Chain Reaction". *Pathology* vol.33, pp.61-65. Australia, 2001.
- <P010227> **CHAN P.K.S.; CHAN M.Y.M.; LI W.W.H.; CHAN D.P.C.; CHEUNG J.L.K. and CHENG A.F.** "Association of Human β -Herpesviruses with the Development of Cervical Cancer: Bystanders or Cofactors". *Journal of Clinical Pathology* vol.54 no.1, pp.48-53. UK, 2001.
- <P010228> **CHAN K.S. Paul; CHIK Ki-Wai; TO Ka-Fai; LI Chi-Kong; HUI Mamie; SHING M.K. Matthew; YUEN M.P. Patrick; TAM S. John and CHENG F. Augustine.** "Clearance of TT Virus after Allogeneic Bone Marrow Transplantation". *Journal of Pediatric Hematology/Oncology* vol.23 no.1, pp.57-58. USA, 2001.01.01.
- <P010229> **IP M.; LYON D.J. and CHENG A.F.B.** "Patterns of Antibiotic Resistance, Serotype Distribution, and Patient Demographics of *Streptococcus pneumoniae* in Hong Kong". *Chemotherapy* vol.47, pp.110-116. Switzerland, 2001.
- <P010230> **LING K.W. Thomas; LIU Y.M. Esther and CHENG F.B. Augustine.** "A 13-Year Study of Antimicrobial Susceptibility of Common Gram-Negative Bacteria Isolated from the Bloodstream in a Teaching Hospital". *Chemotherapy* vol.47, pp.29-38. Switzerland, 2001.
- <P010427> **LING T.K.W.; LIU E.Y.M.; LING J.M.L. and CHENG A.F.B.** "A Study of Extended Spectrum Beta-Lactamase Producing Organisms in Hong Kong". Paper presented in the 3rd International Symposium on Antimicrobial Agents and Resistance, organized by Asian-Pacific Research Foundation for Infectious Diseases. Korea, 2001.04.

- <P010428> **LING K.W. Thomas; FUNG S.C. Kitty and CHENG F.B. Augustine.** "In vitro Activity and Post-Antibiotic Effect of Quinupristin/Dalfopristin (Synercid)". *Chemotherapy* vol.47, pp.243-249. Switzerland, 2001.
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- <P010430> **IP M.; LYON D.J.; YUNG R.W.H. and CHENG A.F.B.** "Macrolide Resistance Determinants in β -Haemolytic Streptococci and *Streptococcus Pneumoniae* in Hong Kong". Paper presented in the 3rd International Symposium on Antimicrobial Agents and Resistance, organized by Asian-Pacific Research Foundation. Korea, 2001.04.
- <P010431> **LYON D.J. and IP M.** "Drug Resistant *S. Pneumoniae* - Trends in Hong Kong". Paper presented in the 3rd International Symposium on Antimicrobial Agents and Resistance, organized by Asian-Pacific Research Foundation for Infectious Diseases. Korea, 2001.04.
- <P010432> **HOUANG E.T.** "Antimicrobial Susceptibilities of *Acinetobacter* Spp from Different Sources in Hong Kong". Paper presented in the 3rd International Symposium on Antimicrobial Agents and Resistance, organized by Asian-Pacific Research Foundation for Infectious Disease Korea, 2001.04.
- <P010433> **CHOW V.; LYON D.J. and CHENG A.F.B.** "MRSA from the Community: Experience in a University Hospital in Hong Kong". Paper presented in the 3rd International Symposium on Antimicrobial Agents and Resistance, organized by Asian-Pacific Research Foundation for Infectious Diseases. Korea, 2001.04.
- <P010541> **YEW W.W.; WONG C.F.; CHAN C.Y.; CHEUNG S.W. and CHENG A.F.B.** "Serological Diagnosis of Tuberculosis Using IgA Detection Against the Mycobacterial Kp-90 Antigen". *International Journal of Tuberculosis Lung Disease* vol.5 no.6, pp.585-587. France, 2001.
- <P010568> **IP Margaret; LYON J. Donald; YUNG W.H. Raymond; CHAN Colin and CHENG F.B. Augustine.** "Macrolide Resistance in *Streptococcus Pneumoniae* in Hong Kong". *Antimicrobial Agents and Chemotherapy* vol.45 no.5, pp.1578-1580. USA, 2001.
- <P010780> **LING J.M.; CHAN E.W.C. and CHENG A.F.** "Molecular Epidemiological Analysis of *Salmonella Enterica* Serotype Derby Infections in Hong Kong". *Journal of Infection* vol.42, pp.145-153. UK, 2001.
- <P010813> **CHAN K.S. Paul; NG Ho-Keung; HUI Mamie and CHENG F. Augustine.** "Prevalence and Distribution of Human Herpesvirus 6 Variants A and B in Adult Human Brain". *Journal of Medical Virology* vol.64, pp.42-46. 2001.
- <P011132> **CHAN C.Y.; AU YEANG C.; HO Y.; CHIN M.L.; YEW W.W. and CHENG A.F.B.** "In vitro Activities of Fluoroquinolones against Mycobacterium Tuberculosis". *Abstracts of the 3rd International Symposium on Antimicrobial Agents and Resistance* Abstracts no.E4. Korea: Asian-Pacific Research Foundation for Infectious Diseases, 2001.04.
- <P011133> **LING T.K.W.; TAM P.C.; LIU Z.K. and CHENG A.F.B.** "The Evaluation of VITEK 2 Rapid Identification and Susceptibility Testing System against Gram-Negative Clinical Isolates". *Abstracts of the 101st General Meeting American Society for Microbiology* p.229. Florida, 2001.05.
- <P011672> **NG K.C.; CHAN S.W.; LYON D.J.; CHEUNG W.L.; CHENG F.B. and RAINER T.H.** "Acute Bacterial Gastroenteritis in Adult Patients Treated in the Emergency Department of a Regional Hospital". *Abstract Book, 5th Annual Scientific Meeting, The Hong Kong Society for Infectious Diseases* p.23. Hong Kong, 2001.03.31.
- <P011678> **CHAN P.K.S.; CHIK K.W.; LI C.K.; TANG N.L.S.; MING M.S.K.; CHEUNG J.L.K.; NG K.C.; YUEN P.M.P. and CHENG A.F.** "Prevalence and Genotype Distribution of TT Virus in

Various Specimen Types from Thalassaemic Patients". *Journal of Viral Hepatitis* vol.8, pp.304-309. UK, 2001.

see also <P002899>, <P002996>, <P003251>, <P003252>, <P003386>, <P004015>, <P004016>, <P007067>, <P010128>, <P010212>, <P010350>, <P010492>, <P010587>, <P010588>, <P011017>, <P011300>, <P011660>, <P011673>, <P011679>

RESEARCH PROJECTS

Psychosocial Outcome Following Phase II Cardiac Rehabilitation in Clients with Acute Coronary Syndromes - Pilot Study

- ✉ CHAN Dominic Shung Kit • CHAU Pak Chun Janita
- ☐ 1 July 2000
- ❖ CUHK Nursing Department Research Grant

Heart disease continues to be the second highest 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. Identification of possible barriers may facilitate health professional to develop strategies to increase clients' participation.

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 (HADS) to assess anxiety and depression, Social Support Questionnaire (SSQ6) to assess social support, State Self-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 cardiac rehabilitation programme.

(MD00312)

An Evaluation of the Effectiveness of a Multisensory Environment on Clients with Learning Disability

- ✉ CHAN Wai Chi Sally • CHIEN Wai Tong • TO Yuen Fung Maggie*
- ☐ 28 May 2001
- ❖ Health Care & Promotion Fund, Hospital Authority

Purpose: The purpose of this project is to promote the psychological health of clients with learning disability by implementing a multisensory environment, and to evaluate the relative impact of this multisensory environment on subjects' emotional

state, level of relaxation, challenging behaviour, maladaptive and adaptive behaviour; as well as to investigate nurses' perception on the benefits and difficulties towards the use of multisensory environment.

Study design: Randomised controlled trial.

Study venue: The Learning Disability Unit in Kwai Chung Hospital.

Intervention: Subjects attend the multisensory environment room for 1-hour session at alternative day for 12 weeks.

Sample: 72 subjects will be recruited from the Learning Disability Unit in Kwai Chung Hospital and randomly assigned to experimental and control group. Registered nurses (RNs) (n=10) working in the learning disability unit will be invited for a semi-structured interview.

Outcome measures: Pre and post assessment using Snoezelen Diary Card, the Behavioural Relaxation Scale, pulse rate, Checklist of Challenging Behaviour, the Behaviour Checklist, medication use and discharge rate, together with a semi-structured interview.

(MD00708)

Preparation for Pregnancy, Labour & the Early Postpartum Period: An Evaluation of a Hospital Based Antenatal Education Program

- ✉ HOLROYD Eleanor Anne • IP Wan Yim • TWINN Sheila Frances
- ☐ 1 January 2001
- ❖ Health Care & Promotion Fund, Hospital Authority

Objectives: To identify, using two consecutive programs at two hospitals, perceptions of women, antenatal educators and service providers of the educational effectiveness of the structural components of the programs in preparing women for pregnancy, labour and early postpartum period. To identify the perceptions of women, antenatal educators and service providers of the educational effectiveness of the processes used in the programs (including course content, skills taught and learning styles) to prepare women for pregnancy, labour and early postpartum period. To identify the perceptions of women, antenatal educators and service providers of the educational outcomes of the programs in preparing women for pregnancy, labour and early postpartum period. To examine the similarities and differences of the educational effectiveness of two consecutive antenatal antenatal education programs on the preparation for pregnancy, labour and early postpartum period. To examine the similarities and differences in the perceptions of the women, antenatal educators and service providers on the educational effectiveness of the programs in preparing for pregnancy, labour and early postpartum period.

Design: A multiple case study approach. The 'case' being defined as the antenatal program.

Sample: Clients (women attend classes at the two hospitals), antenatal educators, service providers.

Outcomes: Educational outcomes for the women concerned will be assessed by (1) Chinese antenatal knowledge questionnaire. (2) Focus groups. (3) Three telephone interviews, each being both structured (to determine skills) and semi-structured to determine women's perceptions of the appropriateness of the knowledge gained. Antenatal educators and service providers perceptions of the contribution of the classes will be assessed by face-to-face semi-structured interviews. (MD20028)

Chinese Families' Experiences with Residential Care Placement of Their Elderly Relatives

✉ LEE Tze Fan Diana • MACKENZIE Ann Elizabeth

□ 1 November 2000

❖ Research Grants Council (Earmarked Grants)

Rapid changes in social and economic structures of Chinese families in Hong Kong have resulted in an increasing number of elderly people moving into residential care homes. However, admitting an elderly relative to residential care is a stressful experience for the families. While a large body of research reveals the different aspects of the families' post-placement difficulties, less is known of the dynamic process through which the families adjust to such placement. Still less is known of this process in Chinese families who are confronted with such a challenge.

This study is to explore the process through which Chinese families in Hong Kong adjust to residential care placement of their elderly relatives. Approximately 20 family members will be invited to participate in a series of in-depth interviews to reveal how their post-placement experiences change over time. These interviews will be conducted within one week of their elderly relatives' admission and then every two months until no new information can be discovered. It is estimated that each informant will be interviewed four times, giving a total of 80 interviews for the study. Results of this study will (1) produce a sound theoretical basis for health care professionals to identify and evaluate appropriate interventions to support the families at particular points in the post-placement period and (2) provide a Chinese cultural perspective to understanding the families' post-placement experiences. (CU00376)

The Nursing Care Needs of Chinese Elders in Residential Care Homes in Britain

✉ LEE Tze Fan Diana

□ 1 January 2001

❖ United Board for Christian Higher Education in Asia Faculty Research Gr.

Being the third largest ethnic minority group in Britain, the Chinese community has increased dramatically with the emigration of families from Hong Kong (Au & Au 1992). Parallel with this increase is the growing number of Chinese elders seeking for residential care in Britain. Yet, there is an extensive literature that addresses the lack of cultural care provided to ethnic elderly (Kayser-Jones 1997). One of the problems identified is care-givers' lack of understanding about the nursing care needs of elders with different ethnic and cultural background.

The purpose of this study is therefore to identify the nursing care needs of Chinese elders residing in residential care homes in Britain. Three residential care homes in London have agreed to provide access to the study. Twenty Chinese elders who are able to communicate and are residing in these homes will be explained of the purpose of the study and invited to participate. Written consent forms will be signed and audio-taped informal interviews will be conducted with the elders to identify their needs at different stages of residence at these homes. The audio-taped data of the interview will then be transcribed and coded for content analysis to identify commonalities and differences in the data. On the basis of these similarities and differences, the needs of Chinese elders residing in residential care homes will be identified. The knowledge thus obtained is of great value in guiding gerontological workers to formulate relevant interventions to address the needs of Chinese elders with dignity and success.

Upon completion of data analysis, two seminars will also be conducted for residential care home workers in London to disseminate the findings of this study and explore ways to better address the nursing care needs of Chinese elders residing in residential care homes in Britain.

(SS00804)

Determining Research Priorities for Critical Care Nurses in Hong Kong: A Delphi Study

✉ LOPEZ Violeta

□ 1 May 2001

❖ CUHK Research Committee Funding (Direct Grants)

Purpose: To determine the most significant problems or questions affecting the welfare of critically-ill patients and their families as well as critical care nurses that can be answered through nursing research.

Design: A two-round Delphi technique.

Sample: A purposive sample of all critical care nurses who are members of the Hong Kong Association of Critical Care Nurses.

Method: A two-round mailed survey using questionnaires developed from round one. First round questionnaire will include questions related to general demographic data (sex, age, qualifications, experience, positions).

Analysis: Descriptive statistics (frequencies, means and standard deviations) will be obtained to rank order each research problem or question identified as well as rank order these within each of the eight domains of nursing research areas: patient care, family care, nurses' competencies, practice standards, physiological and psychological concerns, and technology used in patient management.

Outcome: The results of this study will give direction for critical care nurses as to what areas of investigation have the greatest social relevance and the most impact on patient care. Critical care nurses in Hong Kong will be able to focus their research efforts in determining what patient problems, nursing strategies and approaches are most important and what should be studied first. Documenting nursing research priorities is critical to building the knowledge base for nursing practice. (MD00435)

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	Nursing Management of Oral Mucositis in Cancer Patients (MD99083) ✉ CHANG Anne Marie • MOLASIOTIS Alexandros# •

	CHAN YIP Carmen Wing Han • LEE Yik Mun*
1998-99	A Care Protocol to Reduce Hospital Readmissions of Elderly Residential Care Home Patients with Chronic Obstructive Pulmonary Disease (COPD) (MD98073) ✉ LEE Tze Fan Diana • MACKENZIE Ann Elizabeth • LEE Fung Kam • LAI Shuet Fun, Adela* • LO Lai Fong, Tammi*
1999-00	Developing Reliable and Valid Chinese Measure of Diabetes Empowerment Scale (MD99121) ✉ SHIU Tak Ying • WONG Yee Man Rebecca*
1998-99	The Influence of Extrinsic and Intrinsic Factors on Uptake Rates for Cervical Screening: A Comparison of Perceptions of Hong Kong Chinese Women and Practitioners (MD98010) ✉ TWINN Sheila Frances • HOLROYD Eleanor Anne • ADAB Peymane*
1999-00	Psychometric Evaluation of the Chinese Version of the Parental Stressor Scale: Paediatric Intensive Care Unit (MD99117) ✉ YAM Bernard Man Chung • LOPEZ Violeta

RESEARCH OUTPUTS AND PUBLICATIONS

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RESEARCH PROJECTS

Microsatellite Instability in the Evolution of Cervical Neoplasm and Its Clinical Association

✉ CHUNG Kwok Hung Tony • WONG Yick Fu • CHEUNG Tak Hong • YU Mei Yung (Dept of Anatomical & Cellular Pathology)

☐ 1 April 2001

❖ CUHK Research Committee Funding (Direct Grants)

Cervical carcinoma is the most common female genital tract cancer in Hong Kong. Ninety-five per cent of them are squamous cell carcinoma. The molecular events involved in cervical tumourigenesis are not well understood. Cervical squamous cell carcinoma is preceded by distinct premalignant epithelial changes known as cervical intraepithelial neoplasia (CIN). Infection with specific subtypes of human papillomavirus (HPV) has been strongly implicated in cervical carcinogenesis. However, HPV infection alone is insufficient for malignant transformation of the cervical epithelium. Microsatellites are widely distributed repetitive DNA sequences composed of short tandemly repeated nucleotide motifs. An alteration of microsatellite repeats is the result of slippage owing to strand misalignment during DNA replication and is referred to as microsatellite instability (MSI). These defects in DNA repair pathways as a route for human carcinogenesis are now widely recognised. The association of MSI with disease outcome has been noted in human solid tumours, but the prognostic significance of MSI status in different tumours is still unclear. This project proposes to determine the incidence of MSI in CIN and cervical cancer and its relationship to clinicopathological characteristics and HPV status. Polymerase chain reaction (PCR) based microsatellite assay combined with tissue microdissection with laser and needle systems will be used to examine for MSI in 20 subjects with normal cervix, 80 CINs and 80 cervical squamous cell carcinomas in Hong Kong women. The results from this study will improve our understanding of molecular pathogenesis of cervical cancer, and may define the prognostic significance of MSI status in this neoplasm.

(MD00784)

A Randomized, Double-blind Placebo-controlled Crossover Study of the Effect of Livial (tibolone) on the Dyadic Relationship of Chinese Couples

✉ LAM Po Mui • SHEK Tan Lei Daniel (Dept of Social Work) • LEE Tak Shing Dominic (Dept of Psychiatry) • CHEUNG Wai Yan Grace*

☐ 9 October 2000

❖ Hong Kong Obstetrical and Gynaecological Trust Fund

Livial is a relatively new form of hormone replacement therapy for menopausal women. It has been shown that it can affect climacteric symptoms, elevates mood and increases libido and has a favourable impact on the physiology of the vagina. These effects would be expected to affect the relationship between a woman and her partner. This is a randomized double-blind placebo-controlled crossover study of the effect of Livial (tibolone). The primary outcome measured will be the dyadic relationship of Chinese couples, as assessed by the dyadic adjustment scale. The secondary outcomes are the psychological well being of the couples, as assessed by the general health Questionnaire, and the menopausal symptoms, as assessed by the Greene climacteric questionnaire.

(MD00939)

Quality of Life Measurements in Chinese Women with Urinary Incontinence: A Validation & Clinical Application Study

✉ LEUNG Ho Yin Peter • YIP Shing Kai Alexander • HO CHAN Suzanne (Dept of Community and Family Medicine) • CHUNG Kwok Hung Tony • LEE Tak Shing Dominic (Dept of Psychiatry)

☐ 1 July 2000

❖ Health Services Research Fund, Hospital Authority

This study aims to investigate the reliability, responsiveness and validity of quality of life questionnaire in Chinese women suffering from urinary incontinence. This study also tests the quality of life questionnaire's clinical applicability.

(MD20003)

Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study

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

☐ 4 May 1999

❖ National Institutes of Health

This is a 5-year multi-centre worldwide international collaborative observational study involving 16 centres (Hong Kong as a field centre) and 25,000 pregnant subjects. The aim is to investigate the associations of various levels of glucose intolerance during pregnancy and risks of adverse maternal and perinatal outcomes. The data obtained can be used to develop internationally acceptable guidelines for diagnosis and classification of gestational diabetes mellitus. It will test the hypothesis that

hyperglycaemia in pregnancy, less severe than overt diabetes mellitus, is associated with increased risk of adverse maternal, fetal and neonatal outcomes that is independently related to the degree of metabolic disturbance.
(MD98171)

To Assess the Predictive Value of Ultrasonic Assessment of Umbilical Cord Morphology for Intrapartum Fetal Distress

- ✉ ROGERS Michael Scott • IP Wan Yim (The Nethersole School of Nursing) • LAU Tze Kin • PANG Chi Pui Calvin (Dept of Ophthalmology and Visual Sciences)
- ☐ 1 September 2000
- ❖ Health Services Research Fund, Hospital Authority

Objectives: (1) to determine the difference in operative intervention rates (for fetal distress) between pregnancies with non-coiled and normally coiled umbilical cords; (2) to validate second trimester ultrasonic measurements of umbilical coiling index (UCI) for predicting the occurrence of tight nuchal cord entanglement, operative delivery for fetal distress, and oxidative stress during labour; and (3) to assess the relationships between perinatal outcome measures and the amniotic fluid index, cord entanglement and cord morphology.

Design: (1 & 3) Prospective Observational. (2) Prospective Prediction.

Setting: Department of Obstetrics & Gynaecology, Prince of Wales Hospital, Shatin.

Methods: (1 & 3) Record the incidence of cord entanglement, oligohydramnios, fetal distress and intervention during labour. Measure the UCI and cord arterial lipid peroxide concentrations after birth (2) Measure the second trimester UCI.

Analyses: (1) Comparison of proportions of women undergoing operative delivery for fetal distress in pregnancies with normal and non-coiled umbilical cords (2) Predictive values of UCI for intervention for fetal distress, tight cord entanglement and poor perinatal outcome: ROC curve analysis. Agreement between ultrasound and actual measurements of coiling index will be assessed by Cohen's kappa statistics. (3) The relative contributions of determinants of cord compression to raised lipid peroxidation: multivariate path analysis.
(MD20007)

Development of National Guidelines for Safe Motherhood for Vietnam

- ✉ ROGERS Michael Scott
- ☐ 16 June 2001
- ❖ United Nations Population Fund (UNPFA)

The research will chair a committee of national (Vietnamese) experts on provision of reproductive health services. The aims of this committee are to develop national guidelines on reproductive health and safe motherhood for application in Vietnam.
(MD00412)

A Prospective Observational Study on the Rate of Development of Fetal Hypoxia During the Different Parts of the Second Stage of Labour Using Fetal Pulse Oximetry

- ✉ TSUI Hang Yuet Michelle • SAHOTA Daljit Singh • LAU Tze Kin
- ☐ 1 April 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

The second stage of labour is a stressful period for the fetus as it descends down the maternal pelvis. Adverse fetal outcomes are often attributed to events which occur during second stage. Many advocate instrumental delivery when the total length of second stage exceeds a certain time limit, as it is believed that the length of maternal bearing down effort is associated with a linear fall in fetal pH. The researchers' hypothesis, however, is that it is the latter part of second stage, when the fetal head is lower down in the pelvis and distending the perineum that a more rapid development of hypoxia and acidosis occurs. With the recent development in fetal pulse oximetry which allows non-invasive and continuous measurement of fetal oxygenation status, the researchers are now able to test the above hypothesis and gain better understanding of the development of fetal hypoxia in relation to the duration of the different parts of second stage.

In this study, the rate of change of fetal oxygenation (SpO₂) during the different parts of second stage of labour will be the primary outcome measurement. If the researchers' hypothesis is true, it would be the duration of the latter part of second stage that should be considered in the decision to perform instrumental delivery. This is particularly relevant to the Chinese primigravida, as prolonged second stage is common and often a long time is taken for the fetal head to stretch the perineum before delivery can occur.
(MD00711)

Methylation Profiling of Gene Promoter CpG Islands in Cervical Neoplasm

- ✉ WONG Yick Fu • CHUNG Kwok Hung Tony • CHEUNG Tak Hong
- ☐ 1 February 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Hypermethylation of promoter CpG islands is associated with transcriptional silencing, in particular, in tumour suppressor genes in many types of human cancer, and is believed to be involved in tumour development and progression. Cervical squamous cell carcinoma is a unique and important carcinogenesis model because it develops through a pre-malignant stage of high-grade cervical intraepithelial neoplasia (CIN-H) to invasive cancer. Previously the researchers have detected the methylation of p16 tumour suppressor gene in a subgroup of cervical cancer. In this study they will comprehensively analyze the DNA methylation status of 14 confirmed and putative tumour-suppressor genes that are hypermethylated in different kinds of human cancer. 20 patients with CIN-H and 60 patients with invasive cervical squamous cell carcinoma at different stage will be examined using a highly sensitive methylation-specific polymerase chain reaction method. In addition the researchers will also determine the methylation of these genes in serum DNA in cervical cancer patients. This investigation into methylation profiles in pre-malignant and malignant neoplasms of uterus cervix is likely to advance understanding of the role of gene methylation in cervical tumourigenesis, and may potentially reveal epigenetic targets for cervical cancer intervention, prognostic marker development, and strategies to managing cervical cancer patients. So far no systematic gene methylation analysis in these neoplasms has been reported. This study will be collaborated with Prof. Herman JG, The Oncology Center, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, who is a renown specialist in the study of gene methylation in human cancer. (MD00701)

Psychosocial Morbidity Following Miscarriage: A Prospective Observational Study of Chinese Women in Hong Kong

- ✉ 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
- ☐ 1 November 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Spontaneous abortion is one of the commonest problems complicating early pregnancy. Its common occurrence has tended to obscure the psychological suffering of the women, which has been largely neglected by both the public and the attending professionals. Previous studies have revealed a substantial proportion of women with miscarriage might suffer from major depression in the short term. However, the long term psychological impact of miscarriage has not been studied. In addition, the

psychological reaction of the male partners as well as the effect of miscarriage upon marital relationship have been left unexplored. While miscarriage contributes to a significant proportion of gynaecological admission in our daily practice, data revealing its psychological impact in our local population has been scarce. Furthermore, there has been no interventional study performed to date to help to relieve the psychological stress experienced by these miscarried patients. The researchers thus propose to perform this prospective observational study to assess the prevalence, nature, and progression of psychological and marital morbidity associated with miscarriage in our local population. The results will not only facilitate our understanding in the nature and progression of the psycho-social morbidity following miscarriage, but may also shed light on the type and timing of intervention that we should provide. The study would be expected to help to formulate counseling services we should provide to this group of patients whose psychological well-being are now largely neglected. (MD00600)

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

<u>Edition</u>	<u>Title/Investigators</u>
1997-98	Intratype Variation of Human Papillomavirus Infection in Cervical Cancer: A Regional Perspective in China (MD97054) ✉ CHUNG Kwok Hung Tony • WONG Yick Fu • CHEUNG Tak Hong
1998-99	Prevalence and Intra-type Variation of Human Papillomavirus (HPV) Infection in Cervical Cancers: A Nationwide Perspective of China (CU98248) ✉ CHUNG Kwok Hung Tony • WONG Yick Fu • CHAN Kwok Mei May (Dept of Anatomical & Cellular Pathology)
1998-99	Pro-apoptotic and Anti-apoptotic Regulators in Cervical Neoplasm: Expression of Both Bcl-2 and Caspase Family Members (Bcl-2, Bcl-X, Bax, Mcl-1, Caspase-3 and Caspase-7) (MD98044) ✉ CHUNG Kwok Hung Tony • WONG Yick Fu • CHEUNG Tak Hong • YU Mei Yung (Dept of Anatomical & Cellular Pathology)
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.*
- 1998-99 Evidence for Oxidative Stress and Apoptosis in the Brain Following Perinatal Hypoxicischaemic Insults (CU98251)
 ✎ HAINES Christopher John • FISCUS Ronald Ray (Dept of Physiology) • JAMES Anthony Edward (Laboratory Animal Services Centre) • STADLIN Alfreda (Dept of Anatomy) • WONG Yick Fu • ROGERS Michael Scott
- 1999-00 A Comparison of the Antiatherogenic Properties of Estradiol with Other Cardioprotectants Used in the Treatment of Postmenopausal Women (CU99268)
 ✎ HAINES Christopher John • JAMES Anthony Edward (Laboratory Animal Services Centre) • SAHOTA Daljit Singh • CHOW Tsun Cheung Louis (Dept of Anatomical & Cellular Pathology) • TOMLINSON Brian (Dept of Medicine & Therapeutics) • PANESAR Nirmal Singh (Dept of Chemical Pathology) • BENZIE Iris F. F.* • HUSBAND Alan James*
- 1999-00 The Incidence of Microdeletions of the Azoospermic Factor (AZF) Genes(s) in Individual Sperm from Both Severe Oligospermic and Normospermic Semen (MD99044)
 ✎ HAINES Christopher John • BRITON-JONES Christine May • CHIU Tak Yu Tony • TJER Ching Ching (Lee Hysan Clinical Research Laboratories) • YEUNG Sum Yee Queenie • CHEUNG Lai Ping • WONG Yick Fu
- 1999-00 A Study on Placental Transfer of Nonsteroidal Anti-inflammatory Drugs at Early Gestation (MD99045)
 ✎ LAU Tze Kin • SIU Shing Shun Nelson • YEUNG Hok Keung John (Dept of Pharmacology)
- 1999-00 The Effect of Placental Hypoxia on Trophoblastic Corticotrophin-releasing Hormone (CRH) Secretion in-vitro (MD99046)
 ✎ LEUNG Tse Ngong • LAU Tze Kin • WONG Yick Fu
- 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
- 1997-98 A Prospective Randomised Controlled Study of Using Oral Misoprostol and Vaginal Prostaglandin E₂ for Induction of Labour in Patients with Unfavourable Cervix (MD97122)
 ✎ SAHOTA Daljit Singh • LO Wing Kit • LEUNG Tse Ngong • YUEN Pong Mo • CHUNG Kwok Hung Tony • CHANG Mang Z. Allan
- 1998-99 Customised Growth Assessment in the Local Ethnic Chinese Population (MD98104)
 ✎ SAHOTA Daljit Singh • LAU Tze Kin • LEUNG Tse Ngong • PANG Man Wah Selina • CHANG Mang Z. Allan
- 1998-99 A Comparison of the Effect of Dydrogesterone and Medroxyprogesterone Acetate on the Serum Lipid Profile and Plasma Total Antioxidant Capacity in Chinese Post-Menopausal Women on Oestrogen Replacement (MD98017)
 ✎ TAM Wing Hung • HAINES Christopher John • LAM Wai Kei Christopher (Dept of Chemical Pathology)
- 1999-00 Effect of Antenatal Corticosteroids Therapy on Material 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)
- 1998-99 Is Bat Quasi-monomorphic Tract a Prognostic Indicator for Endometrial Cancer? A Translational Study of a Biomolecular Marker to Clinical Utility (MD98045)
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- 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*
Health) • CHUNG Kwok Hung Tony • LEUNG Peter Ho Yin* • CHEON Cecilia* • LIU John Yu Sun* • WONG Thomas Hong Kwong*
- 1999-00 A Randomized, Double-blind Multi-centre Controlled Trial on Tolterodine versus Oxybutynin in the Treatment of Chinese Women with Overactive Bladder: A Quality of Life and Economic Evaluation Study (MD99094)
✉ YIP Shing Kai Alexander • LAU Tak Fai Joseph (School of Public
- 1999-00 A Follow-up Study of Patients with Postpartum Urinary Retention (MD99107)
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RESEARCH PROJECTS

Genetic Cause of Age-related Macular Degeneration in Hong Kong

- ✉ CHAN Wai Man • PANG Chi Pui Calvin • LAM Shun Chiu Dennis • FAN Shu Ping Dorothy • KWOK Kwan Ho • BAUM Lawrence William (Dept of Medicine & Therapeutics)
- ☐ 1 October 2000
- ❖ CUHK Departmental Funding • CUHK Research Committee Funding (Direct Grants)

Age-related macular degeneration (AMD) is the leading cause of severe visual loss and blindness in the elderly in most developed countries. Its occurrence is pan-ethnic and its etiology multifactorial. There is growing evidence that genetic influences play an important role. Other risk factors include age, cigarette smoking, sunlight, diet and hypercholesterolemia. To date, there is no known cure for AMD despite its high prevalence in our local population. Treatment options are limited and ineffective. The purpose of this proposed project is to reveal in the local population the association of AMD with the environmental and genetic factors. The retina specific ATP-binding transporter (*ABCR*) gene on chromosome 1p13-21 has been shown to be a causative gene of AMD. More than 23 *ABCR* mutations have been reported in Caucasian populations, although no *ABCR* mutation was found in a recent Japanese study. The status in Chinese so far is still not known. The apolipoprotein E (*APOE*) gene on chromosome 19q13.2 is also a susceptibility gene for AMD. *APOE* plays an important role in regulating the metabolism of lipoproteins in plasma and central nervous system. The E4 isoform of *APOE* was shown to have the protective effect from developing AMD. The researchers therefore propose a case-control study on 100 AMD patients and 100 age matched normal control subjects to investigate the effects of known risk factors including diet, smoking, sun exposure, hypercholesterolemia, *APOE* genotype and *ABCR* mutations on the development of AMD. (MD99333)

Clinical Presentation and Genome Mapping of Congenital Cataract

- ✉ FAN Shu Ping Dorothy • PANG Chi Pui Calvin • LAM Shun Chiu Dennis • LEUNG Yuk Fai
- ☐ 1 June 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Cataract is an extremely common eye disease leading to severe visual impairment and even to blindness if

not treated properly. Although most cataracts are senile there is a congenital form of cataract, which also causes visual dysfunction. Study on the genetic factors of congenital cataract may throw light on the etiology of cataract. Recently mutations in the *CRYAA* and *CRYBB2* genes have been shown to be cataract causing. The researchers' preliminary investigation on 3 Chinese families with congenital cataract revealed absence of the reported mutations, suggesting a possible different mutation pattern in Chinese as compared to Caucasians. The researchers therefore propose to screen for sequence alterations in all the known coding and splice regions of these genes in a large number of congenital cataract patients and controls. The researchers' genotypic results will be analysed in the light of the phenotypic features and their study subjects to identify cataract causative *CRYAA* and *CRYBB2* mutations. (MD00950)

Safety of Intravitreal Injection of Various Concentrations of Indocyanine Green Dye

- ✉ KWOK Kwan Ho • LAM Shun Chiu Dennis • PANG Chi Pui Calvin • YAM Hin Fai • LAI Yuk Yau Timothy
- ☐ 1 June 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Histopathologic studies of eyes after macular hole surgery have suggested the proliferation of Muller cells and fibrous astrocytes which restored foveal anatomy. Adjuncts transforming growth factor- β 2, autologous serum, platelet concentrates and laser photocoagulation have been studied to promote formation of a glial scar and to close the edges of the macular hole. Since good visual outcome had been obtained after the removal of internal limiting membrane (ILM) in Terson syndrome, several studies have suggested the removal of ILM in macular hole surgery may relieve tangential traction and promote gliosis. Besides macular hole surgery, the removal of ILM has been advocated in vitrectomy of diabetic patients with severe macular edema. However, visualization of the thin and transparent ILM intraoperatively is very difficult and may preclude its complete removal without damaging other parts of the retina. Recently, the researchers and Kadonosono et al had respectively used indocyanine green (ICG) staining followed by removal of ILM in macular hole surgery with very promising results. ICG is a commonly used intravenous dye for ophthalmic fundus angiogram. It has been proved to be safe through this route of administration, despite the known fact of intraretinal leakage. However, the safety of different concentrations of ICG through intravitreal injection has not been determined. The researchers therefore propose this research to study

this problem. The result can reasonably extrapolate in human eyes for clinical use. It also lays a foundation for further study of ICG-stained ILM in various macular diseases.
(MD00325)

Study on the Use of Single Intraoperative Mitomycin C and Conjunctival Autograft to Prevent Recurrence in the Treatment of Double Head Pterygia

✉ LAM Shun Chiu Dennis • YEUNG Emily Fung-ye* • CHI Chung-chai* • YUEN Kwok-lai*

☐ 1 June 2000

❖ CUHK Departmental Funding

The pterygium is an ocular disease with a multifactorial etiology and is found more commonly in tropical areas where ultraviolet light exposure is high. Many surgical treatments have been described for its treatment. The range of treatment include bare sclera technique, beta irradiation, conjunctival autograft, topical mitomycin C and lamella keratoplasty. However recurrence rate has remained high especially in tropical areas, including Hong Kong. Currently, excision with single intraoperative topical mitomycin C or conjunctival autograft are the most wisely used techniques.

In double head pterygia (nasal and temporal pterygia in one eye), treatment are even more difficult as conjunctival tissue is limited if autograft is chosen and the rare event of scleral melting in topical mitomycin C can be disastrous. Combining the use of the two regimes in the treatment of double head pterygia would seem a more logical approach and is the rationale of the present study.

(MD00753)

Use of Conjunctival-limbal Autografts Versus Intraoperative Application of Mitomycin-C in Treatment of Recurrent Pterygium in Hong Kong

✉ LAM Shun Chiu Dennis • RAO Srinivas Kamalakara# • YU Yau Woon Edward#

☐ 1 July 2000

❖ Research Grants Council (Earmarked Grants)

Pterygium presents as a subconjunctival fibrovascular growth with progressive invasion onto the cornea. Vision is reduced by visual axis obstruction or induced corneal astigmatism. In Hong Kong, pterygium is particularly prevalent, with the treatment procedure second only to cataract surgery. Simple excision of pterygium often results in unacceptable high recurrence rate up to 80% so adjuvant therapies are usually employed, including the use of conjunctival autograft, intraoperative application of mitomycin C or a combination of both. All these methods are reported to achieve a higher

cure rate with reduced recurrence in primary pterygium in the range of 5.3% to 35%.

Recurrent pterygium is more symptomatic than its primary counterpart, much more difficult to remove surgically and the results of using either conjunctival autograft or intraoperative mitomycin-C is less effective and confusing. There is no clinical study of the use of these modified techniques in the treatment of recurrent pterygium in the Chinese population, nor is there any clinical trial on the efficacy of the combined regime in the recurred pterygium in the literature. This study tries to compare the safety and efficacy of the three surgical techniques in the treatment of recurrent pterygium in a standardized clinical trial. This will provide important information about the treatment response of these techniques among local Chinese population.

(CU00052)

A Randomized Trial to Investigate the Ocular-hypertensive Response to Different Dosages of Topical Steroid (0.1% Dexamethasone) in Chinese Children

✉ LAM Shun Chiu Dennis • FAN Shu Ping Dorothy • NG Siu King Joan • YU Bing On Christopher

☐ 1 October 2000

❖ Research Grants Council (Earmarked Grants)

Topical steroids are commonly used anti-inflammatory agents after ophthalmic operations as well as for treating various eye disorders. A sight threatening side effect of topical application of steroids is ocular-hypertensive response (steroid induced glaucoma). The response in adults is well defined and established. Little information, however, is available regarding such response in children. The researchers have recently demonstrated that the ocular - hypertensive response to topical steroids in Chinese children occurs more frequently, more severely, and more rapidly than that reported in adults. Since topical steroid is needed for its anti-inflammatory action in many pediatric conditions, there is a need to study the maximum safe dosage of topical steroid application in Chinese children. A prospective randomized controlled trial to compare the ocular-hypertensive response to different dosages of topical steroid in Chinese children is therefore proposed.

(CU00050)

Retinal Electrophysiological Changes in Patients Following Acute Angle Closure Glaucoma

✉ LAM Shun Chiu Dennis • LAI Timothy Yuk-yau* • CHUA Kien Han John • FAN Shu Ping Dorothy • KWOK Kwan Ho • AU Wai Hing

☐ 1 January 2001

❖ CUHK Departmental Funding

Primary acute angle closure glaucoma (AACG) is due to sudden occlusion of the angle by iris tissue resulting in abrupt rise in the intraocular pressure. Persistently high intraocular pressure can result in irreversible optic nerve damage. Visual loss following AACG is due to retinal ganglion cell loss as a result of the raised intraocular pressure. Histological studies have documented loss of retinal ganglion cells, photoreceptors and retinal pigment epithelial cells in glaucoma. Therefore, electrophysiological study of the retina may reveal changes following an attack of AACG.

Electrophysiological studies used to assess the function of the retina include electrooculography (EOG) and electroretinography (ERG). EOG and ERG measure the gross response of the retina as a whole and readings from EOG and ERG is usually normal unless there is more extensive retinal involvement due to the disease. A relatively new electrophysiologic diagnostic technique known as multifocal electroretinogram (MERG) allows simultaneous recording of focal ERGs from multiple retinal location by cross-correlation techniques. In contrast to EOG or ERG, MERG has the advantage of being able to detect focal abnormality in the central 30-40 degrees of the retina instead of the generalized retina.

This study aims to investigate the disturbance in retinal electrophysiology in patients following acute angle closure glaucoma using EOG, ERG, and MERG.

(MD00552)

A One Year Multi-center, Double-masked, Placebo-controlled, Parallel, Safety and Efficacy Study of 2% Pirezepine Ophthalmic Gel in Children with Myopia

✉ LAM Shun Chiu Dennis • FAN Shu Ping Dorothy

□ 1 January 2001

❖ Valley Forge Pharmaceuticals, Inc.

Myopia is one of the commonest eye diseases worldwide. Different optical and pharmacological methods have been used to control myopic progression. The aim of the study is to evaluate the safety and efficacy of pirezepine in prevention of myopic progression in children.

(MD20040)

Topical Anaesthesia versus Transcutaneous Anaesthetic Injection in Chalazion Surgery

✉ LAM Shun Chiu Dennis • LI Randa T.H.* • LEUNG Tai Shing • NG Siu King Joan • LAI Jimmy Shiu-ming*

□ 1 April 2001

❖ CUHK Departmental Funding

Objective: To determine whether lidocaine 2% gel is an effective anesthetic agent for chalazion surgery.

Design: A randomized controlled clinical trial.

Setting: Specialist Outpatients Clinics in Public Hospitals.

Subjects: Patients of greater than 12 years of age attending our eye clinics requiring incision and curettage for chalazion are recruited over a 6 months period.

Interventions: Patients are randomly allocated into two treatment groups. One group will be given 1.5 ml of 2% lignocaine injection for anesthesia. The other group will be given 1.5 ml of 2% lidocaine gel for anesthesia. Both groups will have incision and curettage 5 minutes after anesthetic administration.

Main outcome measures: Pain experienced during the operation and immediately afterwards will be assessed by a linear zero to one hundred (0-100) analogue pain score.

Results: Pain scores from the topical anesthesia group will be compared with the injection group. An independent t-test or a Mann-Whitney's U test will be used depending on the data distribution and sample size.

Conclusions: The researchers wish to conclude whether 2% lidocaine gel is effective or not in chalazion surgery.

Implications: If 2% lidocaine gel is proved to be an effective anesthetic agent in chalazion surgery, then patients requiring chalazion surgery in the future may avoid the need for injections. If no needles are required, complications from needle injections can be eliminated and the costs of needles and syringes can also be saved. This may therefore be a more cost-effective alternative to be considered by healthcare providers.

(MD00745)

A One-year Multi-center, Double-masked, Placebo-controlled, Parallel, Safety and Efficacy Study of 2% Pirezepine Ophthalmic Gel in Children with Myopia

✉ LAM Shun Chiu Dennis • FAN Shu Ping Dorothy • LAM Robert Fung

□ 1 June 2001

❖ CUHK Departmental Funding

The exact mechanism of myopia (shortsightedness) although remains unknown, both nature and nurture are of importance in the development of this common ocular disorder. Environmental factor such as near work has been shown to associate with myopia in different studies. It is now known that the retina, rather than the ciliary muscle, plays a pivotal role in the control of normal eye growth and elongation.

Different methods have been attempted to reduce the myopic progression. Optical correction by contact lens, bifocal lenses and progressive glasses have been tried. However, the application of these studies was limited because of the small sample size or problems in the study designs.

Pharmacological agent such as atropine has been proven to prevent myopic progression. However, atropine application is associated with side effects, for example mydriasis, cycloplegia and toxicity. It was previously thought that the cessation of accommodation by atropine reduced the myopia progression. On the other hand, other nonaccommodative mechanisms of action had been suggested recently. Inhibition of the scleral chondrocytes might be the mechanism of action. Therefore, newer types of drugs are now attracting attention. Selective anti-muscarinic blocker such as pirenzepine is proposed. This newer medication is selective and thus reduces the side effects of atropine. The children do not need to wear bifocal or progressive lenses for near vision. The photophobia and potential sunlight toxicity will be minimized. In this study, the researchers would like to find out the safety and effectiveness of pirenzepine in arresting myopic progression in Chinese children. (MD00996)

An Observer-masked, Parallel Group, Randomized, 7-day Environment Study of Patanol versus Loratadine in Asian Patients from Hong Kong with Perennial Allergic Conjunctivitis

- ✉ LAW Wai Kee • LAM Shun Chiu Dennis • LEUNG Tai Shing
- ☐ 18 September 2000
- ❖ Alcon Hong Kong Ltd

To compare the efficacy of PATANOL versus Loratadine in the treatment of the ocular signs and symptoms of moderate to severe perennial allergic conjunctivitis.

The primary objective of this study is to demonstrate superiority of Patanol over Loratadine in reducing ocular itching and redness immediately (3, 10, 20 minutes) after the first dose. The primary efficacy variables are ocular: itching & redness immediately after the first dose. The secondary efficacy variable are in-office ocular itching and redness, nasal signs and symptoms (stuffy nose, sneezing, runny nose, itchy nose, postnasal drip), physician's global assessment of ocular and nasal condition. Repeated measures analysis of variance will be used to assess differences between treatments in the primary and secondary efficacy variables. (MD20052)

Role of the Putative Promoter of the *TIGR* Gene on Development of Primary Open Angle Glaucoma

- ✉ PANG Chi Pui Calvin • LAM Shun Chiu Dennis • FAN Shu Ping Dorothy • CHUA Kien Han John • BAUM Lawrence William (Dept of Medicine & Therapeutics)
- ☐ 1 November 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Primary open angle glaucoma (POAG) is a common form of glaucoma, which is a leading cause of visual field defects and blindness in developed countries. It affects about 2% of the world's population and is multifactorial in etiology. In 1997, *TIGR* was identified as a causative gene of POAG. *TIGR* protein is expressed in many eye tissues including trabecular meshwork (TM), which offers resistance to aqueous humor outflow. The *TIGR* gene spans 20 kb in chromosome 1q24-25 and includes 3 exons encoding 504 amino acids. More than 40 sequence variants have been reported in *TIGR* coding regions. Recently the researchers have shown a homozygous Arg46Stop in an elderly woman without POAG. Thus, they have proposed that the known *TIGR* missense mutations probably do not cause glaucoma by inactivating a normal *TIGR* function, but through gain of a pathogenic function. While the *TIGR* coding regions have been actively investigated, the definitive sequence of the *TIGR* promoter is still to be confirmed. However it likely spans at least several hundred bp and is characterized by multiple-consensus steroid hormone-responsive elements and other regulatory motifs.

The researchers therefore propose to sequence the putative promoter region of *TIGR* in POAG patients responsive to steroid, POAG patients non-responsive to steroid, and non-glaucomatous elderly control subjects. Of the putative proximal promoter, 5,000 bp will be studied. The results of this study will throw light on the structural organization of the *TIGR* promoter and will discover promoter sequences that are responsive to steroid treatment. There will be improved basic understanding of the *TIGR* gene and possible clinical applications. (MD00439)

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	Sequence Alterations in the PAX 6 Gene In-Patients with Aniridia or Anterior Segment Dysgenesis and Their Predictive Value for the Development of Glaucoma (MD98105)
	✉ CHUA Kien Han John • LAM Shun Chiu Dennis • PANG Chi Pui Calvin

- CHENG Chak Kwan Arthur ●
FAN Shu Ping Dorothy
- 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 (School of Public Health) ● FAN Shu Ping Dorothy ● CHENG Hong Ming*
- 1999-00 A 12-week, Multi-center, Double-masked, Parallel-group Comparison of the IOP-reducing Effect and Safety of Latanoprost 50µg/ml to That of Timolol 5mg/ml, in Patients with Chronic Angle-closure glaucoma (MD99088)
- ✍ LAM Shun Chiu Dennis ● CHUA Kien Han John ● LAI Shiu Ming Jimmy ● CHEW Paul* ● CHOY Kan* ● MVSCAT Nina*
- 1998-99 Study on Sequence Aberrations in the Mitochondrial Genome in Leber Hereditary Optic Neuropathy (LHON) and determination of their Predictive Value for Clinical Course and Outcome (MD98036)
✍ PANG Chi Pui Calvin ● LAM Shun Chiu Dennis ● LAM Ching Wan (Dept of Chemical Pathology) ● CHENG Chak Kwan Arthur ● FAN Shu Ping Dorothy
- 1998-99 Effects of Genetic Variants of Lipoprotein Lipase on Coronary Heart Disease and Familial Combined Hyperlipidaemia (CU98282)
✍ PANG Chi Pui Calvin ● TOMLINSON Brian (Dept of Medicine & Therapeutics)

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- <P019531> **LAM Shun Chiu Dennis and CHAN Wai Man.** "Images in Clinical Medicine. Choroidal Ischemia in Preeclampsia". *The New England Journal of Medicine* vol.344 no.10, p.739. UK, 2001.03.08.
- <P019979> **LAI Jimmy S. M.; Tham, Clement C.Y. and LAM Shun Chiu Dennis.** "Comparative Study of Intraoperative Mitomycin C and Beta Irradiation in Pterygium Surgery". *British Journal of Ophthalmology* vol.85, p.121. UK, 2001.01.

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RESEARCH PROJECTS

Low Intensity Pulsed Ultrasound Retained Change of Bone Mineral Content of Complex Tibial Fractures

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- ☐ 1 October 2000
- ❖ CUHK Departmental Funding

Objectives: Low intensity pulsed ultrasound was reported to enhance bone healing in uncomplicated closed tibial fractures and distal radial fractures. The researchers investigated the effect of low intensity pulsed ultrasound on the healing of complex fractures.

Materials and methods: Patients who suffered from complex tibial fractures were recruited. 9 of them are open fracture while 4 of them are closed fracture. Average age of patients is 47.3 years and the range of 29-72 years. The patients were randomly assigned to treatment or control group by block randomisation. Patients in treatment group received low intensity pulsed ultrasound (SAFHS 2000, Exogen, New Jersey, USA). The treatment regime was daily application with ultrasound intensity 30mW/cm² (ISATA) for 20 minutes at the fracture site. The treatment period lasted for 3 months and the post-treatment follow-up was another 3 months. The bone mineral content (BMC) of fracture callus was measured by dual energy x-ray absorptiometer (XR-36, Norland, USA). Serum bone-specific activity, a biochemical marker for bone formation, was also assayed.

Results: For ultrasound treatment group, the percentage change in BMC of the fracture site with respect to the baseline (pre-treatment) remained almost the same in treatment and post-treatment period. However the percentage change in BMC of the callus in control group decreased by about 30%. The drop of BMC may be due to the immobilization of fracture by fixation. Ultrasound enhances the bone mineralisation that counteracts the decline of BMC. The ultrasound effect on the callus was sustained after treatment period. In serum BALP activity assay, the increase of activity in the control group was greater than that in the ultrasound treatment group. As referring to the decline of BMC in the control group, the rise of BALP may be due to the feedback of the bone loss as osteoporosis.

Conclusion: Low intensity pulsed ultrasound treatment increases bone mineralisation during fracture healing of complex fractures and its effect sustained to post-treatment.

(MD00354)

Low Intensity Pulsed Ultrasound Enhanced Bone Mineral Content of Tibial Lengthening

- ✉ CHAN Chun Wai* • LEUNG Kwok Sui • CHENG Chun Yiu Jack • NG Kin Wah Bobby • LEE Wing Sze • HUNG Wing Yin Vivian
- ☐ 1 October 2000
- ❖ CUHK Departmental Funding

Objectives: Low intensity pulsed ultrasound was reported to enhance bone healing in closed tibial fracture and distal radial fractures. This study is to investigate the effect of low intensity pulsed ultrasound on the bone mineral density of tibia lengthening.

Materials and methods: 6 patients were performed tibial osteotomy bilaterally. After the distraction ceased, left or right tibia was randomly assigned to treatment or control group by block randomization. Lengthened tibiae in treatment group were subjected to receive low intensity pulsed ultrasound (SAFHS 2000, Exogen, New Jersey, USA). The treatment regime was daily application with ultrasound intensity 30mW/cm² (ISATA) for 20 minutes. The treatment period lasted for 3 months and the post-treatment follow-up was another 3 months. The bone mineral content (BMC) of distraction callus was measured by dual energy x-ray absorptiometer (XR-36, Norland, USA).

Results: In the first half of treatment period, the increase in treatment group (18.7%) was higher than that in control group (16.6%). However, in the second half of treatment period, the percentage increase in BMC in treatment group (15.8%) was less than that in control group (16.9%). There was no significant difference between the treatment and the control group.

Conclusions: Low intensity pulsed ultrasound may enhance bone mineralisation slightly at the early stage of consolidation stage of lengthening. (MD00579)

Normal Position of Cerebellar Tonsil in Chinese Adolescents - An MRI Study

- ✉ CHAU Wai Wang • CHENG Chun Yiu Jack • GUO Xia • Chan YL*
- ☐ 1 October 1999
- ❖ CUHK Departmental Funding

Chiari-I malformation with tonsillar ectopia of herniation is well known to be associated with juvenile idiopathic scoliosis. The researchers' previous study also revealed similar association with adolescent idiopathic scoliosis. Available references were based on adult Caucasian MRI data. The aim of the present study was to define the normal position of the cerebellar tonsil in healthy Chinese adolescents. Sagittal plane total spine MRI imaging (T1 weighted) has been performed on 61 normal subjects (19 boys and 42 girls) 12 to 14 years of age. The standard

reference line connecting the basion and opisthion (BO line) in the best selected MRI sagittal image was used. The perpendicular distance from the tip of cerebral tonsil to the BO line was measured. Results showed that the distance of tonsillar displacement was $-4.03 \text{ cm} \pm 2.63 \text{ cm}$ for boys, and $-3.53 \text{ cm} \pm 2.95 \text{ cm}$ for girls. None of the subjects had tonsil below the reference line. This is in contrast to the reported adult data, which has been used as the "golden standard" for all age groups. (MD99497)

Re-defining the MRI Reference Level for Cerebellar Tonsil - A Study of 225 Adolescents - Normal vs Idiopathic Scoliosis

- ✉ CHAU Wai Wang • CHENG Chun Yiu Jack • GUO Xia • CHAN Y. L.*
☐ 1 October 2000
❖ CUHK Departmental Funding

Purpose: The association of Chiari-I malformation with idiopathic scoliosis has been reported with increasing frequency. However, the normal reference level of inferior displacement of cerebellar tonsils below the plane of the foramen magnum is still controversial as available references were based on studies of small number of adult MRI data. The aims of the present study are to redefine and compare the position of the cerebellar tonsil in adolescents with IS vs normal controls and to correlate the results with severity of the scoliosis.

Methods: Whole spine MRI was performed in 135 patients with AIS with Cobb's angle less than 45 degrees, 29 patients with Cobb's angle more than 45 degrees, and 61 healthy adolescents aged 12 to 14. The standard reference line connecting the basion and opisthion (BO line) in the best selected MRI sagittal image was used. The perpendicular distance from the tip of tonsil to the BO line was defined as negative or positive values when the tonsils lied above or below the BO line respectively.

Results: In all the healthy controls, the tip of the cerebellar tonsil was found to be above the BO line, with a mean distance of $-3.87 \pm 2.95 \text{ mm}$. In the AIS groups, inferior displacement of cerebellar tonsil below the BO line was found in 4 of 135 patients with Cobb's angle less than 45 degrees (3.0%), and in 8 of 29 patients with Cobb's angle above 45 degrees (27.6%).

Conclusion: This study has demonstrated that in adolescents, inferior displacement of the cerebellar tonsils below the BO line from standardized MRI measurements should be regarded as tonsillar herniation and that the currently used normal adult reference level of $+5 \text{ mm}$ is not applicable in adolescents. This has important clinical etiological and prognostic significance since using the new definition; a significant number of patients with AIS

would fall into the abnormal tonsillar herniation group. (MD00378)

The Implications of Preoperative Somatosensory Evoked Potential (SSEP) in Adolescent Idiopathic Scoliosis Patients

- ✉ CHAU Wai Wang • FU Lap Kun • GUO Xia • CHENG Chun Yiu Jack
☐ 1 March 2001
❖ CUHK Departmental Funding

Introduction: Intra-operative neuromonitoring (IOM) during scoliosis surgery is a well established technique in minimizing spinal cord and nerve damage during different stages of operation. However, pre-operative SSEP checking was not routinely done except in a few institutes.

Objectives: The study aimed to find out the number of cases with delayed latencies and amplitudes in pre-operative SSEP checking in lower extremities, and to correlate with the findings during IOM.

Materials and methods: 332 cases of pre-operative SSEP checking from 1996 to 2000 were selected. Posterior tibial nerves SSEPs of both sides were done. Readings of P37 and N45 were recorded on screen. Those patients requiring scoliosis surgery, and those with the pre-operative checking also, were further selected to look for any correlations of readings taken in IOM and the response during wake-up test.

Results: The P37 and N45 values are similar in both sides. The percentage of patients with the delay in both amplitudes and latencies in the percentage of over 5%, 10% and 15% were 8.66%, 5.723%, and 3.539% respectively. All of the patients showed lowered amplitudes and latencies during operation. More time and stimulation had to be taken for having a successful wake-up test.

Conclusions: Pre-operative SSEP checking shows a good and reliable predictive reference for the subsequent IOM monitoring, and gives an alert in performing wake-up test. (MD00430)

Osteopenia in Adolescent Idiopathic Scoliosis (AIS): A Histomorphometric Study

- ✉ CHENG Chun Yiu Jack • TANG Chun Yuen# • GUO Xia • QIN Ling • CHAN C.W.*
☐ 1 December 1999
❖ RGC-Central Allocation Scheme - Group Research

To study the histological features of bone biopsy and to correlate the histomorphometric variables with preoperative bone mineral density (BMD) in patients with AIS. Low BMD has been reported in AIS. However, there is limited information about the

histopathologic changes. Undecalcified and decalcified bone specimens from iliac crest and spinous process of AIS patients obtained intraoperatively were stained with Goldner and H&E stain respectively. Results were correlated with BMD of the lumbar spine (L2-L4) and proximal femur measured preoperatively. Bone histology showed significant less osteocyte count in the trabecular bone characterized with smooth and continuous borders in AIS patients. Histomorphometry confirmed the lower static parameters. The results correlated well with the decreased BMD.
(MD99870)

Asynchrony of Endochondral and Membranous Ossification in Adolescent Patients with Idiopathic Scoliosis (IS)

- ✉ CHENG Chun Yiu Jack • GUO Xia • NG Siu Woon Edmond# • CHEUNG Siu King • HUNG Wing Yin Vivian
- ☐ 1 December 1999
- ❖ Scoliosis Research Society - Etiology Grant

Based on the observation of smaller ratio of posterior to anterior column of thoracic spine in adolescent patients with IS, the researchers' hypothesis is that there is a generalized loss of synchronous coupling of endochondral and membranous ossification in patients with IS. 76 girls with IS aged 12 to 14 with right thoracic scoliosis with Cobb's angle less than 30 degree and 93 age and gender matched normal control subjects entered the study. Body height (BH) was measured to reflect the total body endochondral bone growth and the DEXA measured proximal femoral bone mineral density (BMD) was used to represent membranous bone formation. Results of this study showed significantly lower ratio of BMD to BH in IS patients of all age groups. This finding supported the above mentioned hypothesis that scoliotic deformity of the spine in AIS could be a result of asynchronous endochondral and membranous ossification.
(MD99922)

"Subacute Synovitis of the Hip in Children" A distinct Entity? - A follow up Study of 84 Cases

- ✉ CHENG Chun Yiu Jack • YUNG Shu Hang Patrick • NG Kin Wah Bobby • LAM Tsz Ping
- ☐ 1 January 2000
- ❖ CUHK Departmental Funding

"Subacute Synovitis of the Hip", which runs a more fluctuant clinical progress and slower response to treatment than those of acute transient synovitis, is always posing diagnostic and management challenge in children presented with acute hip pain. This study aims to identify the special features of this distinct

entity, and the important diagnostic parameters in differentiation of acute transient synovitis, subacute synovitis and also septic arthritis in children presented with acute painful pain. From 1985-1999, 427 children have been admitted into Prince of Wales Hospital with subsequent diagnosis of acute transient synovitis, subacute synovitis & septic arthritis. 320 cases with full records are available for review, with 270 cases (85%) having acute transient synovitis, 35 cases (10%) of subacute synovitis and 15 cases (5%) of septic arthritis. Statistical results showed that patient having subacute different significantly from those with acute transient synovitis in terms of age of presentation & duration of symptoms before hospitalization and also on the body temperature on admission, CRP and White Cell count.
(MD99384)

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

- ✉ CHENG Chun Yiu Jack • FUNG Kwai Yau • MAK Arthur*
- ☐ 1 August 2000
- ❖ S K Yee Medical Foundation

The Seating Clinic for Children with Neuromuscular Disease of the Prince of Wales Hospital was first established in November 1994. The clinic is the first of its kind jointly organized by the Rehabilitation Engineering Center of the Hong Kong Polytechnic University, the Department of Orthopaedics and Traumatology (Paediatric Orthopaedics) of the Chinese University of Hong Kong and the Allied Health Division (physiotherapy, prosthetics & orthotics, occupational therapy) of the Prince of Wales Hospital. The Seating Clinic is currently located in the Prince of Wales Hospital. The clinic served children suffering from neuromuscular disorders with special seating and mobility needs. It operates with a multi-disciplinary team of paediatric orthopaedic specialist, rehabilitation engineer, prosthetist and orthotist, physiotherapist and occupational therapist. Children were better positioned in their prescribed seating systems with the right accessories. With these encouraging outcomes, the team now strives to further improve the quality of service by addressing their needs in communication, powered mobility and alternative forms of play. The ultimate goal of 'enhancing function through positioning' still waits to be fulfilled. The application of assistive technology in conjunction with seating intervention was much indicated in this group of children. These needs, though important, were unable to be met without the necessary resources and funding.

An assistive technology device is actually any item, piece of equipment, or product system, whether acquired commercially off the shelf, modified, or customized, that is used to increase, maintain, or improve functional capabilities of individuals with disabilities. Three areas of assistive technology application are proposed in this pilot project. They are assistive technology for communication, computer access and powered mobility. (MD20002)

Can Exogenous Vascular Endothelial Growth Factor (VEGF) Enhance Angiogenesis and Osteogenesis in Posterior Spinal Fusion?

✉ CHENG Chun Yiu Jack • CHOW Pak Ham Patricia (Dept of Anatomy) • GUO Xia • LEE Simon K. M.* • TABATA Yasuhiko*

☐ 1 December 2000

❖ Research Grants Council (Earmarked Grants)

Spinal deformities and degenerative diseases are very common diseases in orthopaedics, many of which would require surgical stabilization and posterior spinal fusion (PSF). Solid bony fusion is most important for the success and outcome of the treatment and failure of which can result in significant morbidity. The nonunion rate in posterior spinal fusion has been reported to range 5-35%. An important area of research is on the biological enhancement of the bony fusion, both in the quality and the rapidity. Angiogenesis has been known to play an important role in spinal fusion process by improving tissue oxygenation, enhancing the transport of nutrients and growth factors and promoting cellular and matrix deposition in the bone fusion area, a mechanism quite similar to fracture healing process.

Most recently, vascular endothelial growth factor (VEGF) has been found to play an important role in mediating capillary invasion and triggering endochondral ossification. However, direct observation of effect of VEGF on spinal fusion has not been reported. The main objectives of this study are to use a well established rabbit PSF model to study the VEGF and VEGF receptors (VEGFR) expression pattern in the standard spinal fusion process and to compare the angiogenesis and osteogenesis effect of exogenous VEGF between different delivery systems in promoting spinal fusion. The outcome of this study will shed light on our understanding the role of angiogenesis and its regulation by VEGF during spina fusion process. The results of the effect of exogenous VEGF treatment will demonstrate the feasibility and possibility of accelerating and improving the quality of the spinal fusion in an optimised delivery system. Success of this new approach could form the basis of further clinical studies to enhance spinal fusion and

decrease the complication and morbidity associated with delayed union or nonunion in PSF. (CU00140)

Virtual Reality (VR) Based Systems for Training on Endoscopic Surgery and Diagnostic Ultrasound Procedures

✉ 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*

☐ 1 March 2001

❖ RGC-Central Allocation Scheme - Group Research

The major advantage of endoscopic surgery (therapeutic) is in minimizing trauma to the body cavity. Although this surgical technique is friendlier to patients, they are more demanding for surgeons. Depth perception is lost as most camera systems transmit only two-dimensional images and much of the tactile sensation is also lost. Conventional training using simulators helps with the initial phase of hand-eye coordination but it is difficult to simulate the actual surgery. Training on animals likewise has its drawbacks as the shape of all four legged animals, being long from front to back and narrow from side to side is in sharp contrast to the human anatomy. On the other hand, ultrasound as a diagnostic procedure has been increasingly used especially in obstetrics because of its non-invasiveness and safety. The skill of obstetric ultrasound examination is particularly difficult to learn because of the unpredictable fetal position in utero and frequent fetal movements. Similar to the endoscopic surgery, hand-eye coordination has to be trained too.

Training the multitude of novice medical officers and interns to acquire the skill of endoscopic surgery and/or obstetric ultrasound examination (diagnostic) is a major task in medical education. Virtual reality (VR) based simulation systems provide a very elegant solution to the problem, because the researchers can provide virtual models of different anatomic structures to simulate different procedures in realism within the virtual environment. In this project, the researchers would focus on the research

and development of the following four virtual reality based training systems:

- (1) Virtual arthroscopic surgery;
- (2) Virtual laparoscopic surgery;
- (3) Virtual thoracoscopic surgery; and
- (4) Obstetric ultrasound examination (diagnostic). (EE20028)

Postural Balance and Gait: A Study on Girls with Idiopathic Scoliosis

✉ GUO Xia • Lau LM Miko* • CHOW Hung Kay, Daniel* • CHENG Chun Yiu Jack

☐ 1 March 2001

❖ Hong Kong Polytechnic University Central Research Grant

Introduction: Abnormality in posterior tibial nerve somatosensory cortical evoked potentials (PTN-SCEPs) was recently observed in some subjects with adolescent idiopathic scoliosis (AIS). This study investigates the biomechanical effects of this abnormality in subjects' postural balance and gait.

Methods: Postural balance and gait of eighteen girls with AIS with Cobb's angle of 25° (eight with abnormal PTN-SCEPs and ten with normal PTN-SCEPs) were measured and compared with eight age-matched normal adolescent volunteers using two force platforms (Advanced Mechanical Technology Inc., USA) and a 3-D motion analysis system (Vicon 370, Oxford Metrics Ltd., UK). All the subjects with AIS had right thoracic curve pattern with apical vertebra at the region between T7 and T9.

Results: It was found that there was no significant difference in postural balance between the subjects with AIS and the controls when the subjects were standing on a solid-base support. When perturbation of proprioception was induced using a foam-base support, all the subjects with AIS (either with or without normal PTN-SCEPs) showed significantly poorer postural balance than the controls with $p < 0.05$. For the gait analysis, all the subjects showed symmetry in the temporal-distance parameters. However, the subjects with AIS and abnormal PTN-SCEPs showed significant asymmetry in their kinetic parameters with $p < 0.05$.

Conclusions: Poorer static postural control and asymmetric kinetic gait pattern in subjects with AIS and abnormal PTN-SCEPs may impose adverse biomechanical effects on the spine. The clinical implication of this study should not be underestimated and further longitudinal studies are worth pursuing.

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(MD00699)

Electromotive Drug Delivery to Bone by the Pulsed Short-circuit Pulsed Direct Current Mode Iontophoresis

✉ HUNG Leung Kim • CHAN Chiu Yeung Raphael (Dept of Microbiology) • LIN Ge (Dept of Pharmacology) • ZHANG Yuanting (Dept of Electronic Engineering)

☐ 1 January 2001

❖ CUHK Research Committee Funding (Direct Grants)

The delivery of drugs to bone is more difficult than to soft tissues. The most common application of drugs to bone is the treatment of bone infections (osteomyelitis) with antibiotics. However this can be further impaired by reduced vascularity, the presence of dead space or necrotic bone. *Iontophoresis*, also known as *Electromotive Drug Administration*, regulates drug delivery by an electric field. Under the electromotive force, drug molecules are guided to move through tissues, thus ensuring a targeted delivery to tissues. Recent experimental studies using the technique to deliver drugs to coronary arteries, urinary bladder, allograft bone or administration of anti-arrhythmic agents have shown positive results. The researchers have previously studied the effects of iontophoresis on charged and

non-charged molecules permeation through skin, and have developed a modified current mode: the pulsed short-circuit pulsed direct current mode (*PSPDC*) (Lui, 1999, Zhao 1996, 1997). The researchers' pilot studies on iontophoresis of ofloxacin delivery through cortical bone has also demonstrated increased drug permeation under iontophoresis (Hung et al 1999). The researchers believe iontophoresis can open up a new way to deliver antibiotics to treat difficult bone infections. In this study they will investigate the effects of the *PSPDC* current mode on bone, the effects of different electric parameters, drug properties and different modes of electrode arrangement. (MD00695)

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

✉ KUMTA Shekhar Madhukar • CHOW Tsun Cheung Louis (Dept of Anatomical & Cellular Pathology) • LEE Simon K. M.* • LEUNG Ping Chung • ZHENG Ming Hao*

□ 1 September 2000

❖ Research Grants Council (Earmarked Grants)

Giant Cell Tumor of bone is an aggressive neoplasm that destroys bone and is notorious for its tendency to recur despite vigorous treatment. The clinical behaviour of this tumor varies from individual to individual and there are no established means as yet, by which one could predict the outcome and progress of patients affected by this tumor. The characteristic feature of this tumor is resorption and destruction of bone, which the researchers postulate is brought about by Osteoclast like giant cells that are recruited and stimulated by special regulatory factors secreted by the cells within this tumor. Destruction of bone occurs just beneath the joint surface of some of the major weight bearing joints and subsequent collapse of this bone results in disability and loss of limb function. The researchers postulate that certain factors such as the Osteoclast Differentiation Factor and the Osteoclast Inhibitory Factor play an important role in mediating this bone destruction. In addition other specialised tissue enzyme systems such as the urokinase-type plasminogen activation (UPA) system (which have been implicated in the process of tissue destruction, tumour invasion and metastasis) also play an important part. In this project, the researchers want to investigate the expression and secretion of these factors with the destructive potential and clinical behaviour of the tumor, so that effective additional treatments may be developed to control this tumor. (CU00142)

Anti-angiogenic and Antiresorptive Actions of Bisphosphonates and COX-2 Inhibitors on Osteosarcoma Cells (Surrogate Osteoblasts)

✉ KUMTA Shekhar Madhukar • LUI Po Yee Pauline# • FU Sai Chuen Bruma (Lee Hysan Clinical Research Laboratories) • CHEUNG Wing Hoi

□ 1 December 2000

❖ CUHK Research Committee Funding (Direct Grants)

Osteosarcoma is an aggressive malignant tumor of bone in which bone formation and bone destruction co-exist. Putative factors that control osteoclastic bone resorption are primarily secreted by osteoblasts in response to environmental changes. Being of osteoblastic lineage, Osteosarcoma cells may function as surrogate osteoblasts, and may mediate tumor-associated bone destruction. Bisphosphonates inhibit the synthesis of osteoclastic factors. Recent evidence also suggests that these drugs may inhibit the synthesis/action of an important class of proteolytic enzymes called Metalloproteinases. *MMP* mediated tissue destruction is part of the process of tumor spread and progression. Neoangiogenesis is an important obligatory component of this process. A large number of putative factors activate this process, VEGF is a prominent cytokine that plays a key role. Angiogenesis is also mediated by prostaglandin synthesis, which may be inhibited using COX-2 inhibitors. It is the researchers' postulate that the individual and combined effects of these drugs may inhibit the invasive potential of Osteosarcoma tumor cells thereby opening up new strategies of treatment. Using Sa-OS2 cell lines the researchers propose to observe the effects of Bisphosphonates and COX-2 inhibitors on expression of osteoclast/osteoblast related factors OPG/OPG-L, proteinases such as MMP-2, MMP-9, angiogenic factors such as VEGF-165. The researchers also propose to use an invasion assay that determines the invasive potential of tumor cells in order to study the effect of these drugs. Osteosarcoma is a tumor that is potentially lethal. Despite intensive therapy, 40-50% of patients will fail with conventional therapy because of drug resistance. This project envisages a novel approach to this problem and may benefit a large number of patients. (MD00642)

Monteggia Fracture in Children - A Review of 30 cases

✉ LAM Tsz Ping • Ma RF* • NG Kin Wah Bobby • CHENG Chun Yiu Jack

□ 1 October 2000

❖ CUHK Departmental Funding

Background: Monteggia fracture of the elbow is still one of the most commonly missed fracture in children. Poor results often result from missed cases. It is important to identify the factors that give rise to poor results so as to enable one to improve in the treatment of Monteggia fracture in children.

Objective: The aim of this study was to review the behavior and treatment results of Monteggia fracture in children.

Methodology: The charts and radiographs of patients with Monteggia fracture and below 16 years old were reviewed retrospectively.

Results: 33 patients were admitted with Monteggia fracture from 1995 to 1999. 30 (90.9%) complete records and radiographs were reviewed. There were 22 boys and 8 girls with an average age of 6.6 years old (range 1.5 to 15.8). None had concomitant injury except one (3.3%) with fracture of distal radius at the same limb. 4 patients (13.3%) had associated nerve palsies including 3 posterior interosseous nerve palsy and 1 median nerve palsy. The nerve palsies were treated conservatively and all recovered spontaneously. When the child was treated within 3 days after injury, all radial head dislocation could be successfully reduced by the close method except one (3.3%) with an intact annular ligament which prevented close reduction. The ulnar fracture was reduced by the close method in 20 cases, and by open reduction in 10 cases. The risk factors for open reduction included an oblique ulnar fracture, delayed treatment and irreducible radial head dislocation. 25 (83.3%) patients returned for clinical assessment. The average follow up was 4 years. All denied any elbow pain. Bruce scoring system was used to assess the injured elbow. 24 (96%) had good to excellent results and 1 (4%) had fair result. The child with fair result had delayed treatment 16 days after injury. 20 cases were treated with intra-medullary K-wire fixation for the ulnar fracture without any complication. 10 cases with oblique ulnar fractures were splinted with intra-medullary K-wires. None had subsequent displacement and all had excellent results according to the Bruce scoring system.

Conclusion and clinical significance: The single most important factor for obtaining good results with Monteggia fracture is not to miss the diagnosis. Nerve palsies associated with Monteggia fracture usually recover spontaneously. The radial head can be reduced by close means when treatment is not delayed. Intra-medullary K-wiring is a safe and effective method for splinting the ulnar fracture. An excellent result is expected when Monteggia fracture in children is treated promptly and appropriately.

(MD00535)

Anterior Spinal Fusion With Halm-Zielke Instrumentation System in Adolescent Idiopathic Scoliosis

✉ LAM Tsz Ping • NG Kin Wah Bobby • CHENG Chun Yiu Jack • Ma RF*

☐ 1 March 2001

❖ CUHK Departmental Funding

Background: Anterior spinal instrumentation and fusion can be very effective for the treatment of certain types of scoliosis particularly for the lumbar and thoracolumbar curves. Early generations of anterior instrumentation systems including the Dwyer and Zielke systems suffer from the drawbacks of easy implant breakage, gradual loss of correction, loss of normal lumbar lordosis and a high rate of pseudoarthrosis. The application of new generation of Halm-Zielke Instrumentation System in the three dimensional correction of the scoliosis deformity was first reported in 1994. .

Objective: The aim of the present study was to evaluate the effectiveness and safety profile of the Halm-Zielke Instrumentation System in the treatment of adolescent idiopathic scoliosis.

Methodology: The charts and radiographs of all patients undergoing surgery for scoliosis with the Halm-Zielke implant from 1999 to 2000 were reviewed and analyzed retrospectively.

Results: 10 patients underwent anterior spinal fusion with Halm-Zielke instrumentation from 1999 to 2000. All patients were included in the study. All were female patients with an average age of 15.7 . The average follow up was 17 months with a range of nine months to 2 years. All had idiopathic scoliosis at the thoracolumbar or lumbar region. 5 patients had the apical vertebra at L1, 3 at T12 and 2 at L2. An average of 4.6 levels were fused. The pre-operative Cobb's angle, apical vertebral rotation (Nash-Moe), apical vertebral translation and trunk shift were 57.1 degrees, 2.3, 6.1cm and 3.3cm respectively. The corresponding post-operative data were 14.2 degrees (75.1% correction), 0.6, 2.2cm (63.9% correction) and 3.4cm respectively. There was one patient with post-operative urinary tract infection which resolved with antibiotics treatment. Otherwise, there was no intra-operative and post-operative complication.

Conclusion and clinical significance: This preliminary report indicates that the Halm-Zielke Instrumentation System is an effective anterior system which provides stable fixation for this early part of follow up in the treatment of severe thoracolumbar or lumbar scoliosis.

(MD00788)

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

✉ 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)

□ 1 January 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 the 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 the research team has been actively involved in the past five years, the mechanism of neo-osteogenesis induced by external mechanical force during distraction phase has not been explored yet.

In this proposal the researchers plan to study the effect of external mechanical stimulation on biological system at 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, 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 PGE2 (one of the downstream effectors of COX-2) and COX-2 inhibitor 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. (MD00652)

Reconstruction of Damaged Physis with 3-D Chondrocytes Pellet Culture

✉ LEUNG Kwok Sui • LUI Po Yee Pauline# • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • CHEUNG Wing Hoi

□ 1 January 2001

❖ AO Research Commission

Physeal injuries are serious injuries in children. The successful treatment of growth plate injury continues to be challenging clinical problem to orthopaedic traumatologists. The current modalities for the repair of growth plate defects have limited success and the goal of accomplishing “functional repair” is seldom achieved. The implantation of 3-D chondrocyte pellet that shows full characteristics of normal physis offers a possible alternative to these methods. As demonstrated in the researchers' previous studies, growth plate chondrocytes could be isolated and grown *in vitro* without the loss of their capacity to differentiate into cartilage. Sufficient cells could be generated to initiate the repair of growth plate and the longitudinal growth by endochondral ossification. The repair tissues underwent developmental transitions as the normal growth plate. In the present study, the researchers aim to produce artificial growth plate in a larger size (larger than 4 mm in diameter) for complete growth plate reconstruction and future clinical application in human. The artificial implant will be grafted to the gap created between the metaphysis and diaphysis of the femur of adolescent rabbit by the modified distraction procedures. The researchers believe that the artificial physis can be implanted in various regions of the long bone and that the creation of a gap will provide an optimal environment for the growth of the implant. After a latency period 5 days post-operation, the osteotomy site will be distracted for 6 days at the rate of 0.5mm/day. The artificial physis will then be implanted before calcification occurs. Long-term follow-up studies for 6 months will be carried out to further confirm the immunological compliance, tissue incorporation, growth potential and functions of the artificial growth plate in the rabbit model. The fact that the transplanted growth plate which can be implanted in various regions of the long bone may help surgeons to operate on virgin areas where scar tissues are minimal. This may also allow easier fixation of the growth plate and enhance its incorporation in the recipient bone. Results obtained from this study hold extremely intriguing possibilities for the treatment of growth plate injuries in children. (MD20039)

Development and Clinical Trials of Compound Yun Zhi (Jiang Su) and Danshen (He Nan) Products

✉ LEUNG Ping Chung • FUNG Kwok Pui (Biochemistry) • LAM Wai Kei Christopher (Dept of Chemical Pathology) • LO Yuk Ming Dennis (Dept of Chemical Pathology)

☐ 1 December 2000

❖ University-Industry Collaboration Prog.: Matching Grant for Joint Research, ITF, Innovation & Tech. Commission • Winsor Health Products Ltd.

Researchers in Institute of Chinese Medicine of The Chinese University of Hong Kong will first make use of animal models to prove the biological activities of the compound products and find out the optimal combination of the two ingredients contained in Yun Zhi and Danshen product. They will then test the pharmaceutical activities of these products in healthy individuals. Clinical trials will also be performed in cancer patients in an attempt to prove that the compound product can on one hand enhance the effects of chemotherapy, perhaps by activating patients' immune system, and on the other hand, alleviate the adverse effects of the drugs. (MD20043)

Associated Osteoporosis of the Host Bone in Tibial Lengthening

✉ NG Kin Wah Bobby • HUNG Wing Yin Vivian • CHENG Chun Yiu Jack

☐ 1 October 2000

❖ CUHK Departmental Funding

Purpose of study: To correlate the stress shielding osteoporosis of adjacent host bone and the callotasis mineralisation changes with frame construct and alignment loss in tibial lengthening.

Method: The researchers studied callotasis and adjacent host bone mineralisation through whole period in achondroplasia patients who had bilateral tibial lengthening. The changes were correlated with frame construct, limb alignment loss and supplementary treatments.

Result: 10 patients (6 F and 4 M) had mean age at operation of 12.44(9.58-14.4)years. 8 Ilizarov Hybrid and 2 Orthofix uniplanar fixator were used. The average lengthening was 9.93, 9.6 cm; the Lengthening Index were 28.81, 29.56 days/cm for left and right tibia respectively. Adjacent host bone mineral density dropped at rate of -0.39 and -0.35% per day during lengthening. Gradual host bone and callotasis interface deformity developed in 4 patients at average of 45.4 (14-224) days after distraction. Frame revision corrected and prevented further deformity.

Conclusion: Stress shielded host bone osteoporosis is universal and may contribute to limb alignment loss during lengthening. Multiplanar fixation prevents deformity in tibial lengthening. Dynamisation, bone

marrow injection and ultrasonic stimulation can help in increasing mineralisation rate. Close BMD monitoring gives quantitative mineralisation progress to allow timely addition of mineralisation enhancing measures.

(MD00633)

Muscle-bone Biological Interaction in Adolescent Idiopathic Scoliosis

✉ QIN Ling • CHENG Chun Yiu Jack • Schonau E*

☐ 1 May 2001

❖ Germany/Hong Kong Joint Research Scheme

Bone mineral acquisition in growing children are closely related level of physical activities (mechanical usage). This is designed to examine the influence of Adolescent Idiopathic Scoliosis (AIS) on the muscle-bone biological and physiological relationship. The well established assessment methodologies using state-of-art research tools for studying muscle-bone interaction in German partner center, which are also newly installed in Hong Kong collaborating center, may allow a new classification of low bone mass and structural characterizations in AIS patients in primary (disease which predominantly affect bone) and secondary bone disorders (diseases which first affect muscle force). (MD20051)

Application of Low Intensity Pulsed Ultrasound for Bone-tendon Junction Repair

✉ QIN Ling • WONG Wan Nar Margaret • LEE Kwong Man, Simon* • LEUNG Kwok Sui

☐ 1 June 2001

❖ CUHK Research Committee Funding (Direct 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. However, its potential beneficial effects on accelerating bone-tendon junction repair have not been reported in the literature.

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. (MD00844)

Treatment of "Floating Elbow" in children

✍ TANG Ning • NG Kin Wah Bobby • CHENG Chun Yiu Jack

☐ 1 October 2000

❖ CUHK Departmental Funding

Objectives: Simultaneous ipsilateral supracondylar fracture of humerus and distal radius also named "Floating Elbow" is an uncommon and serious injury in children. This study is to identify predisposing factors, define injury mechanism and to evaluate the result of sequential percutaneous K-wire fixation in the treatment of this complex fracture.

Methodology: 13 patients with the diagnosis in a 5-year period were included in the study. All except one were treated by close reduction and percutaneous K-wire fixation of both fractures. Sequential reduction and fixation was done first on the unstable radius fracture followed by the supracondylar humeral fracture. Long arm casting was then applied for further immobilization of 4 to 6 weeks. Patients were reviewed with mean follow up 39.2 months (minimal 6 months). Modified Flynn classification was used for functional outcome assessment. The presence of significant joint laxity was also recorded.

Results: The age ranged from 3 to 10 years old (mean 7 yrs.) with M/F ratio of 8:5. All the humeral supracondylar fractures were Gartland extension type (I-4, II-1, III-8). Distal radius fractures included 9 completely displaced metaphyseal fractures, 2 greenstick fractures and 2 minimally displaced Salter Harris type II epiphyseal fractures. The more severely displaced distal radius fractures were associated with higher grades of humeral fractures. Associated ulna fracture was noted in 10 cases. 11 patients (85%) had a good (3) or excellent (8) outcome at final follow-up. There was one patient with fair and poor result respectively. No limitation in ADL /sports and the flexion range reached 125° (145°) were found even in the patient with lowest score. Joint laxity with elbow hyperextension was found in 12/13 of the patients. Average hospital stay was only 2.46 days.

Conclusion: Prompt reduction with proper sequence of reduction and percutaneous k-wire fixation of "Floating Elbow" can yield good functional outcome with short hospital stay. Joint laxity was found to be a common association.

(MD00960)

An Immunohistochemical Study on Expression of Decorin and Biglycan in Bone of Osteopenic Adolescent Idiopathic Scoliosis Girls

✍ TANG Shengping • CHENG Chun Yiu Jack • GUO Xia • LEE Kwong Man, Simon* • QIN Ling

☐ 1 October 2000

❖ CUHK Departmental Funding

Purpose: To detect the two-protein expression pattern in bone of AIS and to explore the possible correlation between the protein expression and bone mineral density parameters.

Methods: Bone biopsy was done during operation on AIS. 33 bone sample include 11 facet, 4 end plates, 4 spinal process, 3 rib and 11 iliac crest. The sample undergone decalcification tissue process and embedded in paraffin. The two-protein expression pattern was estimated by immunohistochemical procedures (avidin-biotin complex method). Bone mineral status was measured before operation.

Results: More positive expression of two protein were detected in cartilage cells and matrix than cortical and trabecular bone and matrix. The difference was significant ($p < 0.05$). Decorin shown more expression at superficial cartilage of facet, biglycan shown more expression in cartilage of facet close to bone. In cortical and trabecular matrix the immunoreaction of biglycan was higher than decorin. All patients show low bone mineral status. The expression of the two proteins in cartilage correlated positively with L2-4 BMD. Biglycan express in cortical bone also correlated with L2-4 BMD.

Conclusion: The two-protein expression pattern in AIS adds more clue to support that the pathogenesis of AIS may be of skeletal origin.

(MD00734)

Sternocleidomastoid Pseudotumor of Infants (SCMPOI) and Congenital Muscular Torticollis (CMT): The Relation Between Spontaneous Regression and Apoptosis

✍ TANG Shengping • CHENG Chun Yiu Jack • Liu ZQ* • QuanXM* • Qin JZ* • Zhang DW*

☐ 1 January 2001

❖ CUHK Departmental Funding

Purpose: To seek evidence that SCMPOI and CMT regression result from apoptosis.

Methods: Forty cases, 19 with pseudotumor and 33 without were investigated by light and electron microscope and TdT-mediated dUTP nick end labelling (TUNEL) technique for in situ cell death detection. The age distribution were as follow: <3 months, 7 cases; 3-8 months, 17 cases; 9-12 months, 7 cases; and >1 year, 11 cases.

Results: There were numerous cells with condensed nuclear and eosinophilic cytoplasm distributing in the proliferation interstitium. The myoblasts contained numerous large vacuoles, margination of heterochromatin, breakdown of cell membrane; the fibroblasts showed karyopyknosis and myelin figure. Muscle showed myelin figure, myofibril lysis and bulla formation. TUNEL techniques detected cell death more significantly in patients with tumour or in patient during 3-12 months age.

Conclusion: Apoptosis might be basic pathological characteristic and induce the mass to disappear. (MD00523)

Osteopenia in Adolescent Idiopathic Scoliosis (AIS): Preliminary Ultrastructural Study

✉ TANG Shengping • CHENG Chun Yiu Jack • GUO Xia • LEE Kwong Man, Simon* • QIN Ling

☐ 1 March 2001

❖ CUHK Departmental Funding

Purpose: To detect the possible association between apoptosis and osteopenia in AIS.

Method: 17 bone samples from operated AIS were examined by electron microscopy. The resources of bone samples include facet, rib, and spinous process.

Result: Sectioned examination of all bone samples by electron microscopy revealed osteocytes with apoptotic appearances such as aggregation of chromatin particles, discontinuous plasma membranes, vacuolated cytoplasm, and lipid formation. The degenerated osteocytes in all bone samples are common phenomenon.

Conclusion: The apoptosis of osteocytes in trabecular bone in AIS may be related to low bone mineral density in AIS. (MD00374)

Bacterial Adherence to Gentamicin-PMMA Beads

✉ WONG Wan Nar Margaret • HUI Mamie (Dept of Microbiology)

☐ 1 October 2000

❖ CUHK Departmental Funding

Gentamicin-PMMA beads are commonly used in the treatment of deep-seated infections. Since the antibiotic is not systemically absorbed, it can provide a high local antibiotic concentration but low serum level, thus minimizing ototoxicity and nephrotoxicity.

It is especially useful in the treatment of chronic osteomyelitis, as the bioavailability of systemically administered antibiotics to the infected bone is low due to the poor perfusion of bone tissue. However, clinical observation of recurrence of osteomyelitis after treatment with gentamicin-PMMA beads raises the suspicion of bacterial adherence to the beads' crevices and emergence of antibiotic resistance. A prospective clinical study of consecutive patients treated with gentamicin-PMMA beads for chronic osteomyelitis within a 12 months period will be examined for:

- (1) the change in bacteriology and antibiotic susceptibility by comparing the pre-treatment, post-treatment bone cultures and the retrieved gentamicin-PMMA beads cultures;
- (2) the presence of bacterial adherence from the retrieved gentamicin-PMMA beads by electron microscopy;
- (3) *in vitro* pharmacokinetics study of the gentamicin-PMMA beads, including gentamicin elucidation in both static and dynamic conditions to simulate *in vivo* condition, by the use of modified Robbins device; and
- (4) *in vitro* induction of bacterial resistance and adherence to the gentamicin-PMMA beads. The result may change the clinical practice of using gentamicin-PMMA beads, and lead to further studies on biomaterials modification.

(MD20030)

Bio-engineered Chondrocyte Pellet as Interposition Material for Acceleration of Bone-tendon Junction Healing and Restoration of Junctional Fibrocartilage Zone

✉ WONG Wan Nar Margaret • QIN Ling • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)

☐ 1 January 2001

❖ CUHK Research Committee Funding (Direct Grants)

The bone to tendon junction (BTJ) is a unique structure composed of a transitional fibrocartilage zone. Many trauma surgery and reconstructive surgeries involve re-establishment of a BTJ. Unfortunately such repair is often technically difficult and the biological healing in BTJ had been shown to be very slow, the fibrocartilage transitional zone often cannot be regenerated, with low subsequent mechanical strength.

The researchers have established a rabbit partial patellectomy model to study BTJ healing. Interposition with autologous articular cartilage was found to enhance BTJ healing. Structural integration at BTJ healing with cartilage interposition was found at 8 weeks, compared with no sign of healing without the cartilage graft. The resultant matrix proteoglycan content resembled those in

normal BTJ, as revealed by Safranin'O/Fast green staining.

The researchers hypothesized that bio-engineered chondrocyte pellet (BCP) can act as an activated artificial cartilage to accelerate BTJ healing, and restore the transitional fibrocartilage zone. The possibility of using allogeneous BCP in accelerating BTJ repair will be investigated.

The objectives of the project are:

- (1) To characterize the BTJ healing and restoration of junction fibrocartilage zone after BCP treatment.
- (2) To follow the proliferation and differentiation of chondrocyte in the BCP in BTJ healing process.
- (3) To investigate the new bone formation process in BTJ healing treated by BCP.

The results of this project will have major contribution and potential.

(MD00373)

Culture of Rabbit Chondrocytes Released from Rib Cage on Calcium Phosphate Ceramic and Collagen Sponge

✉ YEUNG Hiu Yan • LEE Kwong Man, Simon* • CHEUNG Wing Hoi • LAW Lai Pang • TABATA Yasuhiko* • CHENG Chun Yiu Jack

☐ 1 January 1999

❖ CUHK Departmental Funding

Introduction: Biomaterials in orthopaedic conditions are often used as osteoconductive media for bone regeneration. Effort was made to improve the osteoinductive property of the materials *in vivo*. Different growth factors have been incorporated into the material to promote the bone in growth and bone formation. However, the control of release of those growth factors has not been fully explored and the cost of the growth factor production is high. Cell-based biomaterials are alternative development with the aim to overcome the difficulty of protein purification and the cost of production. In the researchers' previous study, multicenters of endochondral ossification were observed in the fusion mass in a HA-TCP rBMP composite model. This shows that chondrocytes may play an important role in bone formation in spinal fusion model. Moreover, it is also well known that chondrocytes can synthesize different kinds of growth factors and morphogenes. The current study attempts to culture chondrocytes on to hydroxyapatite / tricalcium phosphate (HA/TCP) and collagen sponge.

Methods: Chondrocytes were released from the rib cage of 6-week-old New Zealand white rabbit. The cartilage and growth plate of the rabbit rib were treated with serial enzyme digestion to separate the chondrocytes from the extracellular matrix. Immediately after the release procedures, 2M chondrocytes with minimal volume of DMEM containing 10% fetal bovine serum and ascorbic acid was added onto the HA/TCP (10 mm x 5mm x 5mm)

and collagen sponge (5 mm x 5 mm x 3mm) for the cells to settle in the materials. After cultured for 5 weeks, the cell containing biomaterials were examined by stereomicroscope, histology, and cell viability assay to observe the morphology of chondrocytes growing on the materials.

Results: After 5 weeks of culture on the HA/TCP, the chondrocytes were concentrated at the bottom of the HA/TCP toward the bottom of the culture well. Multi-layers of cell and transparent matrix were observed. The pores of the HA/TCP were filled with cells and ingrowth of chondrocytes to the pores could be seen. By MTT assay as cell viability test, the cells appeared on the HA/TCP were able to grow. The chondrocytes directly contact with HA/TCP were laid flat on the material. Chondrocytes also formed matrix on top of the HA/TCP and was shown to be round shaped. Processes extended from a cell to others were observed. Chondrocytes were also grown in a manner of multi-layers and spreading on the collagen sponge. Similar to growing on the HA/TCP, the cells were not formed cluster but apart from each other. From the stereomicroscope, the cultured chondrocytes on collagen sponge were surrounded by extracellular matrix. The nodule of cartilage can be observed within the collagen sponge scaffold. Unlike growing on HA/TCP, all the cells appeared as round shaped and filling the sponge.

Conclusion: In this study, the researchers demonstrated that chondrocytes can be cultured on HA/TCP and collagen sponge and synthesize extracellular matrix. It is known that chondrocytes implantation can escape from the immunological response due to their surrounding extracellular matrix. Although after 5 weeks of culture the cells are still contracted at the bottom of the biomaterial, with further optimization of the culture conditions it is likely that a chondrocyte-based biomaterial can be further tested for implantation in different orthopaedic conditions.
(MD98751)

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

Edition Title/Investigators

1996-97 Health Benefits of Programmed Physical Exercise on the Prevention of Bone Loss in Postmenopausal Women (MD96021)

✉ CHAN Kai Ming • QIN Ling • LAU Edith Ming Chu (Dept of Community and Family Medicine) • WOO Jean (Dept of Medicine & Therapeutics) • LEE Shiu Hung (Dept of Community and Family Medicine)

- 1998-99 The Mechanisms of Delayed Healing and Chronic Disorders in Tendons - Characterization and Regulation of Proteoglycans of Patellar Tendon in a Rat Model (CU98255)
 ✍ CHAN Kai Ming • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • QIN Ling • CHAN Pui Barbara#
- 1998-99 A Cellular and Molecular Study of the Capacity of Cytokines to Promote Tendon and Ligament Healing Following Injury (CU98256)
 ✍ CHAN Kai Ming • LEE Ka Ho Kenneth (Dept of Anatomy)
- 1999-00 The Application of Verbasoside, 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)
- 1999-00 The Application of Verbasoside, 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 Active Living – the Way to Healthy Ageing (ED99033)
 ✍ CHAN Kai Ming • HA Sau Ching Amy (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 “Subacute Synovitis of the Hip in Children” A Distinct Entity? – A Follow Up Study of 84 Cases (MD98168)
 ✍ CHENG Chun Yiu Jack • LAM Tsz Ping • YUNG Shu Hang Patrick • NG Kin Wah Bobby
- 1999-00 Percutaneous Intramedullary Kirschner Wiring for Displaced Diaphyseal Forearm Fractures in Children (MD98169)
 ✍ CHENG Chun Yiu Jack • LAM Tsz Ping • NG Kin Wah Bobby • YUNG Shu Hang Patrick
- 1999-00 Results of Treatment of Scoliosis Patients Undergoing Posterior Instrumentation and Fusion Using the ISOLA Segmental Spinal System (MD99141)
 ✍ CHENG Chun Yiu Jack • LEUNG Ping Chung • NG Kin Wah Bobby • LAM Tsz Ping
- 1999-00 Intestinal Calcium Absorption Measured by Stable Calcium Isotopes in Northern Chinese Adolescents with Sub-optimal Vitamin D Status (MD99142)
 ✍ CHENG Chun Yiu Jack • LEE Tak Keung Warren • Jiang Ji* • Hu Pei* • Hu Xiaopeng*
- 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 The Loss of Synchronous Coupling of Endochondral and Membranous Ossification in Adolescent Idiopathic Scoliosis (MD99140)
 ✍ CHENG Chun Yiu Jack • GUO Xia • NG Siu Woon Edmond# • CHEUNG Siu King • HUNG Wing Yin Vivian
- 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 (School of Public Health) • HO CHAN Suzanne (Dept of

- Community and Family Medicine) • GUO Xia
- 1999-00 Association of Neuropathology with Adolescent Idiopathic Scoliosis – MRI and SEP Studies (MD99109)
 ✎ CHENG Chun Yiu Jack • GUO Xia • CHAN Yu Leung (Dept of Diagnostic Radiology & Organ Imaging)
- 1998-99 Efficiency and Tissue Safety of Transdermal Iontophoresis Treatment of Scar Tissues (MD98107)
 ✎ HUNG Leung Kim • LIN Ge (Dept of Pharmacology) • ZHANG Yuanting (Dept of Electronic Engineering)
- 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#
- 1997-98 A Comparative Study of the Mechanical and Histological Properties of Bone to Bone Union and Bone to Tendon Healing (MD97015)
 ✎ LEUNG Kwok Sui • QIN Ling • CHONG Wai Sing Wilson
- 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* • JAMES Anthony Edward (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)
- 1998-99 Intervention Prevention for Fast Bone Losers Identified with a High Accurate Imaging Peripheral Quantitative Computed Tomography (MD98108)
 ✎ LEUNG Ping Chung • QIN Ling • LAU Edith Ming Chu (Dept of Community and Family Medicine) • DAMBACHER M. A.*
- 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)
- 1999-00 An Evidence Based Study on the Clinical Effects of Two Herbal Preparations Recommended for the Treatment of Diabetic Ulcers (MD99050)
 ✎ LEUNG Ping Chung • YEW Tai Wai David (Dept of Anatomy) • BUT Pui Hay Paul (Dept of Biology) • WONG Wan Nar Margaret
- 1999-00 An Active Comparator-controlled, Parallel-group, 6-week, Double-blind Study, Conducted under In-house Blinding Conditions, to Assess the Safety and Efficacy of MK-0966 versus Naproxen in Patients with Osteoarthritis of the Knee or Hip (MD99084)
 ✎ LEUNG Ping Chung
- 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)
- 1997-98 A Comparative Study of the Mechanical and Histological Properties of Bone to Bone Union and Bone to Tendon Healing - A Goat Model (CU97668)
 ✎ WONG Wan Nar Margaret • QIN Ling • LEUNG Kwok Sui • ZHANG Yuanting (Dept of Electronic Engineering)
- 1999-00 Deleterious Effect of Glucocorticoids on Human Tendon Fibroblast and Possible ‘Rescue’ with Platelet Derived Growth Factor Isoform B (PDGF_{BB}) (MD99052)
 ✎ WONG Wan Nar Margaret • ROLF Christer# • CHAN Kai Ming • CHAN Pui Barbara#

RESEARCH OUTPUTS AND PUBLICATIONS

- <P996552> **CHENG E N M**、**梁國穗**、**馮國培**. 〈擴髓對髓內壓和肺部脂肪栓塞的影響〉. *Chin J Orthop*, vol.9 no.8, p.494-497. 中國, 1999.08.
- <P999211> **LEUNG Kwok Sui**. "The Study of Bone Ingrowth and Extraction of the Flexible Hamburg Humeral Nail". *Osteosynthese International* 8 Supplement 1, pp.S148-S151. Frankfurt, Germany: Johann Ambrosius Barth, 2000.
- <P999571> **CHENG Chun Yiu Jack; TANG Shengping and CHEN MK, Tracy**. "Sternocleidomastoid Pseudotumor and Congenital Muscular Torticollis in Infants: A Prospective Study of 510 Cases". *The Journal of Pediatrics* vol.134 no.6, pp.712-716. USA: Mosby, Inc, 1999.06.
- <P999789> **MAFFULLI Nicola; CHENG Chun Yiu Jack; SHER A. S. H.; NG Kin Wah Bobby and NG Siu Woon Edmond**. "Bone Mineralization at the Callotasis Site After Completion of Lengthening". *Bone* vol.25 no.3, pp.333-338. UK: Elsevier Science Inc., 1999.09.
- <P001024> **QIN L, AU SK, CHOY WY, CHAN KM and LEUNG PC** "Identification of 'Fast Bone Loser' Using pQCT for Prevention of Osteoporosis (in Chinese)". *Abstracts of the '99 National Conference of Sports Medicine*. p.106. Guangzhou, China: The Hong Kong Orthopaedic Association, 2000.11.
- <P001347> **ZHENG, Ming H.; Jiake XU; Peter ROBBINS; Nathan PAVLOS; Stan WYSOCKI; Shekhar M. KUMTA; David J. WOOD and John M. PAPPDIMITRIOU**. "Gene Expression of Vascular Endothelial Growth Factor in Giant Cell Tumors of Bone". *Human Pathology* vol.31 no.7, pp.804-812. 2000.07.
- <P001963> **郭霞、鄭振耀、陳宇亮**. 〈青少年特發性脊柱側凸患者的中樞神經異常〉. 《中國脊柱脊髓雜誌》第 10 卷 第 4 期, 頁 197-199. 中國, 2000.08.
- <P002447> **Leung, P.C.** "Ethics in Medical Practice". *Princess Margaret Hospital 25th Anniversary Commemorative Scientific Conference 2000* p.11. Hong Kong, 2000.10.25.
- <P002461> **LEUNG P.C.** "A Practical Comprehensive Approach to Chinese Medicine Research". Paper presented in the 1st International Conference on Traditional Chinese Medicine: Science, Regulation and Globalization, organized by Institute for Global Chinese Affairs. Maryland USA, 2000.08.30.
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RESEARCH PROJECTS

Quantitative Polymerase Chain Reaction Analysis of Chimerism After Allogeneic Bone Marrow Transplantation

- ✉ CHIK Ki Wai
- ☐ 1 January 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Quantitative approach in the analysis of chimerism after allogeneic bone marrow transplantation (BMT) emerges to become an important pointer of treatment outcome. The recent advances in the transplant methodology such as non-myeloablative preparative regimen, donor lymphocyte infusion, modification of immunosuppressive regimen, cytokine therapy etc demand a more stringent quantitative strategy in assessing chimerism. One of the aims of BMT is to achieve complete engraftment of the donor hematopoietic cells, i.e. complete chimerism. It remains unanswered that at what level of chimerism should medical intervention be applied. Thus, this study will allow the researchers to delineate the dynamics in establishing complete chimerism from a pool of stored peripheral blood specimens of transplant subjects from 1996 to 1999. Currently, the researchers have been able to apply fluorescent *in situ* hybridization (FISH) for our transplant subjects for chimerism study in sex-mismatched transplant. The availability of commercial products for the short tandem repeats study would enable us to study the specific genotypes of almost every subjects for chimerism analysis. Quantitation by fluorescence detection of the polymerase chain reaction products would allow them to calculate the proportion of donor to recipient cells. As the researchers have serial blood samples of the transplant subjects at weekly interval, they would be able to delineate the dynamics of engraftment. The chimerism results will also be correlated with the transplant outcome and FISH data.

(MD00739)

A Randomised, Double-blind, Double-dummy, Parallel-group, Multicentre Study to Compare the Effect on Growth Measured by Stadiometry of Fluticasone Propionate (100µg bd) Administered via Diskus[®] with Budesonide (200µg bd) Administered via Turbuhaler[®] in Prepubescent Children

- ✉ FOK Tai Fai • LEUNG Ting Fan
- ☐ 1 January 2000
- ❖ Glaxo Wellcome China Limited

Current asthma guidelines recommend inhaled anti-inflammatory therapy for asthmatic children not adequately controlled by relief bronchodilators. One popular option is inhaled corticosteroids, but asthma control depends on regular therapy with these drugs for many years. Their long-term safety is therefore the focus of debate. Growth is considered to be a good indicator of children's health. Several studies have shown that frequent treatment with oral steroids has a detrimental effect on growth in children. Clinical trials with inhaled steroids have shown conflicting results. This study aims to compare the effect on growth of treatment with two inhaled steroids, fluticasone propionate and budesonide, in prepubescent children. The growth velocities in these two groups of children, as monitored by stadiometry, will be compared to respective baseline values without inhaled steroid treatment.

(MD99458)

A Cross-sectional, Single-centre Study on the Levels & Sources of Mercury, Cadmium & Lead in a Hong Kong Mother-infant Cohort

- ✉ 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*
- ☐ 1 July 2000
- ❖ Health Care & Promotion Fund, Hospital Authority

Objectives: (1) To evaluate the hypothesis that newborn infants in Hong Kong are at significant risk of prenatal exposure to the three potentially embryotoxic trace metals mercury, cadmium and lead; and (2) to identify the sources of such exposure.

Design: Cross-sectional study for objective (1); and case-controlled study for objective (2).

Setting: A single-centre study at a regional hospital serving a population of one million.

Subjects: Two thousand full-term infants (gestation \geq 37 weeks) delivered consecutively at the hospital and their mothers will be enrolled. Their blood and hair samples will be collected at delivery of the infants for the measurement of mercury, cadmium and lead content. A questionnaire will be used to obtain information from the mothers on possible occupational or household exposure, and dietary intake of these trace metals.

Outcome measures: The body content of the mothers and infants will indicate the risk of prenatal exposure to the three harmful trace metals. Possible sources can be identified by comparing their presence in infants with and without high blood and hair concentration of the trace metals. Further confirmation will be carried out by measuring the trace metal content of the possible sources so identified.

(MD20001)

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

- ✉ LEUNG Ting Fan • LI Man Chim Albert Martin
• WAN Helene
- 1 December 2000
- ❖ Merck Sharp & Dohme (Asia) Ltd

Asthma, the most common chronic disease of children, affects 8-13% of children, with an increasing prevalence in children less than 5 years of age. Asthma exacerbations are an important clinical problem and the most common precipitating factor in preschool children appears to be viral respiratory infections. Some studies suggest that the early use of inhaled corticosteroids can modify the severity, duration or the number of subsequent exacerbation episodes. However, the results are modest and not consistent across studies. Current evidence suggests that respiratory syncytial virus-induced respiratory symptoms may be leukotriene-driven. Montelukast, a potent cysteinyl leukotriene receptor antagonist, may have a role in the treatment of these exacerbation episodes. In clinical trials, montelukast has demonstrated efficacy and tolerability in pediatric patients for the treatment of chronic asthma. The purpose of this study is to investigate the effect of montelukast in children with mild asthma and exacerbations, and whether a 12-month treatment course of montelukast, compared to placebo, can lower the rate of exacerbation episodes in 2-5 year old asthmatic children.

(MD00738)

Evaluation of Chemokines and Eosinophil Functions in Neonates and Their Clinical Relevance to Neonatal Respiratory Diseases

- ✉ LEUNG Ting Fan • NG Pak Cheung • LI Kwai Har Karen • TAM Wing Hung (Dept of Obstetrics & Gynaecology)
- 1 December 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Eosinophils are involved in a wide variety of allergic and inflammatory diseases in human. Functions of these leukocytes as well as chemokines, potent chemotactic cytokines for the recruitment and activation of eosinophils, increased in asthmatic patients whose airways are infiltrated with activated eosinophils. There is a significant overlap in clinical features and pathogenesis between asthma and bronchopulmonary dysplasia in neonates.

Nonetheless, it remains unclear whether eosinophils and chemokines are involved in the pathogenesis of lung diseases in neonates. The first part of this study involves the comparison of several aspects of eosinophil functions and chemokines between neonates and healthy adults. These parameters are then monitored serially in preterm babies with and without respiratory diseases. The possible associations between neonatal lung diseases and chemokines or eosinophil functions can then be assessed. This study may identify laboratory markers that can predict the onset and progression of lung diseases in this group of infants. In addition, we can better understand the roles of eosinophils and chemokines in respiratory diseases in young babies.

(MD00895)

A Randomized, Placebo-controlled and Crossover Clinical Trial of an Elemental Milk Formula in the Treatment of Atopic Dermatitis in Chinese Children

- ✉ LEUNG Ting Fan • LAM Wai Kei Christopher (Dept of Chemical Pathology)
- 1 March 2001
- ❖ SHS International Limited

Atopic dermatitis (AD) is a chronically relapsing inflammatory skin disease. Patients with AD typically present in early childhood with onset before 5 years of age in about 90% of patients. About one third of children with moderate-severe AD have IgE-mediated clinical reactivity to food proteins. Milk, egg, peanut, soy, wheat and fish were responsible for approximately 90% of the food allergens found to exacerbate AD in Caucasian children. In our Chinese AD patients, there is no data on the prevalence of allergies to cow's milk and soybean proteins. The usefulness of elemental milk formulae in alleviating symptoms related to AD therefore remains unclear. A randomized and placebo-controlled study design will be used in this study to investigate the efficacy of an amino acid-based milk formula on the treatment of AD. Fifty young children with eczema will be recruited from the hospital outpatient clinic. The occurrence of IgE-mediated reactions to common food allergens in these subjects will be determined, and their AD-specific clinical scores as well as biochemical markers of AD severity will be evaluated during the treatment and placebo phases of this study. The clinical efficacy and tolerability of this elemental milk formula in local children with AD can then be assessed.

(MD20058)

The Direct Role and Mechanism of the Pro-inflammatory Cytokine IL-1 β on Megakaryocytopoiesis: Expression of IL-1 Receptors and the Signal Transduction Response

- ✉ LI Kwai Har Karen • YANG Mo
 ☐ 1 September 2000
 ❖ CUHK Research Committee Funding (Direct Grants)

Interleukin-1 β (IL-1 β), 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 pilot study, the researchers established that IL-1 β stimulated murine and human megakaryocyte progenitor cell growth. The synergic effect of IL-1 β with thrombopoietin (TPO) was stronger than that of IL-3, IL-6, stem cell factor or flt-3 ligand, suggesting that IL-1 β might be an important cytokine in the regulation of megakaryocytopoiesis. The researchers' hypothesis is that IL-1 β exerts direct stimulatory effects on megakaryocytic cells via its receptors and the transcription factors NF-E2. Their experimental approach is (1) to identify IL-1 RI, IL-1 RII and the receptor accessory protein in cell lines and primary megakaryocytic cells from human bone marrow and cord blood; (2) to investigate the direct effect of IL-1 β on the differentiation of cord blood megakaryocytic progenitors by colony forming assays (CFU-MK) with and without the presence of IL-1 RI inhibitors; and (3) to determine the signal transduction mechanism of IL-1 β on megakaryocytopoiesis by the expression of transcription factors NF-E2.
 (MD00978)

A Hospital-based Study on Disease Burden and Health Costs of Rotavirus Associated Diarrhoea in Hong Kong

- ✉ 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)
 ☐ 1 November 2000
 ❖ CUHK Research Committee Funding (Direct Grants) • Merck & Co., Inc. • World Health Organization

Rotavirus infection is a major cause of child morbidity in developed countries and a major cause of child mortality in developing countries. A number of rotavirus vaccines are under development and the collection of data on disease burden and cost will be of value in determining the potential use of these vaccines in Hong Kong and elsewhere. This study will provide hospital-based information on disease burden and costs related to treatment including out-

of-pocket expenses. Basic clinical data on all children under the age of five years with diarrhoea admitted to two hospitals (one teaching hospital and one regional hospital) in Hong Kong will be collected. Stools will be tested for rotavirus and stool culture performed. A sub-sample of 100 children with rotavirus infection will be recruited from this population to collect detailed information on disease progress and associated costs. Data collected during this study will then be compared with that data collected through Hong Kong's Clinical Management System (CMS). The CMS is a comprehensive computerised database of discharge diagnoses collected for all government hospitals in Hong Kong. The CMS data for participating and non-participating hospitals will be analysed. This will determine the accuracy and completeness of the CMS data and its usefulness for longer term disease surveillance e.g. monitoring rotavirus admission rates after introduction of a vaccine. Mortality data from the Department of Census and Statistics will also be reviewed, although deaths from diarrhoeal diseases are rare in Hong Kong. These data will be used to undertake a cost-effectiveness analysis of rotavirus vaccination in Hong Kong. These data will provide policy makers with information necessary to assess whether rotavirus vaccine should be recommended for routine use in Hong Kong in the future.
 (MD00598)

The Effect of Continuous versus Pulsed Maternal Corticosteroid Treatment on Neonatal Pituitary-adrenal Function

- ✉ NG Pak Cheung • LAM Wai Kei Christopher (Dept of Chemical Pathology) • FOK Tai Fai
 ☐ 1 December 2000
 ❖ CUHK Research Committee Funding (Direct Grants)

The use of exogenous corticosteroids for maternal and fetal indications during pregnancy has raised much concerns about their potential suppressive effects on the fetal and neonatal hypothalamic-pituitary-adrenal (HPA) axis. In the past few years, the researchers have studied the effect of high dose antenatal and postnatal corticosteroid treatment on the HPA axis in preterm infants. Their results suggested that infants whose mother received 1-2 doses of antenatal dexamethasone for treatment of respiratory distress syndrome had normal pituitary-adrenal response at day 7 of life. However, the effect of 'continuous' or multiple 'pulsed' courses of antenatal corticosteroids on the HPA axis in newborns are not known. The researchers' clinical observations (pilot data) suggested that a significant proportion of infants born to mothers who received continuous systemic corticosteroid treatment developed adrenal and/or pituitary insufficiency. This study is, therefore, undertaken to assess the

effect of 'continuous' and multiple 'pulsed' courses of maternal corticosteroid treatment on the pituitary-adrenal function of newborns so as to identify those who are most at risk of adrenocortical insufficiency and thus, likely to require corticosteroid replacement. (MD00593)

A Randomized Controlled Trial of Strength Training Exercise and Diet in the Management of Obesity in Children

✉ 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*

□ 1 July 2000

❖ Research Grants Council (Earmarked Grants)

Objectives: To test the hypotheses that obese children may benefit from strength training exercise by lowering percentage body fat and increase in lean body mass and they will become physically and psychologically fitter after the training.

Design: Randomised controlled trial of a progressive strength training programme plus dietary intervention compared with dietary intervention alone. Participants 80 obese children aged 8-12 years with weight > 120% of ideal body weight will be recruited from children attending schools near our institute. The sample size calculation based on variance estimates from previous studies.

Interventions: Dietary intervention (hypocaloric diet 900-1200 Kcal with adequate protein) to both control and training group. Progressive strength training exercises classes led by professional sport instructors given to training group for 6 weeks, followed by daily practice at home for one year.

Main outcome measures: Anthropometric measurements (weight, height, and skin fold thickness), body composition (lean body mass, fat mass and % total body fat) measured by dual energy x-ray absorptiometry (DEXA), fitness by standard physical fitness tests and treadmill test ($V_{O2_{peak}}$), self esteem and feelings of competence with physical appearance and social acceptance by Marsh's Self-description Questionnaire for Children.

Result: The analysis will be based on intention to treat. Baseline comparisons of variables will be made using t-test or Mann-Whitney test. The baseline values will be subtracted from the values obtained 6 weeks and one year later to obtain change scores. The effects of treatment on the outcome will be measured by means of analysis of covariances with adjustment made for baseline score and patient preference. (CU00060)

Effects of Oxygen Toxicity on Megakaryocytopoiesis and Thrombopoietin Production in Neonates - A Rat Model

✉ YUEN Man Pan Patrick • FOK Tai Fai • LEE Simon K. M.* • LI Kwai Har Karen • YANG Mo

□ 1 September 2000

❖ Research Grants Council (Earmarked Grants)

Oxygen toxicity is an important cause of lung injury in preterm infants receiving mechanical ventilation. Thrombocytopenia is another common complication of these infants. The researchers hypothesize that oxygen toxicity induces the consumption and/or reduces the release of platelets from megakaryocytes in the lungs, leading to thrombocytopenia and a feedback mechanism of increased production of megakaryocytic progenitors in the bone marrow and megakaryocytic promoting cytokines in the circulation. Using a premature rat model of hyperoxic lung injury, the researchers shall perform a randomized controlled study to investigate the mechanism of megakaryocyte and platelet production at multiple levels. The number and morphology of megakaryocytes and platelets will be quantified by assessing the amount of these cells in the blood before and after passing through the pulmonary circulation. The number of lung megakaryocytes will be studied by histochemical staining of a specific marker acetylcholine esterase. To verify the presence of a feedback mechanism, the quantity of functional megakaryocyte progenitors in the bone marrow will be compared in hyperoxic and control animals, using the colony forming assay. The blood level of major megakaryocyte-promoting cytokines will be measured using the enzyme-linked immunosorbent assays. The expression of thrombopoietin in the kidney and liver, which are the major sites of cytokine production, will be analyzed by immunocytochemical staining. The project may provide the basis for a more rational management of thrombocytopenia in newborns with lung diseases. (CU00137)

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

<u>Edition</u>	<u>Title/Investigators</u>
1997-98	Determination of Local Oxygen Consumption by Healthy and Diseased Lungs in a Rabbit Model (MD97064) ✉ FOK Tai Fai • GU Jia Shi • XU Feng# • YIN Ai Tsang Jane
1998-99	Effects of Oxygen Toxicity on Megakaryocytopoiesis (MD98047) ✉ FOK Tai Fai • LI Kwai Har Karen • YANG Mo • XU Feng

- 1999-00 Study of Predisposition Genotypes in Chinese Children with Asthma (MD99053)
 ✉ LEUNG Ting Fan • TANG Leung Sang Nelson (Dept of Chemical Pathology)
- 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*
- 1997-98 Haematopoietic Stem Cells: Characterization and Retrovirus-Mediated Gene Transfer (MD97096)
 ✉ LI Kwai Har Karen • LI Chung Leung*
- 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 (Dept of Clinical Oncology) • TSANG Kam Sze Kent (Dept of Anatomical & Cellular Pathology)*
- 1999-00 Effects of Interleukin -1 β on the Proliferation and Signal Transduction of the Megakaryocytic Lineage (MD99054)
 ✉ LI Kwai Har Karen • YANG Mo
- 1998-99 WHO/GSTF Maternity Advice Study (MD98123)
 ✉ NELSON Edmund Anthony Severn • COWAN S.* • MANGIATERRA V.* • CAFFERATA M.*
- 1998-99 The Effect of Postnatal Systemic Corticosteroids on Serum Leptin Concentration in Preterm, Very Low Birth Weight Infants (MD98050)
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- 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

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- <P001249> **Li, Albert M.; Michael H.M. Chan; T.F. Leung; Robert C.K. Cheung; Christopher W.K. Lam and T.F. Fok.** "Mercury Intoxication Presenting with Tics". *Archives of Disease in Childhood* 2nd ed., vol.83, pp.174-175. UK, 2000.08.21.
- <P001921> **Nelson, E.A.S. and Members of ICCPS Study Group.** "International Child Care Practices Study: Breastfeeding and Pacifier Use". *Journal of Pediatric Gastroenterology & Nutrition* vol.31 suppl.2, p.S28. Philadelphia, USA: Lippincott Williams & Wilkins, 2000.08.
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RESEARCH PROJECTS

Mapping Signal Transduction Networks by Multidisciplinary Approach

- ✉ 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*
- ☐ 1 April 2000
- ❖ RGC-Central Allocation Scheme - Group Research

The contractile action of the EP₃ receptor agonist sulprostone on vascular smooth may have different mechanisms according to the concentration used. A low concentration of sulprostone (3-10 nM) produces little contraction on its own, but markedly synergises with phenylephrine (α -adrenoceptor agonist) or U-46619 (TP-receptor agonist). This contractile action of sulprostone is dramatically enhanced (typically 5-10 fold) by cyclopiazonic acid, which blocks the Ca²⁺ has little effect on sulprostone action. The action of sulprostone is also unaffected by PKC inhibition, but is abolished by the Rho kinase inhibitor Y-27632. At higher concentrations of sulprostone (100-300 nM), the researchers see greater contraction and a more obvious reliance on external Ca²⁺, which in some preparations involves opening of L-type-Ca²⁺-channels. The researchers intend to investigate further the nature of the interaction of sulprostone with non-prostanoid contractile agents at the second messenger level using both isolated vessel rings and CHO cells transfected with human TP and EP₃ receptors.

The mitogen-activated protein kinase (MAPK) pathways are comprised of a three-member protein kinase cascade, of which the extracellular-signal-regulated kinases (ERKs), the Jun N-terminal kinases (JNKs) and the p39 kinases are the best described. The MAPKs are involved in mediating a variety of signals for cell proliferation and differentiation. G protein-coupled receptor-mediated activation of MAPKs can occur via G α or G $\beta\gamma$ -subunits, and utilises members of the Ras and Rho-family of GTPases, as well as receptor and non-receptor tyrosine kinases. The researchers intend to investigate the activation and regulation of MAPKs by G_s and G_q-coupled receptors such as those belonging to the prostanoid receptor family, and by G_i-coupled receptors such as those belonging to the opioid receptor family. These studies in heterologous transfection systems will be followed by studies in physiologically relevant tissues. (BL99452)

Investigation of the Mechanisms Underlying the Contractile Action of Prostanoid EP₃-receptor Agonists on Vascular Smooth Muscle

- ✉ JONES Robert Leslie • KWAN Yiu Wa • GURNEY A. M.*
- ☐ 1 December 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Prostanoid EP₃-receptor agonists (e.g. PGE₂ and sulprostone) induce contraction of vascular smooth muscle that is typified by marked synergism with other agonists such as phenylephrine and U-46619. The researchers' experiments indicate that the contractile action usually involves influx of Ca²⁺ through non-L-type Ca²⁺ channels and a second mechanism possibly related to sensitization of the contractile apparatus to Ca²⁺. In the current project the researchers intend to use the patch-clamp technique to characterise non-L-type current(s) induced by sulprostone in vascular smooth muscle cells of guinea-pig aorta freshly dispersed by collagenase treatment. They will also modulate K⁺ fluxes in the isolated cell, since certain K-channel blockers (e.g. charybdotoxin and TEA) dramatically enhance sulprostone contractions. They have also found that the Rho kinase inhibitor Y-27632 will abolish sulprostone-induced contraction of the guinea-pig aorta, whereas PKC inhibitors such as Ro32-0432 have no effect. The researchers intend to investigate the mechanism of Y-27632. In a few preparations, the sulprostone response is larger than normal and partially susceptible to inhibition by nifedipine. It is possible that in some preparations the basic EP₃ contractile action of sulprostone produces sufficient membrane depolarisation to open L-type Ca²⁺ channels; alternatively, contractile EP₁-receptors may also be present. The researchers have just obtained gifts of novel EP₁ and EP₃ antagonists from a pharmaceutical company. These compounds have much higher selectivity than previous agents and the researchers hope to use them to distinguish the two possibilities.

(MD00779)

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

- ✉ LAM Fu Yuen • CHEW CHENG Siew Boon (Dept of Physiology)
- ☐ 1 November 2000
- ❖ 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. (MD00464)

The Roles of Mast Cells in the Pathogenesis of Aspirin Sensitive Asthma

✉ LAU Hang Yung Alaster • LEUNG Po Sing (Dept of Physiology) • NAGAKURA Toshikazu* • OBATA Toru* • SAITO Hirohisa* • WU Young Yuen Adrian*

☐ 1 November 2000

❖ Research Grants Council (Earmarked Grants)

Aspirin and most non-steroidal anti-inflammatory drugs (NSAIDs) cause severe and prolonged bronchospasm in patients with aspirin sensitive asthma (ASA). The pathogenesis of this hypersensitivity reaction is not well understood but is related to the principle pharmacological actions of these compounds as cyclooxygenase (COX) inhibitors. By inhibiting COX, NSAIDs shunt the metabolism of arachidonic acid (AA) to the lipoxygenase pathway and hence leading to an enhanced synthesis of leukotrienes, in particular, cysteinyl leukotrienes (cys-LT). In fact, levels of cys-LT and their major metabolite, LTE₄ are higher respectively in the tissues and urine of ASA patients. Since the number of activated mast cells are increased in ASA patients, these cells are believed to be a major cellular source of cys-LT and play a pivotal role in the pathogenesis of ASA. By using the novel technique of culturing human mast cells from peripheral blood, the current project will compare mast cells cultured from normal subjects and asthmatic patients with or without aspirin sensitivity. Detection for the expression of key AA metabolizing enzymes and functional studies on these mast cells will provide useful information for defining the exact roles of mast cells in ASA and for the management of asthma in general.

(CU00064)

Effects of Cannabinoid Receptor Directed Ligands on Mast Cells

✉ LAU Hang Yung Alaster

☐ 1 January 2001

❖ CUHK Research Committee Funding (Direct Grants)

Allergic reactions and the underlying inflammation is often initiated by the activation of mast cells. Although the immunological activation of mast cells through the cross-linking of high affinity IgE receptors is well documented, little is known about the physiological regulation of inappropriate mast cell mediator release. Recently, it was proposed that endogenous cannabinoids might act as local autacoids which suppressed inflammation by reducing the activation of mast cells. Since the characterisation of cannabinoid receptors (CB1 and CB2 subtypes) was only established within the last decade, there are only limited literature on the interaction of mast cells and cannabinoids. Initial studies indicated that activation of mast cell cannabinoid CB2 receptors by palmitoylethanolamide might contribute to the endogenous control of inflammation. However, more recent studies had produced contradicting results which suggested that palmitoylethanolamide was unlikely to be an endogenous agonist of the CB2 receptor and the previously reported suppression of mediator release from RBL-2H3 cells was independent of cannabinoid receptor activation. With the recent advance in the pharmacology of cannabinoid receptors and the availability of various cannabinoid receptor direct ligands from commercial sources, this study will aim at solving the current controversies over the interaction of mast cells and cannabinoids. These preliminary studies looking only at the effects of cannabinoid analogues on histamine release from activated mast cells will provide useful background information for evaluating if endogenous cannabinoids possess mast cell modulating actions which can be extended to the future development of new anti-allergic agents. (MD00482)

Identification of Brain Areas Involved in Emesis Control in the Ferret

✉ RUDD John Anthony • YEW Tai Wai David (Dept of Anatomy)

☐ 31 December 2000

❖ Research Grants Council (Earmarked Grants)

Nausea and vomiting can be induced by a wide variety of challenges and often represents a limit of drug therapy. Development of new anti-emetic drugs is reliant on understanding the physiology and

pharmacology of the emetic reflex. The forebrain is involved in emesis control but little is known about the precise connectivity to the reflex brainstem centres. The project will identify which forebrain areas are involved in the emesis induced by cisplatin, apomorphine and copper sulphate using the ferret and c-fos immunocytochemistry. Once the critical brain areas have been identified, the project will investigate the potential of standard anti-emetic drugs to antagonise c-fos expression in the brainstem and forebrain regions. The standard anti-emetic drugs that will be used include the 5-HT₃ receptor antagonist ondansetron and the dopamine D₂ receptor antagonist domperidone. The studies will simultaneously assess the effect of drug treatment on emesis and behaviours that may be relevant to nausea. The studies should increase our understanding of the mechanisms involved in nausea and vomiting necessary for rational anti-emetic development. (CU00066)

Characterization of the Role of Vanilloid Receptors in Emesis and Penile Grooming in *Suncus murinus*

- ✉ RUDD John Anthony
- ☐ 1 January 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

The ultra-potent vanilloid, resiniferatoxin, has a dual action to induce and inhibit emesis when administered peripherally. The emetic mechanism is likely to involve a release of substance P and possibly calcitonin gene related peptide from sensory nerve terminating in the brainstem. The anti-emetic mechanism has been hypothesized to occur due to a subsequent depletion of substance P and/or vanilloid receptor desensitization. The researchers have been interested in the action of vanilloid receptor function in the central nervous system. Using an intracerebroventricular administration technique they demonstrated that resiniferatoxin induces emesis and penile erection and genital grooming in *Suncus murinus*. There is also a subsequent anti-emetic action. The aim of the research project is to confirm the role of the vanilloid receptors in the observed behaviours using a range of vanilloid receptor ligands. The contribution of substance P and dopamine to the emesis and the mechanism of penile erection and genital grooming will be investigated using selective receptor antagonists. The research may lead to novel treatments for emesis and/or sexual dysfunction. (MD00413)

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

Edition Title/Investigators

1998-99	Cellular Mechanisms Involved in the Excitatory Actions of Prostanoid EP ₃ -and IP-Receptor Agonists (BL98001) ✉ JONES Robert Leslie • GURNEY A. M.* • KWAN Yiu Wa • KENNEDY C.* • SNEDDON P.*
1999-00	Delineation of the Second Messenger Pathways Involved in β ₃ -adrenoceptors-mediated Relaxation of Rat Isolated Pulmonary Artery (MD99111) ✉ KWAN Yiu Wa
1998-99	Studies on Anti-inflammatory Neuropeptides in Rat Knee Joints (MD98053) ✉ LAM Fu Yuen
1999-00	Role of Sensory Neuropeptides in Chronic Arthritis (MD99112) ✉ LAM Fu Yuen
1997-98	Chemical and Pharmacological Studies of Beimu, a Commonly Used Antitussive Traditional Chinese Medicine (CU97632) ✉ LIN Ge • KWAN Yiu Wa • HO Yee Ping (School of Pharmacy) • LI Ping*
1999-00	Investigation into Human <i>in vitro</i> Metabolism of Pyrrolizidine Alkaloids and Role of Their Toxic Pyrrolic Metabolites in Inducing Hepatotoxicity (MD99056) ✉ LIN Ge
1998-99	Investigation into the Mechanism of Action of Corticosteroids to Antagonise Cisplatin- and Motion-Induced Emesis (CU98049) ✉ RUDD John Anthony • YEUNG Hok Keung John
1997-98	The Role of Prostacyclin Receptors in Pain Modulation (CU97601) ✉ WISE Helen • JONES Robert Leslie
1999-00	An Investigation into the Multiple Coupling Capacity of Prostacyclin Receptors (CU99253) ✉ WISE Helen • WONG Yung Hou*
1998-99	Metabolic Studies of a Series of Drugs in Horses (MD98082) ✉ YEUNG Hok Keung John • WONG Nai Ching Henry (Dept of Chemistry)

RESEARCH OUTPUTS AND PUBLICATIONS

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- <P002534> **Wong, H.L. and F.Y. Lam.** "Effects of Tachykinin (NK₁) Receptor Antagonists on Adjuvant-Induced Arthritis in the Rat". *Tachykinins 2000 International Tachykinin Conference* p.63. La Grande Mote, France, 2000.10.
- <P002553> **Chan, Shun-Wan; Song-Lin Li; Ge Lin and Ping Li.** "Pharmacokinetic Study and Determination of Imperialine, the Major Bioactive Component in Antitussive *Fritillaria Cirrhosa*, in Rat by High-Performance Liquid Chromatography Coupled with Evaporative Light-Scattering Detector". *Analytical Biochemistry* vol.285, pp.172-175. San Diego, USA, 2000.
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RESEARCH PROJECTS

Establishment of a University Based Drug Development Centre for Anticancer and Cerebro/Cardio-vascular Drugs

✉ CHOW Sing Sum Moses • HO Walter K. K. (Biochemistry) • JONES Robert Leslie (Dept of Pharmacology) • HO Yee Ping • LAU Bik San Clara • LIN Ge (Dept of Pharmacology) • JAMES Anthony Edward (Laboratory Animal Services Centre) • CHOW Hee Lum Albert

□ 1 September 2000

❖ Funding from Other Sponsors • Innovation and Technology Support Programme, ITF, Innovation & Technology Commission

The objective of this proposal is to establish a drug development center at the CUHK for development of anticancer and cerebro/cardio-vascular drugs (both western and Chinese drugs) aimed at meeting the U.S. FDA drug approval process.

The immediate deliverable is the establishment of the infrastructure of the Center. The final deliverable (to be achieved with additional grant) will be the obtaining of approval of Investigational New Drug (IND, the first step in the approval process by FDA recognized as having merit and commercial value). For certain drugs, additional final deliverable will include the completion of Phase 1 and Phase 2a of the clinical trial, due to greater commercial value.

The benefit of having such a Center is primarily to help the local drug industry in developing anticancer and cerebro/cardio-vascular drugs. The Center will provide a new level of drug development capability leading to international recognition of this biotechnology area for Hong Kong. This can lead to potential international marketing of drug products from Hong Kong. (MD20024)

"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"

✉ LEE Kwing Chin Kenneth • CHAN Chung Ngor Juliana (Dept of Medicine & Therapeutics) • TOMLINSON Brian (Dept of Medicine & Therapeutics) • YOU Hoi Sze Joyce

□ 1 November 2000

❖ Research Grants Council (Earmarked Grants)

Insulin resistance is a physiological state in which greater-than-normal amounts of insulin are required to elicit a normal response, thus often leading to an abnormally-high levels of circulating or plasma

insulin. It is also widely recognized that insulin resistance is the common underlying factor of a cluster of metabolic disorders, collectively known as the metabolic syndrome. The major abnormalities associated include type 2 diabetes (preceded by impaired glucose tolerance), hypertension, abnormal lipid levels and obesity.

In the Chinese population, it has been demonstrated that the progression rate of untreated impaired glucose tolerance to type 2 diabetes is about 10% per year. However, while the effects of drug treatment in improving insulin action have been widely investigated in overseas countries, local work is relatively lacking.

The current project is planned to examine the effects of two recently approved agents reported to have beneficial effects on insulin action; namely, orlistat (OL) and rosiglitazone (RSG); in a group of Chinese patients affected by the metabolic syndrome. Both agents do not reduce plasma glucose levels directly. Instead, they act by either increasing the body's insulin sensitivity directly as for RSG or indirectly as for OL by reducing body weight leading eventually to improved metabolic control.

(CU00069)

Pharmacoeconomic Analysis of Tolterodine Comparing with Oxybutynin for the Treatment of Overactive Bladder

✉ YOU Hoi Sze Joyce • LEE Kwing Chin Kenneth • LEUNG Ho Yin Peter (Dept of Obstetrics & Gynaecology) • YIP Shing Kai Alexander (Dept of Obstetrics & Gynaecology)

□ 1 July 2000

❖ CUHK Departmental Funding

Overactive bladder-induced urinary incontinence imposes a significant financial burden on patients, their families, as well as the total healthcare system. The costs of illness associated with overactive bladder mainly include direct medical costs, direct non-medical costs and indirect costs. A pharmacoeconomics analysis would allow one to compare the costs and outcomes of therapies and determine which of the alternatives would produce the best health outcome for the resource invested. The objective of the present study is to compare the pharmacoeconomic impacts of tolterodine and oxybutynin for overactive bladder treatment from the perspectives of a public hospital and patient. (MD20029)

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

✉ 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)

☐ 1 October 2000

❖ Donation from Pfizer Inc.

Non-steroidal anti-inflammatory drugs (NSAIDs) have been the most frequently used medications in controlling symptoms associated with osteoarthritis and rheumatoid arthritis. A recent local study revealed that the most common and potentially serious adverse effect of these agents is gastrointestinal mucosal injury. Recently, celecoxib, a cyclooxygenase-2 (COX-2) selective anti-inflammatory drug has been introduced into Hong Kong. It has been reported that COX-2 inhibitors cause fewer endoscopic ulcers than the conventional non-selective NSAIDs. In view of the mounting resource implications in managing adverse effects due to NSAID therapies, there is a need to compare the economic implications between celecoxib and the most commonly used NSAIDs. This study is designed to compare the economic consequences of celecoxib to NSAIDs (with or without GI protective agents) on adverse GI events from the perspective of a public organization in Hong Kong. (MD20019)

***In vitro* Intestinal Absorption and *in vivo* Pharmacokinetics Evaluation of Baicalein and Baicalin**

✉ ZUO Zhong • LIN Ge (Dept of Pharmacology)

☐ 1 May 2001

❖ CUHK Research Committee Funding (Direct Grants)

Flavonoids, characterized as polyphenolic natural products, are widely distributed both in edible plants and in derived foodstuffs. Although the discovery of flavonoids's health promoting effects has been well described, there is a lack of information concerning the extent to which polyphenolics are absorbed in humans, their metabolism, pharmacokinetics and bioavailability. Even though several studies have provided evidence for the uptake of specific flavonoids in rats and human, few studies have demonstrated the mechanism of flavonoid uptake. Furthermore, it is not clear whether the aglycone or the glycoside is absorbed. In this study, one of the most widely used flavonoid *Baicalein* and its glycoside *Baicalin* are chosen in order to investigate the effect of the sugar moiety on the absorption and also to evaluate their intestinal transport mechanism. The *in vitro* Caco-2 monolayer model will be used to study the transport mechanism as well as to compare

the permeability of baicalein with baicalin. In the mean time, the *in vivo* pharmacokinetic studies on rats will be performed. Knowing both the *in vitro* transport mechanism and the *in vivo* pharmacokinetics of these two pure active flavonoids will help to disclose the traditional mysteries by modern technology. (MD00566)

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

<u>Edition</u>	<u>Title/Investigators</u>
1997-98	Formulation and Evaluation of Oral Traditional Chinese Medicines (TCMs) (MD97023) ✉ CHOW Hee Lum Albert • LEE Kwing Chin Kenneth • HO Yee Ping • HO Suk San Susan • LIN Ge (Dept of Pharmacology)
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 • TOMLINSON Brian (Dept of Medicine & Therapeutics) • LEE Kwing Chin Kenneth
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)
1999-00	A Study to Examine the Potential Saving of Medical Costs in the Management of Impaired Glucose Tolerance and Type 2 Diabetes Mellitus Associated with Orlistat Treatment (MD99145) ✉ LEE Kwing Chin Kenneth • YOU Hoi Sze Joyce • HO Suk San Susan • CHAN Chung Ngor Juliana (Dept of Medicine & Therapeutics) • CRITCHLEY Julian A J H (Dept of Medicine & Therapeutics)#

- 1999-00 A Cost-effectiveness Analysis of High-dose Omeprazole Infusion as Adjuvant Therapy to Endoscopic Haemostasis for Bleeding Peptic Ulceres (MD99148)
✉ LEE Kwing Chin Kenneth • YOU Hoi Sze Joyce • LAU Wan Yee Joseph (Dept of Surgery) • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • CHAN YUNG Man Yee (Dept of Surgery) • HO Suk San Susan • LEE Chi Wai# • CHUNG Sheung Chee Sydney (Dept of Surgery)
- 1999-00 Cost Analysis of Losartan-to-candesartan Switch in Specific Patient Groups (MD99147)
✉ LEE Kwing Chin Kenneth • YOU Hoi Sze Joyce
- 1999-00 Healthcare Resources Utilization Associated with Nonsteroidal Anti-inflammatory Drug-induced Gastrointestinal Complications (MD99149)
- ✉ YOU Hoi Sze Joyce • LEE Kwing Chin Kenneth • KUNG Nam Shing Nelson (Dept of Medicine & Therapeutics) • CHAN Ka Leung Francis (Dept of Medicine & Therapeutics)
- 1999-00 Eradication of Helicobacter Pylori to Prevent Peptic Ulcers Prior to NSAID Therapy – A Cost-effectiveness Analysis (MD99150)
✉ YOU Hoi Sze Joyce • LEE Kwing Chin Kenneth • CHAN Ka Leung Francis (Dept of Medicine & Therapeutics) • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • CHAN YUNG Man Yee (Dept of Surgery) • CHUNG Sheung Chee Sydney (Dept of Surgery)

RESEARCH OUTPUTS AND PUBLICATIONS

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- <P003396> **NG K.F. Alex; YIM T.K. Michael; HO S.S. Susan; LAI C.W. Alex and SANDERSON E. John.** "Clinical Audit of Re-Structuring the Management of Chest Pain and Acute Coronary Syndromes". Paper presented in the Hong Kong Pharmacy Conference 2000: Pharmacy Re-Creation, organized by Pharmaceutical Society of Hong Kong. Hong Kong, 2000.10.22.
- <P003397> **HO S. S.; NG K.F.; YIM T.K.; LAI A. C. and SANDERSON John E.** "Clinical Audit of Restructuring the Management of Chest Pain and Acute Coronary Syndrome". Paper presented in the 35th ASHP Midgear Clinical Meeting, organized by American Society of Health-System Pharmacists. Nevada, USA, 2000.12.
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- <P003764> **ZUO Zhong.** "Piracetam". *Medical Progress* 10th ed., vol.27, pp.36-40. Hong Kong, 2000.10.
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- <P010406> **LEE K.K.; YOU J.H.; HO S.S.; LEUNG W.Y.; THOMAS G.; CHAN T.Y. and CRITCHLEY J.** "A Pharmacoeconomic Analysis of Weight-Reduction Therapy in a Hypothetical Cohort of Obese Chinese Patients with Impaired Glucose Tolerance". *"Value in Health" ISPOR 6th Annual International Meeting* vol.4 no.2, p.116. Arlington, USA: International Society for Pharmacoeconomics and Outcomes Research, 2001.05.
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- <P010624> **YOU J.H.S.; LEE K.K.C.; HO S.S.S.; SUNG J.J.Y.; KUNG N.N.S.; YUNG M.; LEE C. and YEE G.C.** "Economic Analysis of Four Triple Regimens for the Treatment of Helicobacter Pylori-Related Peptic Ulcer Disease in In-Patient and Out-Patient Settings in Hong Kong". *Alimentary Pharmacology & Therapeutics* vol.15, pp.1009-1015. 2001.
- <P010728> **CHANG Qi; ZUO Zhong; ZHU Min; CHOW Moses and HO K.K. Walter.** "Bioavailability of Hawthorn Polyphenols in Rats". *Abstracts of the EUFEPS World Conference on Drug Absorption and Drug Delivery* p.82. Copenhagen, Denmark: European Federation for Pharmaceutical Sciences, 2001.06.
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- <P011153> **XIE J.; DUNN A.; TSIKOURIS J.P.; SUN Y.; FAN C.; KLUGER J.; CHOW M.S. and WHITE C.M.** "A Placebo Controlled Evaluation of the Antifibrillatory Effects of Carvedilol". *Journal of Electrocardiology* vol.34 no.1, pp.25-30. 2001.01.
- <P011154> **CHOW S.S. Moses; FAN Chengde; TRAN Hieu; ZHAO Hong and ZHOU Li.** "Effects of Diaspirin Cross-Linked Hemoglobin (DCLHb) during and Post-CPR in Swine". *Journal of Pharmacology and Experimental Therapeutics* vol.297 no.1, pp.224-229. 2001.04.
- <P011155> **CHOW S.S. Moses; WHITE C. Michael; LAU Chu-Pak; FAN Chengde and TANG Man-Oi.** "Evaluation of CYP2D6 Oxidation of Dextromethorphan and Propafenone in a Chinese Population with Atrial Fibrillation". *Journal of Clinical Pharmacology* vol.41, pp.92-96. 2001.01.
- <P011729> **LEE K.K.; YOU J.H.; HO S.S.; LEUNG W.Y.S.; THOMAS G.N.; CHAN T.Y.S. and CRITCHLEY J.A.J.H.** "A Pharmacoeconomic Analysis of Weight-Neutral Therapy in a Hypertensive Cohort of Older Chinese Patients with Nifedipine". Paper presented in the International Society for Pharmaceutical & Outcomes Research 6th International Meeting, organized by ISPOR. Arlington, VA, USA, 2001.05.

see also <P003394>, <P003395>, <P010330>, <P011444>, <P011709>

RESEARCH PROJECTS

"Functional Studies of a Novel Epididymis-specific Gene, Bin-1b: Role in Epididymal Host Defense and Male Fertility"

✉ CHAN Hsiao Chang • CHEN Xu* • ZHANG Yong Lian*

☐ 1 September 2000

❖ Research Grants Council (Earmarked Grants)

Reproductive tract infections, including sexually transmitted infections, remain a global public health problem. The epididymis, an integral part of the male reproductive system responsible for sperm maturation and storage, is one of the sites readily affected by sexually transmitted diseases and therefore may be the central harbour of bacteria and retroviruses including HIV. However, there is a paucity of information as regard to epididymis host defense mechanisms. The researchers have recently discovered a novel epididymis-specific gene, Bin1b, with structural characteristic similar to that of defensins, a family of antimicrobial peptides. In the present study, they will study defensin-like activities of Bin-1b and elucidate its possible role in epididymis host defense and male fertility. This project would be of both basic research and commercial values with high relevance to Hong Kong considering the increasing rate of sexually transmitted diseases in Hong Kong.
(CU00070)

International Symposium on Cell Signal - from Diseases to Drug Discovery

✉ CHAN Hsiao Chang • WANG Jun (Biochemistry) • FISCUS Ronald Ray • CHEW CHENG Siew Boon • LEUNG Po Sing • YAO Xiaoqiang • WAYE Mary Miu Yee (Biochemistry)

☐ 1 February 2001

❖ Funding from Other Sponsors • General Support Program, Innovation & Technology Commission

The project aims to organize and host in 2001 an international symposium on Cell Signaling with emphasis on diseases and drug discovery.

Cell signaling participates in and affects almost every aspect of life processes. Disruption of signaling pathways impairs body functions leading to diseases and death. The understanding of cell signaling mechanisms and pathways is, therefore, crucial to innovative drug development and our combat against diseases.

This international symposium will bring to Hong Kong a few dozen of world-renowned scientists and experts including a Nobel Laureate in this highly

competitive field of biotechnology. Their up-to-date research findings and the state-of-the-art technologies will help fostering an innovation and technology culture in Hong Kong. Their first hand experience in identifying signaling pathways involved in disease processes, drug actions and the biotechnology in screening related bioactive agents will be invaluable to promote local R&D and drug development. At the same time, innovative applications of the related biotechnology in Traditional Chinese Medicine research, including results from some of the projects sponsored by ITC and Hong Kong companies, will also be presented at the symposium to set examples for local TCM manufacturers to improve their products and to demonstrate to the world the capability of Hong Kong in conducting sophisticated research for innovative development of TCM. This symposium is also a sequel in a series of Beijing-Hong Kong Forum on Life Sciences, aiming to promote exchanges between Hong Kong and the mainland and to enhance the competitiveness of biotechnology/TCM-related industries in this part of the world.

Exhibition of research findings, related technologies and products will also be held at the symposium. Proceedings of the symposium will be published and distributed internationally, which will also provide good references for local pharmaceutical, health care, TCM and food supplements industries. The symposium is expected to attract 300-400 participants world-wide.

(MD00818)

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

✉ FISCUS Ronald Ray • CHEW CHENG Siew Boon • HAN Chide* • WANG Xian*

☐ 1 December 2000

❖ CUHK Research Committee Funding (Direct Grants)

This project will determine if the interactions of nitric oxide (NO) and calcitonin gene-related peptide (CGRP) in blood vessels are diminished during diabetes mellitus and if the synergistic anti-proliferative actions of CGRP and NO in vascular cells involve cAMP-kinase (PKA) and cGMP-kinase (PKG) signaling pathways (potentially important in pathogenesis of diabetic vascular changes).

The hypotheses to be tested are: (1) diabetes damages vascular endothelium, diminishing endothelium-dependent vasorelaxant and anti-proliferative effects of CGRP, (2) diabetes damages perivascular CGRP-containing nerves, diminishing CGRP release, (3) treatment of diabetic animals with nerve growth factor (NGF, a stimulator of CGRP gene expression)

and/or L-arginine (a precursor of NO biosynthesis) protect against excessive smooth muscle cell proliferation and resulting wall thickening, and (4) CGRP and NO inhibit smooth muscle cell proliferation by activating PKA and PKG pathways, respectively.

Streptozotocin-induced diabetic rats will be used as the diabetic model. Cultured vascular smooth muscle cells of normal and diabetic rats will be used to determine involvement of PKA and PKG. The results of this project will provide valuable new information concerning the mechanisms of CGRP and NO interactions in blood vessels as well as insight into their involvement in protecting against the pathogenesis of diabetic vascular complications. (MD00772)

Investigation into Mechanisms of Vascular Action of Purified Neferine from *Nelumbo nucifera* Gaertn in Rat and Mouse Arteries

✉ HUANG Yu • CHAN Wood Yee (Dept of Anatomy) • CHEN Zhenyu (Biochemistry) • KO Wing Hung • YAO Xiaoqiang • YEW Tai Wai David (Dept of Anatomy)

☐ 1 December 2000

❖ CUHK Strategic Research Program

Neferine, an alkaloid isolated from the seeds of *Nelumbo nucifera* Gaertn, has been reported to exert multiple cardiovascular effects, including inhibition of platelet aggregation, thromboxane formation and vascular smooth muscle proliferation. These effects make neferine potentially hopeful as a therapeutic agent. However, little information is available on whether neferine also possesses vasodilator effects in resistance-sized cerebral and coronary arteries from both normotensive and spontaneously hypertensive rats. The researchers will, therefore, examine

- (1) the vasodilator response to neferine and role of endothelium and ion channels in neferine-induced relaxation in small cerebral and coronary arteries;
- (2) the modulatory effect of neferine on gene expression and activity of potassium and calcium channels in vascular smooth muscle cells;
- (3) the beneficial effect of neferine on lipid metabolism through its antioxidant activity;
- (4) the protective effect of neferine on cerebral ischemia-induced damage to central neurons and astrocytes in mice; and
- (5) the effect of neferine on organogenesis to determine whether a new chemical has a teratogenic potential.

This study should provide the pharmacological basis needed for the potentially therapeutic use of neferine and structurally related compounds in the treatment of cerebral and coronary disease. (MD20025)

Studies on the Cellular and Ionic Mechanisms Involved in Estrogen-induced Beneficial Effects on Coronary Artery

✉ HUANG Yu • YAO Xiaoqiang

☐ 1 January 2001

❖ CUHK Research Committee Funding (Direct Grants)

Women experience significantly less incidence of cardiovascular disease such as atherosclerosis, hypertension and stroke in their premenopausal reproductive years than postmenopausal age. Estrogen relaxes vascular smooth muscle *in vitro* and *in vivo* in both animals and humans, and this effect may partly account for the cardiovascular protective effect of estrogen replacement therapy in postmenopausal women. In addition to these well-publicized chronic actions, 17 β -estradiol and progesterone were reported to exert the acute relaxant effects in human blood vessels. However, the precise pathways, and the cellular and ionic mechanisms by which female sex steroid hormones influence the arteries are largely unknown. An increasing amount of evidence suggests that nitric oxide production, modulation of ion channel activity, and regulation of the vascular responsiveness to endogenous vasoconstrictors. The researchers propose to examine the following hypotheses: (1) Estrogen- or progesterone-induced endothelium-dependent relaxation of rat arteries is mediated through increased production of endothelium-derived vasodilators. (2) Estrogen-induced increase of release of endothelium-derived dilators is partly mediated by calcium influx through non-selective cation channels in endothelium. (3) Estrogen- or progesterone-induced decrease in vascular contractility is partly mediated through inhibition of Ca²⁺ channels and activation of K⁺ channels. The primary objective of this study is to investigate the researchers' hypotheses, presenting the cellular and ionic mechanisms linking the estrogen-induced effects in endothelium and vascular smooth muscle to decreased arterial contractility. This study should provide new insight into the ionic mechanisms underlying the protective effects of female steroid hormones against the vascular disease. (MD00545)

Role of Protein Kinase C in Relaxation of Arterial Smooth Muscle by "Classical" and Novel Calcium Antagonists

✉ HUANG Yu • GOLLASCH Maik*

☐ 1 March 2001

❖ Germany/Hong Kong Joint Research Scheme

“Classical” calcium antagonists such as nifedipine are very potent inhibitors of protein kinase C in endothelial cells. Since the nifedipine effects occurred in the low nanomolar range (similar as L-type calcium channels are blocked) protein kinase C has to be considered as major target for 1st and 2nd generation dihydropyridine calcium antagonists in arterial blood vessels. However, it has not been studied whether this putative mechanism is functional important for arterial smooth muscle contraction. Therefore, the researchers want to test the hypothesis that dihydropyridines regulate sustained contraction of arterial smooth muscle by both inhibiting calcium influx and protein kinase C. They specifically propose to test the following hypotheses: (1) The novel dihydropyridine calcium channel antagonist cilnidipine targets the pore-forming α_1C subunit and, thereby, induces a channel state-dependent block of vascular L-type calcium channels. (2) Activation of protein kinase C does not regulate arterial L-type calcium channels. (3) “Classical” dihydropyridine L-type calcium channel antagonists (e.g., nifedipine) interfere with protein kinase C and, thereby, inhibit the sustained contractile phase of arterial smooth muscle by both reducing calcium influx through L-type channels and inhibiting protein kinase C. (4) Novel dihydropyridine L-type calcium channel antagonists (e.g., cilnidipine) inhibit the sustained contractile phase of arterial smooth muscle by reducing calcium influx through L-type channels but not by inhibiting protein kinase C.

(MD20048)

Simultaneous Measurement of Bioelectric and Fluorescent Signals in Intact Epithelial Tissue

✉ KO Wing Hung • Jens LEIPZIGER*

☐ 1 March 2001

❖ Germany/Hong Kong Joint Research Scheme

Epithelial cells characteristically grow as distinct sheets that form the anatomical boundaries between the relatively stable internal environment of the body and the constantly changing environment of the outside world. These transport processes can be controlled by hormones and neurotransmitters binding to specific cell surface receptors located on apical and/or basolateral membranes and so evoking the production of second messenger signals within the cell. One of these important intracellular signaling systems is an increase in intracellular free calcium ($[Ca^{2+}]_i$). Activation of calcium signaling pathway causes an increase in cellular chloride conductances, which is the crucial control point in the secretory mechanism.

Although it is generally believed that data obtained from cultured cells may not be truly reminiscent to those found in native tissues, cell culturing is still a most commonly used experimental approach in studying epithelial transport. However, our recent

data suggest that receptor and ion channel expressions are often altered during cell culture conditions. Moreover, the electrometric techniques that are often used to monitor ion transport in intact tissue do not readily lend themselves to the detailed study of intracellular events. Therefore, there is a need for a technique to be developed that will allow simultaneous measurement of intracellular signaling events and transepithelial ion transport in intact epithelial tissues. The objectives of the project will be to develop a technique that allows the two important parameters, namely transepithelial ion transport and intracellular $[Ca^{2+}]_i$ to be monitored simultaneously in *intact tissue*.

(MD20049)

Association between Pancreatic Angiotensin System and Pancreatic Blood Flow and Ductal Secretion: The Significance of Changes by Chronic Hypoxia in the Rat Pancreas

✉ LEUNG Po Sing • FUNG Man Lung* • NOBILING Rainer*

☐ 1 November 2000

❖ Research Grants Council (Earmarked Grants)

The systemic renin-angiotensin system (RAS) plays an important role in regulating blood pressure and fluid homeostasis. Recently, a local RAS has been demonstrated which may either potentiate the systemic functions or have entirely separate activities that meet the individual tissue needs. The researchers' previous studies have provided evidence that several key elements of RAS are present in the rat pancreas, notably renin and angiotensinogen which are mandatory for intracellular generation of physiologically active angiotensin II. The data support the existence of an intrinsic RAS and such pancreatic RAS may be important for regulating pancreatic blood flow and ductal anion secretion. Interestingly, it is known that the expression of RAS genes is regulated by a number of factors such as hormones, ions and stress. One of these factors, namely hypoxic stress has been shown to result in the upregulation of tissue RAS in the lung, heart and kidney. The activation of RAS by chronic hypoxia should be important in the regulation of the physiological and pathophysiological changes of these tissue functions. In fact, some clinical pancreatic problems such as pancreatitis, alcoholism and transplantation are associated with hypoxia. However, the influence of hypoxia on pancreatic RAS and its significance to changes in pancreatic functions are far less clear. In the present study, the role of pancreatic RAS and the effect of chronic hypoxia on the regulation of pancreatic blood flow and ductal secretion will be elucidated. The reversibility of changes of pancreatic RAS by chronic hypoxia will also be examined. The changes of the pancreatic RAS in response to chronic hypoxia may

be responsible for locally regulating the pancreatic blood flow and ductal anion secretion, which could be important for physiological and pathophysiological events in the pancreas. The significance of changes of pancreatic RAS by chronic hypoxia may have clinical relevance to hypoxia-induced pancreatic injury.
(CU00075)

Changes of Angiotensin Converting Enzyme Activity and Expression in Experimentally Induced Pancreatitis from the Rat Pancreas

✉ LEUNG Po Sing

☐ 1 December 2000

❖ CUHK Research Committee Funding (Direct Grants)

The researchers' previous studies have provided solid evidence for the presence of a local renin-angiotensin system (RAS) in the rat pancreas, which may play a role in the regulation of pancreatic microcirculation and ductal secretion. Such a pancreatic RAS has been demonstrated under the regulation by chronic hypoxia, which would result in the activation of several key RAS component genes. It has been known that prolonged hypoxia causes decreased blood flow to the tissues, which may in turn lead to tissue inflammation and injury. For example, alcohol is believed to induce hypoxia in the pancreas and this could provide mechanism for accounting pancreatic injury such as pancreatitis. Accordingly, the activation of pancreatic RAS by chronic hypoxia and its significance of changes should be important for the physiology and pathophysiology of the pancreas. It is therefore very intriguing to further study the regulation of pancreatic RAS during pancreatic injury such as acute pancreatitis. As angiotensin converting enzyme (ACE) is a critical enzyme of the RAS, which determines the conversion of angiotensin I into physiologically active angiotensin II, the changes of its activity and expression by acute pancreatitis will be of crucial importance.

The present study is aiming at elucidating the expression and activity changes of ACE in experimental pancreatitis using molecular biological, immunohistochemical coupled with a specific ACE assay approaches. The results of the current project should provide useful information on the role of pancreatic RAS in pancreatitis and in chronic hypoxia, and its association with pancreatic injury.
(MD00688)

Changes in the Expression of Renin-angiotensin System in Patients with Idiopathic Dilated Cardiomyopathy: A Activation of the Transcription Factor NF_κB

✉ LEUNG Po Sing • Gerd Wallukat*

☐ 1 May 2001

❖ Germany/Hong Kong Joint Research Scheme

The local renin-angiotensin II system (RAS) of the heart plays a role in the regulation of hypertrophy and myocardial fibrosis in the failing heart muscle. It has been known that local activation of cardiac RAS may trigger the pathogenesis of cardiac function. Chronic hypoxia is able to activate the local RAS of the myocardium and elevate the amount of angiotensin II. Chronic hypoxia has also been demonstrated in dilated cardiomyopathy. Under these conditions, angiotensin II is capable to stimulate the enzyme system NADPH oxidase via the AT₁ receptor. It is possible that, via this cascade, the cardiac myocytes and non-myocytes produce free radicals. The present project is aimed at studying the activation of the NADPH oxidase and the transcription factor, NF κ B in heart tissue samples of patients with dilated cardiomyopathy, and compare them with normal control hearts. The tissues were taken from patients whom were implanted a cardiac assist device. The researchers hypothesize that there is a significant difference in the activity and expression pattern of the NADPH oxidase compounds p47 and p67 phox, the NF κ B and the I κ B between patients who have shown significant improvements under the assist device in comparison to patients with a small improvement. These two patients groups were compared to a healthy control group.
(MD20050)

Regulated Expression and Function of Pancreatic Renin-angiotensin System: Its Significance in Transplanted Pancreatic Islets

✉ LEUNG Po Sing • Carlsson Per-Ola*

☐ 1 May 2001

❖ CUHK Mainline Research Scheme

The researchers' recent studies have provided solid evidence for the existence of an intrinsic, angiotensin-generating system in the pancreas. This locally generated renin-angiotensin system (RAS) has a potential role in finely regulating exocrine and endocrine functions of the pancreas such as ductal anion secretion and islet hormonal secretion. Interestingly, some of these effects seem to be due to the potent vasoconstrictor actions of the RAS system. In fact, the pancreatic RAS has been shown to regulate pancreatic islet microcirculation and hence insulin secretion. Of great interest in this context is that infusion of angiotensin II causes a markedly more pronounced decrease in islet blood flow in transplanted islets when compared to endogenous islets. Interestingly, chronic hypoxia has been shown to induce an upregulation in the local generation of RAS components, including receptors for angiotensin

II, in the pancreas. In transplanted islets, a chronically low tissue oxygen tension and a markedly decreased blood perfusion compared to endogenous islets are seen.

So far, no information is available on RAS in transplanted islets. The present study is therefore aimed at elaborating the expression of RAS in transplanted islets, the influence of chronic hypoxia on this expression, and its significance in the regulation of graft blood perfusion. Theoretically, hyperactivity in local RAS of transplanted islets could cause a vicious cycle resulting in a chronically low graft blood flow. Ultimately, the results of the proposed project will provide information regarding the potential role of pancreatic RAS for islet graft function.

(MD20057)

Trichosanthin as an Antiviral Agent - Mechanism of Action

✉ TAM Michael S C

☐ 1 November 2000

❖ CUHK Research Committee Funding (Direct Grants)

Trichosanthin (TCS) is a type I ribosome inactivating protein possessing anti-viral activity. It is therefore a potential antiviral therapeutic agent. The mechanism of action is generally believed to be mediated through ribosome inactivation but that has not been demonstrated experimentally. The objectives of this study are to (1) characterize the antiviral action of TCS on some selected viruses like Human Immunodeficiency Virus (HIV) and Herpes Simplex virus (HSV), (2) delineate the relationship between antiviral activity and ribosome inactivation and (3), attempt to locate the antiviral region on the TCS molecule.

In the past years, a number of TCS mutants with various ribosome inactivating activities had been made. These compounds can be used to study the correlation between antiviral and ribosome inactivating activities of TCS.

Using molecular biology and chemical coupling techniques, Polyethylene Glycol (PEG) was successfully coupled to any selected sites on the TCS molecule. Such modification can sterically mask the selected site and the activity corresponding to the site is lost. In the researchers' previous study, by measuring the reduction in antigenicity of the modified TCS, 2 sites on the TCS molecule has been mapped as antigenic determinants. Using the same approach, by measuring the reduction in antiviral activity of the modified TCS, it is possible to identify the location on the TCS molecule responsible for its antiviral activity.

In conclusion, this study leads to better understanding of the antiviral activity of TCS, in particular the role

of ribosome inactivation as well as the structure and function relationship.

(MD00577)

Regulation of CNGI Channel Expression by a Natural Antisense Gene

✉ YAO Xiaoqiang • KWAN Hiu Yee

☐ 15 October 2000

❖ CUHK Research Committee Funding (Direct Grants)

Natural (or endogenous) antisense RNAs are endogenous transcripts that exhibit complimentary sequences to transcripts of already known functions, named sense transcripts. They are suggested to play a role in the regulation of expression of their sense counterparts. Up to now, only about a dozen antisense transcripts have been identified in eukaryotic cells. The researchers have recently isolated a cDNA clone from human brain library. This 1.6 kb clone represents a new transcript that is antisense to human CNG1 mRNA. It is likely that it may down-regulate the expression of sense CNG1 channel. This result represents the first discovery of a natural antisense mRNA complementary to any known ion channel.

The researchers will study the functional significance of this anti-CNG1 mRNA and to further localize the anti-mRNA at tissue and cellular level.

(MD00583)

Nucleotide Modulation of Non-selective Cation Channels in Vascular Endothelial Cells

✉ YAO Xiaoqiang • GARLAND Christopher*

☐ 15 November 2000

❖ Wellcome Trust, UK

This project would support a collaboration between Professor C Garland's group in the University of Bath and Dr. X. Yao and his group in The Chinese University of Hong Kong.

The aims would be:

(1) to define the characteristics of the non-selective cation channel present in endothelial cells of small resistance arteries.

(2) to show how this channel links to the release of endothelium-derived hyperpolarizing factor (EDHF).

Of particular interest, the researchers will be showing how the channel is modulated by protein kinase G of which is activated by nitric oxide elaborated by the endothelial cells, and the importance of this interaction in determining the extent and duration of the vasodilatation which is evoked by EDHF in resistance arteries.

The research will rely on the complementary expertise available in the two groups. The ability to isolate and record functional responses from very

small arteries in Professor Garland's group, and in Dr. Yao's group to isolate viable endothelial cells from small blood vessels to which molecular techniques and single channel measurements can be applied. (MD00479)

Protein Kinase G-sensitive Ca²⁺ Influx in Endothelial Cells and Its Role in Vasoregulation

✉ YAO Xiaoqiang • HUANG Yu • YEW Tai Wai David (Dept of Anatomy)

□ 1 December 2000

❖ Research Grants Council (Earmarked Grants)

The hemodynamic force generated by blood flow is considered to be the physiologically most important stimulus for the release of nitric oxide (NO), endothelial-derived hyperpolarizing factor (EDHF), and prostacyclin (PGI₂) from vascular endothelial cells. These factors then act on the underlying smooth muscle cells, causing vasodilation and thus lowering blood pressure. One critical early event occurring in this flow-induced regulation of vascular tone is that blood flow induces Ca²⁺ entry in vascular endothelial cells, which in turn leads to the increased formation and release of NO, EDHF and PGI₂. In the preliminary study, the researchers found a mechanosensitive Ca²⁺-permeable channel in vascular endothelial cells. Evidence from their experiments suggests that this channel is the primary pathway that mediates the flow-induced Ca²⁺ entry in vascular endothelial cells. Therefore it is likely that this channel plays an important role in the regulation of vascular tone.

The researchers propose here to further study the mechanisms by which this Ca²⁺-permeable channel regulates the vascular tone. They will also explore the therapeutic potential of modulating this Ca²⁺ influx pathway as a possible approach for treatment of hypertension. (CU00079)

Analysis of GABAergic Neurotransmission in Rat Globus Pallidus: Correlation of Electrophysiology with Ultrastructural Immunocytochemistry

✉ YUNG Wing Ho • BOLAM John Paul* • YUNG Kin Lam Ken*

□ 1 September 2000

❖ Research Grants Council (Earmarked Grants)

Malfunction of the basal ganglia, which consist of a group of interconnected subcortical nuclei, is the origin of a number of movement disorders including Parkinson's and Huntington's disease. The globus pallidus, one of the nuclei in the basal ganglia, exhibits abnormal neuronal activity under these pathological conditions. Elucidating the factors controlling the activity of pallidal neurons is

therefore essential not only in understanding their normal function, but also their role in the pathophysiology of basal ganglia disorders. In this study, the researchers concentrate on exploring the nature of the main synaptic input, which originates from the striatum and is mediated by the inhibitory amino acid GABA. To fully understand the process of GABA neurotransmission in the globus pallidus, the researchers will define the exact location of GABA-A and GABA-B receptor subtypes and the physiological actions that they mediate. The cellular and subcellular locations of these GABA receptors will be determined by immunocytochemistry using confocal and electron microscopy. These data will be directly correlated with whole-cell recordings from the same neurons. The results will provide a more comprehensive picture of GABA function in the globus pallidus, which could have implications for the search of better treatments for basal ganglia disorders. (CU00080)

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

<u>Edition</u>	<u>Title/Investigators</u>
1997-98	Identification and Functional Studies of VEGF Receptors in Rat Testicular Macrophages (CU97663) ✉ AU Chak Leung • LEE Will M.*
1995-96	Study of Epithelial Electrolyte Transport (MD95029) ✉ CHAN Hsiao Chang • WONG Patrick Yee Ding • CHEW CHENG Siew Boon • KO Wing Hung
1998-99	Research in Epithelial Cell Biology (MD98084) ✉ CHAN Hsiao Chang • CHEW CHENG Siew Boon • FISCUS Ronald Ray • LEUNG Po Sing • WONG Patrick Yee Ding • YAO Xiaoqiang
1999-00	Involvement of CFTR in Mediating Neurohormonal-regulated HCO ₃ ⁻ and Cl ⁻ Secretion by the Endometrial Epithelium (MD99058) ✉ CHAN Hsiao Chang
1999-00	The Cloning of Two Rat Epididymis-specific Novel mRNAs and Their Potential Roles in Sperm Maturation (MD99124) ✉ CHAN Hsiao Chang

- 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)
- 1998-99 Ultrastructural Identification of Apoptotic Cells by Direct Immunogold Detection of Digoxigenin-labeled Genomic DNA in Semithin Sections (MD98056)
 ✍ CHEW CHENG Siew Boon
- 1998-99 Mechanism of Atrial Natriuretic Factor (ANF)-induced Inhibition of DNA Fragmentation and Increased Expression of c-fos, junB and Ornithine Decarboxylase (ODC) Genes in NG108-15 Cells (MD98057)
 ✍ FISCUS Ronald Ray
- 1999-00 Nitric Oxide (NO) Enhancement of Adrenomedullin- and CGRP-induced Vasodilation and Delayed Vasodepression via NO Synthase (iNOS) Gene Expression: Involvement in Endotoxin Shock (MD99059)
 ✍ FISCUS Ronald Ray
- 1997-98 Study on Mechanisms of Vasodilator Effects of Green Tea Epicatechin Isomers in Spontaneously Hypertensive Rats and Normotensive Rats (CU97609)
 ✍ HUANG Yu • CHEN Zhenyu (Biochemistry)
- 1997-98 Interaction between G Protein and K⁺ Channels in Rat Pituitary GH3 Cells (MD97101)
 ✍ HUANG Yu • HESCHELER Jurgen*
- 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*
- 1998-99 Study on Calcium Sparks in Smooth Muscle Cells (MD98117)
 ✍ HUANG Yu • GOLLASCH Maik*
- 1999-00 Electrophysiological and Molecular Studies of Epithelial Potassium Channels (MD99002)
 ✍ HUANG Yu • WILSON Stuart M.*
- 1998-99 The Function of Merkel Cell as a Touch Sensory Receptor (MD98111)
- 1999-00 The Pancreatic Renin-angiotensin System: Its Role and the Effect of Chronic Hypoxia on Pancreatic Ductal Secretion and Blood Flow (MD99061)
 ✍ LEUNG Po Sing
- 1999-00 Changes in the Expression of Renin-angiotensin System in Patients with Idiopathic Dilated Cardiomyopathy (MD99090)
 ✍ LEUNG Po Sing • Dr. Gerd Wallukat*
- 1998-99 Internalization and Routing of Trichosanthin (CU98243)
 ✍ TAM Michael S C • SHAW Pang Chui (Biochemistry) • CHAN Wood Yee (Dept of Anatomy)
- 1999-00 Characterization of Transport Properties of the Rat Efferent Duct with Particular Reference to the Role of Estrogen (MD99006C)
 ✍ WONG Patrick Yee Ding
- 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 Characterization of Transport Properties of the Rat Efferent Duct with Particular Reference to the Role of Oestrogen (MD99062)
 ✍ WONG Patrick Yee Ding
- 1999-00 Patch Clamp Study of Ca-permeable Nonselective Cation Channel in Vascular Endothelial Cells (MD99063)
 ✍ YAO Xiaoqiang • KWAN Hiu Yee
- 1999-00 Isolation and Characterization of An Endothelial Cyclic Nucleotide-gated Cation Channel (CNG) (CU99259)
 ✍ YAO Xiaoqiang • HUANG Yu
- 1999-00 Cannabinoid Modulation of Synaptic Functions in the Basal Ganglia: An Electrophysiological Study (MD99064)
 ✍ YUNG Wing Ho

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RESEARCH PROJECTS

A Study of the Neurobiological Correlates of Behavioural and Psychological Symptoms in Alzheimer's Disease

✉ LAM Chiu Wa • CHIU Fung Kum Helen • TANG Leung Sang Nelson (Dept of Chemical Pathology) • Garcia Barcelo Maria Mercedes*

☐ 1 October 2000

❖ Research Grants Council (Earmarked Grants)

Although memory impairment is a cardinal feature of Alzheimer's disease (AD), behavioral disturbance and abnormal psychological experience are also important dimensions of the clinical syndrome. The term Behavioral and Psychological Symptoms of Dementia (BPSD) is currently adopted to describe the psychiatric manifestations, psychological reactions and behavioral changes associated with dementia.

Prevalence studies on BPSD reported that at least one third of demented patients exhibited significant behavioral and problems during the disease course. Subjects with BPSD constitute higher risk of accidents, morbidity and service utilization. However, the neural mechanism underlying BPSD has not been well defined.

The present proposal aims to examine the detail behavioral phenotypy of BPSD and its association with neurobiological markers. A representative group of AD subjects will be selected for an explorative multi-faceted assessment on different dimensions of neurobiological status. Significant correlations between different neurobiological parameters and behavioural disturbance of AD will be evaluated.

(CU00082)

Attitudes Toward and Cultural Meanings of Suicide in Contemporary Chinese Society

✉ LEE Sing • Arthur Kleinman* • Michael Phillips*

☐ 1 November 2000

❖ Research Grants Council (Earmarked Grants)

In Chinese society, suicide has long been a means of avoiding unbearable situations as well as a partially sanctioned strategy for dealing with a variety of social, political, economic, and moral adversities. Data from China's Disease Surveillance Points death registry system estimates over 300,000 suicides in Mainland China each year. This makes suicide one of the most important causes of death in China. Its rate is very high despite the great value placed on social cohesion in Chinese culture. Besides, it is more common in females than males, three times more frequent in rural than urban areas, and exhibits

less connection with psychiatric disorders such as depression and alcoholism. By contrast, Hong Kong is also a "Chinese" society, but its rate and pattern of suicide are more similar to those of Western countries. These different patterns of suicides are likely to reflect major social, economic and historical differences between Hong Kong and China. Most importantly, suicide remains a major cause of death and economic loss in both Hong Kong and China, and has risen following the recent economic downturn. This is a comparative study that integrates qualitative and quantitative methods for assessing a comprehensive range of cultural attitudes toward and social meanings of suicide in Hong Kong and four rural and urban communities in Mainland China. The results will expand our understanding of suicide in Chinese society and foster the development of effective public campaigns, programs, and policies for reducing suicides in Hong Kong and China. (CU00380)

Mental Health Service Users' Experience of Discrimination in Hong Kong

✉ LEE Sing • Chiu Marcus* • Ching Chi Kong*

☐ 1 December 2000

❖ Equal Opportunities Commission

Stigma against persons with mental illness is universal and as old as mankind. Mental illnesses of various types are very common in Hong Kong. Yet, discrimination against mental health service users is widespread and represents a substantial obstacle toward equal opportunities. It also obstructs the recognition of psychiatric symptoms, causes reluctance to admit mental illness, and delays help-seeking. The present study aims to survey first-hand experience of discrimination from a large group of mental health service users in Hong Kong. It also elicits personal accounts of discriminatory practices and recommendations of how to tackle them from a representative sample of the surveyed subjects. The findings will be disseminated in timely ways that contribute to reducing discrimination against mental illness and promoting equal opportunities. (MD20032)

An Open Trail of the Safety of *WeiniCom* in Detoxification of Heroin Dependence in an Inpatient Setting

✉ LEE Tak Shing Dominic • TANG Jinling (Dept of Community and Family Medicine) • CHIU Fung Kum Helen • LEE Shiu Hung (Dept of Community and Family Medicine)

☐ 1 August 2000

❖ International Drug Abuse Treatment Foundation

Objective: This study serves as a pilot study of a full-scale randomized controlled clinical trial. It aims (1) to obtain a good clinical picture about the safety of *WeiniCom* including severe side-effects, toxic effects, and other possible harms, (2) to gain some first-hand experience with the administration of the drug in inpatient settings, and (3) to characterize the effects of *WeiniCom* in ameliorating withdrawal symptoms.

Design and setting: This study will be phase II trial without a control group in which a series of 30 heroin drug abusers will be given *WeiniCom* as a detoxification treatment in an inpatient setting for 14 days to characterize the treatment and possible severe side effects and harms of the treatment. The followup of the patients will continue for one month upon the completion of the treatment.

Subjects: Patients who fulfilled the DSM-IV criteria of opiate dependence will be recruited from the inpatients of the substance abuse clinic at the Prince of Wales Hospital. Every patient will be asked to sign a written informed consent form before they are finally entered the study.

Study Outcome: Patients' symptoms and complaints will be recorded whenever reported during the whole course of the trial. Physical examination and laboratory investigations will be conducted at days 0, 1, 3, 14, and at the end of the one-month followup. The score of withdrawal symptoms, score of craving for heroin, treatment retention self-reported heroin use and urine toxicology will also be assessed daily. (MD20015)

Charcoal Burning Suicide in Hong Kong

✉ LEE Tak Shing Dominic • CHAN Sau Man Sandra • CHUNG Wai Sau Dicky • Chan Po Man Kathy* • Yip Siu Fai Paul*

☐ 1 September 2000

❖ Health Care & Promotion Fund, Hospital Authority

Objectives: (1) To identify risk factors of charcoal burning suicides;

(2) To understand the psychological, social and economic contexts where charcoal burning suicide occurs.

Design: A retrospective cases study compounded with a prospective qualitative investigation using ethnographic interviews.

Setting: The case study will be conducted at the Coroner's Court. The qualitative study will be conducted in three district general hospitals.

Participants: [Quantitative study] All charcoal burning suicide deaths occurring between November 1998 and January 2000 will be examined. A total of 160 cases is anticipated. As control comparison, 160 age-gender matched non-charcoal burning suicide deaths occurred over the same time span will be examined.

[Qualitative study] 20 consecutive survivors of charcoal burning suicide will also be recruited for ethnographic interviews. They will be recruited by the consultation liaison psychiatrists of the participating centers.

Methods: [Quantitative study] Each coroner case record (including suicide notes, police statements, medical reports, toxicology laboratory findings) will be reviewed. Data pertaining to socio-demographic characteristics and putative factors will be collected.

[Qualitative study] Participants will be interviewed in a semi-structured manner, based on an inventory of guiding questions. The ethnographic interview will be followed by a semi-structured psychiatric diagnostic interview to ascertain current and past psychiatric diagnosis.

Outcome: [Quantitative study] Odds ratios of putative factors.

[Qualitative study] Central themes and coding categories will be identified and interviews will be coded for presence or absence of the identified themes. Attention will be focused on subjectivity, motives, interpersonal dynamics, and various local impacts.

Conclusion: The qualitative and quantitative data will be triangulated to make sense of the charcoal burning epidemic. Efforts will also be made to search for intervention that may reverse the current trend.

(MD20036)

An In-depth Study on the Psychotropic Substance Abuse Problem in Hong Kong

✉ LEE Tak Shing Dominic

☐ 9 October 2000

❖ Action Committee Against Narcotics

Objectives: (1) To identify various factors and underlying reasons at a microscopic level relating to psychotropic substance abuse; (2) To conduct in-depth qualitative and ethnoepidemiological analyses on the relationship between rave culture and drug abuse in Hong Kong; (3) To investigate into the pattern of drug progression amongst psychotropic substance abusers and whether there has been and will likely be, a transition from opiate drug abuse to psychotropic substance in Hong Kong in the overall drug scene; (4) To recommend a strategy to combat the psychotropic substance in Hong Kong based on findings obtained.

Method: Fifty informants will be interviewed by the Principal Investigator using mini-ethnography. Also, the PI will visit and observe different kinds of venue where PS are being used. This participant observation, as well as other informal interviews, will compliment the ethnographic interviews in the data collection.

Results: Grounded in the phenomenological tradition, mini-ethnography is a research methodology commonly used to collect qualitative data. With no-

perception of the studied phenomenon/population, the ethnographer lives in the local world of the informants and participants in the communal activities to achieve an in-depth and local understanding of the experience of the informants as well as the meanings to understand the phenomenon of drug abuse.

Potential values: Well-conducted qualitative studies will inform drug and social policy makers as to the relationship between rave culture and psychotropic drug abuse and whether there has been (or will be) a real shift in the pattern of drug use. (MD20045)

Patients' and Their Relatives' Satisfaction with Electroconvulsive Therapy

✉ TANG Wai Kwong • UNGVARI Gabor Sandor • LEUNG Shung Pun • LEUNG Chi Ming • YIP Ka Chee • NG Yin Kwok • DUNN Eva* • CHUNG K F* • NG F S* • LEUNG W H* • YIU G C*

☐ 25 November 2000

❖ Lee Hysan Endowment Research Grant

Electroconvulsive therapy (ECT) is a safe and effective treatment in psychiatry. A few hundred patients receive and benefit from ECT every year in Hong Kong. ECT facilities are available in nearly all psychiatric units in Hong Kong. ECT has been widely accepted by psychiatrists and mental health professional (Finch 1999; Kalayam 1981). On the other hand, there is a wide spread negative view among the lay public. Survey on the patients' view and experience in ECT in western populations found that patients had positive attitude towards ECT (Goodman 1999, Water 1999, Petinnati 1994). There is no data on the level of satisfaction of ECT among Chinese patients. Such information is important in : (1) optimizing the delivery of ECT; (2) revealing patients' gaps in knowledge and their understanding about ECT; (3) providing more accurate information on ECT to the lay public. Hence the researchers propose to measure patients' experience with ECT and patients' and their relatives' knowledge and attitude on ECT. Sixty patients who have received ECT and their relatives will be recruited among several psychiatric units in Hong Kong over 3 months. After obtaining their written consents, a research assistant will administer a questionnaire 2 to 3 weeks after the completion of their ECT courses to collect information on their experience, knowledge and attitude on ECT. In addition, the research assistant will administer the Brief Psychiatric Rating Scale (Overall & Gorham, 1962) and Hamilton Depression Rating Scale (Hamilton 1967) to rate the severity of patients' psychotic and depressive symptoms, respectively. (MD00663)

Prospective Memory in Patients with Schizophrenia and Its Relationship with Retrospective Memory, Executive Functions, and Daily-life Adjustment

✉ UNGVARI Gabor Sandor • AU Wing Cheong* • CHU Man Keung* • TANG Wai Kwong • SHUM H K David*

☐ 15 August 2000

❖ Research Grants Council (Earmarked Grants)

One of the most commonly reported problems by patients with schizophrenia is memory deficit. This is a debilitating problem because it affects everyday functioning of these patients and hinders rehabilitation efforts. Past research has focused mainly on patients' ability of recalling past information or retrospective memory (RM) but neglected an important memory process known as prospective memory (PM) or the ability to remember to perform intended actions in the future. Given its future and behavioral orientation, PM is considered different from and more complex than the traditional construct of RM. Available evidence has indicated that patients with schizophrenia suffer from some kind of PM impairments but systematic research in this area is still lacking. PM is relevant to the management and rehabilitation of schizophrenia because PM is essential for maintaining an organized daily routine of life and coping with social demands. For both theoretical and practical reasons, the researchers propose a study to assess the nature and extent of PM impairment and their relationship with RM, prefrontal executive functions, and daily-life adjustment in patients with schizophrenia. The researchers will compare patients with schizophrenia with matched normal controls (100 each) on performances of three PM tasks (event-, time-, and activity-based), RM tests, and prefrontal function tests. For the patient group, symptom profiles and functional capacities for daily living will be evaluated against performance on PM tasks. Findings will provide useful information for improving the assessment, management, and rehabilitation of PM problems in patients with schizophrenia. The data collected will also advance our understanding of PM processes and their relationship with RM and executive functions. (CU00330)

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	A Clinical Trial of the Motivational Strategy for Engaging Early Drug Abusers (MD99118)

- ☞ CHEUNG Kin Leung Ben • TANG Jinling (Dept of Community and Family Medicine) • CHAN Shiu Yee Cynthia (Dept of Community and Family Medicine)
- 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* • 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*
- 1999-00 Duplication of the *CYP2D6* Gene in Hong Kong Chinese (MD99113)
- ☞ CHOW Lok Yee • CHIU Fung Kum Helen • UNGVARI Gabor Sandor • GARCIA BARCELO Maria Mercedes#
- 1998-99 Outcome and Cultural Context of Anorexia Nervosa in Hong Kong (CU98029)
- ☞ LEE Sing • HSU L. K. George*
- 1999-00 Attitudes Toward and Social Meanings of Suicide in Contemporary Chinese Society (SS99004)
- ☞ LEE Sing • PHILLIPS Michael* • KLEINMAN Arthur*
- 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)
- 1999-00 Development of a Local Drug Abuse Treatment Outcomes Measure (MD99119)
- ☞ LEE Tak Shing Dominic
- 1999-00 An Open-label Pilot Study to Assess the Effect of Venlafaxine-XR in the Treatment of Chinese Patients in Hong Kong with Neurasthenia (MD99126)
- ☞ WING Yun Kwok • LEE Sing • LEE Tak Shing Dominic • CHAN Shiu Yee Cynthia (Dept of Community and Family Medicine)

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RESEARCH PROJECTS

Step Beyond Limits: Learning Effective Multiple Intelligence

- ✉ LAU Tak Fai Joseph • LEUNG Kit Sang (Centre for Clin. Trials & Epidemiological Research) • WONG Wing Sze (Dept of Psychiatry)
- ☐ 1 July 2000
- ❖ Yaumatei Catholic Primary School (a.m.) funding from Quality Education Fund

The project evaluates an innovative educational programme aiming to enhance the understanding of the basic concept of 'multiple-intelligences' in primary school teachers in Hong Kong. Seminars and workshops focusing on the utilization of the eight intelligences in educational settings were delivered to 960 teachers from 28 primary schools in a two-year period. The evaluation exercise employed a pre- vs. post-programme design, in which quantitative data were collected before and after the educational programme by using structural questionnaires designed by independent researchers. The structural questionnaires were designed to evaluate teachers' knowledge, competence, and confidence in applying what they have acquired from the programme. (ED00961)

Growing Up to a Balanced Life

- ✉ LAU Tak Fai Joseph • WONG Wing Sze (Dept of Psychiatry)
- ☐ 1 July 2000
- ❖ Chai Wan Faith Love Lutheran School funding from Quality Education Fund (QEF)

To evaluate a project helping teachers to learn the basics of multiple intelligence and provide them with ideas and suggestions for them to apply the concepts to their teaching subjects. (ED20022)

The 2000 Survey of Drug Use among Students

- ✉ LAU Tak Fai Joseph • CHAN Kam Kuen (Centre for Clin. Trials & Epidemiological Research)# • WONG Chung Kwong (Dept of Psychiatry)# • WONG Wing Sze (Dept of Psychiatry) • LAU Man Chun Mason (Centre for Clin. Trials & Epidemiological Research) • Choi Yuen Wan*
- ☐ 1 September 2000
- ❖ Action Committee Against Narcotics

The Center will conduct a large-scale survey to collect information on the extent of the drug abuse by

students of secondary schools and Institute of Vocational Education (IVE). The objectives of the Survey include:

- (1) To obtain information about the drug use pattern of students;
- (2) To assess students' knowledge of and attitudes towards drug use;
- (3) To find out students' exposure to the risk of drugs;
- (4) To find out the reasons why students use drugs; and
- (5) To examine if there are personal and family variables associated with the abuse of psychotropic substances.

About 122,000 students will be selected for enumeration in this survey, comprising:

- (a) 85,000 students in Chinese-speaking Schools (F.1-F.7);
- (b) 10,000 students in all English Schools foundation and International Schools (F.1-F.7); and
- (c) 26,000 students from full-time and part-time day courses of the Vocational Training Council's Institute of Vocational Education. (MD20035)

The Hong Kong Men Who Have Sex with Men Study – A Study of Behavioural Surveillance, Bisexual Behaviours and Need Assessment

- ✉ LAU Tak Fai Joseph • SIAH Poh Chua (Centre for Clin. Trials & Epidemiological Research)#
- ☐ 1 September 2000
- ❖ Council for the AIDS Trust Fund

There are four main objectives in this study, which are to setup a behavioral surveillance system for MSM (men who have sex with men) population in Hong Kong, to understand the diversity of the types of risk behaviors and its relationship to AIDS prevention, to understand the mechanism of behavioral change, and to understand the bridge between the MSM and female populations. To minimize response and sampling bias, an interactive computerized call-in method will be used. 15,000 men of above 18 years old will be screened by a short questionnaire to see if they have practiced MSM behaviors. Those who report to have practiced MSM behavior will be interviewed with an in-depth questionnaire to meet the above-mentioned objectives. (SS20006)

The Development of an Instrument to Measure Discrimination Toward People Living with HIV/AIDS (PLWA) in Hong Kong and to Improve the Acceptance of PLWA among Secondary Students

- ✉ LAU Tak Fai Joseph • TSUI Hi Yi (Centre for Clin. Trials & Epidemiological Research)
- ☐ 1 March 2001

❖ Council for the AIDS Trust Fund

The present study has four main objectives, which are to develop an instrument to measure discriminatory attitudes toward people living with HIV/AIDS (PLWA) in the community, to apply this instrument to a school setting to examine whether secondary students are more or less discriminatory toward PLWA than adults in Hong Kong, to develop an information pamphlet aiming at removing misconception and improving supportiveness of PLWA by secondary school students, and to distribute such materials to secondary school students and evaluate the impact of receiving such information. (SS20014)

✉ LAU Tak Fai Joseph • LEE Shiu Hung (Dept of Community and Family Medicine)

1998-99 Evaluation of a program for Frequent Travellers Crossing the China-Hong Kong Border (MD98147)

✉ LAU Tak Fai Joseph • SIAH Poh Chua (Centre for Clin. Trials & Epidemiological Research)#

1999-00 Enhancing Children's Emotional Intelligence (ED98037)

✉ LAU Tak Fai Joseph • CHAN Kam Kuen (Centre for Clin. Trials & Epidemiological Research)#

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

1999-00 Emotional Education for Primary School Students (ED99058)

✉ LAU Tak Fai Joseph • CHAN Kam Kuen (Centre for Clin. Trials & Epidemiological Research)#

Edition Title/Investigators

1997-98 Understanding the Adolescent Project - Pilot Implementation and Evaluation Study (ED97026)

✉ LAU Tak Fai Joseph • CHOI Yuen Wan* • LAI Yee Ching Kelly (Dept of Psychiatry) • OBORNE David* • HOH Ying*

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 (Centre for Clin. Trials & Epidemiological Research)# • BROW Tin*

1997-98 The Development of Indicators to Track Awareness, Attitude and Behaviours (MD97129)

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<P010793> **劉德輝.** <香港愛滋病服務非政府組織的發展方向> 《社聯季刊》 第 158 期, 頁 3-6. 2001.

see also <P002267>, <P002652>, <P003999>, <P011022>, <P011060>

RESEARCH PROJECTS

Impact of Continuous Ventilation on Pulmonary Injury After Cardiopulmonary Bypass

✉ ARIFI Ahmed A* • NG Sze Hang Calvin# • HO Ming Hei Anthony (Dept of Anaesthesia & Intensive Care) • WAN Song • YIM Ping Chuen Anthony

□ 1 June 2001

❖ CUHK Research Committee Funding (Direct Grants)

Cardiopulmonary bypass (CPB), which is required in the majority of cardiac operations, is known to cause lung injury with subsequent morbidity and mortality. The role of maintaining lung ventilation during CPB has not been scientifically studied. The researchers will conduct a case-controlled randomized clinical trial in patients undergoing coronary artery bypass grafting (CABG) to evaluate the relationship between neutrophil activation, the systemic inflammatory response, haemodynamic changes, and pulmonary dysfunction after CPB. In particular, the researchers will assess the potential influence of maintaining lung ventilation throughout CPB on these parameters. Thirty patients for CABG will be randomized into ventilated or non-ventilated groups. Standardized anesthesia and surgical technique will be used. Differential leucocyte count, neutrophil activation (cell surface adhesion molecules CD11b, CD45), inflammatory cytokines (tumor necrosis factor- α , Interleukins 6, 8, 10) and proteolytic enzymes (myeloperoxidase, matrix metalloproteinase-9, tissue inhibitor metalloproteinase-1) will be determined in the blood samples and in the bronchoalveolar lavage fluid taken at 7 time points during and after CABG. Haemodynamic changes and pulmonary function will be determined by two specialist monitors connected to the patient via the ventilator and a thermodilution arterial catheter. Pulmonary gas exchange, extravascular lung water, lung dynamic compliance, and cardiac output will be recorded as outcome parameters. The study is expected to last for one year. The knowledge obtained will help to elucidate the pathophysiology of lung injury after CPB and allow us to assess the role and feasibility of continuous lung ventilation during CPB in an attempt to further improve on our clinical practice. (MD00456)

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

✉ BURD David Andrew Ross • HO Wai Sun • POON Kwok Man

□ 1 December 2000

❖ CUHK Research Committee Funding (Direct Grants)

The use of laser treatment of skin lesions is widely established in current medical practice. The biological effects of laser exposure are, however, poorly understood. The researchers' previous studies in a melanoma cell model have suggested that laser energy may interfere with cell cycle control mechanisms and cause cells to exhibit features associated with increased malignant potential.

Post burn keloid scarring is a major cause of disability from functional loss and deformity due to distortion of anatomical features. Disability and deformity can lead to economic deprivation and social isolation.

Keloid scar tissue exhibits lack of normal cell-matrix interaction leading to an over production of matrix components. Many attempts have been made to control this proliferative excess, therapeutically, with varying degrees of success. The use of laser treatment of post-burn keloid is currently being evaluated clinically in many centres. There is a concern, however, that the biological behaviour of keloid fibroblasts may be altered by exposure to laser energy.

This project seeks to gain a further understanding of the fundamental biology of cells exposed to laser energy with the goal of identifying both potential therapeutic and harmful effects in vitro.

(MD00824)

A Multi-centered Randomized Controlled Trial Comparing Standard Oesophagectomy Versus Primary Chemo-irradiation without Surgery as the Treatment for Squamous Oesophageal Cancer

✉ CHAN Chi Wai Angus • CHUNG Sheung Chee Sydney • GRIFFITH James Francis (Dept of Diagnostic Radiology & Organ Imaging) • KWOK Po Yin Samuel • LEONG Heng Tat • LEUNG Sing Fai (Dept of Clinical Oncology) • ONG Lina Lilian

□ 1 July 2000

❖ Research Grants Council (Earmarked Grants)

Cancer of the oesophagus is notorious for its grave prognosis with an overall 5-year survival rate of 10-20%. Surgical resection with curative intent remains the most effective treatment for this disease. To improve the survival, a better treatment approach is in need to manage patients with oesophageal cancer. Unfortunately, the use of preoperative adjuvant chemotherapy or adjuvant radiotherapy does not confer any survival benefit to patients with localized oesophageal cancer as proven in most randomized studies. However, the combination of chemotherapy and radiotherapy has greater clinical efficacy in

achieving complete pathological regression of the tumour as well as the response rate as shown in the researchers' preliminary results. In fact, treatment of squamous oesophageal cancer by primary chemo-irradiation without surgery is now feasible. The researchers will conduct a multi-center randomized trial to evaluate the efficacy and the patients' survival by comparing primary chemo-irradiation without surgery versus standard surgical resection as the treatment for squamous oesophageal cancer. Those patients with residual cancer after primary chemo-irradiation will have salvage oesophagectomy to control the disease. Over a 3-year period, a total of 200 patients will be recruited from 4 different hospitals with 100 patients being randomized into each treatment arm. Treatment outcomes will be compared on an intention-to-treat analysis basis. (CU00084)

A Functional and Molecular Study of Mitochondria in the Progress of Carcinogenesis of Urinary Bladder Tumours In Rats

- ✉ CHAN Siu Foon Peter • CHAN Leung Franky (Dept of Anatomy) • CHEN Guangfu
- ☐ 30 October 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Bladder cancer is the commonest malignant tumour of the urinary tract, with over 90% being transitional cell carcinoma (TCC), the rest being squamous cell carcinoma (SCC) and adenocarcinoma. A great deal of work is needed to be done to understand its carcinogenesis.

The researchers have developed an animal model to study aspects of bladder cancer carcinogenesis: high incidence of TCC had been induced in SD rats and Balb/c mice by feeding the animals with drinking water containing the carcinogen N-butyl-N-(4-hydroxybutyl) nitrosamine (BBN). Their study demonstrated the sequential changes, by light and electron microscopy, from normal transitional epithelium to hyperplasia to papilloma to full grown carcinoma. Also it was found that during tumour development, there were significant increases in the number of mitochondria and lysosomes together with a decrease in fusiform vesicles.

Using the same animal model, the researchers design experimental studies to investigate the aspects of energy supply in bladder cancer carcinogenesis:

- (1) Using light and electron microscopy, enzyme histochemistry and immunogold labelling, they will study the sequential morphological changes and co-relate such changes to mitochondrial enzyme activities.
- (2) Using enzyme histochemistry, they will study the activities of the key enzymes of carbohydrate metabolism in pre-neoplastic and neoplastic cells.

(3) By means of enzyme assays with immunohistochemistry and immunoblotting and protein expression levels, they will investigate the activities of several important mitochondrial enzymes involved in oxidative phosphorylation, particularly cytochrome c oxidase.

It is hoped that the studies will shine light on an area of carcinogenesis where relatively few studies have been focused.

(MD00894)

Kupffer Cells Kill Tumor Cells by Generating Inducible Nitric Oxide synthase

- ✉ CHEN Gong George • LAI Bo San Paul
- ☐ 31 October 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Kupffer cells are the resident macrophages of the liver and constitute 80-90% of the body's total macrophages mass. It is well known that activated macrophages have the capacity to recognize and kill tumor cells and circulating micrometastases. Evidence has shown that there is a reverse correlation between the number of Kupffer cells in liver and the occurrence of liver cancers, suggesting Kupffer cells may have a suppressive role in the development of liver cancers. However, experimental data available to support such clinical findings are very limited. Among more than 100 substances that are known to be secreted by macrophages, inducible nitric oxide synthase (iNOS) is of central importance. Nitric oxide (NO) sensitizes or cause tumor cells to death by a number of mechanisms, some requiring cell-to-cell contact and others dependent on the elaboration of soluble effector molecules such as TNF- α , interleukin 1, interleukin 10 and cytolytic proteases. The activation of macrophages is known to be associated with an increased level of reactive oxygen species (ROS). The researchers' previous study has shown that the production of iNOS is fine-tuned by ROS. Therefore, the researchers hypothesize that Kupffer cells destroy tumor cells by producing iNOS which is subjected to ROS regulation.

(MD00339)

Altered Expression and Mutations of the HBV Transactivator X Gene in Hepatocellular Carcinoma and Liver Cirrhosis

- ✉ CHUI Ka Keung Albert • CHEN Gong George • LAU Wan Yee Joseph
- ☐ 1 June 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

Hepatitis B virus (HBV) infection, which is a major risk factor for the development of hepatocellular

carcinoma (HCC), is endemic in many regions of the world including Eastern Asia, China and Hong Kong. The *HBX* gene of HBV has been postulated to play an important role in the viral pathogenesis by transactivating viral and critical cellular genes, but its function in cellular transformation is still unclear. The researchers' recent work has demonstrated that HBX affects the expression of proapoptotic molecule, Bid and the researchers have also analyzed HBx expression in HCC by immunohistochemical staining. Strong cytoplasmic expression of HBx was found in the cirrhotic tissues adjacent to the HCC, while low or undetectable expression was found in the tumors. However, the *HBX* gene from HCC, cirrhotic tissues and sera of hepatitis patients contains multiple numbers of mutation in various regions. The wild-type *HBX* sequence was then fused with the reporter gene *GFP* (Green Fluorescent Protein) and the chimeric gene was transfected into HepG2 cells. HBx fusion protein localized in distinct foci in the cytoplasm of the transfected cells and gradually migrated toward the nuclear region and initiated apoptosis. These data indicate that the major target of HBx is in the cytoplasm, and that this transactivator may play an important role in liver cirrhosis or at the early stages of the tumorigenic process.

The researchers proposed: (1) to further analyze the protein and mRNA expression of the *HBX* gene in a larger cohort of HCC and liver cirrhosis from Hong Kong; (2) to determine the mutation frequency and hot-spots of *HBX* from HCC and cirrhotic liver; and (3) to elucidate if the mutated *HBX* may be defective in inducing apoptosis, cell growth, subcellular localization and/or other cellular responses. (MD00305)

A Randomized Trial on the Need for Cholecystectomy in Elderly Patients After Endoscopic Sphincterotomy for Bile Duct Stones

✉ 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

☐ 1 September 2000

❖ CUHK Research Committee Funding (Direct Grants)

Stones in the common bile duct cause jaundice, pancreatitis and cholangitis. Endoscopic treatment is preferred in those presenting with acute cholangitis, biliary pancreatitis and in elderly patients with comorbid illnesses. After successful endoscopic sphincterotomy, surgical removal of the gall bladder is traditionally offered in prophylaxis against future gallstone migration and biliary symptoms. A wait-and-see strategy may however be appropriate in elderly patients as surgical morbidity and mortality

increase with age. Currently it remains uncertain whether to proceed to cholecystectomy or to leave gallbladders in situ. A prospective randomized controlled trial is required to compare early elective laparoscopic cholecystectomy or expectant management in elderly patients. (MD00455)

Non-invasive Assessment of Patients with Thalamic Brain Haemorrhage for Surgical Indications: A Study with Continuous Compliance Monitoring (CM) and Transcranial Doppler Ultrasonography (TCD)

✉ 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 (Dept of Diagnostic Radiology & Organ Imaging)

☐ 1 November 2000

❖ CUHK Research Committee Funding (Direct Grants)

Thalamic brain haemorrhage accounts for 30% of spontaneous intracerebral haemorrhage, which carries a 15% mortality. Patients with thalamic hemorrhage are complicated by intraventricular hemorrhage and hydrocephalus. There has not been any objective clinical criteria as to when (1) cerebrospinal fluid (CSF) diversion to alleviate hydrocephalus, and (2) evacuation of the deep-seated haematoma are indicated.

The researchers hypothesise that continuous compliance monitoring (CM) and transcranial Doppler ultrasonography (TCD) may predict which patient will require CSF diversion and/or haematoma aspiration.

They propose to study 20 consecutive patients in an eight-month period with thalamic hemorrhage complicated by intraventricular hemorrhage and hydrocephalus (10 patients with haematoma size <25ml and 10 patients ≥25ml). Continuous monitoring in the intensive care unit to include arterial blood pressure (ABP), intraventricular intracranial pressure (ICP) and compliance, and TCD (blood flow velocity of the middle cerebral artery) will be carried out to correlate with clinical outcome (incidence of CSF diversion and the 6-month Glasgow Outcome Scale scores).

This will be the first systematic study of thalamic hemorrhage correlating clinical condition with intracranial pressure, compliance and TCD parameters. The results of this pilot study will (1) document the natural history of the clinical, ICP, CM and TCD parameters, and (2) provide clinical guidance for whether CSF shunting and / or aspiration of the deep-seated haematoma is necessary. (MD00487)

Kinetics of Circulating EBV DNA Following Nasopharyngectomy for Recurrent Nasopharyngeal Carcinoma

✉ TO Wai Hei Edward • LO Yuk Ming Dennis (Dept of Chemical Pathology) • JOHNSON Philip James (Dept of Clinical Oncology)

☐ 1 April 2001

❖ CUHK Research Committee Funding (Direct Grants)

There is a very high incidence of nasopharyngeal carcinoma (NPC) in Guangdong province of southern China and Hong Kong with a yearly incidence rate between 10 and 50 per 100,000. It is actually the third most common cancer among the male populations, and the eighth most common cancer among the female. Epstein-Barr virus (EBV) is a human B-lymphotropic herpes virus. The association between EBV and NPC was first observed in 1966. It had been demonstrated that cell-free EBV DNA can be detected in the plasma and serum of NPC patients. Until recently, the development of a real-time quantitative PCR assay allows the quantitative measurement of tumour-derived EBV DNA in the circulation of NPC patients.

There is much recent interest in the diagnostic applications of tumour-derived DNA in the plasma and serum of cancer patients. However, the biology of this phenomenon is relatively poorly understood. In the current project the researchers propose to elucidate one of the fundamental parameters of this phenomenon, namely, the kinetics of tumour DNA clearance from the plasma.

In their previous study, the researchers have established the kinetics of EBV DNA clearance following radiotherapy for NPC. The median half-life of EBV DNA clearance has been determined to be 3.8 days. However, this half-life is a *composite* of two processes: the rate of tumour cell death; and the rate of clearance of tumour DNA which is released by the dying tumour cells. In the current study, the researchers would like to determine kinetics of process. This can only be addressed if the tumour is removed from a single time point, such as at surgery. The principal investigator has extensive experience in performing nasopharyngectomy for recurrent NPC and the co-investigators are experts in circulating DNA. The researchers' combination of complementary expertise thus makes them a highly efficient group for answering this important question. One of the co-investigators (Dennis Lo) has carried out a previous study looking at fetal DNA clearance following caesarean section. This previous study has demonstrated the feasibility of the proposed research strategy and established that fetal DNA is cleared from the maternal circulation with a half-life of the order of minutes. It is important to establish whether tumour DNA clearance also follows this rapid kinetics.

(MD00426)

A Systematic Review of the Effectiveness of Ofloxacin Otic Solution for the Treatment of Suppurative Otitis Media

✉ TONG Chi Fai Michael • Generoso T Abes* • Noel L Espallardo*

☐ 1 September 2000

❖ CUHK Departmental Funding

This is a collaborative research projects with other Asian centres in determining the effectiveness of ofloxacin otic solution for the treatment of suppurative otitis media compared with other antibiotics. The researchers' role is to provide necessary data in relation to previous studies performed in their Unit and to participate in investigators' discussion meetings.

(MD20013)

Clinical Efficacy and Safety of Tolterodine Prolonged Release Capsules 2 mg qd Compared to Placebo in Children with Symptoms of Urinary Urge Incontinence Suggestive of Detrusor Instability: A Phase III Randomised, Double Blind, Multinational Study

✉ YEUNG Chung Kwong • Sihoe Dart Yin Jennifer* • Shit Kam Yee Frances*

☐ 1 January 2001

❖ Pharmacia Hong Kong Limited

Bladder instability is a significant problem in children 5 years and above. The aim of the study is to compare the clinical efficacy and safety of tolterodine prolonged release capsules 2mg qd with placebo in children with symptoms of urinary urge incontinence suggestive of detrusor instability. The primary objective is to compare the clinical efficacy of tolterodine PR 2mg qd and placebo regarding the change in number of incontinence episodes/week after 12 weeks treatment. The secondary objective is to compare the clinical efficacy of tolterodine PR and placebo with regard to change in mean number of micturitions per 24hr; change in mean urinary volume voided per micturition; change in patient's well-being; and safety and tolerability. This is a double blind, randomized, placebo-controlled, multinational, multi-center study with two parallel groups. Each patient will be randomized to receive either tolterodine PR 2mg qd or placebo for 12 weeks. All statistical tests will be two-sided and the level of significance will be 0.05. Quantitative variables will be summarized using descriptive statistics and the change from baseline will be estimated within groups and compared between treatment groups by analysis of variance (ANOVA). Qualitative variables will be

summarized using frequency tables and treatment groups will be compared using the chi-square test. (MD20038)

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

✉ YEUNG Chung Kwong • SIHOE Dart Yin Jennifer* • SHIT Kam Yee*

☐ 1 June 2001

❖ Pharmacia Asia Limited

Tolterodine is a potent drug used in patients with symptoms of bladder instability. Its use in adults has been established from previous study which showed a lower incidence of side-effects and reduced urinary symptoms. This is a follow-up study with the objective to document the long-term safety and efficacy of treatment in children.

Materials and Method: Children 5-15 years of age who took part in the researchers' previous randomised, double-blind, multinational study are recruited to continue in this follow-up open-label multicentre multinational study. All are given tolterodine prolonged release capsules and followed-up regularly for a period of 12 months. The safety and tolerability of tolterodine is assessed by detailed documentation of adverse events during treatment. In addition, clinical and subjective efficacy variables are assessed from micturition charts, bladder scans for post-void residual volumes and haematological investigations. The study results will be analysed in a descriptive manner. (MD00637)

Novel Strategies for the Treatment of Vein Graft Failure: Investigations Using a Porcine Model

✉ YIM Ping Chuen Anthony • ARIFI Ahmed A* • JEREMY Jamie* • WAN Song

☐ 31 December 2000

❖ Research Grants Council (Earmarked Grants)

The saphenous vein from the leg is the most commonly used means of bypassing blocked coronary arteries surgically. Unfortunately, in a large number of cases, these vein grafts undergo a process of narrowing due to the multiplication of cells in the implanted vein. This process is responsible for the blockage of more than 50% of all grafts within 10 years and as such is an enormous problem in terms of both the prolongation of life of patients with heart disease and cost to Health Services worldwide. To date, no drug has proved successful in preventing this problem. However the researchers recently found in experimental pigs that there is an increase in the levels of substance called endothelin and a decrease

in a substance known as nitric oxide in vein grafts. Since endothelin promotes and nitric oxide inhibits the multiplication of cells in the vein, the researchers proposed that these changes are involved in the vein graft disease and failure in man. This research project, therefore is designed to specifically investigate the effect of drugs that block endothelin and enhance nitric oxide formation in a pig model of bypass surgery. This research could have far reaching consequences for the millions of patients receiving saphenous vein grafts for blocked arteries. (CU00091)

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	The Use of Octreotide in Adhesive Small Bowel Obstruction - A Prospective Double-Blinded Randomized Controlled Trial (MD98113) ✉ CHAN Chi Wai Angus • CHUNG Sheung Chee Sydney • LEE Wai Hung Danny • NG Enders Kwok-wai • LAU Yun Wong James • WONG Kin Hung Simon • LAW Ka Bo Bonita Angela
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
1999-00	Does Acid Suppression Reduce Rebleeding in Peptic Ulcers after Endoscopic Haemostasis - A Double Blind Placebo-controlled Randomized Trial (CU99315) ✉ CHUNG Sheung Chee Sydney • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • LEE Kwing Chin Kenneth (School of Pharmacy) • LAU Yun Wong James
1999-00	Coronary Endothelial Function Related to Open Heart Surgery and Its Protection (CU97280) ✉ HE Guo Wei
1999-00	Protection of Coronary Endothelium-smooth Muscle Function During Cardiac Surgery (CU99246)

- 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
- 1997-98 The Determination of Kupffer Cell Kinetics During the Evolution of Cirrhosis and the Potential Role of Kupffer Cells in Preventing the Development of Liver Metastases in the Presence of Cirrhosis (CU97648)
 ✍ LAU Wan Yee Joseph • LEOW Chon Kar# • LIEW Choong Tsek (Dept of Anatomical & Cellular Pathology) • LAI Bo San Paul
- 1998-99 The Bioenergetic Basis of Liver Regeneration Following Partial Hepatectomy in Man - A ³¹P Magnetic Resonance Spectroscopy Study (CU98214)
 ✍ LAU Wan Yee Joseph • MANN Darren Vivian • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • HJELM Nils Magnus (Dept of Chemical Pathology)# • LAM Wai Man Wynn (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*
- 1998-99 Cerebral Haemodynamic Tests in Traumatic Brain Injury (TBI): Do Abnormalities Such as Hypoperfusion, Hyperperfusion and Impaired Autoregulation Require Treatment? A Correlative Study with Intracerebra (CU98223)
 ✍ POON Wai Sang • LAM Ming Kuen Joseph • HJELM Nils Magnus (Dept of Chemical Pathology)# • LAM Wai Man Wynn (Dept of Diagnostic Radiology & Organ Imaging) • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • CHAN Matthew Tak Vai (Dept of Anaesthesia & Intensive Care)
- 1997-98 The Effect of Indoor Pollution on the Development of Rhinitis in Office Workers in Hong Kong (MD97019)
 ✍ VAN HASSELT Charles Andrew • TONG Chi Fai Michael • TSANG King Yin Raymond* • WOO Kong Sang John • LAU Tak Fai Joseph (School of Public Health) • WONG Ming Chung (Centre for Clin. Trials & Epidemiological Research) • NG Heung Ling Margaret (Dept of Anatomical & Cellular Pathology) • YU Tak Sun Ignatius (Dept of Community and Family Medicine)
- 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)
 ✍ VAN HASSELT Charles Andrew • TONG Chi Fai Michael • LEE Y.S. Kathy* • CHIU S. N.* • WONG K.C. Terence*
- 1999-00 Evaluation of Swallowing Problems in Patients with Nasopharyngeal Carcinoma after Radiotherapy – A Phase I Prospective Study (MD99066)
 ✍ VAN HASSELT Charles Andrew • KU Ka Ming Peter • CHEUNG D. M. C. (Dept of Diagnostic Radiology & Organ Imaging)* • KEW Jacqueline (Dept of Diagnostic Radiology & Organ Imaging)# • LEUNG Sing Fai (Dept of Clinical Oncology) • YUEN H Y (Dept of Diagnostic Radiology & Organ Imaging)* • TONG Chi Fai Michael • MARSHALL J N*
- 1999-00 A Preliminary Study on Thallium-201 Single Photon Emission Computed Tomography (Tl-201 SPECT) in Evaluating Primary and Post-Radiotherapy Nasopharyngeal Carcinoma (MD99114)
 ✍ VAN HASSELT Charles Andrew • AHUJA Anil Tejbhan (Dept of Diagnostic Radiology & Organ Imaging) • KU Ka Ming Peter • TONG Chi Fai Michael • LEUNG Sing Fai (Dept of Clinical Oncology) • CHAN Kam Wing (Dept of Diagnostic Radiology & Organ Imaging) • YUEN Hok Yuen (Dept of Diagnostic Radiology & Organ Imaging)

- 1998-99 A Comparative Study of the Physiological Changes with Pneumoperitoneum During Laparoscopic Surgery in Infantile Versus Adult Animals (CU98224)
 ✉ YEUNG Chung Kwong • AUN Sui Tee Cindy (Dept of Anaesthesia & Intensive Care) • GOMERSALL Charles David (Dept of Anaesthesia & Intensive Care) • FOK Tai Fai (Dept of Paediatrics) • LAU Wan Yee Joseph
- 1995-96 Video Assisted Thoracic Surgery (MD92192)
 ✉ YIM Ping Chuen Anthony
- 1997-98 Investigation of the Efficacy of External Stenting of Saphenous Vein Bypass Grafts in Preventing Deleterious Graft Wall Changes Following Coronary Artery Bypass Surgery (CU97647)
 ✉ YIM Ping Chuen Anthony • SANDERSON John Elsby (Dept of Medicine & Therapeutics) • CHOW Tsun Cheung Louis (Dept of Anatomical & Cellular Pathology)
- 1998-99 Induction of Proinflammatory Cytokine mRNA Expression in Myocardium after Clinical Cardiopulmonary Bypass (MD98065)
 ✉ YIM Ping Chuen Anthony • WAN Song • IZZAT Mohammad Bashar# • WAYE Mary Miu Yee (Biochemistry)
- 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 • WAN Song* • JEREMY Jamie*

RESEARCH OUTPUTS AND PUBLICATIONS

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RESEARCH PROJECTS

Plasma DNA, Prognosis and Cerebrovascular Disease: A Prospective, Observational Study

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Background: Cerebrovascular accidents are catastrophic cerebral events that may be caused either by thromboembolic ischaemia or haemorrhage. The two pathologies are sometimes difficult to differentiate on clinical and radiological grounds. Computerised axial tomography may discriminate between different causes of stroke but may fail to accurately quantify the degree of underlying tissue damage. Discriminating between haemorrhagic and ischaemic stroke is important as early anticoagulation may benefit the latter. Plasma DNA increases within minutes of mechanical traumatic injury and is useful as a predictor of post-traumatic complications. Although the mechanisms leading to such increases are unknown, it is postulated that active liberation contributes significantly to the phenomenon. Currently there is no information on changes of plasma DNA in the early period after the onset of stroke. The amount of DNA liberated into plasma may reflect the underlying pathology, the extent of tissue damage and serve as a good marker. Therefore, this study is designed to investigate whether plasma DNA increases in acute cerebrovascular accidents and may have prognostic significance.

Study Design: Prospective, observational trial investigating patients with neurological abnormalities suggestive of a cerebrovascular accident and comparing them with healthy controls.

Participants: Eighty adult patients will be recruited from the Emergency Department of the Prince of Wales Hospital.

Laboratory methods: After a single blood sample is withdrawn from the patients, centrifuged plasma will be used for quantitative analysis of DNA by measuring the β -globin gene using the polymerase chain reaction.

Outcome measure: Plasma DNA in patients who develop haemorrhagic stroke, ischaemic stroke and 'stroke mimic'.

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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	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) ✉ RAINER Timothy Hudson • COCKS Robert Anthony (Dept of Surgery) • CHEUNG Nai Kwong • LAM Kwok Wai (Centre for Clin. Trials & Epidemiological Research) • JACOBS Philip* • NG Ying Chu*

RESEARCH OUTPUTS AND PUBLICATIONS

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- <P011270> **XU L.Y. Shirley; CHOOK P.; CHAN S.W.; QIAO M.; LIU T.Y. Belinda; IP K.L. Ricky; WOO L.F. Jean; CRITCHLEY A.J.H. Julian; CELERMAJER S. David and WOO K.S.** "Psychological Stress, Dietary Habits and Metabolic Syndrome in Westernized Chinese". *Journal of Hong Kong College Cardiology (9th Annual Scientific Congress, Hong Kong College of Cardiology)* vol.9, p.89. Hong Kong, 2001.04.
- <P011518> **LAM K.W. Peggio; RAINER H. Timothy and WONG M.C. Eric.** "Classification Tree for Early Prediction of Organ Failure in Trauma Patients". *Workshops Proceedings, The 5th Pacific-Asia Conference on Knowledge Discovery and Data Mining* pp.145-148. Hong Kong: World Association for Sexology, 2001.

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RESEARCH PROJECTS

Identification of the DNA Sequence Element That Regulates the Strand Bias in Somatic Hypermutation of Immunoglobulin Genes

- ✉ CHUI Yiu Loon • CHING Kar Keung
- ☐ 1 February 2001
- ❖ CUHK Research Committee Funding (Direct Grants)

The immunoglobulin gene V(D)J segments that encode the antigen-binding region of antibody undergo an enormously high rate of somatic mutation during an immune response. This hypermutation, which takes place in the activated B cells within the germinal centres of secondary lymphoid organs, enables rapid improvement of antibody binding to the antigens - a phenomenon known as affinity maturation. One characteristic feature of somatic hypermutation is the preference of one strand of DNA over the other for mutation. The mechanistic basis for the strand bias is unknown. Using a transgenic approach, the researchers have previously shown that the non-immunoglobulin sequences substituting part or nearly all of the light chain VJ can still undergo hypermutation. However, for some of those non-immunoglobulin sequences, the characteristic strand bias in hypermutation is no longer detectable. The researchers have followed up on this observation and found that a stretch of the VJ from FR1, CDR1 to the 5' half of FR2 may contain a sequence element responsible for directing the hypermutation in a strand-specific manner. Absence of this stretch of sequence, which is about 130bp long, corresponds with the disappearance of strand bias in hypermutation of the non-immunoglobulin sequences. The researchers propose to generate a series of the gene constructs containing a non-immunoglobulin sequence in the VJ region, in which the DNA stretch from FR1 to the first half of FR2 is progressively shortened, to pinpoint the sequence element. A novel

cell transfection approach instead of the lengthy transgenic one will be used to address this study. (MD00465)

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	Generation of Monoclonal Antibodies Against the Epstein-Barr Virus Latent Membrane Protein 1 Variants in Hong Kong Nasopharyngeal Carcinoma (CU98271) ✉ CHUI Yiu Loon • HUANG POON Wai Sin Dolly (Dept of Clinical Oncology) • CHEUNG Siu Tim (Dept of Anatomical & Cellular Pathology)# • LO Kwok Wai (Dept of Anatomical & Cellular Pathology)
1999-00	Functional Analysis of a Novel Gene that Modulates Life and Death (MD99030) ✉ CHUI Yiu Loon • CHAN Yeuk Hon John (Dept of Clinical Oncology)#
1998-99	Production of Recombinant Human Telomerase and Anti-Telomerase RNA Probe to Examine Their Diagnostic Utility in Autoimmune Disease (MD98097) ✉ LIM Pak Leong • LEUNG Tze Ming • WONG Kong Chiu (Dept of Medicine & Therapeutics)
1999-00	Production of Recombinant Human Telomerase and Anti-telomerase Antibody and RNA Probes to Examine their Diagnostic Utility in Autoimmune Disease and Cancer (MD99031) ✉ LIM Pak Leong • LEUNG Tze Ming

see also <P006585>

RESEARCH OUTPUTS AND PUBLICATIONS

<P016584> **LEE Kwong Man Simon; YE Guilan; YUNG Wing Ho; LEUNG Kwok Sui and LEUNG Ping Chung.** "In Situ Model for Studying Potassium Currents in Various Growth Plate Chondrocyte Subpopulations". Life Sciences vol.69, pp.721-728. USA: Elsevier, 2001.

see also <P002939>, <P003208>, <P006594>, <P007737>, <P008557>, <P010539>, <P010540>, <P016792>, <P019737>, <P019948>

RESEARCH PROJECTS

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

Edition Title/Investigators

1999-00 Web-based Medical Education
Development (Web-MED) (MD99136)
✉ HAZLETT Clarke Blaine • CHANG
Mang Z. Allan (Dept of Obstetrics &
Gynaecology) • CHEAM Teo Seng#
• YIP Pak Yiu Simon • Dr
NICHOLLS John* • LAU Y L*

RESEARCH OUTPUTS AND PUBLICATIONS

<P002678> **GORDON Fill; HAZLETT Clarke; CATE Olle Ten; MANN Karen; KILMINSTER Sue; PRINCE Katinka; O'DRISCOLL Elizabeth; SNELL Linda and NEWBLE David.** "Strategic Planning in Medical Education: Enhancing the Learning Environment for Students in Clinical Settings". *Medical Education 2000* vol.34, pp.841-850. 2000.04.

<P002679> **SPIKE N.; ALEXANDER H.; ELLIOTT S.; HAZLETT C.; KILMINSTER S.; PRIDEAUX D. and ROBERTS T.** "In-Training Assessment - Its Potential in Enhancing Clinical Teaching". *Medical Education 2000* vol.34 no.10, pp.858-861. 2000.

see also <P002202>, <P010981>, <P011543>, <P018863>