



**Faculty of
Medicine**

RESEARCH PROJECTS

Comparison of Respiratory Effects of Sevoflurane & Halothane in Children

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

☐ 1 July 1999

❖ CUHK Departmental Funding

Inhalational anaesthetics play an essential role in paediatric anaesthesia, Halothane has been the most commonly used agent for its ability to produce a rapid and smooth induction of anaesthesia. Sevoflurane, a relatively new agent with low blood: gas partition coefficient can thus provide rapid induction of anaesthesia and faster recovery. This study aims to compare the carbon dioxide ventilatory response of sevoflurane & halothane in children who are scheduled for surgery.

(MD99074)

Plasma Lignocaine Level Following Topical Anaesthesia Applies to the Airway By the Aspiration Techniques

✉ CHUNG David Chi Wai • HO Ming Hei Anthony • TAY Beng Aik

☐ 30 September 1999

❖ CUHK Departmental Funding

Topical anaesthesia of the airway by aspiration of lignocaine is a technique developed by the authors. Blood level of lignocaine will be measured in the study.

(MD99130)

Use of IV Lignocaine to Attenuate the Pressor Response to Tracheal Intubation

✉ CHUNG David Chi Wai • HO Ming Hei Anthony • TAY Beng Aik

☐ 22 March 2000

❖ CUHK Departmental Funding

To test the hypothesis that IV lignocaine target-controlled infusion can attenuate the pressor response to tracheal intubation in anaesthetized patients.

(MD99131)

Incidental Heparin Exposure and Development of Heparin Induced Thrombocytopenia

✉ HO Ming Hei Anthony

☐ 1 July 1997

❖ CUHK Departmental Funding

Heparin is often used in invasive monitoring lines to prevent thrombosis at the tip of the catheter *in vivo*. The small amount of exposure to heparin in that situation may cause the development of heparin induced thrombocytopenia in susceptible patients. This prospective study aims to determine the incidence of this syndrome in patients undergoing knee or hip replacement and in whom an arterial or central venous line has been placed with continuous heparinized saline or plain saline flushing. It also compares the incidence of line thrombosis when saline with or without heparin is used for continuous flushing of the lines.

(MD97187)

Predicting the Post-cardiopulmonary Bypass Coagulation Function

✉ HO Ming Hei Anthony • LEE Anna

☐ 1 August 1998

❖ CUHK Departmental Funding

The researchers are completing the study of 156 patients undergoing cardiac surgery to see if they can predict the post-surgical coagulation function during cardiopulmonary bypass. The technique involves taking blood from the bypass machine and neutralizing the blood with heparinase *in vitro*. The processed blood is then analyzed and the coagulation results are compared against those obtained after completion of bypass and systemic protamine administration. If the prediction is accurate, early correction of the causes of excessive mediastinal bleeding, including the request for fresh frozen plasma, if needed, can be made.

(MD98167)

Accuracy of Arterial and Venous Blood Identification Through Inspection

✉ HO Ming Hei Anthony • CHUNG David Chi Wai • TAY Beng Aik • YEO Patricia*

☐ 1 August 1999

❖ CUHK Departmental Funding

Clinicians' ability to visually identify venous and arterial blood is tested. This has implications on the use of inspection to help identify venous blood during central venous cannulation.

(MD99080)

Regional Anaesthesia for Cardiac Surgery

✉ 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)*

□ 1 January 2000

❖ CUHK Departmental Funding

Regional anaesthesia may decrease cardiac ischemia, pulmonary impairment, and pain after cardiac surgery. There may be implications on patient mortality and morbidity, and cost.
(MD99081)

Bilateral Thoracic Paravertebral Block for Patients Undergoing Coronary Artery Bypass Grafting – A Randomised Controlled Trial

✉ 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

□ 1 June 2000

❖ CUHK Research Committee Funding (Direct Grants)

Thoracic epidural anaesthesia/analgesia (EA) as an adjunct to general anaesthesia in cardiac surgery provides haemodynamic stability, analgesia, improved pulmonary function for early tracheal extubation, reduced cardiac ischaemia, and is potentially cost saving. However, the concern for spinal haematoma in the presence of profound anticoagulation, routinely needed in conventional cardiac surgery, is a strong deterrent for most anaesthetists.

Bilateral paravertebral block theoretically has all the advantages of EA in cardiac surgery but without the risk of spinal haematoma. This approach has apparently never been attempted before. We wish to study the anti-anginal, haemodynamic, metabolic, respiratory, and analgesic effects of thoracic paravertebral block in coronary artery bypass grafting (CABG). The secondary aim is to study the pharmacokinetics of ropivacaine after bilateral paravertebral bolus injection followed by continuous infusion in cardiac surgery.

If this study shows that paravertebral block can be beneficial (decreased cardiac ischaemia, superior analgesia, shorter intensive care stay), the implications are enormous given the huge number of cardiac cases done yearly in Hong Kong and the rest of the world. It will also set the stage for a larger outcome study.

50 patients for non-emergent CABG will be randomized into two groups. Group one will receive bilateral paravertebral catheterizations before surgery and will receive a bolus plus a continuous infusion of ropivacaine throughout surgery and postoperative intensive care. Group two (control) will not receive any block. The anaesthesia, perfusion, and surgery of

both groups will otherwise be the same. The effects of the block on haemodynamics, metabolic changes, cardiac ischaemic byproducts, postoperative analgesic requirements, respiratory parameters, pain and sedation score, and time to tracheal extubation will be compared. The absorption pharmacokinetics of ropivacaine will be measured after the initial bolus and during the infusion.

(MD99096)

The Preventive and Resuscitative Role of Lung Isolation in Systemic Air Embolism After Lung Trauma

✉ HO Ming Hei Anthony • GIN Tony • CHUNG David Chi Wai

□ 1 June 2000

❖ International Trauma Anesthesia and Critical Care Society

Systemic air embolism after lung trauma is caused by the entrance of air from bronchioles via traumatic fistulas into pulmonary vessels. The condition is exacerbated by positive pressure ventilation.

By isolating the injured lung from ventilation in a dog model, the researchers aim to prove that systemic air embolism can be prevented and stopped. In addition, they wish to determine the duration of non-ventilation of the injured lung required for the fistulas to close so that bilateral ventilation can resume.
(MD99134)

Use of Heliox in Peripheral Airway Obstruction – A Systemic Review

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

□ 1 June 2000

❖ CUHK Departmental Funding

Heliox reduces turbulence and airflow resistance through narrowed airways. This is a systematic review of randomized trials on the use of heliox in patients with disease involving narrowing of the peripheral airways. The question is whether heliox is superior to air during acute attacks of small airway obstruction. Measurements of interest include blood gases, respiratory mechanics, clinical scores. Relevant trials have been identified by electronic databases, reference lists, and hand-searching. Two authors will independently extract the data using a standardized data collection form. Meta-analysis will be done using the DerSimonian and Laird random-effects mode.

(MD99135)

Ropivacaine as an Intrathecal Agent, PII – The Effects of Baricith

✉ KHAW Kim Sun • CRITCHLEY Lester
Augustus Hall • NGAN KEE Warwick Dean

☐ 1 December 1999

❖ CUHK Departmental Funding

Ropwacaine is a new local anaesthetic which can be used as an intrathecal agent for spinal anaesthesia. The researchers propose to study whether the addition of glucose to increase the baricity will change the quality of the block.
(MD99073)

Haemodynamic Changes During Spinal Anaesthesia for Caesarean Section in Patients with Multiple Gestation: Quantification and Comparison with Singleton Pregnancies

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

☐ 1 August 1999

❖ CUHK Departmental Funding

Patient with multiple gestation frequently require delivery by Caesarean section. In keeping with standard anaesthetic recommendations, our normal practice is to use regional anaesthesia in these cases. However, one of the commonest side effects of spinal anaesthesia is the potential to cause hypotension. The incidence of hypotension and vasopressor requirement may be increased in multiple pregnancies compared with singleton pregnancy because of potentially greater aortocaval compression and higher spread of spinal anaesthesia. However, although standard obstetric anaesthesia textbooks have highlighted this potential increased risk of hypotension this has not been clearly quantitated in the literature. Therefore, this prospective study was designed to specifically examine the haemodynamic changes associated with spinal anaesthesia in patients with multiple gestation, with a comparison with a control group of patients with singleton pregnancies.
(MD99079)

Randomized Comparison of Spinal and Epidural Anaesthesia for Caesarean Section in Parturients with Severe Preeclampsia

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

☐ 1 September 1999

❖ CUHK Departmental Funding

The optimum method of anaesthesia for parturients with severe preeclampsia undergoing Caesarean section is controversial, although most recommend regional anaesthesia. Of regional techniques, epidural anaesthesia has usually been preferred to

spinal anaesthesia because the latter has been thought to be associated with a greater risk of severe hypotension. However, this has recently been challenged: spinal anaesthesia has the advantages of rapid onset of reliable, high quality surgical and may offer a viable alternative to general anaesthesia, particularly in circumstances when there is urgency to deliver the fetus. The objective of this prospective, randomised study is to compare spinal and epidural anaesthesia for Caesarean section in patients with severe preeclampsia. Major outcomes to be compared will be maternal haemodynamic status and early neonatal outcome
(MD99076)

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

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

☐ 1 October 1999

❖ CUHK Departmental Funding

Parturients who are receiving epidural analgesia in labour frequently require delivery by Caesarean section. In most cases, anaesthesia is provided by extending the epidural block. However, a potential adverse effect of rapidly extending epidural block is hypotension from rapid onset of sympathetic block and peripheral vasodilatation. One of the most commonly adopted techniques used to reduce hypotension in epidural and spinal anaesthesia is intravenous fluid preload immediately prior to administration of anaesthesia. However, although this is widely practised, the efficacy of intravenous preload has been recently questioned. Furthermore, in emergency cases when there is often relative urgency to deliver the fetus, has recently been suggested that it may not be warranted to delay anaesthesia in order to complete preloading. However, the majority of studies that have addressed hypotension during regional anaesthesia for Caesarean section investigated elective cases and there are few data available on emergency or labouring patients. Previous studies have shown labouring patients to be less susceptible to hypotension, possibly because of the autotransfusion that occurs with uterine contractions. The objective of this randomised double-blind study will be to evaluate the efficacy of intravenous preload of lactated Ringer's solution 20 ml/kg on the incidence and severity of hypotension associated with spinal anaesthesia in labouring parturients presenting for emergency or semi-emergency Caesarean section. The primary outcome will be the incidence of hypotension according to predefined criteria.

Neonatal outcome will be a secondary outcome and will be assessed clinically and biochemically. (MD99078)

Randomized Double-blind Comparison of Obstetric Outcome After Epidural Labour Analgesia Using Ropivacaine or Bupivacaine

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

☐ 15 May 2000

❖ Health Services Research Fund, Hospital Authority

Epidural analgesia is the most effective method of providing analgesia in labour, but its use has been associated with an increased risk of instrumental delivery and Caesarean section. Recently a new local anaesthetic drug, ropivacaine, has been introduced into clinical practice in Hong Kong. Compared with the current standard epidural local anaesthetic bupivacaine, ropivacaine has the advantage of greater specificity for sensory block over motor block. This means that ropivacaine used for epidural analgesia may result in greater patient mobility and less perineal muscle relaxation, with potentially less effect on the progress of labour. Prospective randomized comparisons of ropivacaine with bupivacaine have show comparable analgesia, but a reduction in instrumental delivery rate in patients who received ropivacaine using moderately high concentrations. However, this may not be relevant to the use of low concentrations of local anaesthetics as is common in many units, including Prince of Wales Hospital. Therefore, the researchers have designed a prospective, randomized double-blind study to compare low concentration infusions ropivacaine with low concentration bupivacaine, both with fentanyl. The primary outcomes that will be compared between groups will be the proportion of patients achieving normal vaginal delivery. Subgroup analysis will be performed to compare the rates of instrumental delivery (forceps delivery and vacuum extraction) and surgical delivery (Caesarean section). Secondary objectives that will be compared will include: analgesia, motor block, hypotension and patient satisfaction and neonatal outcome. (MD99116)

Ultrasound Guided Peripheral Nerve Block

✉ 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)

☐ 1 March 2000

❖ CUHK Departmental Funding

The researchers use ultrasound to guide the needle placement during various nerve blocks. They aim to show the feasibility of using this adjunct to assist in needle positioning in particularly difficult nerve blocks. (MD99132)

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

Edition Title/Investigators

1998-99 Context Sensitive Half-time of Remifentanyl After Long Neurosurgical Procedure (MD98163)

✉ CHAN Matthew Tak Vai • TAM Yuk Ho • CHUI Po Tong • GIN Tony • POON Wai Sang (Dept of Surgery)

1998-99 Dose Response of Cisatracurium Besilate in Children During Intravenous Anaesthesia (MD98162)

✉ CHAN Matthew Tak Vai • CHEE Yee Eot • AUN Sui Tee Cindy

1998-99 The Electroencephalographic Effects of Regional Anaesthesia and Their application During Combined Regional and General Anaesthesia (CU98044)

✉ CHUNG David Chi Wai • MORLEY Andrew Peter# • CHAN Matthew Tak Vai

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#

1997-98 Hypotension During Spinal Anaesthesia: How Should the Vasopressor be Given? (MD97185)

✉ CRITCHLEY Lester Augustus Hall • YU S. C.*

1998-99 The Use of Dihydroergotamine in Spinal Anaesthesia (MD98158)

✉ CRITCHLEY Lester Augustus Hall

1998-99 Intraocular Pressure Changes in Patients with Intracranial Hypertension (MD98154)

✉ HO Ming Hei Anthony • CHUNG David Chi Wai • JOYNT Gavin Matthew • YEO Victor*

- 1997-98 Thoracic Paravertebral Infusion of Bupivacaine for Post-thoracotomy Analgesia. What is the Most Effective Concentration? (MD97184)
 ✉ KARMAKAR Manoj Kumar • LOW S. John Matthew# • NG Siu Keung • YIM Ping Chuen Anthony (Dept of Surgery) • LEE T. W. (Dept of Surgery)*
- 1998-99 Arteriovenous Plasma Concentration of Ropivacaine Following Epidural Administration (MD98156)
 ✉ KARMAKAR Manoj Kumar • CHUNG David Chi Wai • KWOK Wing Hong • CHEE Yee Eot
- 1998-99 Comparative Systemic Absorption of Ropivacaine and Bupivacaine Following Caudal Epidural Administration in Children (MD98155)
 ✉ KARMAKAR Manoj Kumar • AUN Sui Tee Cindy • YEUNG Chung Kwong (Dept of Surgery) • CHAN S. C.*
- 1998-99 Spinal Anaesthesia for Caesarean Section Using Ropivacaine (MD98159)
 ✉ KHAW Kim Sun • NGAN KEE Warwick Dean • LEE Bee Beng • 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
- 1998-99 Randomised Double-blind Comparison of Ephedrine and Metaraminol for the Treatment of Hypotension During Spinal Anaesthesia for Caesarean Section (MD98150)
 ✉ NGAN KEE Warwick Dean • KHAW Kim Sun • LEE Bee Beng • LAU Tze Kin (Dept of Obstetrics & Gynaecology)
- 1998-99 Randomized Double-Blind Evaluation of Ropivacaine-Adrenaline as an Epidural Test Dose (MD98151)
 ✉ NGAN KEE Warwick Dean • KHAW Kim Sun • LEE Bee Beng
- 1998-99 Dose-Response Investigation of Ephedrine by Intravenous Bolus for the Prevention of Hypotension During Spinal Anaesthesia for Caesarean Section (MD98152)
 ✉ NGAN KEE Warwick Dean • KHAW Kim Sun • LEE Bee Beng • LAU Tze Kin (Dept of Obstetrics & Gynaecology)
- 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

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000178> **Ngan Kee, Warwick D.; Kim S. Khaw; Bee B. Lee; Tze K. Lau and Tony Gin.** "A Dose-Response Study of Prophylactic Intravenous Ephedrine for the Prevention of Hypotension During Spinal Anesthesia for Caesarean Delivery". *Anesthesia and Analgesia* vol.90 no.6, pp.1390-1395. USA, 2000.06.
- <P000179> **Ngan Kee, W. D.; T. K. Lau; K. S. Khaw and B. B. Lee.** "Metaraminol Vs Ephedrine for Maintaining Arterial Pressure During Spinal Caesarean Section". *Abstracts of the 12th World Congress of Anaesthesiologists* Abstracts no.P3.2.06, p.96. Canada, 2000.06.06.
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- <P000624> **Gin, T.; M. Chan; A. Chan and P.M. Yuen.** "Duration of Rocuronium Block in Postpartum Patients". *Anaesthesia & Intensive Care* vol.28 no.2, pp.215-216. Australia, 2000.04.
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- <P000776> **Gin, Tony.** "Postoperative Nausea and Vomiting". *Australian and New Zealand College of Anaesthetists* p.54. Australia, 2000.05.
- <P000777> **Critchley, L.A.H.** "The Haemodynamic Profile of Dihydroergotamine During Spinal Anaesthesia". *Anaesthesia & Intensive Care* vol.28 no.2, p.226. Australia, 2000.04.
- <P000778> **Kwok, Wing-Hong; Manoj Karmakar; Yee-Eot Chee and Po-Tong Chui.** "Single Shot Femoral Three-in-One Nerve Block Using a Long Catheter Versus a Short Catheter". *Australian and New Zealand College of Anaesthetists* p.100. Australia, 2000.05.
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- <P000780> **Morley, Andrew; James Derrick and David Chung.** "Epidural Blockade and Intraoperative Isoflurane Requirements". *Australian and New Zealand College of Anaesthetists* p.74. Australia, 2000.05.
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- <P000790> **Yap, F.H.Y.; G.M. Joynt and T.A. Buckley.** "Serum Albumin and Mortality Risk in Critically Ill Patients". Paper presented in Poster Presentation at 20th International Symposium on Intensive Care and Emergency Medicine. Brussels, Belgium, 2000.03.

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- <P985053> **Yu, Sui-Cheun; Warwick D. Ngan-Kee and Anne Kwan.** "Prolongation of Postoperative Analgesia After Elective Caesarean Section by Addition of Pethidine to Intrathecal Bupivacaine". Paper presented in Australian and New Zealand College of Anaesthetists Annual Scientific Meeting. Australia, 1999.05.09.
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- <P990355> **Aun, C.S.T.** "New i.v. Agents". *British Journal of Anaesthesia* vol.83 no.1, pp.29-41. UK, 1999.07.
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- <P992683> **Chan, Fred; Matthew Chan; David Sun; Ronald Boet; Joseph Lam; Stephanie Ng and Wai Poon.** "Defining Abnormal Acetazolamide Reactivity Test in Patients with Carotid Artery Stenosis - A Comparison with CO₂ Reactivity". *Journal of Neurosurgical Anaesthesiology* vol.11 no.4, p.334. USA, 1999.10.
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see also <P000863>, <P001767>, <P993018>, <P993541>

RESEARCH PROJECTS

Evaluation of Clonality and Genetic Progression in Metachronous Bilateral Breast Cancers

- ✉ CHANG Alexander Russell • LO Kwok Wai • NG Ho Keung
- ☐ 1 June 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Breast cancer has now become the top cancer among women in Hong Kong and constitutes a major health problem. The incidence of breast cancer is on the rise. Many patients have bilateral diseases, with the second cancer usually developing within 10 years of the initial cancer, despite apparent complete excision. Many of these apparently distinct tumors are clonal. Specific genetic abnormalities can be identified for the prediction of future contralateral recurrences. In the present proposal, the researchers intend to examine 40 bilateral breast cancer samples from 20 patients. Each tumor will be microdissected and subjected to investigation of the allelic status on 50 microsatellite loci of multiple chromosomal arms. The patterns of allelic loss of the bilateral tumors of each patient will be analyzed for the assessment of clonality and progression of this cancer. Special emphasis will be laid on the specific chromosomes 1, 3, 8, 11 and 17. The clonality of these paired samples will be further confirmed by investigation of the X-chromosome inactivation and p53 gene mutation. (MD99097)

Comprehensive Study of Nasopharyngeal Carcinoma Genome by High-resolution Allelotyping

- ✉ HUANG POON Wai Sin Dolly • LO Kwok Wai • TEO Man Lung Peter (Dept of Clinical Oncology) • TO Ka Fai
- ☐ 15 August 1999
- ❖ CUHK Research Committee Funding (Direct 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. High-resolution allelotyping will be used to screen for chromosomal deletion throughout the entire NPC genome. Thirty to forty microdissected NPC tumors of early and advanced stages will be included in the study, using 400 highly polymorphic microsatellite

markers. The frequency of chromosomal deletion and the extent of deleted regions on all 22 autosomal arms will be identified. Consistent patterns of genetic changes in NPC samples including deletion and microsatellite instability will be correlated with disease progression and tumor behavior. The resulting high-resolution allelotypes will also identify regions of the genome that may harbor genes important for the development and progression of NPC. Detailed deletion mapping of these chromosomal regions by additional genetic markers in the target regions will be selected for LOH analysis to locate the candidate NPC-associated genes. (MD99021)

The Study of Genetic Alterations of the PTEN/MMAC/Gene in Multiple Myeloma and Its Relation to Plasmacytoma Development

- ✉ NG Heung Ling Margaret • WONG Hing Nam# • LEI Ieng-Kit Kenny (Dept of Clinical Oncology)*
- ☐ 1 April 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Multiple myeloma (MM) is a haematological malignancy affecting mainly the elderly. However, there is a trend that younger people (age < 40 y.o.) are increasingly involved. Although the diagnosis can be easily made by the recognition of the characteristic triad of bone marrow plasma cell infiltration, paraprotein secretion and osteolytic lesions, the treatment outcome remains dismal with a median survival of 3.5 years. To date, a definitive cure has not been reported. Based on the molecular data of IgH gene rearrangements of the MM cells, the final transformation event of this disease is probably derived from the late stage B lymphoid cells. PTEN, a newly identified tumor suppressor gene on chromosome 10q23.3, has a dual specificity characterized by its phosphatase domain and homology to tensin. It has been postulated that PTEN might act to inhibit invasion and metastasis through modulation of the cytoskeleton. An association of its mutational inactivation with the metastatic phenotype in neoplasms has also been observed. Recently, PTEN deletion was also observed in a significant proportion of follicular (B-lineage) lymphomas in addition to its characteristic pathogenetic t(14,18). Thus far, alteration of PTEN has not been examined in MM. It may be of importance to study the genetic alteration of this gene in MM as proposed in this study to address two issues: (1) MM is B-lineage neoplasm which may have pathogenetic links with lymphomas through a lymphoplasmacytic transition; (2) MM is basically a disseminated disease with the main tumor load being found in bone marrow. The molecular control of

tumor progression and dissemination (extramedullary involvement) is not clear.
(MD99067)

Follow-up Study on Genetic Events Regulating Telomerase Activity in Gliomas

- ✉ NG Ho Keung • PANG Chung Sean Jesse
- ☐ 1 December 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

Telomeres are the very ends of linear eukaryotic chromosomes. Human telomeres contain the repeat TTAGGG, which may be reiterated in tandem up to 15 kilobases. Telomeres undergo programmed shortening during cell division in somatic cells. When these chromosome ends are critically shortened, it may lead to an exit from the cell cycle, i.e. senescence. An enzyme called telomerase using integral RNA as a template, can synthesize telomeric repeats to overcome the end-replication problem and compensate for the telomeric loss. It is believed that telomerase is activated in immortal (cancer) cells, so that these cells can escape from replicative senescence and proliferate indefinitely. The researchers have previously examined the telomerase activity of a wide range of gliomas and demonstrated a positive correlation between histologic grade and the proportion with telomerase activity. In this follow up project, they propose to study a broad range of gliomas but will focus on non-astrocytic tumors, especially the oligodendrogliomas and ependymomas. These tumor groups are more slowly growing than the astrocytic tumors and potentially curable. Molecular events with hTERT and hTBP1 expression and pRb and p16INK4a expression will be studied. The significance of this study is two fold: further understanding of molecular pathogenesis of gliomas and providing more clues to future clinical diagnosis and therapy based on telomerase activity.
(MD99022)

Genomic Study of Selected Groups of CNS Tumours: A Combined Approach with Allelotyping, Molecular Cytogenetic and Microdissection Studies

- ✉ NG Ho Keung • PANG Chung Sean Jesse • LO Kwok Wai • HUANG POON Wai Sin Dolly • POON Wai Sang (Dept of Surgery)
- ☐ 31 December 1999
- ❖ Research Grants Council (Earmarked Grants)

This is an extension of the researchers' previous grant (CUHK4278/97M, Molecular Genetics of CNS Tumors). Recent years have seen a vast increase in our understanding of the molecular genetics of brain tumors. The advent of new molecular technology

and the refinement of existing technology continue to make a major impact on cancer research. In this application, the researchers aim to examine three selected groups of brain tumors: astrocytic tumors in childhood, paired recurrent astrocytic tumors in adults and gliomas with oligodendroglial components. Gliomas are the most important primary cancers of the brain and astrocytic tumors are the commonest type. The diffuse high-grade astrocytic tumors have very limited prognosis. However, subgroups of diffuse astrocytomas occurring in childhood and those in adults that develop from pre-existing low-grade tumors seem to have a better prognosis. Conversely, although most pediatric pilocytic astrocytomas are circumscribed instead of diffuse and have excellent prognosis, there are subgroups that seem to have a worse prognosis than the prototype. Likewise, gliomas with oligodendroglial components are recognised to be susceptible to chemotherapy and should be delineated from the rest of the astrocytic tumors. Although some information about the molecular genetics of some of these tumors is already available, the researchers intend to conduct a comprehensive genomic analysis by allelotyping, molecular cytogenetic and laser capture microdissection analysis. These techniques complement each other, examine all chromosomes in details, yield fine sites of potential cancer genes, and allows the development of routine diagnostic adjuncts. These genetic surveys will be performed on expanded series of these groups accumulated and partly analyzed in our laboratory in the last year. Such information will be critically important in future understanding of these tumors and provide a genetic basis for rational clinical management.
(CU99277)

Comprehensive Analysis of Epstein-Barr Virus (EBV) Genotypes in EBV Associated Lymphoproliferative Lesions and Normal Controls

- ✉ TO Ka Fai • CHEUNG Siu Tim# • LO Kwok Wai
- ☐ 1 October 1999
- ❖ Research Grants Council (Earmarked Grants)

Epstein-Barr virus (EBV) shows a strong association with nasopharyngeal carcinoma (NPC) and distinct subsets of EBV associated lymphoproliferative lesions (EBV-LP). Variation of EBV genotypes in diverse EBV-associated diseases and among different geographic regions has been demonstrated. Viral strain variations present in different tissues may represent tissue tropism or selection under evolution pressure. The researchers had delineated the prevalent EBV strain in EBV-associated NPC of which the disease shows a high incidence in our locality. In contrast, detail-sequencing analysis on EBV strain variants in EBV-LP and normal lymphoid

tissues is scanty. This underscores the importance of the present study for a comprehensive survey of EBV stain variations in EBV-associated lymphoproliferative lesions and normal subjects. EBV specific cytotoxic T lymphocyte (CTL) responses could be observed in healthy EBV life long carrier and also in-patients with EBV-associated malignancy. Escape of immunosurveillance could be possible by restriction on viral gene expression. Strain sequence variations could also result in change of potential CTL recognition epitopes and lead to failure of elimination. As latent membrane protein 1 (LMP1) and latent membrane protein 2 (LMP2) are frequently expressed in NPC and subsets of EBV-LP, there is an increasing interest in the identification of the potential target epitopes within these two viral proteins. The issue is not clear, however, on whether or not these CTL recognition epitopes are antigenically conserved among different EBV strains. Present study will thus further focus on the sequences variations of LMPs on potential CTL recognition epitopes, and to examine if distinct sequences would be observed in EBV-LP compared to normal subjects. Further investigation on the HLA type, in complementary to LMP1 and LMP2 sequence variations, would also be included. The results would contribute to the future development of vaccine and immunotherapy.
(CU99301)

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

Edition Title/Investigators

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)

1998-99 Detection of Helicobacter Pylori DNA in Serum and Plasma by Real-time Polymerase Chain Reaction (MD98022)
 ✍ CHAN Wing Yee • LO Yuk Ming Dennis (Dept of Chemical Pathology) • NG Enders Kwok-wai (Dept of Surgery)

1996-97 Cervical Screening Programme (MD96223)
 ✍ CHANG Alexander Russell

1996-97 Application of Comparative Genomic Hybridization to the Detection of DNA Imbalances in Sinonasal T-cell Lymphoma (MD96010)
 ✍ CHOW John Hei Sing • WONG Nathalie (Dept of Clinical Oncology) • WOO Kong Sang John (Dept of Surgery)

1997-98 Determination of the Presence and Type of EBV in Colorectal Carcinoma and Lymphoma by *in situ* Hybridization for EBER and Characterization of LMP1 by PCR-RFLP and PCR-SSCP (MD97029)
 ✍ CHOW John Hei Sing • NAIR Gopinathan Raj# • CHAN Wing Yee

1996-97 Molecular Pathology of the Precancerous Lesions in Nasopharyngeal Carcinoma (CU96639)
 ✍ HUANG POON Wai Sin Dolly • TO Ka Fai • LO Kwok Wai • LEUNG Sing Fai (Dept of Clinical Oncology)

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 • PANG Chung Sean Jesse • LO Kwok Wai

1998-99 Antigen Processing in an Epstein-Barr Virus Positive Nasopharyngeal Carcinoma Cell Line (C666-1) (MD98023)
 ✍ HUANG POON Wai Sin Dolly • CHEUNG Siu Tim#

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)

- 1997-98 Studies on the Molecular Genetics of CNS Tumors (CU97671)
✉ NG Ho Keung • HUANG POON Wai Sin Dolly • LAM Yeng Po Paula# • LO Kwok Wai • PANG Chung Sean Jesse • POON Wai Sang (Dept of Surgery)
- 1998-99 Biological Studies of the Endothelial Cells in Glioblastoma Multiforme (MD98024)
✉ NG Ho Keung • TO S.S.Tony*

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000564> **Chow, L.T.C.; J. Griffith; W.H. Chow and S.M. Kumta.** "Monostotic Fibrous Dysplasia of the Spine: Report of a Case Involving the Lumbar Transverse Process and Review of the Literature". *Arch Orthop Trauma Surg* vol.120, pp.460-464. USA: Journal of Hong Kong College of Radiologists, 2000.
- <P000683> **Chan, Michael W.Y.; Tin Lap Lee; Joanna H.M. Tong; Kwok Wai Lo; Wai Sang Wong; Lung Wai Chan; Fernand Mac-Moune Lai and Ka Fai To.** "Hypermethylation of 5'CPG Islands of Death Associated Protein (DAP) Kinase in Urinary Bladder Cancer". *Proceedings of the American Association for Cancer Research* vol.41, p.496. San Francisco, USA: American Association for Cancer Research, 2000.04.
- <P000717> **Wong, Ivy H.N.; Margaret H.L. Ng; Ng Dolly P. Huang and Joseph C.K. Lee.** "Aberrant P15 Promoter Methylation in Adult and Childhood Acute Leukemias of Nearly All Morphologic Subtypes: Potential Prognostic Implications". *Blood* vol.95 no.6, pp.1942-1949. 2000.
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- <P001055> 陳志強。〈免疫細胞化學在細針吸取細胞學診斷中的應用〉。《癌症早期診斷現代技術——細針吸取細胞病理學》舒儀經、關秀編。頁95-111. 中國北京: 人民衛生出版社, 2000.05.
- <P001056> **Chang, Alexander R.** "Maintaining Laboratory Standards in Cytology". *Annals of Contemporary Diagnostic Pathology 1999/2000* vol.3, pp.19-25. Hong Kong, 2000.
- <P001114> **Wong, Ivy H.N.; Philip J. Johnson; Paul B.S. Lai; Wan Y. Lau and Y.M. Dennis Lo.** "Tumor-Derived Epigenetic Changes in the Plasma and Serum of Liver Cancer Patients Implications for Cancer Detection and Monitoring". *Annals of the New York Academy of Sciences* vol.906, pp.102-105. New York, USA, 2000.04.
- <P001149> **Yu, S.C.H.; C.T. Liew; W.Y. Lau; T.W.T. Leung and C. Metreweli.** "Percutaneous Biopsy of Tiny (≤ 1 cm) Liver Lesions for Pre-Operative Tumour Staging". *Proceedings of 4th World Congress of IHPBA* vol.2 no.2, p.272. Brisbane, Australia: ISIS Medical Media, UK, 2000.
- <P001236> **Tsang, K.S.; C.K. Li; M.M.K. Shing; K.W. Chik; T.T. Lau; A.P.Y. Wong; K. Li; Y. Leung; A.K.W. Lie and P.M.P. Yuen.** "Transplantation of Positively Selected CD34+ Cells in the Prophylaxis of Graft Versus Host Disease and Tumour Cell Purging". *Hong Kong Society of Flow Cytometry 5th Annual Symposium* p.5. Hong Kong: Hong Kong Society of Flow Cytometry, 2000.01.08.
- <P001364> 陳志強、袁勤。〈遠程病理學〉。論文發表於遠程醫學教育系統應用培訓班, 主辦機構為香港中文大學. 香港與武漢, 2000.01.11.
- <P001365> **Chang, Alexander R.** "The Pap Smear in the New Millennium: The Old and the New". Paper presented in The Pap Smear Test in the New Millennium: Inaugural Hong Kong Symposium, organized by The Chinese University of Hong Kong. Hong Kong, 2000.01.15.

- <P001366> **Chang, Alexander R.** "Overcoming Laboratory Problems Associated with the Setting up of a Free Community Pap Test Clinic: A Hong Kong Experience". Paper presented in the 13th International Symposium of Foundation for Promotion of Cancer Research, organized by Foundation for Promotion of Cancer Research. Tokyo, Japan, 2000.04.27.
- <P001388> **Lai, Fernand M.M.; Philip K.T. Li; Paul C.L. Choi; Ka-Fai To; Angela Y.M. Wang; Chi-Bon Leung; Cheuk-Chun Szeto; Teresa Y.H. Wong; Siu-Fai Lui and Edmund K.M. Li.** "Histological Appraisal of Lupus Nephritis". *Hong Kong Journal of Nephrology* vol.2 no.1, pp.13-18. Hong Kong, 2000.04.
- <P001395> **To, Ka Fai; Paul C.L. Choi; Cheuk Chun Szeto; Philip K.T. Li; Nelson L.S. Tang; Chi Bon Leung; Angela Y.M. Wang; Kelvin K.L. Ho; Teresa Y.H. Wong; Sui Fai Lui and Fernand Mac-Moune Lai.** "Outcome of IgA Nephropathy in Adults Graded by Chronic Histological Lesions". *American Journal of Kidney Diseases* vol.35 no.3, pp.392-400. Philadelphia, USA, 2000.03.
- <P001713> **Ely, Kim A.; Gary Tse; Jean F. Simpson; Rick Clarfeld and David L. Page.** "Diabetic Mastopathy - A Clinicopathologic Review". *American Journal of Clinical Pathology* vol.113, pp.541-545. USA, 2000.04.
- <P001714> **Gobbi, Helenice; Gary Tse; David L. Page; Sandra J. Olson; Roy A. Jensen and Jean F. Simpson.** "Reactive Spindle Cell Nodules of the Breast Aftercore Biopsy or Fine-Needle Aspiration". *American Journal of Clinical Pathology* vol.113, pp.288-294. USA, 2000.02.
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- <P001745> **Lam, P.Y.P.; E. Di Tomaso; H.K. Ng; J.C.S. Pang; M.F. Roussel and N.M. Hjelm.** "Expression of P19^{INK4d}, CDK4, CDK6 in Glioblastoma Multiforme". *British Journal of Neurosurgery* vol.14 no.1, pp.28-32. UK, 2000.
- <P001746> **Ng, H.K.; J.Y.M. Tse and W.S. Poon.** "Cerebellar Astrocytoma Associated with Von Hippel-Lindau Disease: Case Report with Molecular Findings". *British Journal of Neurosurgery* vol.13 no.5, pp.504-507. UK, 2000.
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- <P002034> **Tsang, K.S.; Li C.K.; Chik K.W.; Wong A.P.; Lau T.T.; Li K.; Pong H.N.; Shing M.M. and Yuen P.M.** "Up-Regulation of Cell Growth Associated with an Extra Y Chromosome in a Child with Beta-Thalassemia Major Having Undergone Hematopoietic Stem Cell Transplant". *Journal of Pediatric Hematology/Oncology* vol.22 no.2, pp.133-136. USA, 2000.03.
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RESEARCH PROJECTS

Embryological Basis of Congenital Heart Disease: A Study of Neural Crest Cell Migration Using A Mouse Mutant and A Transgenic Marker

- ✉ CHAN Wood Yee • COPP A. J.*
□ 1 December 1999
❖ Research Grants Council (Earmarked Grants)

Congenital heart disease is one of the commonest types of birth defect (3 to 12 in 1,000 livebirths) and is the fourth most important cause of childhood death in developed countries. However, in 90% or more of cases, no known cause has been identified and the embryological basis of cardiac birth defects is still speculative. It has been suggested from studies on the chick embryo that normal cardiac development require the participation of a group of embryonic cells known as the cardiac neural crest. Cardiac neural crest cells are derived from the developing central nervous system (neural tube) of the embryo and are able to migrate ventrally from the dorsal side of the embryo towards the heart. Defective migration of cardiac neural crest cells has been proposed to lead to the abnormal development of the heart and great vessels in the chick embryo. In the present study, a mouse mutant, which is shown to have major congenital heart defects, will be used as an animal model to study heart defects and a transgene will be employed as a genetic marker to trace neural crest cell migration. Cell labelling, micro-transplantation and whole embryo culture techniques will also be used. The present study will provide information on the role of cardiac neural crest cells in both normal heart development and in the origin of heart defects, and will also evaluate the feasibility of restoring the normal heart development by microsurgical transplantation. (CU99275)

A Study of the Role of *Bcl-2* in Neural Tube Defects Using Normal and Mutant Mouse Embryos

- ✉ CHAN Wood Yee • COPP A. J.*
□ 1 January 2000
❖ CUHK Research Committee Funding (Direct Grants)

Neural tube defects (NTDs) which occur in about 1 to 8 per 1,000 livebirths are among the commonest birth defects that result in infant mortality and serious disability. NTD is a group of defects in which the neural tube has failed to complete neurulation, and NTDs include anencephaly, spina bifida and encephalocele. Epidemiological and animal studies have indicated that most isolated NTDs are multifactorial in nature, possessing both genetic and

environmental components. Several genes have been identified to be involved in regulating mammalian neurulation. Circumstantial evidence has indicated that the proto-oncogene *bcl-2* appears to be the gene which is strongly associated with NTDs, but a direct proof of the proto-oncogene *bcl-2* in NTDs is still lacking. In the present study, in order to find out the role of *bcl-2* in NTDs, we plan (1) to determine the morphological features and *bcl-2* expression patterns in both normal embryos and mutant embryos with NTDs; (2) to genetically alter the *bcl-2* expression in normal embryos to determine whether alteration of the *bcl-2* expression induces NTDs; and (3) to genetically alter the *bcl-2* expression in NTD mutant embryos to ascertain whether alteration of the *bcl-2* expression corrects NTDs. Special attention will be paid to the relationship between the *bcl-2* expression and the development of NTDs. The results of the present study would provide us with insights into the pathogenetic mechanism of NTDs and also give us information on the therapeutic value of gene transfer in NTDs.

(MD99023)

A Study on the Ability of Sertoli Cells to Promote Regeneration of Retinal Ganglion Cells

- ✉ CHO Yu Pang Eric
□ 1 June 2000
❖ CUHK Research Committee Funding (Direct Grants)

Transplantation of neuronal and non-neuronal cells into the damaged central nervous system has been an extensively studied means to promote functional recovery of damaged neurons. In this study, the researchers explore the potential of Sertoli cells derived from the testis as a promoter of neural regeneration, based on its unique immuno-privileged property and its ability to produce many biologically active factors. The ability of Sertoli cells to stimulate retinal ganglion cells to regenerate their axons after injury will be assessed both *in vitro* and *in vivo*, and compared with another transplant, the peripheral nerve, which has previously been shown to be a good substrate for stimulating axonal regeneration in the mature central nervous system. (MD99098)

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

- ✉ CHOW Pak Ham Patricia • O wai Sum*
□ 1 June 1999
❖ Committee on Research and Conference Grant, University of Hong Kong

Reactive species (ROS) is known to damage plasma membrane and induce DNA strand breaks in sperm. A correlation between ROS activity and infertility in the male has also been noted in human. In the hamster, the researchers have shown that surgical removal of male accessory sex glands results in a lowering in the number of pups born. Defects in oocyte activation and a delay in DNA replication during the first cleavage have also been noted. They propose that this is the consequence of ROS damage on sperm that are not exposed to and consequently protected by male accessory sex gland secretions. This study will give an insight into the function of the male accessory sex gland secretions. It has important implication in the management of male infertility/subfertility in both clinical and veterinary practice.
(MD98170)

Histological and Morphological Effects of Tadenan on the Response of the Rabbit Bladder to Partial Outlet Obstruction

- ✉ CHOW Pak Ham Patricia • LEVIN R* • GOSLING John Arthur*
 ☐ 1 August 1999
 ❖ Laboratories DEBAT

In previous study of the partially obstructed rabbit urethra, the researchers have used electron microscopy to investigate the fine structure of smooth muscle cells and autonomic nerves within the bladder wall. They have shown that the smooth muscle cells and autonomic nerves undergo progressive damage in response to partial outflow obstruction. Mitochondria within the muscle cells become swollen and disrupted and the endoplasmic reticulum is markedly dilated reducing the myofilaments to the cell periphery. In addition, autonomic nerves show structural evidence of disruption since most of the terminal regions contain numerous abnormal inclusions and other signs of damage. The purpose of the present study is to use this experimental model to investigate the effects of Tadenan® on the structural changes which the researchers have described in their previous investigations. This compound is a plant extract which has been shown in clinical practice to alleviate the signs and symptoms associated with urethral occlusion due to human benign prostatic hypertrophy. Partially obstructed animals will be prepared by Dr Levin and sacrificed at selected postoperative intervals. Some animals will be treated with Tadenan® during the period of partial obstruction whilst other will receive placebo and serve as controls. Tissues will be examined using electron microscopy and the fine structure of bladder smooth muscle and autonomic nerves will be determined and compared with the findings of their previous study. By so doing it is intended to identify those tissue components upon which Tadenan® has a

beneficial effect and thereby improve our understanding of the mechanism of action of this compound.
(MD99013)

Effects of Ribosome-inactivating Proteins on Motor and Ganglionic Neurons

- ✉ KWONG Wing Hang
 ☐ 31 August 1997
 ❖ CUHK Departmental Funding

This project studies the effects of ribosome-inactivating proteins on motor, spinal sensory, and autonomic neurons. Ricin and trichosanthin will be used. Some plant proteins that possess similar amino-acid sequences but are less toxic will also be used for comparison. The mechanisms of axonal uptake, retrograde axonal transport, and the sequence of events leading to neuronal death will be studied. Experiments will be carried out on adult rats and peripheral neurons-Schwann cells culture. The researchers have observed in a preliminary study that some types of neurons are more susceptible to the toxins than the others. It is hoped that this study will provide a better understanding on the specificity of neural toxins.
(BL97043)

Systemic Application of Curcumin, an NF κ B Inhibitor, to Enhance Skeletal Muscle Healing Following Traumatic Injury

- ✉ LEE Ka Ho Kenneth
 ☐ 1 June 2000
 ❖ CUHK Research Committee Funding (Direct Grants)

Skeletal muscle is frequently the site of tissue injury due to trauma, disease and surgery. However, there is still no effective treatment available which can enhance the repair of skeletal muscle. This repair progress is especially inefficient in the elderly, and patients with cancer and AIDS. In this study, the researchers will investigate whether systemic administration of curcumin, a pharmacological inhibitor of the transcription factor NF κ B, can enhance muscle regeneration following experimentally induced injuries. They will freeze damage the tibialis anterior of 8-10 week-old male ICR mice and then inject 0.1% curcumin or its vehicle (DMSO) into the peritoneum. They will then determine the kinetics and extent of muscle regeneration *in vivo* after curcumin treatment. Biochemical and histological analyses will be performed 1-4 days after induced muscle injury. They will also investigate in cell culture how curcumin can act to stimulate both cell myogenic cell proliferation and differentiation. Flow cytometry will

be used to quantify cell proliferation and serum induction tests will be utilized to determine myoblast fusion and differentiation efficiency. They have already generated some preliminary data suggesting curcumin can promote myoblast proliferation by inhibiting NF κ B activation in culture. If they are able to demonstrate that curcumin can promote muscle growth and differentiation *in vivo*, then potentially they would possess a therapeutic drug for treating muscle injuries and enhancing the performance of athletes.
(MD99099)

Cloning and Sequencing of an Immunomodulatory Protein

- ✉ LIU Wing Keung Ken • NG Tzi Bun (Biochemistry)
- 1 August 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

Mushroom has long been considered as health food in Asian countries partly because it is very delicious and partly because it is highly nutritious. It contains relatively high levels of proteins, part of them have been reported to possess immunomodulatory activities, thus collectively termed as fungal immunomodulatory proteins (FIPs). The researchers have recently isolated a novel protein designated as VVL from the edible mushroom, *Volvariella volvacea*. This protein possesses potent proliferative and stimulating activities towards mouse lymphocytes, but the mechanism underlying its activities is not clear. Cloning of the gene encoding VVL is thus necessary to provide more protein for use in studies on its structure-function relationship. The sequence of the VVL gene will be obtained using "Rapid Amplification of cDNA Ends" technique (RACE), and thereafter for cloning and detailed chemical and biological characterization. The amino acid sequence derived from the VVL gene will be compared with that from the native VVL isolated from mushroom fruiting bodies. It is anticipated through this sequence to obtain insight into the functional domain of the FIPs.
(MD99024)

A Study of the Pathogenetic Mechanism of Renal Agenesis

- ✉ SHUM Sau Wun Alisa • WOOLF Adrian S.*
- 1 December 1999
- ❖ Research Grants Council (Earmarked Grants)

The main aim of this study is to establish the cellular and molecular mechanisms that can lead to renal agenesis induced by retinoic acid.

Renal agenesis (absence of kidney) is a clinically significant birth defect with high mortality and incidence rate. Renal agenesis has been reported to occur in cases of excess intake of vitamin A during pregnancy and it is also highly associated with the caudal regression syndrome. To help develop further information on the pathogenetic basis of this defect, a mouse model will be used. This mouse model of renal agenesis is induced by maternal administration of retinoic acid (an active metabolite of vitamin A). In this study, the researchers firstly propose to determine the primary tissue being affected in the kidney rudiments. Their preliminary data have shown that kidney rudiments could be rescued from degeneration if cultured *in vitro* in the presence of serum. This represents some hope that the genetic pathways which lead to renal agenesis can be interrupted. As growth factors are important in controlling various processes during kidney development (including the death and survival of cells), they secondly propose to characterise the expression of various growth factors and their receptors in the retinoic acid-treated kidney rudiments and thirdly, replenish these growth factors in an attempt to rescue the defect. Results of these proposed studies would provide not only important information on the pathogenetic mechanisms of renal agenesis, but also pave the way towards deriving methods for early detection, prevention and treatment of the defect *in utero*.
(CU99283)

The Effects of Prolonged Neonatal Auditory Stimulation on the Development, Maturation and Aging of the Auditory Midbrain of the Senescence Accelerated Mice (SAM)

- ✉ YE W Tai Wai David • CHAN Wood Yee • POON W.F.Paul*
- 1 November 1999
- ❖ Research Grants Council (Earmarked Grants)

It has long been known that environmental influences including auditory stimuli during the pre- or post-natal periods have effects on the subsequent development of the nervous system. It is believed that early sensory input during infancy may help or even enhance normal development of the nervous tissues while over-exposure to loud noise at an early stage of development may have harmful effects on the maturation of neuronal cells. However, the biological mechanisms whereby the external stimuli, particularly prolonged stimulation, affect subsequent development, maturation and aging of the nervous system are not well understood. In the present study, the researchers propose to analyze the immediate and long-term effects of prolonged auditory stimulation (one month) of different intensities occurred during the early postnatal development on the subsequent neuronal changes in the midbrain. The functional

integrity, morphological features and biochemical changes of the midbrain inferior colliculi will be examined in the senescence-accelerated mice immediately after the prolonged stimulation, and later in the middle age and old age. The results of the present study will establish whether neonatal sensory stimulation produces adverse effects on the subsequent development, maturation and aging of the central nervous system, or, on the other hand, exerts protective effects on the nervous centers against subsequent aging. The results would also provide important information on possible therapeutic value and problems of prolonged neonatal sensory stimulation on the nervous system. (CU99260)

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

Edition Title/Investigators

- | | | | |
|---------|--|---------|--|
| 1998-99 | A Study of Gene Expression of Gonadotropin-Releasing Hormone and its Receptor in Normal and Neoplastic Rat Prostates (MD98093) ✉ CHAN Leung Franky | 1998-99 | Effect of Drug on the Nuclear Matrix of Hepatocellular Carcinoma Cells <i>in vitro</i> (MD98026) ✉ CHEW Eng Ching |
| 1996-97 | Identification of the Molecular Determinants in the Retina that Govern Axon Pathfinding in the Chiasm of Mammals (CU96623) ✉ CHAN Sun On | 1998-99 | Induction of Retinal Ganglion Cell Regeneration by the Equineurium of a Peripheral Nerve (MD98027) ✉ CHO Yu Pang Eric |
| 1997-98 | The Role of SPARC, an Extracellular Matrix-Associated Protein, in Ovarian Tumor Growth and Invasion (CU97610) ✉ CHAN Wood Yee • MOK S. C.* | 1998-99 | The Influence of Mature Astrocytes on the Survival and Regeneration of Adult Retinal Ganglion Cells (CU98265) ✉ CHO Yu Pang Eric |
| 1998-99 | Migration of Secondary Neural Crest Cells to the Bowel: A Study of Normal and Congenitally Aganglionic Mutant Mice (MD98025) ✉ CHAN Wood Yee | 1998-99 | Male Accessory Sex Glands and Abnormalities in Embryo Development: The Role of Growth Arrest Specific 6 (Gas6) Gene (MD98029) ✉ CHOW Pak Ham Patricia • LEE Ka Ho Kenneth |
| 1997-98 | Development of a Novel Diagnostic Kit for Early Detection of Human Cervical Cancer: Identification and Generation of a Monoclonal Antibody (MD97003) ✉ CHEW Eng Ching • LEE Chuen Kwun Joseph (School of Chinese Medicine) • CHEW CHENG Siew Boon (Dept of Physiology) • LIU Le-he* | 1998-99 | Ampullary Gland, Ventral prostate and Embryo Implantation (CU98030) ✉ CHOW Pak Ham Patricia • O Wai Sum* |
| 1997-98 | Application for Development of a Novel Nuclear Matrix Laboratory for Both Research and Teaching at Prince of Wales Hospital (MD97008) ✉ CHEW Eng Ching | 1998-99 | Role of Fibroblast Growth Factor Isoforms in the Development of the Mammalian Limb Musculature (CU98273) ✉ LEE Ka Ho Kenneth • PAULIN Denise* |
| | | 1998-99 | Regulation of Apoptosis and Differentiation by a Novel Gene BRE that Modulates TNF- α Action (MD98094) ✉ LEE Ka Ho Kenneth • CHAN Yeuk Hon John (Dept of Clinical Oncology)# • YEW Tai Wai David |
| | | 1996-97 | Mechanisms Underlying the Immunomodulatory and Antitumor Activities of Selected Lectins (CU96667) ✉ LIU Wing Keung Ken • NG Tzi Bun (Biochemistry) • OOI Vincent Eng Choon (Dept of Biology) • CHANG Shu Ting (Dept of Biology) |
| | | 1997-98 | The Effect of Mushroom Extract on the Tumor Vascular System in Inbred Mice - A Scanning Electron Microscopic Study (MD97102) ✉ LIU Wing Keung Ken • KONERDING Moritz* |
| | | 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.*
 1997-98 The Role of Wilms' Tumor Gene (WT1) and Apoptosis in the Development of Renal Agenesis (MD97106)
 ✎ SHUM Sau Wun Alisa • HASTIE Nicholas D.* • TSE K. W. Herman • MENKE Aswin*
- 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*
- 1998-99 A Study to Determine the Role of Glutamic Acid Decarboxylase (GAD) in the Pathogenesis of Caudal Agenesis Associated with Diabetic Pregnancy (MD98028)
 ✎ SHUM Sau Wun Alisa
- 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
 1994-95 Apoptosis in the Developing, Diseased and Aging Nervous Systems (MD95061)
 ✎ YEW Tai Wai David • CHAN Wood Yee • CHO Yu Pang Eric • DIXON John Stuart# • LEUNG Ping Chung (Dept of Orthopaedics & Traumatology) • SHUM Sau Wun Alisa • John Arthur GOSLING • YU Mang Chung
- 1995-96 Aging Changes in the Human Central Nervous System (MD95185)
 ✎ YEW Tai Wai David
- 1997-98 Microglial Reaction Pattern in Normal and SCID (Severe Combined Immunodeficient) Mice (MD97103)
 ✎ YEW Tai Wai David • SCHUMACHER U.* • LORKE D. E.*
- 1998-99 Neural Plasticity in the Auditory Midbrain: A Combined Histological and Electrophysiological Study (MD98030)
 ✎ YEW Tai Wai David • POON W.F.Paul*

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000569> **Yew, David T.; T.K. Lam; D. Tsang; Y.K. Au; Winnie W.Y. Li and M.O.M. Tso.** "Changes of Cytochemical Markers in the Conjunctival and Corneal Epithelium after Corneal Debridement". *Cellular and Molecular Neurobiology* vol.20 no.4, pp.465-481. 2000.
- <P000616> **Yau, Kin; W.W.Y. Li and D.T. Yew.** "Changes in Leucine Uptake in the Retina of the Hamster after Traumatic Detachment". *Biological Signals and Receptors* vol.9, pp.23-37. Switzerland, 2000.
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RESEARCH PROJECTS

Studies on Fish Prolactin

- ✉ CHENG Hon Ki Christopher
- 1 March 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Two cDNA clones encoding for goldfish prolactin have been identified from a pituitary cDNA library. The coding regions of these clones, containing four silent mutations, encode for the same polypeptide. However, the 3'-untranslated regions of these two clones are substantially different from each other to indicate that there are two different genes for prolactin in goldfish. This observation, suggested by genomic Southern blot analysis, is in concordance with the fact that goldfish is a tetraploid. The two prolactin genes might have derived from recent gene duplication before the divergence of goldfish from other Cypriniforms. In this study the researchers intend to clone the prolactin genes from goldfish by genomic PCR and by genomic library screening. The regulation of prolactin gene expression in goldfish would also be studied. (BL99017)

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

- ✉ FUNG Kwok Pui
- 1 August 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

Antioxidants are commonly found in plant extracts from Traditional Chinese Medicine (TCM) and natural sources. Some of the antioxidants have been found to be effective in preventing cancer formation but not many reports on their effects in suppressing growth of tumour cells are found. In this proposal, the researcher will examine the probable anti-tumour activities of five pure antioxidants isolated from TCM and natural sources. They are purpurogallin, morin, propyl gallate, lithospermic acid B and tanshinone IIA. The optimal conditions of these antioxidants to exert their anti-tumour activities in tumour bearing animals will be worked out. Because all these antioxidants are planar in structure, whether this structural property is essential for the activity will be scrutinized. Other possible anti-tumour mechanisms, such as arrest in cell cycle progression in tumour cells, inhibition of protein kinases and activation of p53 expression in tumour cells, and

activation of immune system in the host, will also be investigated. The possibility of these antioxidants in counteracting the multidrug resistance of tumour cells *in vivo* will be examined. Finally, the probable cardioprotective effects of these antioxidants on the doxorubicin-or mitomycin-C-treated tumour bearing mice will be investigated. Whether the antioxidants can exert additional or synergistic effects on suppressing tumour growth in these combined treatments will be examined. It is hoped that from this study a novel anticancer mode using these antioxidants will accrue.

(MD99025)

Function & Regulation of a Gene Encoding a Heat Shock-like Protein

- ✉ LEE Cheuk Yu • WAYE Mary Miu Yee • FUNG Kwok Pui • TSUI Kwok Wing
- 1 September 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

Ability to adapt to stress is essential for the survival of organisms living in an often hostile environment. They have developed complex mechanisms to combat the myriad insults that beset organ systems and cellular constituents after trauma. Ischemic stress of the heart is one type of stress involving reduced blood supply to tissues and consequent anoxic injury of the heart muscle. An array of integrated responses have evolved in man and in animals that work in concert to counteract that stress. These include the early production of heat shock proteins which are postulated to stabilise and repair essential cellular proteins that might have been denatured by pH or free radical insult. They help maintain the integrity of the myofibrils and the muscle's contractile functions.

In the course of their work in a RGC-supported project on genes of the cardiovascular system, the researchers identified a novel gene that encodes a new member of the small heat shock protein (sHSP) family, termed HSPL27 (for Heat-Shock-Protein-Like). The gene is abundantly expressed in the human heart, slightly expressed in kidney, and not at all in a host of other tissues tested. Sequence analysis of the gene showed it to be very similar to a known human HSPL27 gene and to another sHSP capable of inhibiting actin polymerisation in chick embryos (CIAP). Preliminary results from experiments conducted in their laboratory and those done in collaboration with A. Suzuki showed that, interestingly, HSPL27 is not inducible by heat, but HSPL27 and another heart-specific sHSP protein MKBP (myotonic dystrophy protein kinase binding protein) interact and then complex with DMPK, a serine/threonine protein kinase postulated to be involved in the pathogenesis of a type of muscular dystrophic condition characterised by loss of muscle

tone (myotonic dystrophy). MKBP is also not induced by heat shock but it does show the characteristic response of HSPs in being redistributed to insoluble fractions upon stress. This interaction is clinically significant in that it associates a specific muscular dystrophic condition with a stress response system. The researchers now propose to further study the function of HSPL27 via a two-prong approach: firstly, they will examine HSPL's interaction with the MKBP protein and in view of HSPL27's similarity to CIAP, also its ability to induce F-action fragmentation, through antisense oligodeoxynucleotide and site-directed mutagenesis/transfection experiments. The researchers will also examine the sequence characteristics of HSPL27's promoter region, with a view to identifying putative transcription factors that regulate gene expression and elucidate thereby its function. At the conclusion of this study, they expect to have a clearer picture of whether HSPL27 acts to protect cardiac function, and, if so, what the molecular mechanism might be. They hope, in particular, to be able to define the possible role that HSPL27 might play in the pathogenesis of myotonic dystrophy. (MD99026)

Chemopreventive and Hormone-replacement Therapeutic Evaluations on Some Dietary Phytoestrogens

- ✉ LEUNG Lai Kwok
- ☐ 1 June 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Estrogen replacement therapy has been a dilemma for postmenopausal women. Although the estrogen given may alleviate the symptoms arising from lacking estrogen, the risk of breast cancer is also increased. Recently specific estrogen receptor mediators (SERMs) has been attracting tremendous attention since the drugs are antiestrogen in the breasts and acting like estrogen in the other tissues. The phenomenon has been attributed to the expression of different estrogen receptor (ER) isoform in the tissues. Phytoestrogens are estrogenic chemicals derived from plant origin. Because of their differential binding affinity to the isoforms of estrogen receptor, phytoestrogens have been proposed to be the natural SERMs. The objective of this project is to estimate the medicinal value of several phytoestrogens by using a cell culture system. MCF-7 cell transfected with ER responsive element reporter construct will be used to determine the phytoestrogens' ER binding properties. The phytoestrogen will be administered alone in various concentrations or competing with 0.1 nM 17 β -estradiol to illustrate their agonistic or antagonistic activities on ER. The chemoprevention values will

be measured by cell proliferation and apoptosis assays in non-transfected MCF-7 cells. Past results indicated estrogen may change the expressions of Bcl-2 family proteins, so this project also looks into the Bcl-2 family proteins affected by phytoestrogens. The overall goal of this project is to evaluate the health benefits of dietary phytoestrogens, and this can be the scientific basis for convincing women to turn to those phytoestrogen-rich food items. (MD99100)

Determining the Chemopreventive Potential of Tea Phytochemicals

- ✉ LEUNG Lai Kwok
- ☐ 30 June 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Heterocyclic aromatic amines (HAA) and polycyclic aromatic hydrocarbons (PAH) are mutagens and animal carcinogens that can be found in foods which undergo heating or processing. Recently cooking oil has also been demonstrated releasing PAHs in the air when heated in frying pans or woks. One of the better-known carcinogens, benz[a]pyrene (BP), is a PAH. Its carcinogenicity originates from the DNA damaging property upon metabolism. Past work has illustrated that the genotoxic intermediate of BP is catalyzed by cytochrome p450 (CYP) 1A enzymes. Phytochemicals in tea, mainly catechins, are inhibitors of CYP1A1 enzyme as shown in past studies. The current study is to evaluate the possibility of these tea phytochemicals inhibiting the transformation and preventing the DNA-adduct formation. Following this vein, the underlying mechanism will be investigated. (BL99028)

The Role of LIM Domain Proteins in Heart Growth and Development

- ✉ TSUI Kwok Wing • CHAN Wood Yee (Dept of Anatomy) • FUNG Kwok Pui • LEE Cheuk Yu • LEE Sau Tuen Susanna (Biochemistry) • WAYE Mary Miu Yee
- ☐ 1 September 1999
- ❖ Research Grants Council (Earmarked Grants)

In Hong Kong, heart diseases are the second leading causes of death in 1997. These diseases affect mainly elderly people and will continue to dominate the mortality statistics as the population ages. Based on the resources established by the cardiovascular expressed sequence tags (ESTs) sequencing project and a former grant from the Research Grants Council, the researchers have isolated three LIM domain protein genes, which are preferentially or abundantly expressed and developmentally regulated in human

heart. Moreover, previous results have shown that two of the protein genes are differentially expressed in chemical hypoxia and hypertrophic cardiomyopathy, and one is down-regulated in embryonal-rhabdomyosarcoma cell line. Together with other preliminary results, they believe that the further characterization of these LIM domain proteins should be an important step towards the understanding of cardiovascular development and diseases. To uncover the functional significance of these three proteins, the researchers will investigate their roles in myogenic differentiation using green fluorescent protein tagged recombinant proteins express in mouse muscle myoblast cell line. They will also clarify the location and time of their gene expression using mouse model. Finally, they will disrupt the function of one of the genes in mouse and study the corresponding changes in the phenotype of the heart. They believe that the elucidation of the functional role of LIM domain proteins could enable new approaches for diagnosis and treatment of human heart diseases. (CU99305)

Cell Cycle Control: Regulation of CDC25B Phosphatases by Calmodulin and CaM Kinase

- ✉ TSUI Kwok Wing • WAYE Mary Miu Yee • DUCOMMUN Bernard*
- 1 February 2000
- ❖ France/Hong Kong Joint Research Scheme

A number of studies that have been published over the last few years suggest that calmodulin plays a role in cell cycle control. At the G1/S transition, the nuclear accumulation of calmodulin and its association with DNA polymerase suggest an involvement in the regulation of the replication machinery. The involvement of calmodulin and CaM kinases in G2 and in mitosis is less documented. It has been shown that several inhibitors are able to block the function of calmodulin both at G2/M and at the metaphase/anaphase transitions. These observations suggest that calmodulin may play a role in the regulation of these two cell cycle checkpoints. Members of the 14-3-3 chaperone family also appear to play a role in the control of cell proliferation and to regulate the G2/M checkpoint. Interestingly, both CaM kinase and 14-3-3 appear to target the CDC25 phosphatase. CaM kinase II might directly activate CDC25C. In contrast, 14-3-3 acts by sequestering CDC25C in the cytoplasm and inhibit therefore the activation of nuclear CDK1-cyclinB at mitosis. An interesting issue is to determine whether calmodulin and 14-3-3 proteins are acting on separate pathways on CDC25 function or whether they are both part of a more complex regulatory mechanism that still remains to be unravelled. The aim of this project is to determine whether calmodulin can regulate the function of CDC25B in a 14-3-3-dependent or

independent manner and to examine the consequences of these interactions on cell cycle progression. (BL99008)

Mitotic Gene Conversion in Asexual Diploid *Candida albicans*

- ✉ WANG Jun
- 1 October 1999
- ❖ Research Grants Council (Earmarked Grants)

Two features make *Candida albicans* an attractive organism for genetic study. First, it is the most important human fungal pathogen and second, like other obligate diploid, it has a unique life cycle that is free of meiosis. Very little is known about the genetic mechanism of mitotic recombination in this asexual diploid. In the last two years the researcher's research group has accumulated evidence that gene conversion (nonreciprocal transfer of genetic information) plays an important, perhaps seven predominant, role in the mitotic segregation of heterozygous alleles in this and other fungi of similar life cycle. They seek to further define the genetic significance of gene conversion in this meiosis-free, obligate diploid using strains heterozygous at *ADE1* or *ADE2* locus and carry additional selectable marker of *URA3* gene. The study represents the first attempt to systematically study the mitotic recombination in an obligate diploid cell and to assess mitotic recombination events in the absence of meiotic processes. The heterozygotes constructed in this study will also be used as testers to screen chemical or physical reagents that promote mitotic recombination or loss of heterozygosity in eukaryotic cells and to delineate the underlying mechanism. (CU99158)

DNA Fingerprinting Technology for Detection of Genetically Modified Organisms and Identification of Chinese Population

- ✉ WANG Jun
- 1 April 2000
- ❖ Molecular Technology Innomed Limited • University-Industry Collaboration Prog.: Industrial Research Chair Scheme, ITF, Innovation & Tech. Commission

The objectives of this project are:

- (1) to develop a reliable, efficient & versatile detection system for GMO, and
- (2) to establish and commercialize a new short tandem repeats (STR) based technology for paternity & forensic analysis.

(BL99029)

Structural and Functional Studies of Human 14-3-3 Epsilon Protein

✉ WAYE Mary Miu Yee • LEE Cheuk Yu • FUNG Kwok Pui • TSUI Kwok Wing

□ 15 August 1999

❖ CUHK Research Committee Funding (Direct Grants)

14-3-3 proteins belong to a highly conserved multigene family of small acidic proteins that associate with cell cycle and cell death regulators, oncogenes, and signalling molecules. A number of functions have been proposed for 14-3-3 proteins, including inhibition of protein kinase C (PKC), activation of Raf-1 protein kinase, regulation of the biosynthesis of neurotransmitters and determination of the timing of cell division. Since 14-3-3 proteins associate with a number of proto-oncogenes and oncogenes, they might play an important role in tumor development. To date, 14-3-3 proteins are suggested to be a multifunctional regulator of cellular signals mediated by two types of Ca²⁺-dependent protein kinases: PKC and calmodulin-dependent protein kinase (CaM kinase). While the inhibition of PKC by 14-3-3 proteins has been well characterized, the relationship between CaM kinase and 14-3-3 proteins remains to be elucidated. It has been shown those two isoforms of the 14-3-3 protein associate with Cdc25. Cdc25 is complexed primarily with 14-3-3 epsilon and to a lesser extent with 14-3-3 zeta. The association of these 14-3-3 proteins with Cdc25 varies dramatically during the cell cycle: binding is high during interphase but virtually absent at mitosis. Recently, the researchers found that the epsilon isoform of human 14-3-3 proteins (h1433 ϵ) can also interact with calmodulin, which is a calcium-binding protein that participates in the signal transduction pathway through the interaction with CaM kinase. The biological relevance of the interaction between h1433 ϵ and calmodulin will be examined. The effect of h1433 ϵ on the activity of CaM kinase will be determined. (MD99027)

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 | Molecular Mechanism of Metallothionein Gene Regulation (BL97018) ✉ CHAN King Ming |
| 1998-99 | Cloning of Common Carp Metal Regulatory Element Binding Proteins (BL98005) ✉ CHAN King Ming |

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| 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) |
| 1996-97 | Structure-function Studies on Fish Growth Hormone and Prolactin: A Protein Engineering Approach (CU96320) ✉ CHENG Hon Ki Christopher • CHAN King Ming • NG Tzi Bun |
| 1998-99 | IGF Gene Expression Studies in Fish (BL98006) ✉ 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* |
| 1996-97 | Tumour Necrosis Factor- α : Biological Activities and Action Mechanism in Health and Diseases (MD96127) ✉ FUNG Kwok Pui • CHAN Leung Franky (Dept of Anatomy) • CHENG Hon Ki Christopher • CHOY Yuen Min (Biochemistry) • KONG Siu Kai (Biochemistry) • KWOK Tim Tak • LEUNG Kwok Nam (Biochemistry) • WAN Chi Cheong 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 |
| 1997-98 | Discovery of Traditional Chinese Medicine (TCM) - Derived Saponins with Anti-Tumour and Cardiotoxic Activities for Use as Health Food Supplements or Therapeutics (MD97085) |

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|---------|---|---------|--|
| | <p>✍ FUNG Kwok Pui • WONG Nai Ching Henry (Dept of Chemistry) • CHANG Yen Albert# • HUI Yongzheng* • YU Biao*</p> | 1998-99 | <p>Isolation and Characterization of Ribosome - Inactivating Proteins with Novel Features (CU98331) ✍ NG Tzi Bun</p> |
| 1998-99 | <p>Glucose transporter as an anti-tumour target (CU98148) ✍ FUNG Kwok Pui • LEE Cheuk Yu</p> | 1997-98 | <p>Structural and Functional Studies of Human 14-3-3 ε Protein (BL97041) ✍ TSUI Kwok Wing</p> |
| 1998-99 | <p>Mechanistic Study of the Anti-tumour Effect of Step-down Hyperthermia (MD98031) ✍ FUNG Kwok Pui</p> | 1998-99 | <p>Characterization of the Human 14-3-3 Epsilon Protein (MD98032) ✍ TSUI Kwok Wing</p> |
| 1998-99 | <p>Organization of 8th International Symposium of Society of Chinese Bioscientists in America (BL98024) ✍ FUNG Kwok Pui • TSANG David Sau Cheuk (Biochemistry) • WONG Ricky* • WAYE Mary Miu Yee • KONG Siu Kai (Biochemistry) • CHAN King Ming • FONG Wing Ping (Biochemistry) • TSUI Kwok Wing • WONG Raymong* • CHAN Vivian* • CHUNG Stephen* • WU Rudolf* • CHAU F. T.*</p> | 1997-98 | <p>Molecular and Immunological Characterization of Endothelin Converting Enzymes (CU97320) ✍ WAN Chi Cheong David</p> |
| | | 1998-99 | <p>The role of pre-synaptic motor neuron acetylcholinesterase in neuromuscular synaptogenesis (CU98140) ✍ WAN Chi Cheong David • TSIM Karl W. K.*</p> |
| | | 1998-99 | <p>The Biological Significance of the Adenine Auxotrophic Heterozygosity in the Obligate Diploid Fungus <i>Candida Albicans</i> (BL98011) ✍ WANG Jun</p> |
| 1998-99 | <p>The Role of Growth Factor Signalling and c-Jun Expression in the Anti-tumor Effect of Natural Polysaccharides (CU98141) ✍ KWOK Tim Tak • CHOY Yuen Min (Biochemistry)</p> | 1996-97 | <p>Molecular Cloning and Characterization of Human Heart cDNAs Coding for LIM Domain Containing Proteins (CU96313) ✍ WAYE Mary Miu Yee • LEE Cheuk Yu • FUNG Kwok Pui</p> |
| 1998-99 | <p>The Role of Mitochondria in the Response of Cells to Anticancer Drugs (BL98008) ✍ KWOK Tim Tak</p> | 1997-98 | <p>Sequence Analysis of the SLIM1(FHL1) Gene (BL97017) ✍ WAYE Mary Miu Yee • BENTLEY David R.* • ROSS Mark*</p> |
| 1997-98 | <p>Atherosclerosis Genes (MD97037) ✍ LEE Cheuk Yu • WAYE Mary Miu Yee • FUNG Kwok Pui</p> | 1998-99 | <p>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*</p> |
| 1995-96 | <p>Natural and Synthetic Anti-human Immunodeficiency Virus and Anti-Lymphoma Compounds (BL95036) ✍ NG Tzi Bun • WONG Nai Ching Henry (Dept of Chemistry) • FONG Wing Ping (Biochemistry) • WAN Chi Cheong David • YEUNG Hin Wing (Biochemistry)#</p> | | |
| 1997-98 | <p>Natural Products with Anti-Human Immunodeficiency Virus Activity (CU97688) ✍ NG Tzi Bun • WAN Chi Cheong David • FONG Wing Ping (Biochemistry) • Yeung Hin Wing*</p> | 1998-99 | <p>Molecular Study of FHL2 – a Four and a Half LIM-Domain Protein Specifically Expressed in Heart (BL98012) ✍ WAYE Mary Miu Yee • LEE Cheuk Yu • FUNG Kwok Pui • TSUI Kwok Wing</p> |

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*

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- <P000756> **Fung, K.P.; W.K. Kan and P.C. Leung.** "Bioinformatics for Chinese Medicine". Paper presented in the 3rd Symposium on Herbal Medicine - Taking Herbal Medicine into the Global Mainstream Healthcare System in the 21st Century, organized by Institute of Bioagricultural Science, Academia Sinica. 2000.03.
- <P001798> **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- Induced Apoptosis Via Mitochondrial Damage". *Life Sciences* vol.67, pp.725-732. USA, 2000.
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- <P002536> **Au, T.K.; R.A. Collins; T.L. Lam; T.B. Ng; W.P. Fong and D.C.C. Wan.** "The Plant Ribosome Inactivating Proteins Luffin and Saporin are Potent Inhibitors of HIV-1 Integrase". *Federation of European Biochemical Society Letter* vol.471, pp.169-172. USA, 2000.03.
- <P002551> **Chim, Stephen S.; Kwok-Pui Fung; Mary M.Y. Waye; Cheuk-Yu Lee and Stephen K.W. Tsui.** "Expression of Replication Factor C 40_RDa Subunit 2 is Down-Regulated During Neonatal Development in Rat Ventricular Myocardium". *Journal of Cellular Biochemistry* vol.78, pp.533-540. New York, USA, 2000.06.12.
- <P002564> **Tsui, S.K.W.; M.M.Y. Waye; C.Y. Lee; K.P. Fung and S.S. Chim.** "Subtracted cDNA Libraries of Hyperplastic and Hypertrophic Neonatal Hearts". *Proceedings of the Human Genome Meeting 2000* ed. by Tsui, L.C. p.24. Vancouver, Canada: The Human Genome Organization, 2000.04.
- <P002566> **Chan, Kwok-Keung; Stephen K.W. Tsui; Sai-Ming Ngai; Simon M.Y. Lee; Masayo Kotaka; Mary M.Y. Waye; Cheuk-Yu Lee and Kwok-Pui Fung.** "Protein-Protein Interaction of FHL2, a LIM Domain Protein Preferentially Expressed in Human Heart, with HCDC47". *Journal of Cellular Biochemistry* vol.76, pp.499-508. New York, USA, 2000.01.24.
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- <P002569> **Sugiyama, Yuki; Atsushi Suzuki; Masaru Kishikawa; Rika Akutsu; Tomonori Hirose; Mary M.Y. Waye; Stephan K.W. Tsui; Shosei Yoshida and Shigeo Ohno.** "Muscle Develops a Specific form of Small Heat Shock Protein Complex Composed of MKBP/HSPB2 and HSPB3 During Myogenic Differentiation". *The Journal of Biological Chemistry* vol.275 no.2, pp.1095-1104. Bethesda, MD, USA, 2000.01.14.

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- <P993446> **Ng, T.B.; W.Y. Chan; H.X. Wang; F. Liu; X.Y. Ye; C.S. Cheung and W.F. Mok.** "Mushroom (*Coriolus Versicolor*) Polysaccharopeptide Elicits Analgesia But Does Not Adversely Affect Ovarian Steroidogenesis, Ovulation, Gestation and Embryonic Development in Mice". *Advanced Research in PSP 1999* ed. by Qing-Yao Yang. pp.204-214. Hong Kong: Hong Kong Association for Health Care Ltd, 1999.12.
- <P994060> **Fu, R.Z.; Wang J.; Zhang Y.B.; But P.P.H.; Li N. and Shaw P.C.** "Differentiation of Medicinal Codonopsis Species from Adulterants by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism". *Planta Medica* vol.65, pp.648-650. Germany, 1999.10.
- <P994564> **Choi, R.C.Y.; Man, L.S.; Wan D.C.C. and Tsim K.W.K.** "Analysis of Human Acetylcholinesterase Promoter by *in vitro* Transfection". *Proceedings of the 8th International Symposium of Society of Chinese Bioscientists in America* p.POS-M21. Hong Kong: SCBA, 1999.08.
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- <P994607> **Ip, Alice Lai Fong and David C.C. Wan.** "Isolation and Characterization of ECE-2 from Rat Hypothalamus and Rat C6 Gloma Cells". *Abstracts of the 8th International Symposim of Society of Chinese Bioscientists in America* p.POS-H60. Hong Kong, 1999.08.
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- <P994612> **Kotaka, Masayo; Sai-Ming Ngai; Merce Garcia-Barcelo; Stephen K.W. Tsui; Kwok-Pui Fung; Cheuk-Yu Lee and Mary M.Y. Waye.** "Characterization of the Human 36-KLISTDa Carboxyl Terminal LIM Domain Protein (HCLIM1)". *Journal of Cellular Biochemistry* vol.72, pp.279-285. 1999.
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- <P994614> **Tse, Paul M.F.; T.B. Ng; W.P. Fong; R.N.S. Wong; C.C. Wan; N.K. Mak and H.W. Yeung.** "New Ribosome-Inactivating Proteins from Seeds and Fruits of the Bitter Gourd *Momordica Charantia*". *The International Journal of Biochemistry and Cell Biology* vol.31, pp.895-901. 1999.
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- <P994624> **Chan, Kwok-Keung; S.K.W. Tsui; S.M. Ngai; S.M.Y. Lee; M.M.Y. Waye; C.Y. Lee and K.P. Fung.** "Protein-Protein Interaction of FHL2, a LIM Domain Protein Preferentially Expressed in Human Heart, with HCDC47". *Proceedings of 8th International Symposium of Society of Chinese Bioscientists in America* ed. by Eva Lee. p.171. Hong Kong, China, 1999.08.

see also <P000506>, <P000803>, <P000945>, <P001386>, <P002562>, <P002570>, <P002571>, <P003707>, <P006094>, <P008150>, <P008174>, <P009754>, <P991337>, <P992319>, <P992559>, <P992695>, <P992696>, <P992760>, <P992761>, <P992812>, <P993705>, <P994061>, <P994462>, <P994620>, <P994621>, <P994622>, <P994623>, <P994625>, <P996427>, <P996549>, <P996928>

RESEARCH PROJECTS

Non-invasive Prenatal Screening of β -thalassaemia by Molecular Analysis of Maternal Plasma

- ✉ CHIU Wai Kwun Rossa • LO Yuk Ming Dennis
 - LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Tse Ngong (Dept of Obstetrics & Gynaecology)
- 1 May 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

β -thalassaemia is an inherited condition of prime significance to Southern Chinese populations. It is an autosomal recessive condition caused by decreased synthesis of β -globin chains. β -thalassaemia major, β -thalassaemia in its severest form, is a condition which requires life-long blood transfusions and chelation therapy. In Hong Kong, the carrier rate is estimated to be 3.4%. With an average rate of 70,000 births per year in Hong Kong, it is estimated that approximately 80 pregnancies per year will involve a fetus at risk of β -thalassaemia major or intermedia. Currently in Hong Kong, prenatal diagnosis and genetic counselling are offered to couples whose pregnancy is at risk. Fetal tissue for genetic testing is conventionally obtained by chorionic villus sampling or amniocentesis, both of which, despite marked technical improvements, are associated with the risk of abortion of 2-3% and 1%, respectively. With the discovery of circulating fetal DNA in maternal plasma, the potential for non-invasive prenatal genetic testing is becoming a reality. The successful application of such approach has been demonstrated by the prenatal determination of fetal RhD status by molecular analysis of maternal plasma. The current study is designed to apply this approach for the development of a non-invasive prenatal test for β -thalassaemia through the analysis of maternal plasma. (MD99101)

Mitochondrial Genome in Wolff-Parkinson-White Syndrome

- ✉ LAM Ching Wan • John Elsby SANDERSON (Dept of Medicine & Therapeutics) • WONG Lee-Jun C* • FONG Win Hon*
- 1 October 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

Wolff-Parkinson-White (WPW) syndrome is a conduction defect of the heart. The prevalence of this disease is high approximately 0.1% of the general population. Some patients with WPW present with sudden cardiac death. The genes involved in causing

this atrioventricular accessory pathway have not been identified. Now, there is preliminary evidence that WPW syndrome is associated with mitochondrial DNA mutations. However, no large study has been performed to investigate the whole mitochondrial genome in a significant population of patients. Determination of the extent of mitochondrial involvement in WPW syndrome and identification of the mitochondrial mutations involved will have both diagnostic and therapeutic implications for this disease. Information on the phenotypic expression of different contributing mutations will be important to the development of methods for preventing, diagnosing and treating WPW syndrome. The new findings will influence the current understanding of the molecular and biophysical basis of arrhythmogenesis. (MD99028)

Signal Transduction for Dexamethasone-Induced Apoptosis of Human Eosinophils in Allergic Inflammation

- ✉ LAM Wai Kei Christopher • WONG Chun Kwok • HJELM Nils Magnus#
- 1 October 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

Eosinophils are the principal effector cells of late-phase inflammation in allergic diseases. Inhibition of eosinophil apoptosis has been proposed as a key pathogenetic mechanism for the eosinophilia in bronchial asthma and atopic dermatitis. Glucocorticoids which have been shown to accelerate apoptosis of eosinophils is usually used for the treatment of allergic inflammation. However, the molecular mechanism by which glucocorticoids accelerate eosinophil apoptosis is still unknown. Considerable attention has recently been focused on the roles of different intracellular signal transduction pathways including mitogen-activated protein kinases (MAPK), nitric oxide, NF- κ B and caspases in the control of apoptosis in granulocytes.

This project aims to utilise our established (1) human blood eosinophil culture and (2) MAPK assay techniques to elucidate the roles of different signal transduction regulators including MAPK, NF- κ B, NO, caspases in dexamethasone treated eosinophils. It will study the (1) effect of dexamethasone on the intracellular MAPK (ERK, JNK, p38 MAPK), NO, NF- κ B, caspases in human peripheral blood eosinophils, (2) relationship between the activation of the above different regulators and eosinophils apoptosis, and (3) effect of specific inhibitors of MAPK, NO synthetase, NF- κ B, caspases on the apoptosis of dexamethasone treated eosinophils. Understanding of these intracellular control mechanisms will widen our knowledge of the immunopathogenesis of allergic diseases and the

mechanisms of the pharmacological activity of dexamethasone, thereby providing further biochemical basis for the design of more effective pharmacological agents for the treatment of allergy. (MD99029)

Investigation into Plasma DNA Abnormalities in Pre-eclampsia

✉ LO Yuk Ming Dennis • HJELM Nils Magnus# • LAU Tze Kin (Dept of Obstetrics & Gynaecology) • LEUNG Tse Ngong (Dept of Obstetrics & Gynaecology)

☐ 1 September 1999

❖ Research Grants Council (Earmarked Grants)

Pre-eclampsia is an important cause of maternal and fetal morbidity and mortality. Clinical manifestations of pre-eclampsia include hypertension, oedema and proteinuria. Potential sudden and rapid clinical deterioration may result in convulsions, coma and death. The aetiology and molecular pathogenesis of this disorder remain incompletely understood. The researchers have recently shown for the first time that cell-free fetal DNA is present in maternal blood and have obtained preliminary data indicating a 5-fold elevation in maternal plasma fetal DNA in pre-eclamptic individuals. This project aims to obtain further data on the production and clearance mechanisms of fetal DNA in pre-eclampsia and to determine whether plasma DNA analysis may be used to predict the disorder prior to its clinical manifestation. (CU99255)

Development of Plasma DNA-Based Diagnostic Technology

✉ LO Yuk Ming Dennis • HJELM Nils Magnus# • JOHNSON Philip James (Dept of Clinical Oncology)

☐ 1 September 1999

❖ Industrial Support Fund, Industry & Technology Development Council

This project is based on recent work demonstrating the existence of cell-free DNA of tumoral and fetal origins in circulation to develop new diagnostic assays for cancer detection and prenatal diagnosis. Towards the first goal, hepatocellular carcinoma will be used as a model system. This project may allow the development of rapid molecular assays for the early detection of this tumour, thus potentially improving the chance of survival from this disease. For the latter goal, the prenatal determination of fetal blood group type will be used as a model. The resultant assays may improve the management of sensitised pregnant women with fetomaternal blood group incompatibilities and may serve as a model

system for the non-invasive prenatal diagnosis of other single gene disorders. (MD99015)

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 | Mutation Screening of a New Oncogene: The Human Smoothed (SMO) in Sporadic Basal Cell Carcinoma (MD97112) ✉ LAM Ching Wan • XIE J* • MCCORMICK F* • TO Ka Fai (Dept of Anatomical & Cellular Pathology) • YUEN W. F.* • LEE K. C.* |
| 1998-99 | The Role of Mitogen-activated Protein Kinases (MAPK) in Regulating Apoptosis of Eosinophils in Allergic Inflammation (MD98033) ✉ LAM Wai Kei Christopher • WONG Chun Kwok • HJELM Nils Magnus# |
| 1998-99 | Novel Analyte Assay in Experimental and Human Cataract (MD98089) ✉ LAM Wai Kei Christopher • PETERS T J* |
| 1997-98 | Trafficking of Nucleated Cells between Fetus and Mother (CU97670) ✉ LO Yuk Ming Dennis • CHANG Mang Z. Allan (Dept of Obstetrics & Gynaecology) • HJELM Nils Magnus# |
| 1997-98 | Development of a Rapid and Accurate Molecular Assay for the Diagnosis of Chromosomal Aneuploidies (MD97044) ✉ LO Yuk Ming Dennis • HJELM Nils Magnus# • LAM Ching Wan |
| 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 |
| 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)

✉ TANG Leung Sang Nelson • YEO
Winnie (Dept of Clinical Oncology)

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000051> **Max, Mongelli; Yiu Kwan; Law Lap Kay; Magnus Hjelm and M. S. Rogers.** "Effect of Labour and Delivery on Plasma Hepatic Enzymes in the Newborn". *The Journal of Obstetrics and Gynaecology Research* vol.26, pp.61-63. Asia, 2000.02.
- <P000175> **Tang, N. L. S.; Hui J.; Law L. K.; Cheung K. L. and Fok T. F.** "Genetic Mutations of Prevalent Metabolic Diseases in Hong Kong Chinese". *Chinese Congress of Clinical Chemistry & Laboratory Medicine 2000 - Frontier in Clinical Chemistry and Laboratory Medicine* p.49 (SC5-4). Hong Kong: Hong Kong Society of Clinical Chemistry & Chinese Society of Clinical Chemistry, 2000.06.11.
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- <P000203> **Chan, L.; Y. Mak; B. Tomlinson; L. Baum; X. Wu; J. Masarel and C. Pang.** "Compound Heterozygosity of Leu 252 Val and Leu 252 Arg Causing Lipoprotein Lipase Deficiency in a Chinese Patient with Hypertriglyceridemia". *European Journal of Clinical Investigation* vol.30, pp.33-40. Blackwell Science Ltd, 2000.
- <P000204> **Lo, Y. M. Dennis; Sing-Fai Leung; Lisa Y. S. Chan; Anthony T.C. Chan; Kwok-Wai Lo; Philip J. Johnson and Dolly P. Huang.** "Kinetics of Plasma Epstein-Barr Virus DNA During Radiation Therapy for Nasopharyngeal Carcinoma". *Cancer Research* vol.60, pp.2351-2355. USA, 2000.
- <P000228> **Lo, Y. M. Dennis.** "Fetal DNA in Maternal Plasma". *Annals of the New York Academy of Sciences* vol.906, pp.141-147. New York, USA, 2000.04.
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- <P000232> **Zhang, J.; C. Fidler; M. F. Murphy; P. F. Chamberlain; I. L. Sargent; C. W. G. Redman; N. M. Hjelm; J. S. Wainscoat and Y. M. D. Lo.** "Determination of Fetal RhD Status by Maternal Plasma DNA Analysis". *Annals of the New York Academy of Sciences* vol.906, pp.153-155. New York, USA, 2000.04.
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- <P000787> **Wong, C.K.; J.P. Zhang; C.W.K. Lam; C.Y. Ho and N.M. Hjelm.** "Sodium Salicylate-Induced Apoptosis of Human Peripheral Blood Eosinophils is Independent of the Activation of C-Jun N-Terminal Kinase and p38 Mitogen-Activated Protein Kinase". *International Archives of Allergy and Immunology* vol.121, pp.44-52. Switzerland, 2000.

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- <P000813> **Tang, Nelson Leung-Sang; Hui Joannie; Law Lap-Kay; To Ka-Fai; Cheung Kam-Lau; Hjelm N. Magnus; Patrick Man-Pan Yuen and Fok Tai-Fai.** "Primary Carnitine Deficiency in the Chinese". *Chinese Medical Journal* vol.113 no.4, pp.376-380. PR China, 2000.04.
- <P001165> **Lam, Ching-Wan; Ying-Tat Mak; Yuk-Ming Dennis Lo; Sui-Fan Tong; Ka-Fai To and Fernand Mac-Moune Lai.** "Molecular Genetic Analysis of a Chinese Patient with Fabry Disease". *Chinese Medical Journal* 2nd ed., vol.113, pp.186-188. Beijing, China, 2000.02.
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- <P001762> **Lai, Kar Neng; Ka Bik Lai; Christopher C.K. Lam; Tak Mao Chan; Fu Keung Li and Joseph C.K. Leung.** "Changes of Cytokine Profiles During Peritonitis in Patients on Continuous Ambulatory Peritoneal Dialysis". *American Journal of Kidney Diseases* vol.35 no.4, pp.644-652. USA, 2000.
- <P001766> **Lo, Y.M.D.; S.F. Leung; L.Y.S. Chan; K.W. Lo; J. Zhang; A.T.C. Chan; J.C.K. Lee; N.M. Hjelm; P.J. Johnson and D.P. Huang.** "Plasma Cell-Free Epstein-Barr Virus DNA Quantitation in Patients with Nasopharyngeal Carcinoma". *Annals of the New York Academy of Sciences* vol.906, pp.99-101. New York, USA, 2000.04.
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RESEARCH PROJECTS

Gene Expression Profile Analysis of Human Prostate Cancer Cell Lines with or without Metastatic Feature

- ✉ JOHNSON Philip James • ZHONG Sheng
 ☐ 1 May 2000
 ❖ CUHK Research Committee Funding (Direct Grants)

Prostate cancer remains an important cause of death in men despite new treatment modalities. The high and persistent mortality resides in part in the presence of occult metastases at the time of treatment. The molecular events that define the metastatic prostate cancer cell remain incompletely understood. To delineate the molecular events that are responsible for metastasis, the researchers will apply representational differences analysis (RDA) in combination with a recently developed cDNA arrays technique to study altered gene expression profiles in cell line HL-7 and BE1, which were derived from primary and metastatic prostate cancer of a single patient. If identification of the altered gene expression profile in HL-7 and BE1 by RDA coupled with cDNA array is successful, novel genes responsible for metastases will be isolated. This information may provide insights on the mechanism of prostate cancer and development of anti-metastasis therapy for this cancer.
 (MD99102)

A Comprehensive Cytogenetic Characterization on Nasopharyngeal Carcinoma Cell Lines and Xenografts by Spectral Karyotyping and Comparative Genomic Hybridization

- ✉ LEUNG Sing Fai • WONG Nathalie
 ☐ 1 May 2000
 ❖ CUHK Research Committee Funding (Direct Grants)

Conventional cytogenetic studies on primary Nasopharyngeal Carcinoma (NPC) have been difficult due to the poor tumour growth *in vitro*. NPC cell lines and xenografts therefore represent invaluable source of material for the understanding of chromosomal alterations present in this malignancy. Their comprehensive karyotypic analysis has, however, been hampered by the many complex rearrangements found and the presence of marker chromosomes of uncertain origin. Much information on breakpoints and recurring translocations was hence unable to be extrapolated from these materials. *Spectral Karyotyping* (SKY) is a newly developed technique that allows the unprecedented discernment of chromosome rearrangements, and *Comparative Genomic Hybridization* (CGH) is a technique that

enables the genome-wide survey of regions of chromosomal gains and losses in a single experiment. Both techniques have been successfully developed within the researchers present investigative team. They therefore propose in here to apply SKY and CGH analysis to the study of chromosomal changes in 4 NPC xenografts (xeno-666, xeno-2117, xeno-1915 and xeno-S13) and 3 cell lines (HK-1, CNE-1 and CNE-2). In this study, almost all presently available NPC xenografts and cell lines will be analyzed. They anticipate information regarding recurring genetic aberrations and non-random breakpoints would be identified and such information would serve entry points for further investigations of genes residing on these sites in the NPC tumorigenesis.
 (MD99103)

A Comprehensive Genome Analysis on Hepatocellular Carcinoma by Spectral Karyotyping and Comparative Genomic Hybridization

- ✉ LEUNG Wai Tong Thomas • WONG Nathalie • JOHNSON Philip James
 ☐ 1 August 1999
 ❖ CUHK Research Committee Funding (Direct Grants)

Cytogenetic studies can provide an overall view of the numerical and structural chromosomal aberrations present. However, in the case of hepatocellular carcinoma (HCC), a common and highly malignant cancer in Hong Kong, cytogenetic information has been limited. This is largely due to the low mitotic index *in vitro* and the frequent unrecognizable chromosomal rearrangements found. Comparative genomic hybridization (CGH) is a molecular cytogenetic tool that allows the identification of regions of DNA sequences gains and losses in the entire tumour genome without the need of cell culture. However, the detection of chromosome translocations and the ability to distinguish between different sub-clones are limited in CGH, and such analyses remain the strength of karyotyping. Spectral Karyotyping (SKY) is a newly developed technique that allows structural chromosomal abnormalities to be confidently discerned by assigning a specific color to each chromosome. SKY is therefore an ideal technique to the study of complex chromosomal rearrangements detected in HCC. The combined application of CGH and SKY, whereby CGH can provide information on numerical aberrations and SKY on structural rearrangements, can offer a comprehensive picture into the genomic abnormalities of any tumour studied. In the present study, the researchers propose to apply SKY and CGH to the study of genetic aberrations in HCC. By doing so, they expect to gain invaluable information on the genetic alterations of HCC, which can be used

for correlation with tumour staging, metastatic potential and clinical outcome.
(MD99032)

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

✉ MOK Shu Kam Tony • CHAN Anthony Tak Cheung • LEUNG Wai Tong Thomas

□ 1 September 1999

❖ Roche Hong Kong Limited

This is the first world wide multi-center study on the use of Herceptin (Trastuzumab) in patient with HER-2 positive non- small cell lung cancer. Eligible patients will be screened for HER-2 positivity by immunohistological stain of the pathological specimen. Only the positive case will be randomized to receive either gemcitabine plus cisplatin, or gemcitabine plus cisplatin and Herceptin. The primary endpoints include response rate and survival. Toxicity and safety of these regimen will also be documented.
(MD99016)

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

✉ MOK Shu Kam Tony • LEUNG Wai Tong Thomas • CHAN Anthony Tak Cheung

□ 1 September 1999

❖ SmithKline Beecham International

Topotecan has been shown to be an effective drug in treatment of small cell lung cancer. As a single agent the response rate is about 40% in-patient with or without prior chemotherapy. Oral topotecan is potentially equal effective as intravenous infusion. This randomized study enrolls patients with prior chemotherapy for small cell lung cancer that relapse greater than or equal to 90 days after the initial treatment. Primary endpoints include response rate and survival.
(MD99019)

Investigation of Beta-Galactoside Alpha2, 6-sialyltransferase Activity and Its Regulation in Hepatocellular Carcinoma

✉ MOK Shu Kam Tony • JOHNSON Philip James • LAI Bo San Paul (Dept of Surgery) • POON Chuen Wai

□ 1 September 1999

❖ CUHK Research Committee Funding (Direct Grants)

Hepatocellular carcinoma (HCC) is prevalent in Hong Kong and China. Despite of well-recognized etiological factors including hepatitis B virus and cirrhosis, the manner in which these factors interact and the molecular mechanism by which they lead to HCC remains unclear. This investigation team, using isoelectric focusing, has identified AFP isoforms that are produced specifically by HCC and subsequently have defined the molecular structures of the predominant AFP isoforms. The presence of the HCC-specific isoforms is due to incomplete sialylation of the AFP glycoprotein molecules. In addition, many laboratories have indicated the importance of abnormal cellular sialylation in oncogenesis of other malignancy. Further understanding of the pathophysiological mechanism producing these highly specific isoforms should provide us valuable information relating to the oncogenesis of HCC.

Sialylation of AFP is known to be controlled by beta-galactoside alpha2, 6-sialyltransferase (ST6GalII). In this project the researchers plan to investigate the ST6GalII activities and the mechanism of its regulation during the development of HCC using HCC tissues and normal (control) liver tissues. Research plan is as follow:

- (1) Prof. P Lai will provide the fresh frozen surgical specimens (malignant and non-malignant liver tissues);
- (2) The ST6GalII activities will be measured by sialyltransferase activity assay;
- (3) To investigate the cause of the changed activities, the ST6GalII enzyme concentrations and the presence of inhibitors will be investigated by immunoassays, immunoprecipitation assay and Western blot analysis; and
- (4) If the change in ST6GalII activities is found to be caused by the change in the enzyme concentrations, the regulation of the ST6GalII production on gene transcription and mRNA alterate splicing levels will be investigated by Northern blot analysis.

(MD99033)

A Multicentre Phase III Trial of Taxotere and Doxorubicin vs. 5-Fluorouracil, Doxorubicin & Cyclophosphamide in Patients with Unresectable Locally Advanced Breast Cancer

✉ YEO Winnie

□ 1 March 2000

❖ Aventis Pharma Ltd.

Neoadjuvant chemotherapy for unresectable locally advanced breast cancer.
(MD99144)

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 | <p>Detection, Purification and Identification of Isoforms of Serum Glycoproteins: Use as Diagnostic and Dedifferentiation Markers in Cancer (CU97654)</p> <p>✉ CHAN Anthony Tak Cheung • JOHNSON Philip James • HJELM Nils Magnus (Dept of Chemical Pathology)# • HO Chung Shun (Dept of Chemical Pathology)</p> |
| 1997-98 | <p>An Open-Label Phase II Study of a 28-day Oral Regimen of 5-Fluorouracil Plus 776C85 in Patients with Advanced Nasopharyngeal Carcinoma (FUMB2011) (MD97180)</p> <p>✉ CHAN Anthony Tak Cheung • LEUNG Wai Tong Thomas • JOHNSON Philip James</p> |
| 1997-98 | <p>The Role of Biological Markers as Prognosticators in Undifferentiated Nasopharyngeal Carcinoma (MD97114)</p> <p>✉ CHAN Anthony Tak Cheung • HO King Wah Stephen* • TEO Man Lung Peter • CHIU Kwok Wing Samuel • JOHNSON Philip James</p> |
| 1998-99 | <p>A Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Effect of Cisplatin / Epinephrine Injectable Gel (Product MPI 5010) When Administered Intratumorally for Achievement of Treatment Goals in Recurrent or Refractory Squamous Cell Carcinoma of the Head and Neck (MD98011)</p> <p>✉ CHAN Anthony Tak Cheung • LEUNG Wai Tong Thomas • MOK Shu Kam Tony • YU Simon* • JOHNSON Philip James</p> |
| 1998-99 | <p>Analysis for Chromosomal Anomalies in Hepatocellular Carcinoma by Conventional Cytogenetics and Comparative Genomic Hybridization (CU98264)</p> <p>✉ JOHNSON Philip James • WONG Nathalie • LAI Bo San Paul (Dept of Surgery)</p> |
| 1998-99 | <p>Specific Inactivation of a Suppressor Gene PML in Small Cell Lung Cancer (CU98280)</p> |
| 1998-99 | <p>The Study of Genomic Alterations in Breast Cancer by Comparative Genomic Hybridization (MD98098)</p> <p>✉ JOHNSON Philip James • WONG Nathalie • TANG Leung Sang Nelson (Dept of Chemical Pathology)</p> |
| 1998-99 | <p>A Specific Isoform of Alpha-fetoprotein for the Diagnosis of Hepatocellular Carcinoma (MD98128)</p> <p>✉ JOHNSON Philip James • POON Chuen Wai</p> |
| 1997-98 | <p>Alterations of the Growth and Transformation-Suppressor PML in Hepatocellular Carcinoma and Nasopharyngeal Carcinoma (CU97653)</p> <p>✉ LEUNG Sing Fai • CHAN Yeuk Hon John# • CHAN Anthony Tak Cheung • LIEW Choong Tsek (Dept of Anatomical & Cellular Pathology) • JOHNSON Philip James</p> |
| 1996-97 | <p>Randomised Trial of Radiotherapy Alone Versus Concomitant Radiotherapy and Chemotherapy in Locoregional Advanced Nasopharyngeal Carcinoma (MD96152)</p> <p>✉ LEUNG Wai Tong Thomas • CHAN Anthony Tak Cheung • TEO Man Lung Peter • LEUNG Sing Fai</p> |
| 1997-98 | <p>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)</p> <p>✉ LEUNG Wai Tong Thomas • CHAN Anthony Tak Cheung</p> |
| 1997-98 | <p>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)</p> <p>✉ LEUNG Wai Tong Thomas • JOHNSON Philip James • CHAN Anthony Tak Cheung • YEO Winnie</p> |
| 1997-98 | <p>Phase I/II Study of Topotecan and Oral Etoposide in Treatment of Small Cell Lung Cancer (MD97012)</p> |

- 1997-98 MOK Shu Kam Tony • CHAN Anthony Tak Cheung • YEO Winnie • YIM Ping Chuen Anthony (Dept of Surgery) • JOHNSON Philip James
- 1997-98 Molecular Prognostication of Therapeutic Response of Liver and Lung Cancers (MD97082)
 1997-98 MOK Shu Kam Tony • CHAN Yeuk Hon John#
- 1998-99 Universal DNA Amplification by Degenerate Oligonucleotide-Primed PCR in the Study of Genomic Aberrations in Nasopharyngeal Carcinoma (MD98037)
 1998-99 MOK Shu Kam Tony • WONG Nathalie • TO Ka Fai (Dept of Anatomical & Cellular Pathology)
- 1998-99 OGT 719-003 HCC Study (BL98040)
 1998-99 MOK Shu Kam Tony • LEUNG Wai Tong Thomas • 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)
 1998-99 MOK Shu Kam Tony
- 1997-98 High Dose Adjuvant Chemotherapy and Peripheral Stem Cell Transplant for High Risk Breast Cancer Patients (MD95266)
 1997-98 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)
 1997-98 YEO Winnie • KWAN W. H.* • LEUNG C. M.*
- 1997-98 Phase II Study of Taxotere and Epirubicin for Metastatic Breast Cancer (MD97177)
 1997-98 YEO Winnie • MOK Shu Kam Tony • LEUNG Wai Tong Thomas • CHAN Anthony Tak Cheung • JOHNSON Philip James • KWAN W. H.* • LAM K C* • TSE K. K.* • CHIU K W*
- 1997-98 Phase II Trial to Document the Efficacy and Tolerability of Daily Dose of 2.5mg Femara in Postmenopausal Chinese Women with Advanced or Metastatic Breast Cancer as Second Line Hormonal Treatment after Tamoxifen (MD97165)
 1997-98 YEO Winnie • KWAN W. H.* • MOK Shu Kam Tony • CHAN Anthony Tak Cheung • LEUNG Wai Tong Thomas • JOHNSON Philip James
- 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)
 1997-98 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)
 1997-98 YEO Winnie • JOHNSON Philip James • LEUNG Wai Tong Thomas
- 1997-98 Phase II Trial to Document the Efficacy and Tolerability of Daily Dose of 2.5mg Femara in Postmenopausal Chinese Women with Advanced or Metastatic Breast Cancer as Second Line Hormonal Treatment After Tamoxifen (FEM-HK-01) (MD97179)
 1997-98 YEO Winnie • KWAN Wing Hong • MOK Shu Kam Tony • LEUNG Wai Tong Thomas • CHIU Kwok Wing Samuel • JOHNSON Philip James
- 1998-99 A Prospective Study Using Sequencing Analysis to Determine Mutation Variants of Hepatitis B Virus (HBV) Genome and their Incidence in Cancer Patients with HBV Reactivation during Chemotherapy (MD98038)
 1998-99 YEO Winnie • STEINBERG Joyce Leta# • ZHONG Sheng • TAM Siu Lun John (Dept of Microbiology) • CHAN Yeuk Hon John# • JOHNSON Philip James

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000020> **Leung, T. W. T.; G. Cheng; C. H. Chui; S. K. W. Ho; F. Y. Lau; J. K. J. Tjong; T. C. C. Poon; J. C. O. Tang; W. C. P. Tse; K. F. Cheng and Y. C. Kong.** "Yuehchukene, a Bis-Indole Alkaloid, and Cyclophosphamide Are Active in Breast Cancer *in vitro*". *Chemotherapy* vol.46, pp.62-68. 2000.01.
- <P000024> **Johnson, Philip J.** "Benign and Malignant Tumors of the Liver". *Liver Disease Diagnosis and Management* 1st ed., pp.310-320. Philadelphia: Churchill Livingstone, 2000.
- <P000621> **Leung, Thomas W.T.; Wan-Yee Lau; Stephen Ho; Simon Yu and A.M.Y. Tang.** "Post-Operative Adjuvant Intra-Arterial Lipiodol-Iodine-131 for Operable Hepatocellular Carcinoma Reduced Recurrence and Prolonged Survival - Report on a Prospective Randomised Study after Longer Follo". *HPB (Proceedings - 4th World Congress of IHPBA)* vol.2 no.2, p.171. Brisbane, Australia: ISIS Medical Media, UK, 2000.
- <P000707> **Zhong, Sheng; Winnie Yeo; C.K. Lin; Mandy Tang; Xiao-Rong Lin; M. Ho; P. Hui and Philip J. Johnson.** "New Genotype of TT Virus and Its Prevalence in Hospitalized Patients of Hong Kong". *Journal of Tumor Marker Oncology* vol.15 no.1, p.62. Hong Kong: The International Academy of Tumor Marker Oncology Inc Publishers, 2000.03.23.
- <P000708> **Lau, Kwok Kwong; Kwok Wai Wong; Wing Chong Ho; Thomas Sik To Lai; Kam Cheong Lee and Thomas Wai Tong Leung.** "Hepatocellular Carcinoma Presenting with Right Supraclavicular Lymph Node Metastasis and Superior Mediastinal Syndrome". *Liver* vol.20, pp.184-185. Denmark, 2000.04.
- <P000744> **Zhong, Sheng; Winnie Yeo; C.K. Lin; Xiao-Rong Lin; M.W.M. Tang; W.M. Ho; P. Hui and Philip J. Johnson.** "Quantitative Analysis of TT Virus Dna in Peripheral Blood of Patients with Cancers". *Journal of Tumor Marker Oncology* vol.15, p.61. Hong Kong: The International Academy of Tumor Marker Oncology Inc. Publishers, 2000.03.23.
- <P000802> **Chan, Anthony Tak Cheung.** "Multimodality Approaches to the Treatment of the Hepatocellular Carcinoma". *Journal of Tumor Marker Oncology* vol.15, pp.29-30. Austria, 2000.03.
- <P000807> **Fan, Chung-Sze; Nathalie Wong; Sing-Fai Leung; Ka-Fai To; Kwok-Wai Lo; Siu-Wah Lee; Tony S.K. Mok; Philip J. Johnson and Dolly P. Huang.** "Frequent *c-myc* and *Int-2* Overrepresentations in Nasopharyngeal Carcinoma". *Human Pathology* vol.31 no.2, pp.169-178. 2000.02.
- <P000939> **Mok, Tony S.K.; Benny Zee; Anthony T.C. Chan; Winnie Yeo; Wei Tse Yang; Anthony Yim; Sing Fai Leung; Binh Nguyen; Thomas W.T. Leung and Philip Johnson.** "A Phase II Study of Gemcitabine Plus Oral Etoposide in the Treatment of Patients with Advanced Nonsmall Cell Lung Carcinoma". *Cancer* vol.89 no.3, pp.543-550. USA, 2000.
- <P000989> **Yeo, Winnie.** "Quality of Life". *Oncology Forum* vol.3 no.3, p.14. Hong Kong, 2000.01.
- <P000991> **Teo, Peter Man Lung; Sing Fai Leung; Wai Yee Lee and Benny Zee.** "Intracavitary Brachytherapy Significantly Enhances Local Control of Early T-Stage Nasopharyngeal Carcinoma: The Existence of a Dose-Tumor-Control Relationship above Conventional Tumoricidal Dose". *International Journal of Radiation Oncology Biology Physics* vol.46 no.2, pp.445-458. USA, 2000.
- <P000992> **Wong, T.M.; W. Yeo; L.W. Chan and T.S.K. Mok.** "Hemorrhagic Pyelitis Ureteritis and Cystitis Secondary to Cyclophosphamide: Case Report and Review of the Literature". *Gynecologic Oncology* vol.76, pp.223-225. 2000.
- <P000993> **Yeo, Winnie.** "Palliative Care in the Future". *Oncology Forum* vol.3 no.3, p.2. Hong Kong, 2000.
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RESEARCH PROJECTS

A Population-based Cohort Study on Phytoestrogens Intake and Bone Loss in Chinese Early Postmenopausal Women

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

☐ 1 October 1999

❖ Health Services Research Fund, Hospital Authority

Objectives: The study aims to test the hypothesis that high level of phytoestrogens consumption is associated with reduced bone loss during early menopausal years in Chinese women.

Design: An 18 months prospective study will be carried out in 450 Hong Kong Chinese menopausal women (within the first 7 years of menopause). Subjects will be recruited from population based samples. Data collection will be conducted through face to face interview using validated structured questionnaire. Repeated measurements will be taken at 9 months and then at 18 months followup.

Main outcome measures: The outcome variables will be bone changes in the group belonging to the high isoflavonoid intake group compared with the other intake groups. Comparison will also be made for subjects with high cumulative phytoestrogens intake with those with lower level of intake over the study period. Comparison of bone changes among different intake levels will also be made.

Results: Besides the usual descriptive statistics used to summarize the baseline data, the outcome variable, change in bone mineral density will be related to the baseline phytoestrogens intake as well as cumulative intake categories using the multiple regression model, controlling for the presence of the confounding factors.

Conclusions: This will be the first population-based cohort study of phytoestrogens consumption and bone loss in Chinese early postmenopausal women. The results will have vast implications for prevention strategies for bone loss and osteoporosis in postmenopausal women and subsequent fracture risks. (MD99011)

Preventive Medicine Activities by Hong Kong Doctors

✉ James Arthur DICKINSON • CHAN Shiu Yee Cynthia • TANG Shao Fen Joyce

☐ 1 July 1999

❖ Health Services Research Fund, Hospital Authority

Objective: To ascertain the beliefs of doctors in primary care in Hong Kong about preventive activities they should undertake and the factors that affect their activities in this field. This study will use qualitative focus groups and interviews with a wide range of different primary care doctors, followed by development of a questionnaire survey of a stratified sample of 400 doctors.

The participants will be primary care doctors: Family Physicians and general practitioners, including specialists who are undertaking substantial amounts of adult primary care, in government, hospital and private clinics.

The researchers expect that the first part of the project will produce a rich understanding about practitioners' understanding of the role and possibilities of preventive activities along with their beliefs about their role in this field and difficulties in practice for primary care doctors. The survey will produce detailed information about what Hong Kong doctors do and the limits to their capability. This will then allow better planning about continuing medical education and policy change that will assist them to do their work better, and use resources more effectively.

(MD99007)

Cholesterol Management in Primary Care in Hong Kong

✉ James Arthur DICKINSON • WUN Yuk Tsan Kyran Patrick

☐ 1 May 2000

❖ Parke-Davis, A Division of Warner-Lambert (HK) Ltd.

High levels of lipids in the blood are an important risk factor for coronary heart disease. Treatment reduces the risks of heart and vascular disease and death, therefore, primary care doctors treat patients with this problem using a variety of drugs. Because of the compartmentalized nature of the Hong Kong Health Care System, it is difficult for private practitioners to treat patients consistently in Hong Kong.

This study will pilot a method to evaluate the effectiveness of treating patients with high blood lipids in primary care to determine the extent to which the recommended target levels are achieved, and to find factors associated with those target levels. The study will identify areas and approaches for future larger scale studies on the improvement of such management in Hong Kong. (MD99120)

Tai Chi and Resistance Training Exercise - Would These Really Improve the Health of the Elderly?

✉ 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*

☐ 1 September 1999

❖ Research Grants Council (Earmarked Grants)

The objectives of the study are to investigate and compare the health benefits of Tai Chi and Resistance Training Exercise in elderly Hong Kong Chinese. A randomized controlled trial will be conducted. 150 elderly men and women will be allocated to Tai Chi for 3 times a week; Resistance Training Exercise for 3 times a week, or placebo. Insulin sensitivity, lipid profile, urine catecholamine levels, muscle strength, coordination, bone mineral density and quality of life will be measured at baseline, 6 months and 12 months. The changes in the three intervention groups will be compared.
(CU99303)

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

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

☐ 1 October 2000

❖ New Zealand Dairy Board

Two hundred postmenopausal Chinese women were randomized to receive 800mg calcium equivalent of milk powder or placebo. Bone density and biochemical markers were studied every 6 months for 2 years. The effects of milk supplementation on preventing bone loss in postmenopausal Chinese women will be studied.

This is a 12 month extension of the project. The study results will be formally analysed at 12 months, 24 months and 36 months after Anlene supplementation.
(MD99068)

A randomised, multi-centre, double-dummy, parallel-group comparison of Seretide RPID (50/100µg strength) twice daily with budesonide BADPI 400 µg twice daily in steroid experienced adolescents and adults with reversible airways obstruction

✉ LEE Albert • NG VENTURA Lorna

☐ 1 September 1999

❖ Glaxo Wellcome China Limited

A 12 week treatment study to compare the effectiveness, safety and tolerability of inhaled Seretide (50/100µg strength) twice daily versus inhaled budesonide 400µg twice daily in treating

steroid experienced patients with reversible airways. Please note that steroid naive patients will not be eligible to participate in the study. Eligible patients are required to participate in a 2 week run-in period, a 12 week treatment period, and may complete an optional 2 week follow up period. Patients are expected to attend 4 scheduled study visits, and an optional visit if required. Patients will be permitted to use rescue Ventolin throughout the study as required. Patients are required to complete a Daily Record Card (DRC) capturing morning and night peak flow, day and night time symptoms scores, rescue Ventolin usage and any adverse events throughout the study. Randomisation is 1:1 and approximately 400 patients will be recruited in hospital centres throughout the Asia-Pacific region. Primary assessment is based on the efficacy on mean morning PEF during 12 week treatment period, using the predicted lung function as the normal range. Urinary cortisol measurements will be taken for safety. Countries involved are Hong Kong, Malaysia, Philippines, Singapore, Taiwan and Thailand.
(MD99122)

Multi-centre Influenza Trial of RWJ-270201

✉ LEE Albert • TSANG Kwong Ka • LEE Shiu Hung (School of Public Health)

☐ 1 February 2000

❖ Johnson & Johnson (Hong Kong) Limited

Introduction: RWJ-270201 is one of a new class of anti-viral drugs, called neuraminidase inhibitors, which has been shown to be a potent and selective inhibitor of influenza A and B neuraminidases in both *in vivo* and *in vitro* preclinical testing. It is also efficacious in humans with experimentally induced influenza.

Objective: To assess the efficacy and safety of RWJ-270201 for the treatment of acute influenza A and Influenza B infections in healthy adults.

Setting: In this study centre, subjects will be recruited at the Accident and Emergency Department of a district general hospital in Hong Kong.

Study Design: This is a randomized, double-blind, placebo-controlled, multi-centre study. Approximately 450 healthy adults, presented with flu-like symptoms, in the Asia-Pacific region will be enrolled and randomly assigned to one of the three treatment groups, including a placebo group.

Outcomes: All subjects will maintain diary cards for four weeks, recording relevant information on course of the disease. In addition, clinical laboratory tests, cultures, influenza-related complications and adverse events will be monitored during the follow-up visits.

Conclusion: RWJ-270201, if proven to be efficacious and safe, can contribute to the treatment of acute influenza A and influenza B infections in healthy adults.
(MD99128)

Provision of Service for Design of Statistical System for Logging Air Pollution Related Disease

- ✉ WONG Tze Wai • WUN Yuk Tsan Kyran Patrick • YU Tak Sun Ignatius • TAM Wai San Wilson • LAU Tai Shing (Dept of Statistics) • WONG Chit Ming* • Anthony Hedley* • LAM Tai Hing* • THACH T. Q.*
- ☐ 1 November 1999
- ❖ Environmental Protection Department, HKSAR Government

The objective of this consultancy is to design a record system for the use in primary health care setting for capturing time series data of illnesses related to air pollution. The data so obtained should be amenable to statistical analysis to investigate the relation with air pollutant concentrations on a daily basis. The purpose of the study is to determine the magnitude of the effect air pollution on illnesses seen in primary care settings so that a comprehensive health audit of air pollution can be performed. The appropriate "tool" for the study is to be developed in this Consultancy. (MD99070)

The Study of the Short Term Effects of Air Pollution on Morbidity of the General Population and the Associated Cost of Illness

- ✉ WONG Tze Wai • WUN Yuk Tsan Kyran Patrick • YU Tak Sun Ignatius • TAM Wai San Wilson
- ☐ 1 May 2000
- ❖ Environmental Protection Department, HKSAR Government

Data on illnesses of the respiratory and cardiovascular systems are collected on a daily basis from 10 to 12 private family physicians for 9 to 12 months. Corresponding data on daily air pollutant concentrations are obtained to provide time series datasets to find out the association between morbidity in the community and air pollution. A Poisson regression model will be constructed to adjust for cyclical and other variations. Risk estimates of morbidity increase will be desired for a unit increase in pollutant concentration. The associated cost of illnesses for various morbidities will be estimated using Summary data on cost of illnesses from published sources. The study provides an overall estimate of the effects of air pollution on primary case (non-hospitalized illnesses) and their costs. (MD99125)

Lung Cancer Mortality in Relation to Silicosis: A Cohort Study of Hong Kong

- ✉ YU Tak Sun Ignatius • WONG Tze Wai • CHAN Chi Kuen Alan* • LEUNG Chi Chiu* • TAM Cheuk Ming*
- ☐ 1 October 1999
- ❖ Research Grants Council (Earmarked Grants)

Occupational exposure to crystalline silica dust is a well known cause for silicosis - a pneumoconiosis (with lung fibrosis) and one of the most common occupational diseases in Hong Kong. The International Agency for Research on Cancer has recently classified respirable crystalline silica as a confirmed human carcinogen for lung cancer but there is still a lot of debate in the literature about the strength of the evidence.

The current study will look at the mortality experience of a cohort of silicotic patients registered in the Pneumoconiosis Clinic of the Department of Health from 1981 to 1997 inclusive. The occurrence of deaths from lung cancer in the cohort will be compared to that of the general population of Hong Kong taking into consideration sex, age and calendar time at death. Adjustments for smoking (a well-known cause for lung cancer) and occupational exposures to other known lung carcinogens will be made.

If lung cancer deaths are really more common among patients with silicosis, and especially if a dose-response relationship can be demonstrated, more stringent preventive measures should be called for in order to protect workers exposed to silica dust from this deadly disease. (CU99328)

A Study on the Neurobehavioural Effects of Occupational Exposure to Organic Solvents Among Printing Workers in Hong Kong

- ✉ YU Tak Sun Ignatius • WONG Tze Wai
- ☐ 1 October 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

The present study will look into the neurobehavioural effects (such as memory, mood, psychomotor performance) of long term exposure to organic solvents among industrial workers in Hong Kong. Male printing machine operators from two printing factories will be included as the study group as they have constant significant exposure to organic solvents due to their job nature and working environment. The subjective neurobehavioural symptoms will be obtained through a standardized questionnaire and the objective neurobehavioural tests performance will be assessed using the Neurobehavioural Core Test Battery of the World Health Organization. Results from the study group will be compared to those of a non-exposed control group comparable in age and educational background. Different indices of

exposure, including the air concentration of organic solvents in the current working environment, years of exposure, the level of metabolites in urine and a composite cumulative exposure estimate, will be used to assess the exposure of the individual worker. The dose-response relationships between different exposure indices and neurobehavioural deficits will be explored with a view of establishing 'safe' exposure standards which will be able to protect the majority of the workers exposed to organic solvents at work.
(MD99034)

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

Edition Title/Investigators

1997-98 Computer-Assisted Interactive Tutorials on Clinical Problem Solving in Family Medicine (MD97022)
 ✎ CHAN Shiu Yee Cynthia • WUN Yuk Tsan Kyran Patrick • CHAN Keith*

1997-98 Qualitative Study of HIV/AIDS Risk Behaviour among Hong Kong's Teenage "Street Roamers" and Approaches for Harm Reduction (MD97094)
 ✎ CHAN Shiu Yee Cynthia • TANG Shao Fen Joyce

1997-98 Developing Problem Based Learning Tutorials in Family Medicine (MD97130)
 ✎ CHAN Shiu Yee Cynthia • WUN Yuk Tsan Kyran Patrick • James Arthur DICKINSON

1996-97 A Randomized Controlled Trial of the Effect of Milk Supplementation on the Rate of Bone Loss in the Post Menopausal Women in Hong Kong (MD96136)
 ✎ LAU Edith Ming Chu

1997-98 A Randomized, Parallel-Group Study to Compare the Effects on Bone Density of Oral Alendronate and Calcium Supplementation or Calcium Supplementation Dose in Chinese Patients on High Dose Inhaled Steroid (MD97098)
 ✎ LAU Edith Ming Chu • WOO Jean (Dept of Medicine & Therapeutics) • LAI Kei Wai Christopher (Dept of Medicine & Therapeutics)

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 Collagen Type I Alpha I Gene, Estrogen Receptor Gene, and Lifestyle Factors in the Etiology of Osteoporosis in Chinese (MD98099)
 ✎ LAU Edith Ming Chu • HO CHAN Suzanne • WOO Jean (Dept of Medicine & Therapeutics) • CRITCHLEY Julian A J H (Dept of Medicine & Therapeutics)

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*

1998-99 Smoking and Health in Hong Kong Women (MD98119C)
 ✎ LAU Edith Ming Chu • WOO Jean (Dept of Medicine & Therapeutics) • HEDLEY A J* • LAM T H* • AU T K* • YAU Helen* • IP Shirley*

1997-98 Social Costs of Drug Abuse in Hong Kong (SS97030)
 ✎ LEE Albert • CHEUNG Yuet Wah (Dept of Sociology) • CHIEN James M. N.* • LEE Shiu Hung (School of Public Health) • LAM K C*

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RESEARCH PROJECTS

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

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□ 1 September 1999

❖ CUHK Research Committee Funding (Direct Grants)

Radiation therapy is an important treatment modality for brain tumours and cancer of the head and neck regions. However, the use of high radiation dose is limited by delayed radiation reactions of the normal brain, the pathophysiology of which is incompletely understood. Recent advances in magnetic resonance has enabled the study of brain metabolites by magnetic resonance spectroscopy, and the study of cerebral vascular perfusion by magnetic resonance perfusion imaging. Whilst these offer a new opportunity to study the pathophysiology of radiation effect on the brain, the inherent difficulty in distinguishing tumour tissue and brain tissue inflicted with radiation-induced injury could introduce uncertainty in the study findings in patients with cerebral tumours. Nasopharyngeal carcinoma is a very commonly occurring cancer in Hong Kong. It is regularly treated by radiation therapy and part of the temporal lobes are frequently incidentally irradiated. Late radiation-induced injury to the temporal lobes is one of the most important long term complication for these patients. Already an important clinical problem to be studied by itself, radiation-induced temporal lobe injury also offer an opportunity of a model of the response of a normal brain to therapeutic radiation. The researchers therefore propose to study longitudinally temporal lobe lesions after radiation therapy in 50 patients using magnetic resonance spectroscopy and perfusion imaging with the objectives of documenting the vascular perfusion and metabolite changes in late delayed radiation-induced injury of the brain and its evolution with time, and identifying prognostic factors in perfusion and metabolites in the prediction of progressive severe changes.
(MD99035)

Phosphorous-31 Magnetic Resonance Spectroscopy in the Evaluation of Progressive Brain Tumour versus Radiation-induced Brain Injury

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❖ Germany/Hong Kong Joint Research Scheme

The diagnosis of progressive brain tumour after radiation therapy is important in both the prognosis and further management of the disease. Morphological differentiation from radiation induced injury on computed tomography (CT), or magnetic resonance imaging (MRI) has not been successful as considerable overlapping of imaging features exists for both conditions.

Recent studies have shown the potential of proton magnetic resonance spectroscopy (MRS) in differentiating progressive brain tumour and radiation induced injury. A significant elevation of choline (Cho)/ creatine (Cr) ratio is seen in spectra of progressive tumour as compared to radiation-induced injury. Elevation of choline is attributed to the increase of cell membrane synthesis in tumour. However, there is an overlap of value with those of radiation necrosis since choline may also be elevated from necrosis related-myelin breakdown, Cho/Cr ratio may be elevated, especially in the more severe radiation necrosis, which may mimic progressive tumour.

An increase of phosphomonoester (PME) signal intensity has been shown to be proportional to the rate of membrane phospholipid synthesis and it is seen in brain tumour P-31 MR spectra, whereas radiation-induced injury, being a catabolic process, would result in elevation of phosphodiester (PDE) signal. The PME/PDE ratio therefore would in principle be different in tumour associated with a rapid membrane synthesis or tissue growth from necrosis with catabolic membrane breakdown. The objective of the project is to study the PME/PDE intensity ratio on phosphorous-31 magnetic resonance spectroscopy (P-31 MRS) in patients with suspicion of progressive brain tumour after radiation therapy or radiation induced brain injury, with the aim of increasing the specificity of diagnosis of progressive brain tumour against radiation induced brain injury.
(MD99091)

To Study the Correlation Between Color Power Angiography Ultrasound Measurement of Breast Tumor Vasculature and Immunohistochemical Analysis of Microvessel Density for the Quantitation of Angiogenesis

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Tumor angiogenesis (or neovascularisation) is the formation of new capillaries from the existing vascular network that is upregulated in cancer and is essential for both tumor growth and dissemination. Histologic microvessel density measured by immunohistochemical staining of endothelial cells is a recognized surrogate of tumor angiogenesis. This method is invasive and limited by random sampling error due to intratumoral heterogeneity.

Breast cancer is the second leading cause of cancer death in women in Hong Kong and is rising in incidence with an annual incidence of 34 per 100 000 population. Breast tumors are ideally suited for Doppler ultrasound studies due to their superficial location. Neovascularity has been documented as a chaotic arrangement of vessels in all directions with arteriovenous shunts showing abnormal high-velocity signals at Doppler imaging in rat carcinoma, as well as *in vivo* breast carcinoma in several large series. Color power angiography (CPA) ultrasound after the

administration of a blood pool microbubble contrast agent has the ability to aid characterization of tissue microvessels.

The aim of this study is to quantitate *in vivo* angiogenesis by CPA ultrasound of primary breast cancers with and without contrast, and to determine the relationship between ultrasound derived characteristics of tumor microvessels and histologic capillary density. A quantitative ultrasound model for the measurement of tumor vascularity, comparable to histologic microvessel count, will be established. This will have the advantage of allowing the entire tumor volume to be sampled, and will be a cheap, noninvasive, easily reproducible method for estimating tumor angiogenesis in diagnostic practice. It will be applicable for predicting prognosis, response to standard systemic treatment and anti-angiogenic agents, not only for breast cancer but also for a wide range of other malignancies.

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RESEARCH PROJECTS

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

✉ CHAN Chung Ngor Juliana • NG Chor Yin • LEE Shao Chin • LEE Suk Kuen • Clive Stewart COCKRAM • CRITCHLEY Julian A J H

☐ 1 June 2000

❖ CUHK Research Committee Funding (Direct Grants)

Diabetes mellitus is a common disease occurring in about 10% of our general population, with type 2 diabetes being the predominant form. About 17% of patients with type 2 diabetes have early onset of disease (≤ 40 years). 50% of them are obese and 50% have positive family history. In their previous studies, the researchers have found 12% of the early onset diabetes can be accounted by mutations in mitochondrial gene, hepatocyte nuclear factor-1 α , glucokinase and amylin.

Obesity is an important risk factor for diabetes and genetic defects have been associated with development of diabetes and insulin resistance. In this study, the researchers aim to investigate for the prevalence of mutations or polymorphisms in 4 obesity-related genes which have never been studied in Chinese type 2 diabetic patients. These include the melanocortin-4 receptor which is involved in the leptin signalling pathway for the control of appetite, the uncoupling protein-2 and -3 which are involved in thermogenesis and energy metabolism, and TNF- α which stimulate lipolysis, induce apoptosis and inhibit differentiation of adipose tissues and associated with insulin resistance.

Searching for mutations or polymorphisms in these genes in both lean and obese early onset type 2 diabetics will provide important insight on the genetic modifying effects on the development of obesity-related diabetes in our population. These polymorphisms may also serve as markers for screening susceptible individuals which will allow early diagnosis and treatment to be made.

(MD99037)

Laser Therapy of Hypertrophic Scars

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

☐ 31 December 1999

❖ Research Grants Council (Earmarked Grants)

Introduction: Hypertrophic burn scars are not only disfiguring but also functionally disabling. Pulse dye laser (PDL) is a vascular laser that targets at the hemoglobin and the surrounding blood vessel that lead to selective vascular destruction. As vascular proliferation is an essential part of a scar formation, by removing these vessels, scar formation could be inhibited. Unlike patients with lighter skin types, Asian patients have more melanin in their dermis. This melanin can act as a competing target chromophore for hemoglobin, causing an increased risk of adverse effects. Furthermore, most studies looked at the role of pulsed dye laser in treating chronic hypertrophic scar, its role, as a preventive measure has not been studied. Study assessing the effectiveness and adverse effects of pulsed dye laser in the prevention and treatment of hypertrophic scar in Chinese subjects is therefore necessary.

Objective: To assess the role of pulsed dye laser therapy in (a) Treatment of chronic hypertrophic burn scars (b) Prevent the formation of hypertrophic burn scar

Subjects: (a) 70 patients with burn scar in areas where hypertrophic scar is prone to develop (b) 70 patients with linear post burn erythematous hypertrophic scars will be recruited for the study.

Treatments: At 8-week intervals for a period of 12 months, half of a hypertrophic scar on an individual patients will be treated with laser while the other half of the scar will be untreated and served as control. Each laser treatment will consist of application of 585nm flashlamp pumped pulsed dye laser (PDL) to the hypertrophic scars with an 8.0J/cm² and 3-5mm spot size.

Measurement: Scar will be mapped with a translucent paper at the first appointment so as to ensure consistency of location. During each visit, patients are assessed before laser therapy by clinical photographs, ultrasonography (for thickness), cutometer (viscoelasticity) and clinical rating (change in colour, consistency and other symptoms such as pain, dysesthesia, itchiness, hypersensitivity and blistering).

(CU99299)

Eradication of Helicobacter Pylori Infection for Secondary Prevention of Upper Gastrointestinal Hemorrhage in Patients with Ischemic Heart Disease and Stroke: A Prospective Randomized Study

✉ CHAN Ka Leung Francis • SUNG Joseph Jao Yiu • LUK Yiu Wing* • LAI Moon Sing* • LI Ting Ho* • LI Michael Kin Kong*

☐ 1 July 1999

❖ Health Services Research Fund, Hospital Authority

Background: Ischemic heart disease and stroke are amongst the five leading causes of death in Hong

Kong. Aspirin, a non-steroidal anti-inflammatory drug (NSAID), has been well documented in preventing these dreadful conditions. However, aspirin is also a major cause of peptic ulcer bleeding which results in significant morbidity and mortality. The risk of gastrointestinal (GI) toxicity of aspirin is much higher in patients with past history of upper GI bleeding. Prevention by acid-suppressive drugs, though effective, is expensive and requires life-long treatment. Previously we showed that *helicobacter pylori* infection significantly contributes to the development of NSAID-induced peptic ulcers. Our recent pilot study suggests that curing the infection alone is as effective as long-term acid suppressive treatment (omeprazole) in preventing recurrent ulcer bleeding in high-risk aspirin users with past history of GI bleeding.

Objective: To study whether eradication of *H. pylori* alone is effective for secondary prevention of aspirin-associated upper GI bleeding in patients with ischemic heart disease or stroke.

Design: 6-month prospective randomized controlled trial.

Subjects: Patients are eligible if they: (1) have *H. pylori* infection, (2) require aspirin for ischemic heart disease or stroke, and (3) have past history of peptic ulcer bleeding. *Interventions:* Eligible patients are randomized to receive either omeprazole as maintenance or 1-week of anti-helicobacter therapy followed by placebo for 6 months. Endoscopy is performed if patients develop upper GI bleeding or severe epigastric pain. *Outcome Measure:* The primary endpoint is the cumulative incidence of upper GI bleeding. The number of patients needing treatment and the costs needed to prevent one event of upper GI bleeding in the two treatments arms are compared.

(MD99009)

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

✉ CHOW Chun Chung Francis • Clive Stewart COCKRAM

☐ 1 May 2000

❖ Novo Nordisk Health Care (Asia Pacific) Pte Ltd

Primary Objective:

To study the glycaemic efficacy, as measured by HbA_{1c}, of five different doses of DRF2593 compared to placebo in oral hypoglycaemic agent (OHA)-and/or diet-treated patients with type 2 diabetes.

Secondary Objectives:

To study the safety of five different doses of DRF2593 compared to placebo in OHA-and/or diet-treated patients with type 2 diabetes.

To study the effect of five different doses of DRF2593 on fasting plasma free fatty acids(FFA) and triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol, VLDL cholesterol, total ApoB, plasma glucose, insulin and flucosamine compared to placebo in OHA-and/or diet-treated patients with type 2 diabetes.

Trial Design:

This is a 4-month randomised, multi-centre, double-blind, parallel-group, placebo-controlled trial to investigate the efficacy and safety of five doses of DRF2593 in OHA-and/or diet-treated patients with type 2 diabetes. The trial will include a screening visit (Visit 1) to assess patients' eligibility. Eligible patients previously treated with OHAs will undergo a 4-week OHA wash-out period before randomisation, whereas eligible patients previously treated with diet only will proceed to Visit 2 after a one-week run-in period. At Visit 2 all patients will be randomised to receive one daily dose of DRF2593 0.25 mg, 0.5 mg, 1.0 mg, 2.0 mg and 5.0 mg or placebo tablets for 16 weeks.

(MD99129)

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

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

☐ 1 October 1999

❖ Research Grants Council (Earmarked Grants)

Diabetes mellitus is a common chronic disease occurring in about 10% of our general population. Genetic factors have been implicated in this disease as about 40% of diabetic patients give a positive family history of diabetes. Type 2 diabetes is the predominant form of diabetes in our population. In contrast to Caucasians, the prevalence of autoimmune Type 1 diabetes is low even in-patients with early onset of disease.

Type 2 diabetes is genetically and phenotypically heterogeneous. The candidate gene and positional cloning approaches have been used to identify genes involved in its pathogenesis. In this study, the researchers shall carry out a genome-wide search for Type 2 diabetes genes in Chinese. From a previous RGC-supported study, they have recruited 60 families with early-onset Type 2 diabetes. 100 affected sib-pairs (ASPs) will be identified. Initially, microsatellite markers with significant linkage to Type 2 diabetes in other ethnic groups will be genotype for testing of linkage in our population. Subsequently, a genome-wide search will be conducted with microsatellite markers at an average interval of 10 centiMorgans (cM). The results will be analyzed by two-point and multipoint linkage

analysis to identify susceptibility loci and for exclusion mapping. These data will allow us to identify susceptibility loci associated with Type 2 diabetes characterized by defect in pancreatic β cell function. Further studies on the identification of the responsible gene(s) will improve our understanding of the pathogenic mechanism of diabetes. It will also enable us to identify subjects at risk of Type 2 diabetes.
(CU99292)

Nocturnal Nasal Positive Pressure Ventilation Plus Oxygen Therapy versus Oxygen Alone in Severe Stable Chronic Obstructive Pulmonary Disease

- ✉ HUI Shu Cheong David
- 20 September 1999
- ❖ Health Services Research Fund, Hospital Authority

Chronic Obstructive Pulmonary Disease (COPD) is a common disease in our community affecting 7% of the elderly Chinese. Long-term domiciliary oxygen therapy (LTOT) with minimum use 15 hrs daily has been shown to improve 5-year survival in patients with respiratory failure due to COPD by delaying the progression of pulmonary hypertension and terminal right heart failure. Currently a large number of patients in our community are already on LTOT. In the hospital setting, non-invasive positive pressure ventilation (NPPV) has been shown to greatly lower the need for intubation in selected patients with COPD exacerbations, reducing morbidity and mortality as well as hospital length of stay. In contrast, evidence for use of NPPV in patients with severe but stable COPD is not as clear. Since 1992, only one controlled trial conducted in the U.K. has shown favourable results for the use of NPPV in patients with severe stable COPD with improvement in daytime and nocturnal carbon dioxide level, total sleep time and quality of life scores after 3 months of NPPV use compared to oxygen therapy alone while 3 other overseas studies yielded conflicting results. In H.K., there is no data at all concerning the use of NPPV in such patients. This is the first study in H.K. to determine prospectively whether COPD patients with respiratory failure already on LTOT will benefit from the addition of home NPPV with reference to sleep efficiency, daytime arterial blood gases, exercise capacity, lung function, quality of life scores and hospital admission rates.
(MD99017)

The Effect of Adrenergic Receptor Blockade on Myocardial Collagen and Ventricular Remodeling in Heart Failure Post Myocardial Infarction

- ✉ John Elsby SANDERSON • CHOW Tsun Cheung Louis (Dept of Anatomical & Cellular Pathology) • CHOW Sing Sum Moses (School of Pharmacy) • WOO Kam Sang
- 1 October 1999
- ❖ Research Grants Council (Earmarked Grants)

Increased sympathetic activity is a recognized feature of heart failure whatever the cause. Although initially supporting the failing heart, prolonged excessive activation of the sympathetic nervous system has many potentially adverse effects including myocyte loss and arrhythmias. Clinical studies (including our own) have confirmed that blockade of the sympathetic nervous system with beta-adrenergic receptor antagonists can have beneficial haemodynamic and symptomatic effects in patients with heart failure. However, there is little information on the role of adrenergic stimulation in the regulation of myocardial extracellular matrix and the process of ventricular remodeling which occurs post myocardial infarction and which leads to a progressive decline in ventricular systolic function, diastolic dysfunction, and finally the syndrome of heart failure. The researchers plan therefore to study using a well-established post-infarction heart failure model to determine (1) if carvedilol has a superior effect compared to the standard β -blockers metoprolol and propranolol on myocardial total collagen and collagen mRNA levels, (2) if α -receptor blockade alone is equally effective by using the specific α_1 -receptor antagonist (Doxazosin) and (3) whether reduced myocardial gene expression of transforming growth factor β -1, a potent fibrogenic cytokine, is associated with adrenergic inhibition. Thus, this study tests the hypothesis that adrenergic blockade, of α - or β -receptors or both, may have an important effect on myocardial collagen post interaction, and thus the process of left ventricular remodeling. This study may have important implications for the management of patients post myocardial infarction and may lead to the development of new therapies if adrenergic inhibition is shown to modulate transformation growth factor β_1 expression.
(CU99340)

The Effects of α - and β -adrenoreceptor Stimulation on Collagen Production in Cultured Cardiac Fibroblasts

- ✉ John Elsby SANDERSON • LAI Ka Bik
- 1 May 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

In previous studies the researchers have demonstrated in a rat coronary ligation model that the adrenergic antagonist, carvedilol has an inhibitor effect on

myocardial collagen in the non-infarcted myocardium whereas the selective β_1 adrenoceptor antagonist metoprolol had no effect on myocardial collagen. The question is whether this is due to the additional β_1 antagonism property that carvedilol possesses or a nonspecific growth inhibiting, antiproliferative action possibly mediated through other cytokines or secondary messengers. The researchers will study the effect of stimulation of β_1 , and adrenergic receptors and the antagonist carvedilol, metoprolol and propranolol on production of collagen and fibrogenic cytokines such as TGF, TNF, and IL-1 in isolated cultured cardiac fibroblasts. There is little knowledge about the role of sympathetic adrenergic stimulation on fibroblast function and this will be the first detailed study to look at the potential important action of the sympathetic nervous system on collagen production and the healing process. (MD99104)

A Study of Aspirin versus Warfarin for the Prevention of Stroke among Chinese Patients with Nonvalvular Atrial Fibrillation

- ✉ KAY Li Chi Richard • John Elsbj SANDERSON
□ 1 December 1999
❖ CUHK Research Committee Funding (Direct Grants)

As in many other communities, stroke in Hong Kong is among the top three causes of death as well as being the leading cause of disability. Among Chinese, approximately 70% of all strokes are due to ischaemic brain infarction of which 15% are related to atrial fibrillation, which is itself a very common disorder especially in the elderly. Studies from the Europe and North America have demonstrated that both aspirin and warfarin are highly effective in preventing ischaemic strokes in patients with atrial fibrillation. Warfarin is generally more effective than aspirin, but it has to be given in doses that carry a higher risk of bleeding, including notably intracranial haemorrhage. However, under carefully controlled conditions warfarin is still regarded as the treatment of choice. No equivalent study confirming this has ever been performed in a Chinese population. The study, which will compare the effects of aspirin, low-dose warfarin and high-dose warfarin, seeks to address this question objectively by means of a randomised clinical trial. The researchers believe that until such a study is successfully performed, the correct treatment for our fibrillating patients will remain a matter of speculation. (MD99038)

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)

- ✉ LEUNG Wai Yee Nancy
□ 1 March 2000
❖ Glaxo Welcome

Lamivudine is a nucleoside analogue with potent inhibitory effect on the hepatitis B virus. In the Asian multicenter trial, clinical benefit has been observed with extended duration of treatment over 5 years. However, a proportion of the treated patient developed drug resistant virus with associated relapse of hepatic activity. Adefovir diproxil is a nucleotide analogue with potent antiviral effect. It has been demonstrated to be effective against hepatitis B virus resistant to Lamivudine. The present randomized trial will evaluate and compare the therapeutic efficacy and safety of Lamivudine plus Adefovir or Lamivudine plus placebo in patients who have developed Lamivudine resistant hepatitis B. (MD99115)

A Double-blind, Parallel Group, Placebo Controlled, Multi-center, Phase IIIA Study to Assess the Safety and Efficacy of Oral Famciclovir (Three Times a Day) for the Treatment of Chronic Hepatitis B in Asian Population

- ✉ SUNG Joseph Jao Yiu • LEUNG Wai Yee Nancy • TSANG Woon Choy Steven
□ 7 August 1996
❖ SmithKline Beecham International

Preliminary data from an ongoing study in patients with chronic hepatitis B shows that treatment with famciclovir results in significant reductions in HBVDNA and ALT. The objectives of this study is to evaluate the safety and efficacy of famciclovir at 500mg three times a day for 52 weeks for the treatment of chronic hepatitis B in an Asian population. The primary efficacy parameters include: the percentage change from baseline in the levels of HBV DNA at the end of the double-blind treatment period and; the change in the total liver histologic activity index (Ishak) from the pre-treatment period to the end of the one year double blind treatment period for patients with two evaluable biopsies. (MD96222)

A Double-blind Placebo Controlled Clinical End-points of Lamivudine in Patients with Hepatitis B Related Cirrhosis

- ✉ SUNG Joseph Jao Yiu • CHAN Ka Leung Francis • TSANG W. C. Steven* • CHAN L. Y. Henry* • HUI Y.*

□ 29 November 1998

❖ Glaxo Wellcome China Limited

A five year study of lamivudine versus placebo to establish the rate clinical endpoints in chronic hepatitis B patients with cirrhosis confirmed on biopsy. Primary endpoint is progression of disease, as indicated by Childs-Pugh score increase of two or more points, development of hepatocellular carcinoma, spontaneous bacterial peritonitis (with proven sepsis). Renal insufficiency defined as a 2-fold increase in serum creatinine compared to baseline or bleeding oesophageal varices. Randomisation is 2(lamivudine): 1 (placebo), and approximately 600 patients will be recruited in hospital centres throughout the Asia-Pacific region. Patients are followed up for a maximum of 5 years on blinded therapy, with assessments every 3 months. Upon reaching a clinical endpoint, patients may switch to open label lamivudine for a maximum of 3 years, or 1 year post-local marketing approval, whichever is sooner. A data safety monitoring board will assess the data in a ongoing basis and, with statistical stopping rules, may terminate the study. (MD98164)

Gastric Cancer – A Study on Genetic and Bacterial Mechanisms

✉ SUNG Joseph Jao Yiu • YU Jun • Peter Malfertheiner* • Matthias Ebert*

□ 1 January 2000

❖ Germany/Hong Kong Joint Research Scheme

Gastric cancer ranks second in cancer incidence and still top the list of cancer-related mortality worldwide. The process of carcinogenesis is a multi-step development from chronic inflammation to pre-malignant lesions (gastric atrophy, intestinal metaplasia and dysplasia) before the final appearance of gastric cancer. The development of gastric cancer involves both genetic factors of the host and environmental factors including H. pylori infection and dietary habits. Previous studies conducted in different parts of the world suggest a geographical variation in both genetic mechanisms and H. pylori strains which might account for the differences in clinical pictures of different ethnic groups. This study aims to investigate the relationship of H. pylori infection and E-cadherin expression in gastric cancer and premalignant lesion and compare the H. pylori strains (cag A, vac A and ice A) in Hong Kong and Germany for their correlation with E-cadherin mutation. (MD99092)

The Role of Vascular Permeability and Fibrosing factors in Longitudinal Change of Peritoneal Solute Kinetics

✉ SZETO Cheuk Chun • LI Kam Tao Philip

□ 1 November 1999

❖ CUHK Research Committee Funding (Direct Grants)

Background: In Hong Kong, most of the end-stage renal failure patients are treated with peritoneal dialysis. Peritoneal fibrosis is an important causes of patient morbidity and treatment failure. The permeability of this lining plays a critical role in the success of treatment. However, prospective data on longitudinal change of peritoneal transport kinetics is scarce. The association of various fibrosing factors and progressive change of clinically determined peritoneal characteristics is not clear. Although morphologic studies and mathematical models predict that capillary endothelium is the major site of resistance of peritoneal transport, the role of capillary permeability in determination of peritoneal kinetics has not been studied.

Objective: To investigate the relationship between expressions of vascular permeability factor (VPF), other fibrosing factors and the progressive change in peritoneal permeability.

Patient & Method: 100 peritoneal dialysis patients will be studied for 2 years. Peritoneal equilibration test (PET) will be performed regularly. Serum and spent dialysis solution will be collected. The contributions of VPF and other fibrosing factors are assessed by their gene expression and protein concentration in spent dialysate. The data will be correlated with change in peritoneal kinetics by serial PET.

Significance & Potential: This project will provide important data on the effect of fibrosing factors on the progressive change in peritoneal transport characteristics. It will support further application for RGC grant, in which the researchers aim to study the interaction of fibrosing factor, peritonitis, hypersonic dialysis solution, and peritoneal sclerosis a large-scale prospective project. (MD99039)

The Participation of the Actin Cytoskeleton in Insulin-mediated Glucose Uptake in Rat Skeletal Muscle Cells

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

□ 1 October 1999

❖ CUHK Research Committee Funding (Direct Grants)

The stimulation of glucose transport across the plasma membrane by insulin in skeletal muscle and fat tissues is crucial to the maintenance of glucose homeostasis. Despite intense research effort, the molecular mechanisms of insulin-induced translocation of glucose transporters from the

intracellular storage compartment to the cell surface remain unclear. Given the fact that insulin causes rapid reorganisation of actin filaments below the plasma membrane into membrane ruffles, the researchers hypothesised that the actin cytoskeleton may participate in the translocation of glucose transporters to the plasma membrane in response to insulin.

They will study the molecular mechanisms whereby the cytoskeleton facilitates movement of glucose transporters. The dynamic turnover of the actin cytoskeleton will be perturbed by treatment with latrunculin B and jasplakinolide, which disrupts and stabilises actin filaments respectively. The effects of these agents on insulin-induced actin remodelling, translocation and internalisation of glucose transporters on the cell surface will be studied by indirect immunofluorescence and confocal laser scanning microscopy.

These experiments should reveal how insulin may control the movement of glucose transporters. The knowledge acquired would provide the foundation to examine the specific defects associated with insulin resistance in Type II diabetes mellitus in a novel manner.

(MD99040)

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

✉ WONG Ka Sing Lawrence • E. B. RINGELSTEIN*

☐ 1 July 1999

❖ Germany/Hong Kong Joint Research Scheme

Stroke is the third leading cause of mortality and a leading cause of disability in adult in Hong Kong. In Chinese stroke patient, middle cerebral artery stenosis is the most commonly found vascular lesion in patients with acute ischomic stroke. Yet the stroke mechanism (thromboembolic or hemodynamic) in patients with middle cerebral artery stenosis remains uncertain. Recent advances in ultrasonology enable us to monitor the occurrence of microemboli signals (MES) in the cerebral circulation. Studies of MES in patients with carotid stenosis have shown that it occurred commonly in acute stroke but much less commonly in asymptomatic patients, suggesting MES may be a marker of active thrombotic process. There have been no published data on the detection of MES in acute stroke patients with middle cerebral artery stenosis. The researchers will perform a study on 100 acute stroke patients with middle cerebral stenosis in order to document the frequency of MES and correlate its occurrence with thrombotic markers. In this project, they will incorporate the expertise of the Germany partner in the technique of MES and the experiences of the investigation of middle cerebral artery stenosis in Hong Kong. For the Hong Kong

investigators, the expertise in MES of the Germany partner will help to improve the quality of the data collection. For the Germany investigators, the experiences of examining a substantial number of patients with middle cerebral artery stenosis is only possible in Asia. This project will also help to establish collaboration between the two institutions so that future studies of advance technique in ultrasound (such as contrast agent and color-coded transcranial duplex studies) are possible. In the clinical setting, finding of this study may guide us towards a better strategy in secondary stroke prevention in these high-risk patients.

(MD99005)

A Pilot Study of Early and Aggressive Lipid-lowering Therapy for Atherosclerotic Stroke

✉ WONG Ka Sing Lawrence • LO See Kit Raymond* • TOMLINSON Brian • LAM Wai Man Wynn (Dept of Diagnostic Radiology & Organ Imaging) • LAM Wai Kei Christopher (Dept of Chemical Pathology) • KAY Li Chi Richard

☐ 1 January 2000

❖ CUHK Research Committee Funding (Direct Grants)

Stroke is a major cause of mortality and morbidity in Hong Kong. About one quarter of stroke is recurrent stroke. Therefore, secondary stroke prevention is a very important strategy in stroke management. Stroke is a heterogenous disease with a variety of different pathophysiology. Atherosclerosis is the most common cause of ischemic stroke. In patients with coronary atherosclerosis, the use of a class of cholesterol-lowering agents, HMG-CoA inhibitors, greatly reduce future vascular events (including stroke) and death. However, there has not been a randomised trial to study the effect of HMG-CoA inhibitor in stroke patients. Before a large trial which may need to recruit thousands of patient, a pilot study is required to provide data regarding the magnitude of the potential benefits or risks of such therapy. Without the background data, it is impossible to calculate the power of a definitive study. The researchers will conduct a pilot study in the Prince of Wales Hospital and Shatin Hospital to randomise stroke patients with ultrasonographic evidence of atherosclerosis to either early aggressive lipid therapy or usual care. Outcome events include new stroke, transient ischemic attack, acute coronary syndrome and vascular death. For the safety assessment, they will monitor the occurrence of haemorrhagic stroke which is associated with low cholesterol level. They plan to recruit 100 patients for this pilot study.

(MD99041)

The Role of Phytoestrogens in Women's Health

- ✉ 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)
- 1 January 2000
- ❖ CUHK Strategic Research Program

This project seeks to examine various aspects of phytoestrogens in relation to the health of Hong Kong Chinese. A laboratory assay for isoflavones (daidzein and genistein) has recently been set up in the Lee Hysan Laboratories. Expertise in population dietary surveys and in the use of traditional Chinese medicine exists within the research group. The proposed series of studies will examine the effect of phytoestrogens on calcium metabolism, the effect of soy extract on health outcomes, the relationship between dietary phytoestrogen consumption and bone mineral density, an analysis of preparations recommended for menopausal women for phytoestrogen content, and a comparison of health outcome between one of these preparations involving hormone replacement therapy with that of a newer selective oestrogen receptor modulators. Results obtained from these studies have considerable potential for making a significant contribution towards improving the health of women at and after the menopause. (MD99069)

A Study of the Acceptability and Effectiveness of Hip Protectors in Elderly Chinese in the Institutional Setting

- ✉ WOO Jean • SUM Cecilia*
- 1 July 2000
- ❖ Health Services Research Fund, Hospital Authority

Objectives: To evaluate acceptability of a newly designed hip protector and to determine if it is effective in reducing the incidence of hip fractures as a result of falls.

Design & Setting: Randomized trial of use of hip protectors versus none, in nonacute Hospital Authority hospitals with long term care facilities.

Subjects: Elderly subjects admitted to the above institutions who are at risk of falling.

Intervention: Wearing of hip protectors developed in Australia.

Outcome measure: (1) Number of hours per day subjects agree to wear hip protectors; (2) Number of fractures per fall.

Results & Conclusion: It is hoped that these newly designed hip protectors will have a good compliance rate and will result in a statistically significant reduction in hip fracture as a result of falls. (MD99010)

Chinese Atherosclerosis in the Aged and Young (Cathay Study)

- ✉ WOO Kam Sang • WOO Jean • John Elsby SANDERSON • CRITCHLEY Julian A J H • CHENG Gregory • LAM Ching Wan (Dept of Chemical Pathology) • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research)
- 1 January 1997
- ❖ Donation from Chinese Atherosclerosis Trust • Donation from Hong Kong Heart Foundation • Donation from Hong Kong Institute of Heart Health Promotion

Background: Atherosclerosis (hardening of blood vessels) is the leading cause of morbidity and mortality (mostly due to heart attacks or stroke) in most western countries and in China now in process of modernization. The researchers' previous studies suggested an increased intima-media (internal lining) thickness (IMT) of carotid (neck) artery as marker of subclinical atherosclerosis in westernized Chinese in Sydney and Hong Kong, as compared with native Chinese in southern Chinese village. These findings inspire a possibility of relative protection of rural Chinese, and westernization (modernization) is associated with higher risk for developing atherosclerosis [*hypothesis 1*], and subscribe to a model of gene-environment interaction in atherogenesis [*hypothesis 2*].

Objective: To further confirm and test these 2 hypotheses, and in particular the effect of modernized dietary patterns in a bigger subjects sample.

Methods: In this landmark collaborative project, the researchers systematically study 500 asymptomatic Chinese, aged 18-70 years having lived in Hong Kong, Sydney, and San Francisco respectively for > 15 years, and similar rural Chinese in northern China (Yu County of Shanxi Province and Beijing). High resolution ultrasonography of carotid artery (for IMT measurement of common carotid artery) and of brachial artery (for endothelium-dependent FMD) will be performed, using uniform operation procedure and automatic computerized measurement package. Dietary and lifestyle patterns will be evaluated using a validated food frequency questionnaire and by trained interviewers. Blood will be taken after >12 hours fasting for novel risk factors including full lipid profiles, antioxidants, phytoestrogen, thrombotic factors, homocysteine and molecular genetic profiles. Age and gender-matched groups and active smokers

from each locality will be compared, as well as group of vegetarians in Hong Kong.

Significance & Potential: This collaborative project will provide an unique opportunity to identify adverse and protective dietary and lifestyle factors, and the underlying mechanisms predisposing to increased atherosclerosis, in the Chinese in particular. (MD96224)

A Double-blind, Randomized Study on Valsartan vs Diuretics in Essential Hypertension: The Impact of Antihypertensive Therapy on Arterial Endothelial Function

✉ WOO Kam Sang • FUNG Wing Hong • John Elsby SANDERSON • Dr. Chiu R C W*

☐ 1 January 1998

❖ Donation from Novartis Co.

Background: Hypertension is an important medical problem in the twentieth century and antihypertensive treatment prevents stroke and heart failure. However, it is uncertain whether this is purely an effect of blood pressure-lowering, or a therapeutic attribute of additional pharmacological effect of specific antihypertensive drugs. A key question is whether some drugs have any advantage in prevention and control of atherosclerosis or other target organ disease, compared with traditional antihypertensive agent such as diuretics. Flow mediated dilatation of arteries (FMD) as a sensitive indicator of vascular reactivity (endothelial function) by high resolution ultrasonography is a recent advance in diagnostic modality; abnormality in vascular reactivity identified emerges as a sensitive markers of early atherosclerosis and a reliable index of cardiovascular health in hypertensive subjects. Valsartan (Diovan) is one of a new class of antihypertensive agents, known as angiotensin II blocker (inhibitors) with a potent and specific competitive angiotensin II antagonistic action at the AT-1 subtype receptor, which mediates essentially all the known effects of angiotensin II on the cardiovascular system.

Objective: The study will directly compare the application of valsartan with hydrochlorothiazide in treating essential hypertension. Primary endpoint: Changes in arterial endothelial function. Secondary endpoints: Blood pressure control, left ventricular mass and arterial wall stiffness.

Study Design: This is a parallel group, double blind and randomised study. Patients with sitting blood pressure >160/95 mmHg after 4 week's placebo washout will be enrolled. They were then given a 24-week active treatment period with either valsartan 80mg/160mg or hydrochlorothiazide 12.5mg/25 mg with addition of a β -blocker if necessary. Blood pressures, FMD and LV mass were measured at baseline, week 12 and week 24, and arterial stiffness (by applanation tonometry) were measured at

baseline and week 24. Comparisons on these end points will be made between the 2 treatment groups.

Significance: This study will document the impact of antihypertensive treatment using specific angiotensin II blocker on improving endothelial function, as compared with a nonspecific blood pressure lowering agent (diuretic) This effect of proven, will be of great implication in medical treatment of a very common medical problem in modern society.

(MD97188)

Hyperhomocysteinaemia and Arterial Endothelial Dysfunction: An Emerging Strategy for Prevention of Atherosclerosis

✉ WOO Kam Sang • WOO Jean • John Elsby SANDERSON • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • FUNG Kwok Pui (Biochemistry) • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research)

☐ 1 August 1999

❖ Research Grants Council (Earmarked Grants)

Homocyst(e)ine (HC) is a highly reactive amino acid from metabolism of animal protein, damaging to endothelial cells (internal lining) of arteries in both cell culture and animal studies. High blood level of homocyst(e)ine (HHC) is emerging as a new risk factor in humans, for development of sick endothelial lining (endothelial dysfunction, an key early event in atherogenesis) and premature atherosclerotic diseases (heart attack and stroke).

This novel project will evaluate the prevalence of HHC among patients with coronary heart disease (CAD) and propose to confirm HHC as an independent risk factor for endothelial dysfunction in CAD [*Hypothesis 1*]. This will be critically assessed in a case-control design comparing the vascular reactivity of brachial artery (an indicator of overall arterial endothelial function) of HHC coronary and matched normal HC coronary patients, using high-resolution ultrasound.

In testing the hypothesis that endothelial dysfunction in HHC subjects is amenable to homocyst(e)ine-lowering intervention such as folic acid supplementation [*Hypothesis 2*], HHC subjects (both normal asymptomatic and CAD) will be given folic acid (5mg/day) or placebo for 8 weeks in a double-blind randomized and cross-over fashion. Vascular reactivity, homocyst(e)ine and folate assay will be performed at baseline and at end of each treatment periods. Folic acid supplementation will be continued for one year to document its long-term effect.

This project will provide the scientific basis for a new innovative but simple strategy of using folic acid supplementation in prevention of atherosclerosis, the leading killer of modern society.

(CU99282)

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)

✉ WOO Kam Sang • John Elsby SANDERSON • FUNG Wing Hong* • CHAN W M Wilson*

☐ 1 December 1999

❖ Merck Sharp & Dohme (Asia) Ltd

This project will test 2 important hypotheses in managing acute coronary syndrome, a potentially sinister manifestation of coronary artery disease related to acute rupture of atherosclerotic plaque of coronary artery:

- (1) Plaque - stabilizing regimen using IIB-IIIa glycoprotein receptor inhibitor (tirofiban), aspirin plus either low molecular heparin (enoxaparin) or unfractionated heparin (UH) is well tolerated with acceptable adverse effect in the Chinese;
- (2) Early aggressive simvastatin (40-80mg) treatment will reduce a composite of cardiovascular events after acute coronary syndrome as compared with usual care secondary preventive programme.

In the first phase ('A' phase) of the project, patients with acute coronary syndrome will be randomized to take open label tirofiban (Aggrastat) (intravenous bolus 10µg/kg then infusion of 0.1µg/kg/min for 48-108 hours), aspirin (80-160mg orally) and enoxaparin (1mg/kg q 12 hrs) or UH (5000 U IV bolus, then 5000-1000 U/hr). In the second phase ('Z' phase), stable patients will be randomized at 48-120 hrs after admission, in double-blinded placebo-controlled fashion, to receive either usual care secondary preventive programme (dietary and life style modification for 4 months, followed by Simvastatin 20 mg daily for 8 months), or early Simvastatin (dietary and lifestyle modification plus simvastatin 40 mg/day for 1 month, followed by Simvastatin 80 mg/day for 11 months). The tolerability and adverse effects (bleeding complications in particular), composite of cardiovascular events (mortality, coronary surgery, and recurrence of angina, myocardial infarction, heart failure and hospital readmission) will be monitored for at least 1 year. Comparisons will be made on these end points between the treatment groups in A or Z phases. (MD99072)

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 | Cost-effective Approaches to Gastro-intestinal and Antihypertensive Drug Prescribing: An Economic Impact Study of Intervention Mechanisms in the In-patient and Out-patient Setting (MD96023) ✉ CHAN Chung Ngor Juliana • LEE Shing Cheung (School of Pharmacy) • CHANG Sophie (School of Pharmacy)# • CRITCHLEY Julian A J H |
| 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 • Clive Stewart COCKRAM • CRITCHLEY Julian A J H |
| 1997-98 | Phenotypic and Genotypic Characterisation of NIDDM (Type 2 Diabetes Mellitus) and their Interactions with Environmental Factors (CU97682) ✉ CHAN Chung Ngor Juliana • YEUNG Tok Fai Vincent • CHOW Chun Chung Francis • Clive Stewart COCKRAM • 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 • Clive Stewart COCKRAM • CRITCHLEY Julian A J H |
| 1998-99 | Screening for Mutations in the Glucokinase and Hepatocyte Nuclear Factor-1α Genes in Chinese Patients with Early-onset Type 2 Diabetes and A Positive Family History (MD98100) ✉ CHAN Chung Ngor Juliana • NG Chor Yin • Clive Stewart COCKRAM • 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 • Clive Stewart COCKRAM • NG Chor Yin • LEE Shao Chin • LEE Suk Kuen • THOMAS Neil G • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • WONG Wing Kin Gary (Dept of Paediatrics)
- 1997-98 NSAID-Induced Peptic Ulcer Bleeding: Protection at a Lower Cost? (MD97004)
 ✎ CHAN Ka Leung Francis • SUNG Joseph Jao Yiu
- 1998-99 A Randomized, Double-blind Study to Evaluate the Safety and Antiviral Activity of Three Doses of FTC in Patients Chronically Infected with Hepatitis B (FTCB-102) (MD98161)
 ✎ CHAN Ka Leung Francis • LEUNG Wai Yee Nancy • SUNG Joseph Jao Yiu
- 1998-99 A Multicenter, Double-blind, Parallel Group Study Comparing the Efficacy and Incidence of Gastroduodenal Ulcer Associated with SC-58635 100MG BID with that of Diclofenac 50MG BID Taken for 12 Weeks in Patients with Osteoarthritis or Rheumatoid Arthritis in Hong Kong (MD98149)
 ✎ CHAN Ka Leung Francis • SUNG Joseph Jao Yiu • LI Kwok Ming Edmund • WOO Jean
- 1996-97 The Role of the Renal Kallikrein-kinin System in the Regulation of Sodium Balance and Blood Pressure in Chinese Subjects in Relation to a Family History of Hypertension, Low/Normal Renin Hypertension or NIDDM Albuminuric Status (CU96675)
 ✎ CHAN Yan Keung Thomas • CHAN Chung Ngor Juliana • YOUNG Robert Peter# • TOMLINSON Brian • CRITCHLEY Julian A J H
- 1998-99 A Study on the Drug-Related Death Cases in Hong Kong (MD98080)
 ✎ CHAN Yan Keung Thomas • CRITCHLEY Julian A J H • CHAN Tai Wai David*
- 1998-99 Effect of Alendronate on Patients with Primary Hyperparathyroidism (MD97175C)
 ✎ CHOW Chun Chung Francis • Clive Stewart COCKRAM • LI J. K. Y.* •
- CHAN W. B.* • KWOK Chi Yui Timothy • SO W Y*
- 1998-99 IND Filing and Phase I Clinical Trial of a Malaria Vaccine TBV25H - Phase I Clinical Trial Component (MD98005)
 ✎ CRITCHLEY Julian A J H • TOMLINSON Brian • THOMAS Neil G • SEPHTON Carmen L.*
- 1998-99 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 (MD98101)
 ✎ CRITCHLEY Julian A J H • CHAN Chung Ngor Juliana • NG Chor Yin • Clive Stewart COCKRAM • SCHERER Stephen W.* • TSUI Lap Chee*
- 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*
- 1997-98 Matrix-Metalloproteinases (MMPs) and their Specific Inhibitors (TIMPs) in Tuberculous Pleural Effusions (MD97132)
 ✎ HUI Shu Cheong David • LAI Kei Wai Christopher • HOHEISEL Gerhard*
- 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
- 1996-97 The Role of Cytokine Growth Factors in the Control of Myocardial Collagen Turnover and the Development of Left Ventricular Diastolic Dysfunction in Patients with Heart Failure (CU96670)
 ✎ John Elsby SANDERSON • CHOW Tsun Cheung Louis (Dept of Anatomical & Cellular Pathology) • WOO Kam Sang

- 1998-99 A Multinational, Multicentre, Randomised, Double-Blind Study to Assess the Efficacy and Tolerability of Nifedipine GITS 20 mg Compared to Placebo in Low Body Weight Patients with Mild to Moderate Hypertension (MD96219C)
 ✎ John Elsby SANDERSON • TOMLINSON Brian
- 1998-99 The SYMPHONY Trial: A Phase III, Multicenter, International, Randomized, Double-Blind, Aspirin-Controlled Trial to Evaluate the Efficacy and Safety of Sibrafiban (Ro 48-3657), an Oral Platelet Glycoprotein IIb/IIIa Antagonist, as Therapy for the Prevention of Secondary Vascular Events in Patients after an Acute Coronary Syndrome (MD97176C)
 ✎ John Elsby SANDERSON • CALIFF, Robert*
- 1998-99 The Paragon-B Trial (MD98146)
 ✎ John Elsby SANDERSON • CHIU C. W.* • TANG Kare Hung* • FUNG Wing Hong*
- 1998-99 The 2nd Symphony Trial – Sibrafiban Versus Aspirin as Therapy for the Long Term Prevention of Secondary Vascular Events Post Acute Coronary Syndromes (MD98125C)
 ✎ John Elsby SANDERSON
- 1996-97 Pilot Study of Clomethiazole in the Treatment of Intracerebral Haemorrhage (MD96055)
 ✎ KAY Li Chi Richard • WONG Ka Sing Lawrence • AHUJA Anil Tejbhan (Dept of Diagnostic Radiology & Organ Imaging)
- 1998-99 The Efficacy of a Community Nurse Specialist in Preventing Hospital Readmission of Older Patients with Chronic Lung Disease and Cardiac Failure (MD98075)
 ✎ KWOK Chi Yui Timothy • WOO Jean • LAU Edith Ming Chu (Dept of Community and Family Medicine) • LEE Tze Fan Diana (Dept of Nursing) • TANG So Kum Catherine (Dept of Psychology)
- 1998-99 Association of Plasminogen Activator Inhibitor (PAI-1) Gene Polymorphism with Diabetic Nephropathy Among Type 2 Diabetic Patients in Chinese (MD98126)
 ✎ LI Kam Tao Philip • WONG Teresa*
- 1998-99 The Effect of Hydroxychloroquine on Serum Lipids, Apolipoproteins and Lipoprotein(a) in Patients with Systemic Lupus Erythematosus (MD98039)
 ✎ LI Kwok Ming Edmund • TOMLINSON Brian • LAM Wai Kei Christopher (Dept of Chemical Pathology) • TAM Lai Shan
- 1995-96 A Follow-On Study to Determine the Safety and Efficacy of Long Term Lamivudine Treatment in Patients with Chronic Hepatitis B Infection (NUCB 3018) (MD95267)
 ✎ SUNG Joseph Jao Yiu • LEE Yuk Tong • TSANG Woon Choy Steven • Leung Wai Yee Nancy* • CHAN Ka Leung Francis • CHAN Lek Yuen*
- 1995-96 *Helicobacter pylori*: Mode of Transmission and Carcinogenesis (MD95255)
 ✎ 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*
- 1997-98 The Use of Endosonography and MR Angiography in Predicting the Risk of Variceal Bleeding in Portal Hypertension (CU97657)
 ✎ SUNG Joseph Jao Yiu • CHAN Yu Leung (Dept of Diagnostic Radiology & Organ Imaging) • CHUNG Sheung Chee Sydney (Dept of Surgery) • LAM Wai Man Wynn (Dept of Diagnostic Radiology & Organ Imaging) • LEE Y. T.*
- 1998-99 Does *Helicobacter Pylori* Cause Or Protect Against Gastro-Esophageal Reflux In Asia (CU98260)
 ✎ 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*
- 1996-97 Study of the Metabolic Syndrome in Hong Kong Chinese: Investigations of the Phenotypic Characteristics and Underlying Genotypes in Patients with the Metabolic Syndrome Presenting with Dyslipidaemia, Non-insulin Dependent Diabetes Mellitus, Hypertension or

- Atheromatous Vascular Disease (MD96027)
 ✎ TOMLINSON Brian • CHAN Chung Ngor Juliana • CRITCHLEY Julian A J H • YOUNG Robert Peter# • PANG Chi Pui Calvin (Dept of Ophthalmology and Visual Sciences) • ARUMANAYAGAM Manoharan (Dept of Chemical Pathology)# • CHAN Yu Leung (Dept of Diagnostic Radiology & Organ Imaging) • CHAN Yan Keung Thomas • John Elsby SANDERSON • Clive Stewart COCKRAM • YEUNG Tok Fai Vincent • CHOW C. C.*
- 1997-98 Wynnie (Dept of Diagnostic Radiology & Organ Imaging) • CHAN Yu Leung (Dept of Diagnostic Radiology & Organ Imaging)
- 1997-98 A Prospective Study of Asymptomatic Patients with Middle Cerebral Artery Stenosis (CU97673)
 ✎ WONG Ka Sing Lawrence • LAM Wai Man Wynnie (Dept of Diagnostic Radiology & Organ Imaging) • YEUNG Tok Fai Vincent • CHAN Yu Leung (Dept of Diagnostic Radiology & Organ Imaging) • KAY Li Chi Richard
- 1997-98 The Effects of Different Doses of Vitamin E on Atheroma Formation and Indices of antioxidant Activity and Oxidative Stress in Cholesterol-Fed Rabbits (MD97047)
 ✎ TOMLINSON Brian • JAMES Anthony Edward (Laboratory Animal Services Centre) • BENZIE Iris F. F.* • ARUMANAYAGAM Manoharan (Dept of Chemical Pathology)# • SAHOTA Daljit Singh (Dept of Obstetrics & Gynaecology) • CRITCHLEY Julian A J H • HAINES Christopher John (Dept of Obstetrics & Gynaecology)
- 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 Wynnie (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 Effects of Homocysteine on Platelet Aggregation *in vitro* (MD98040)
 ✎ TOMLINSON Brian • CRITCHLEY Julian A J H
- 1998-99 Clinical Trial for GLYB 3001 in Acute Stroke (MD98145)
 ✎ WONG Ka Sing Lawrence
- 1998-99 An Open-Label Study to Evaluate the Efficacy and Safety of 80 mg Simvastatin in Patients with Hyperlipidaemia (MD98120C)
 ✎ TOMLINSON Brian • TANG Leung Sang Nelson (Dept of Chemical Pathology) • CHAN, Michael*
- 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
- 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
- 1996-97 Domiciliary Pulmonary Rehabilitation Program: A Randomised Controlled Clinical Trial (MD96017)
 ✎ WOO Jean • LUM Christopher* • HUI E.* • LEUNG Chung Chuen Roland
- 1995-96 Regress of Cerebral Artery Stenosis Study (MD95268)
 ✎ WONG Ka Sing Lawrence • KAY Li Chi Richard • LAM Wai Man
- 1997-98 Provision of Health Services - Elderly Residents in Nursing Homes Using Telemedicine (MD97005)
 ✎ WOO Jean • HJELM Nils Magnus (Dept of Chemical Pathology)# • TSUI Hung Tat (Dept of Electronic Engineering) • ZHANG Yuanting (Dept of Electronic Engineering)
- 1998-99 Quality of Life Assessment for Palliative Care (MD98003)

- 1998-99 A Multicenter, Double-Blind, Randomized, Parallel Group Study to Compare the Antihypertensive Efficacy of Losartan Versus Candesartan Cilexetil in Patients with Mild to Moderate Hypertension (MD98088)
 ✍ WOO Jean • LO See Kit Raymond*
 ✍ WOO Kam Sang • John Elsby SANDERSON • CHIU C. W.* • YIP Thomas* • KWONG S. K.*

RESEARCH OUTPUTS AND PUBLICATIONS

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Dept of Medicine & Therapeutics

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RESEARCH PROJECTS

Clinical Significance of Human Herpesvirus 7 Infection in Bone Marrow Transplantation

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☐ 1 October 1999

❖ Research Grants Council (Earmarked Grants)

Bone marrow transplantation is used with increasing frequency for treatment of haemic diseases, solid tumours and genetic disorders. Herpesviruses, in particular cytomegalovirus (CMV) and human herpesvirus 6 (HHV-6), are recognized important pathogens in marrow graft recipients. The role of the recently isolated herpesvirus, human herpesvirus 7 (HHV-7), however is still undefined. Preliminary *in vitro* and *in vivo* data suggest HHV-7 may be associated with delayed engraftment, CMV disease, rash and encephalitic illnesses. However the available information is limited and inconclusive. To prove the pathogenic role of a ubiquitous latent viral infection is difficult and requires independent confirmations. The researchers propose a 3½-year in-depth prospective study on paediatric marrow graft recipients to elucidate the association between HHV-7 infection and adverse clinical events, in particular the duration to engraftment incidence and severity of graft-versus-host disease, CMV disease, hepatitis, neurological and rash illnesses. During the course of study, they will also establish methods for monitoring of viral activity as well as for strain differentiation. This study will produce essential data for the formulation of preventative and treatment strategies, and to provide guidance for future development of diagnostic assays and molecular epidemiological studies pertaining to this novel human herpesvirus. (CU99248)

Quinolone and Multidrug Resistance in *Acinetobacter* spp

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☐ 1 October 1999

❖ Research Grants Council (Earmarked Grants)

Acinetobacter spp are important nosocomial pathogens associated with a growing number of hospitals acquired infections worldwide. In hot, humid regions, such as Hong Kong, *Acinetobacter* infection is endemic and sometimes caused by strains resistant to multiple antibiotics, including fluoroquinolones, resulting in therapeutic problems. The researchers' previous work shows that (1) there is a significant difference between Hong Kong and

Europe in the distribution of species in isolates from clinical and environmental sources; and (2) some genospecies appear to be of greater epidemiological significance than previously appreciated. Using strains obtained from their patients, healthy subjects and the environment, the researcher will study (1) multidrug and fluoroquinolone resistance and (2) the bacterial and resistance characteristics of epidemic and non-epidemic multidrug resistant strains in endemic situations, e.g., in the Intensive Care Unit. For this, the researchers will examine the mutation in quinolone target genes, intracellular accumulation of antibiotics and chemicals, and outer membrane proteins, and also clone the gene(s) involved in multidrug resistance. This study should improve the understanding of the evolution of multiply resistant epidemic clones. Thus, we may be in a better position to recognise them and formulate measures that would minimise their emergence and dissemination in the control of hospital-acquired infection.

(CU99290)

Speciation of Unclassifiable *Acinetobacter* from Hong Kong

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☐ 1 January 2000

❖ CUHK Research Committee Funding (Direct Grants)

Acinetobacter is an important nosocomial pathogen in our region with a prevalence of infection higher than elsewhere. To devise an effective program for the prevention of hospital-acquired *Acinetobacter* infections, it is important to understand the ecology of clinically significant genospecies. The results of the researchers' work so far on the distribution of *Acinetobacter* genospecies in Hong Kong are unexpected, showing that it is significantly different from that in Europe. A high proportion (18%) of their isolates cannot be genospecified by the commonly used method: amplified ribosomal DNA restriction analysis (ARDRA) which has been based on profiles obtained from European isolates. Recently, Dr. Dijkshoorn, their collaborator and an authority on *Acinetobacter* speciation, has validated the high-resolution amplified-fragment length polymorphism (AFLP) analysis, using ³²P radiolabelling. The purpose of this application is (1) to validate sequencing of ARDRA products and fluorescent AFLP for the genospeciation of acinetobacters and (2) using these two methods and the classical phenotypic approach, to determine the relatedness of their unclassifiable strains to the known genospecies. The results of the project is likely to show that some strains belong to known genospecies and their recognition will thus expand the ARDRA data base. Successful validation of

fluorescent AFLP and sequencing of ARDRA products will establish these two techniques as rapid means for speciation of *Acinetobacter* isolates. Strains that remain unclassifiable may belong to so-far-undescribed species. Their delineation will be the basis for an earmarked grant application in 2000. (MD99042)

Mechanisms of Macrolide, Lincosamide, Streptogramin (MLS Group) Resistance in Drug-resistant *Streptococcus Pneumoniae* and Other Streptococci

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

☐ 1 November 1999

❖ Research Grants Council (Earmarked Grants)

Clinical resistance to penicillin and other antimicrobial agents in *Streptococcus pneumoniae* has emerged rapidly in many parts of the world in recent years. This rapidly evolving pattern of antimicrobial resistance in many key pathogens is now causing major public concern. As over 50% of all human antibiotic consumption belong to the B-lactam group, emphasis is now placed on new applications of existing classes of antimicrobials and their new derivatives. Currently, interests have re-focused on the macrolide, lincosamide, and streptogramin (MLS) groups of antibiotics. Some of the new MLS agents e.g. quinupristin/dalfopristin, ketolides are active against multi-drug resistant pathogens. However, in recent years, new mechanisms of resistance have also been detected giving varying resistance patterns to individual agents in this MLS group of antibiotics. The relative importance of these mechanisms in gram positive bacteria has not been elucidated. With new antibiotics in this group being developed, knowledge of the prevalence and distribution of these resistance determinants would be important to enable one to establish appropriate antibiotic guidelines for the treatment of infections. The aims of the present study are to develop molecular methods for the detection of macrolide, lincosamide, and streptogramin resistance genes in *S. pneumoniae* and other streptococci; to determine the prevalence of related macrolide resistance determinants in clinical isolates from Hong Kong, and to investigate the distribution of these antibiotic resistance determinants in chromosomal DNA and plasmids in streptococci. (CU99331)

Effects of Respiratory Pathogens on an *in vitro* Nasal Ciliated Epithelial Monolayer Cell Culture Model

✉ IP Margaret • LEE Wai Chung (Dept of Surgery) • VAN HASSELT Charles Andrew (Dept of Surgery) • CHENG Fun Bun Augustine

☐ 1 June 2000

❖ CUHK Research Committee Funding (Direct Grants)

The adherence of bacterial pathogens to eukaryotic cells is the initial step in colonization and infection of the host. The ability of certain respiratory pathogens e.g. *Streptococcus pneumoniae* to adhere to specific sites on host tissues has been investigated by using various cell culture models, including human nasopharyngeal, alveolar, and bronchial epithelial cells. In order to colonize these areas, the pathogens have to bypass the mucociliary clearance of the nasal epithelial cells which are often the first sites of encounter for any host interactions to occur. In the past, observations had been made using animal models and organ cultures which were cumbersome and measurements difficult to assess.

In this study, the researchers aim to determine the possible mechanisms of damage by various pathogens on respiratory epithelium using an *in vitro* nasal ciliated epithelial monolayer cell culture model. These bacterial pathogens include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. This study will utilize a primary cell culture system using human nasal ciliated epithelia recently developed at the Department of Surgery, The Chinese University of Hong Kong. The cell culture will be prepared using strips of human nasal ciliated epithelium obtained from the turbinates of patients admitted for surgery. Bacteria will be cultured, washed, pelleted and resuspended in culture media and incubated in the cell culture system. Three parameters will be observed; namely the ciliary beat frequency (CBF) of the ciliated cells, the adherence of the organism to the nasal epithelial cells and the microscopic effects of both ciliated and non-ciliated epithelial cells will be examined. Data obtained will facilitate further understanding in the host-pathogen interactions involved in bacterial infections of the respiratory tract and provide information towards the novel intervention strategies in the prevention of such infections. (MD99105)

Mechanisms of Fluoroquinolone-resistance in *Salmonella Typhimurium* in Hong Kong

✉ LING Mei Lun Julia

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❖ CUHK Research Committee Funding (Direct 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 which codes for subunit A of the enzyme. Other mechanisms include mutations in the *gyrB* gene which codes for subunit B of the enzyme; mutations in the *parC* gene which codes for topoisomerase IV, another target enzyme of fluoroquinolones; and reduced intracellular accumulation of antibiotics because of changes in the bacterial cell envelope. *Salmonella typhimurium* remains the most common salmonellae isolated in Hong Kong and 75% of strains are resistant to one or more antibiotics. The researchers' previous study showed that 9% of *S typhimurium* isolated in Hong Kong from 1989 to 1995 had reduced susceptibility to fluoroquinolones. The main objective of this project is to use molecular biological techniques to elucidate the mechanisms of resistance to fluoroquinolones in these isolates and those isolated in 1996 - 1998. Elucidation of the mechanisms of resistance will provide a basis on which the pharmaceutical industry modifies the chemical structure of their drugs to widen the antibacterial spectrum. It will also aid health care professionals to devise appropriate measures to prevent the emergence and spread of antibiotic resistance. (MD99043)

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

1998-99 TT Virus Infection in Patients with Haemophilia and Transfusion-Dependent Thalassaemia (MD98103)
 ✎ CHAN Kay Sheung Paul • CHIK Ki Wai (Dept of Paediatrics) • CHENG Fun Bun Augustine • LI Chi Kong (Dept of Paediatrics)

1997-98 *In-vitro* Activity of Tazocin in Comparison with Other Commonly Used Antibiotics against Clinical Isolates (MD97147)

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1998-99 Studies on the Production of Proinflammatory Cytokines in Human Macrophages Induced by Microbial Pathogens and in Cerebrospinal Fluids from Patients with Meningitis – a Search for Interleukin 1- α (MD98041)
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1997-98 Acinetobacter Genospecies: Their Distribution in Hong Kong and Evaluation of PCR Identification Methods (CU97625)
 ✎ HOUANG Ting Sou Elizabeth • CHU Yiu Wai • PITT Tyrone Leslie*

1998-99 The Role of Skin Fatty Acid Profiles in the Carriage of Acinetobacter spp (MD98042)
 ✎ HOUANG Ting Sou Elizabeth • CHU Yiu Wai • CHEUNG S. W.*

1997-98 Molecular Epidemiology of Penicillin- and Multidrug-Resistant Streptococcus pneumoniae (CU97607)
 ✎ IP Margaret • LYON Donald James • CHENG Fun Bun Augustine

1998-99 Surveillance of Antibiotic Resistance in the Community – an Approach to Reduce Bacterial Resistance to Antimicrobial Agents (MD98166)
 ✎ LING Mei Lun Julia • CHAN Wai Chi • CHENG Fun Bun Augustine

1998-99 Rapid Detection and Identification of Medically Important Fungi by Molecular Methods (MD98043)
 ✎ Mamie HUI • IP Margaret • CHAN Kay Sheung Paul • CHENG Fun Bun Augustine

1996-97 A Multicentre Study to Determine the Efficacy of High-Dose Interferon Alpha-2b in the Treatment of Chronic Hepatitis B Virus Infection in Asia (MD96180)
 ✎ TAM Siu Lun John • CHENG Fun Bun Augustine • LEUNG Nancy*

RESEARCH OUTPUTS AND PUBLICATIONS

- <P001475> **Chan, P.K.S.; Lam C.W.; Li W.H.; Chan M.Y.M.; Cheung J.L.K. and Cheng A.F.** "AF234529 Human Papillomavirus Type 58 Strain E6HK1 E6 Protein Gene Complete Cds". *GenBank USA: National Center for Biotechnology Information*, 2000.03.28.
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- <P001525> **Hui, Mamie; Paul K.S. Chan; Ho-Keung Ng; Jo L.K. Cheung and Augustine F.B. Cheng.** "A Survey for the Presence of Human Herpesvirus 6 Genomic Sequences in Various Anatomical Positions of the Brain". Paper presented in 9th International Congress on Infectious Diseases, organized by International Society for Infectious Diseases. Argentina, 2000.04.12.
- <P001527> **Bridges, Carolyn Buxton; Jacqueline M. Katz; Wing Hong Seto; Paul K.S. Chan; Dominic Tsang; William Ho; K.H. Mak; Wilina Lim; John S. Tam; Matthew Clarke; Seymour G. Williams; Anthony W. Mounts; Joseph S. Bresee; Laura A. Conn; Thomas Rowe; Jean Hu-Primme** "Risk of Influenza A (H5N1) Infection Among Health Care Workers Exposed to Patients with Influenza A (H5N1) Hong Kong". *The Journal of Infectious Diseases* vol.181, pp.344-348. USA, 2000.
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- <P001533> **Chan, K.S.P.** "Emerging and Re-Emerging Infectious Diseases". Paper presented in Chinese Congress of Clinical Chemistry & Laboratory Medicine 2000. Hong Kong, 2000.06.11.
- <P001534> **Chan, P.K.S.** "H5N1 Avian Influenza in Hong Kong 1997". Paper presented in the 10th Asian Congress of Pediatrics, organized by the Chinese Taipei Pediatric Association. Taiwan, 2000.03.26.
- <P001535> **Lyon, D.J.; Fung K.S.C.; Chan R.F.Y.; Ho D.Y.M. and Cheng A.F.B.** "A Ten Year Review of Methicillin Resistant Staphylococcus Aureus in a Hong Kong Hospital". Paper presented in the 4th Decennial International Conference on Nosocomial and Healthcare - Associated Infections. USA, 2000.03.05.
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RESEARCH PROJECTS

Compliance with Complex Medication Regimes in HIV/AIDS Patients

✉ Alexandros MOLASIOTIS • Violeta LOPEZ • CHUNG Rita*

☐ 1 November 1999

❖ Council for the AIDS Trust Fund

This study aims to assess the factors contributing to compliance with complex medication regimes in HIV/AIDS patients, and assess the effectiveness of a psychosocial intervention in improving long-term compliance rates in those patients characterised as non-compliant. Around 120 HIV patients in one outpatient HIV clinic in Hong Kong will be screened for compliance and related factors through a battery of psychometric tests. Those that will be non-compliant will be asked to join a program that will assist them in managing their medication schedule. This is mainly an education program that empowers the patient and provides positive reinforcement, counseling and lifestyle modification. Compliance assessment will be carried out in the intervention patients 3 times over 6 months in order to assess the long-term effectiveness of this approach to medication management. High compliance rates in HIV patients receiving antiretroviral drugs is necessary in order to improve survival, make treatment more effective and decrease drug costs associated with failed treatments. (MD99020)

The Chinese Translation of the Revised Piper Fatigue Scale and Symptom Distress Scale

✉ CHAN YIP Carmen Wing Han

☐ 1 July 1999

❖ CUHK Departmental Funding

The objectives of the study are:

- (1) Assessing equivalence between the English and Chinese versions of Revised Piper fatigue scale (PFS) in bilingual healthy university students;
- (2) Assessing the reliability and validity of the Chinese version of PFS and Symptom Distress Scale (SDS);
- (3) Collecting fatigue data from a sample of healthy university students and cancer patients.

A cross-sectional approach and cross-over design was used to collect data from bilingual university students using the Chinese and English versions of revised PFS. They also received a Chinese version of the POMS (Profile of Mood) fatigue subscale to complete and return to the research assistant.

The cancer patients in the oncology unit of a teaching hospital were asked to independently complete the

Chinese versions of fatigue subscale of POMS, revised PFS and SDS.

All data were analysed using SPSS program. Data from patients indicated that the Chinese version of revised PFS achieved high alpha coefficients of 0.9678 and the SDS of 0.8599. The POMS fatigue sub-scale was correlated with the revised PFS (0.681) and the SDS (0.793), both at 0.01 level. Data from students indicated that the Chinese and English versions of PFS were correlated (0.969) and paired samples t test showed no difference of the fatigue level obtained from both versions. Both cancer patients and healthy students reported a medium level of fatigue (4.88 - 4.99 from a range of 0-10). (MD99138)

Nursing Management of Oral Mucositis in Cancer Patients

✉ CHANG Anne Marie • Alexandros MOLASIOTIS • CHAN YIP Carmen Wing Han • LEE Yik Mun*

☐ 9 April 2000

❖ Health Services Research Fund, Hospital Authority

A two-phase study will be used to determine the effectiveness of guidelines in reducing oral mucositis in patients receiving chemotherapy in an acute hospital. During phase I data will be collected from 75 patients about current oral outcomes and the nurses' practice in caring for those patients. Phase II will use a quasi-experimental design for comparing the outcomes of 75 patients in the experimental and 75 in the control ward. The oncology patient outcomes to be compared are the level, severity and prevalence of mucositis and other oral symptoms. The nursing practice outcomes are the assessment and management of mucositis and the nurses' knowledge of mucositis. Following collection of baseline nursing data from both wards, nurses in the experimental wards will receive an education programme on the implementation of the mucositis guidelines and follow-up at 1-month. This education programme will be provided to nurses in the control ward at the end of the study. The main outcome measures for patients re Oral Mucositis Assessment, Oral Symptoms and for nurses are The Oral Nursing Care Monitor and Nurses Knowledge of Mucositis. Data will be analysed using t-test to compare experimental and control ward patient outcomes and nursing knowledge. Chi-square will be used to compare the level of nurses' adherence to the guideline. Spearman's correlation coefficient will be used to determine relationships between the major variables. The findings from this study will provide information on the effectiveness of the mucositis guidelines of the nursing management of mucositis in terms of level of mucositis and oral symptoms in cancer patients.

(MD99083)

The Inter-generational Dynamics of Aged Care

- ✉ Elizabeth Anne HERDMAN
- 2 May 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

This study proposes to examine the link between inter-generational dynamics and aged care. By the year 2016 it is estimated that approximately 13% of the population of Hong Kong will be over 65 years. Since the elderly utilize a disproportionate number of health services the demand for health care is expected to increase as the numbers of over 65s increases. The next few decades will see a significant need for increased numbers of nurses in aged care in both the community and hospital sectors. However, overseas and local research indicates that nurses have negative attitudes towards caring for the aged. In general studies have found an association between negative attitudes towards the aged and willingness to care for them. The proliferation of studies has not, however, extended our knowledge of the problem of how to generate an interest in aged care. In particular there are few studies:

- (1) relate attitudes to behaviour;
- (2) attempt to understand the underlying reasons for negative attitudes towards the aged or;
- (3) examine the role the social context plays in shaping attitudes and behaviour.

This study proposes to examine the proposition that there are inter-generational factors that contribute to the lack of interest by nurses in aged care. An examination of inter-generational dynamics may prove a more useful approach to understanding the problems of providing sufficient qualified nurses to meet the needs of an ageing population.

(MD99106)

The Chinese Women's Childbirth Expectations

- ✉ IP Wan Yim
- 1 July 1999
- ❖ CUHK Student Campus Work Scheme

In a review of western studies about childbirth expectation, Evan (1995) concluded that there is homogeneity in childbirth expectation across women populations. Expectations regarding support from nursing staff and support from their partners are always rated high both by high-risk and low-risk pregnant women (Bramadat, 1990 & Heaman et al., 1992). Stollte (1987) also found that more primiparas than multiparas rated their labour as "not like" what they had expected. Women having attended childbirth preparation class usually have more positive expectations for their experience.

Nevertheless, researchers claim that childbirth expectations might not be met for women. (Astbury, 1980; levy & McGee, 1976; Stolte, 1987). The incongruence between a woman's expectations for childbirth and the actual birth experience would result in more labour pain and emotional disturbance (Fridh et al., 1988; Lipson & Tiden, 1980).

In Hong Kong, no study has been done before to evaluate the women's childbirth expectation. As a beginning step toward more appropriate preparation of pregnant women for their childbirth experience, local research is needed to determine and understand the expectations that Hong Kong Chinese women have for their childbirth experience. Therefore, the purpose of this study is to explore the expectations of Hong Kong Chinese pregnant women about the care they will receive during labour. The results of this study will help address the type of childbirth preparation needed to be provided by health professionals.

(MD99137)

The Relationship Between Chinese Women's Feelings of Control During Labour and Obstetric Outcomes

- ✉ IP Wan Yim
- 1 July 1999
- ❖ CUHK Departmental Funding

Practitioners and researchers in obstetrical areas have long recognised the special importance of the concept of control to the childbearing women. Control or mastery during labour is always regarded as the key to childbirth satisfaction (Humenick & Bugen, 1981). As early as 1970s, women's desire to actively participate in her labour is found to be contributing to a positive childbirth experience (Davenport-slack & Boylan, 1974). It has been well established that more obstetric interventions a woman experiences, in particular the amount of drug used, the less control she feels and the less satisfied she feel (Knapp, 1996). On the other hand, perceived quality of partner support and perceived quality of relationship with caregiver has a positive relationship with perceived control.

However, there are many research questions which have not yet been answered. For example: the relationship between individual childbirth expectations and experiences of control during labour, and the impact of incongruence between expectations and perceived outcomes on experiences of control during childbirth. Therefore, the purpose of this study is to answer the following questions:

- (1) What are the feelings of control during labour among Chinese women?
- (2) What is the relationship between the feelings of control during labour and physiological outcomes of labour?

The findings of this study will help health care professionals gain more understanding about the local women's perception of control during labour and its association with the obstetric outcomes.

(MD99139)

Developing Reliable and Valid Chinese Measure of Diabetes Empowerment Scale

✉ SHIU Tak Ying • WONG Yee Man Rebecca*

☐ 12 May 2000

❖ Health Care & Promotion Fund, Hospital Authority

Objectives: Two objectives are derived to fulfil the aim of the study. First, to examine the cultural equivalency of the Chinese measure of Diabetes Empowerment Scale (DES). Second, to test the reliability and validity of the Chinese DES.

Design: A study incorporating a qualitative and quantitative component, undertaking at two stages will enable the psychometric properties of the Chinese DES to be established. The first stage will involve the examination of cultural equivalency and content validity of the Chinese DES while the second stage will establish construct and criterion validity as well as internal consistency and test-retest reliability of the instrument.

Setting: A diabetes centre of a regional hospital provides the setting of the study.

Subjects: Adult outpatient (N=130, aged 18 to 65, Type 1 and Type 2) who are attending the centre for diabetes care and education during a data collection period of 7 clinic days.

Results and conclusion: To our best knowledge, this is the first time for the DES to be translated in Chinese and psychometrically tested for the reliability and validity among Hong Kong Chinese. If the Chinese DES is found to be reliable and valid, it will provide an instrument as an outcome measure for diabetes research using empowerment as a theoretical framework. In addition, results of the proposed study may provide important information on the patients perceived self-efficacy level in relation to diabetes self-care.

(MD99121)

Psychometric Evaluation of the Chinese Version of the Parental Stressor Scale: Paediatric Intensive Care Unit

✉ YAM Bernard Man Chung • Violeta LOPEZ

☐ 15 May 2000

❖ Health Services Research Fund, Hospital Authority

Objectives: (1) To translate the English version of the Parental Stressor Scale: Paediatric Intensive Care Unit (PSS:PICU) to Chinese and (2) To evaluate the

psychometric properties of the Chinese version of the PSS:PICU (CPSS:PICU).

Design: A methodological study design will be used in this study to explore the following research questions: (1) What is the internal reliability of the CPSS:PICU? and (2) What is the construct and convergent validity of the CPSS:PICU?

Setting: Two hospitals with designated PICU in Hong Kong island and Kowloon will be used in this study.

Subjects: For a reliability coefficient of .70, with a confidence interval computed at 95% level of confidence, a convenience sample of 130 parents (mothers and/or fathers) will be asked to participate in this study.

Procedure: The first step is to translate the PSS:PICU into Chinese and to establish content validity of the translated version. Secondly, parents will be asked to complete the CPSS:PICU and the Chinese version of Part A of the State-Trait Anxiety Inventory within 48 hours after their child's admission to PICU.

Data analysis: Statistical tests to measure internal consistency, subscale to total correlations, construct validity and convergent validity will be calculated.

Results: The findings of this study will be submitted for publication in local and international refereed journals.

Conclusion: The validated CPSS:PICU will be used for future research to identify parental stressors in PICUs in Hong Kong.

(MD99117)

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 Clinical Management of Chemotherapy-Induced Nausea and Vomiting with Adjuvant Progressive Muscle Relaxation Training and Imagery Techniques in Breast Cancer patients (MD98006) ✉ Alexandros MOLASIOTIS • YUNG Ha Ping Hilary# • MOK Shu Kam Tony (Dept of Clinical Oncology) • YAM Bernard Man Chung |
| 1997-98 | Promoting Independent Learning and Clinical Competence through Implementing Contract Learning in a Clinical Context (ED97001) ✉ CHAN Wai Chi Sally • CHIEN Wai Tong |
| 1997-98 | An Evaluation of the Implementation of Case Management in the Community Psychiatric Nursing Service (MD97084) ✉ CHAN Wai Chi Sally • Ann Elizabeth MACKENZIE • CHAN |

- Oi Wah* • KU Man Wing, Betty* • LEUNG Lai To, Winnie*
- 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 • Ann Elizabeth MACKENZIE • LEE Fung Kam • LAI Shuet Fun, Adela* • LO Lai Fong, Tammi*
- 1998-99 The Qualitative Experiences of Postnatal Depression in Hong Kong Chinese Women (MD98066)
✍ LEVY Valerie Anne • CHAN Wai Chi Sally • LEE Tak Shing Dominic (Dept of Psychiatry) • CHUNG Kwok Hung Tony (Dept of Obstetrics & Gynaecology)
- 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)
- ✍ Sheila Frances TWINN • Eleanor Anne HOLROYD • ADAB Peymane*
- 1998-99 Nursing Management of Peripheral Intravascular Access Devices (MD98077)
✍ Violeta LOPEZ • CHANG Anne Marie • Alexandros MOLASIOTIS • CHAN David* • TONG Wah Kun*
- 1998-99 Comparative Analysis of Patient-Controlled Analgesia Versus Traditional Intramuscular Injection in Chinese Women Undergoing Elective Gynaecological Surgery (MD98074)
✍ WOOTTON LAW Siu Yin • WILLS Shuc Han Betty# • CHANG Anne Marie • IP Wan Yim • CHEUNG Tak Hong (Dept of Obstetrics & Gynaecology)

RESEARCH OUTPUTS AND PUBLICATIONS

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- <P000398> 黃金月、王慧蓮、李潔明、吳慕賢、翁夏萍、陳慧慈、楊笑明。〈中國護理教育發展趨勢分析〉。《中華護理雜誌》第35卷第6期，頁333-337。中國，2000.06。
- <P000409> 李子芬。〈老年病康復中護理的重要性〉。Paper presented in the 2000 HA Shanghai Geriatric Scientific Forum, organized by the Renji Hospital, Shanghai, China 上海，中國，2000.05。
- <P000410> **Lee, Tze-Fan Diana.** "Adjusting to Residential Care Placement: A Grounded Theory Study of Chinese Elders". PhD. Dissertation. 292 pgs. Hong Kong: The Chinese University of Hong Kong, 2000.
- <P000436> **Chan, Carmen.** "Evidence-Based Practice in the Management of Mucositis". Paper presented in the 2nd Hong Kong Nursing Symposium on Cancer Care 2000, organized by Departments of Nursing & Clinical Oncology, the Chinese University of Hong Kong. Hong Kong, 2000.01.21.
- <P000444> **Chan, Carmen and Molassiotis Alexander.** "The Experience and Perceptions of Fatigue in Chinese Cancer Patients". Paper presented in the 2nd Hong Kong Nursing Symposium on Cancer Care 2000, organized by Departments of Nursing & Clinical Oncology, The Chinese University of Hong Kong. Hong Kong, 2000.01.21.
- <P000495> **Leung, Ka Yi and Sally Chan.** "Preventing Youth Suicide in Hong Kong: Psychiatric Nurses' Contributions". *The Hong Kong Nursing Journal* vol.36 no.1, pp.7-15. Hong Kong, 2000.

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- <P000498> **Lam, Lai-Wah and Ann E. Mackenzie.** "Coping with a Child with Down Syndrome: The Experiences of Mothers in Hong Kong". *Abstracts of the 6th Annual Conference: Qualitative Health Research* pp.253-254. Alberta, Canada: International Institute for Qualitative/Methodology & University of Alberta, 2000.04.06.
- <P000580> **Ip, Wan Yim.** "Chinese Husbands' Presence During Labour: A Preliminary Study in Hong Kong". *International Journal of Nursing Practice* vol.6 no.2, pp.89-96. Melbourne, Australia, 2000.
- <P000581> **Chang, Anne and Ann Mackenzie.** "Contributions & Challenges in Clinical Nursing Research". Paper presented in the Health Services Research Committee Symposium, organized by Hospital Authority. Hong Kong, 2000.02.21.
- <P000582> **Wills, Betty S.H.; Yvonne Wootton and Joe Thomas.** "Health Care Professionals' Knowledge and Attitude Towards Post-Exposure Prophylaxis". *Abstracts of the 6th Annual Conference: Qualitative Health Research*, p.255. Alberta, Canada: University of British Columbia, 2000.04.
- <P000583> **Ip, Wan Yim.** "Relationships Between Partner's Support During Labour and Maternal Outcomes". *Journal of Clinical Nursing* vol.9 no.2, pp.265-272. UK, 2000.03.
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- <P000918> **Chan, Carmen and Sally Chan. ed.** *14th Anniversary Commemorative Monograph of Hong Kong Society for Nursing Education.* 34 pgs. Hong Kong: Medcom Limited, 2000.03.
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- <P001085> **Ng, Dominic Tin-Fu; Sally W.C. Chan and Ann Mackenzie.** "Case Management in the Community Psychiatric Nursing Service in Hong Kong: Describing the Process". *Perspectives in Psychiatric Care* vol.36 no.2, pp.59-66. USA, 2000.
- <P001086> **Mackenzie, Ann.** "The Art and Science of Collaboration Among Health Professionals". Paper presented in Hospital Authority Convention 2000: Quality in Practice, organized by Hospital Authority. Hong Kong, 2000.05.09.
- <P001087> **Holroyd, Eleanor.** "Chinese Daughters' Care-Giving Obligations Towards Elderly Parents: Discontinuities and Continuities". *Women of South China* ed. by Tam M.S. 22 pgs. Hong Kong, 2000.
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- <P001090> **Nahas, Violeta Lopez.** "Nursing Management of Peripheral Intravascular Access Devices". Abstracts of the 20th Anniversary of the Aga Khan University School of Nursing International Conference: Regional Collaboration in Nursing Education, Practice and Research. Karachi, Pakistan, 2000.05.
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- <P001093> **Nahas, Violeta Lopez.** "Maintaining Clinical Credibility as a Nurse Teacher in a Postgraduate Tertiary Specialization Program". *Clinical Nurse Specialist* vol.14 no.4, pp.184-188. USA, 2000.
- <P001095> **Holroyd, Eleanor Anne.** "Hong Kong Chinese Daughters' Caregiving Obligations Towards Their Elderly Dependant Parents: Implication for Community Nurses". Paper presented in the 6th International Middle East Nursing Conference-Celebrating Success in the New Millenium: International Reflections on Nursing Heritage Jordan, 2000.05.
- <P001096> **Twinn, Sheila.** "Developing Programmes for the Prevention of Cervical Cancer Amongst Hong Kong Chinese Women: An Evaluation of Focus Groups as a Method of Needs Assessment". Paper presented in the Royal College of Nursing Research Society Annual Conference, organized by University of Sheffield. England, 2000.04.13.
- <P001097> **Molassiotis, Alexander; Bernard M.C. Yam and Flora Y.S. Chan.** "The Effectiveness of Progressive Muscle Relaxation Training and Guided Imagery in Managing Chemotherapy Induced Nausea and Vomiting Among Breast Cancer Patients in Hong Kong". Paper presented in the 2nd Hong Kong Nursing Symposium on Cancer Case 2000: Developments in Cancer Nursing, organized by Dept of Nursing & Dept of Clinical Oncology, CUHK. Hong Kong, 2000.01.
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RESEARCH PROJECTS

Microsatellite Instability in the Evolution of Cervical Neoplasm

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☐ 1 June 2000

❖ Germany/Hong Kong Joint Research Scheme

Cervical squamous cell carcinoma is preceded by distinct premalignant epithelial changes known as cervical intraepithelial neoplasia (CIN). An alteration of microsatellite repeats in genome, that is referred to as microsatellite instability (MSI), reflects defects in DNA repair pathways and it has now been recognized as a probable route for human carcinogenesis. This project proposes to determine whether this mechanism is important in the evolution from premalignant to a malignant conditions of the cervix. The results from this study will improve our understanding of molecular pathogenesis of squamous cell cervical cancer. (MD99093)

A Comparison of the Antiatherogenic Properties of Estradiol with Other Cardioprotectants Used in the Treatment of Postmenopausal Women

✉ 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*

☐ 31 December 1999

❖ Research Grants Council (Earmarked Grants)

Unlike the situation in many developed countries, the incidence of coronary artery disease (CAD) in Hong Kong and in other parts of Asia is steadily increasing. One of the risk factors for CAD in women is the menopause, but the administration of estrogen to postmenopausal women has been shown to reduce CAD risk. However, long term use of estrogen is associated with an increased risk of endometrial and possibly breast carcinoma. As an alternative to conventional estrogen replacement, two other pharmaceutical interventions (selective estrogen receptor modulators [SERMS] and phytoestrogens) have recently become available. Each of these preparations has a selective action on estrogen receptors, and both appear to be protective against breast and endometrial cancer whilst having a similar but less potent effect than estrogen on serum lipids. The direct anti-atherogenic effects of the SERMS and

phytoestrogens have not been thoroughly evaluated. Using an ovariectomized, cholesterol-fed, rabbit model, the researchers will compare the effects of SERMS and phytoestrogens with those of estrogen on atheroma formation. Outcome parameters will include measurements of serum lipid concentrations, total antioxidant activity, the area of staining for atheroma in the aorta and the measurement of plaque depth. The results of this study will determine whether these newer interventions protect against atheroma formation in a similar manner to estrogen. These data will be of considerable value in determining the best treatment strategies for postmenopausal women and to curb the expected increase in cardiovascular disease in Hong Kong. (CU99268)

The Incidence of Microdeletions of the Azoospermic Factor (AZF) Genes(s) in Individual Sperm from Both Severe Oligospermic and Normospermic Semen

✉ 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

☐ 30 June 2000

❖ CUHK Research Committee Funding (Direct Grants)

Over 20 years ago the presence of gross deletions of portions of the Y-chromosome long arm (Yq) in azoospermic men was demonstrated. More recently, discrete microdeletions of the Yq have been found in some azoospermic and oligospermic men. Deletion analysis of men with aberrant Yq suggests that gene(s) termed azoospermic factor (AZF) reside in the region that carries the deletions and such genes may play an important role in spermatogenesis.

Intracytoplasmic sperm injection (ICSI) is an established fertility treatment in which a single sperm from a male with severe oligospermia is injected into the oocyte of the female partner to enable fertilization of the oocyte. ICSI allows men with spermatogenic defects to achieve biological paternity.

However, Yq microdeletions occur in 9-30% of males undergoing treatment with ICSI. Therefore the Yq microdeletion may be transmitted from father to son. The currently used method to detect Yq microdeletions is carried out on leukocyte DNA and this does not allow the detection of individuals who may be mosaic. This has serious implications in that the screening methods currently used will not reflect the real risk of transmitting AZF microdeletions from father to son.

This project will identify Yq microdeletions in single sperm and will therefore address directly the issue of mosaicism. This will provide a more accurate assessment of the incidence of Yq microdeletions in

infertile men, and it will also allow couples to be more accurately counselled before they proceed with assisted reproductive technology using ICSI. (MD99044)

A Study on Placental Transfer of Nonsteroidal Anti-inflammatory Drugs at Early Gestation

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

☐ 1 October 1999

❖ CUHK Research Committee Funding (Direct Grants)

The objective of this study is to investigate the potential placental transfer of 3 commonly prescribed Non-steroidal Anti-inflammatory Drugs (NSAIDs) in the first trimester of pregnancy. In this study, the concentration of naproxan, dichlofenic acid or mefenamic acid in matched samples of maternal serum, amniotic fluid, extra-coelomic fluid and fetal tissue will be measured by High Performance Liquid Chromatography following a standard dose of the respective drug in the patient. Since NSAIDs is one of the commonest group of drugs prescribed by general practitioners worldwide, it is not uncommon for pregnant women reporting a history of first trimester exposure to NSAIDs leading to undue anxiety and worry. Little is known about possible fetal effects during the first trimester. This study should provide useful information on the potential for placental transfer of these drug which will facilitate patient counselling. (MD99045)

The Effect of Placental Hypoxia on Trophoblastic Corticotrophin-releasing Hormone (CRH) Secretion in-vitro

✉ LEUNG Tse Ngong • LAU Tze Kin • WONG Yick Fu

☐ 1 October 1999

❖ CUHK Research Committee Funding (Direct Grants)

Levels of corticotrophin-releasing hormone (CRH) are raised in maternal, fetal and umbilical cord plasma in pathological pregnancies such as pre-eclampsia, intrauterine growth restriction and preterm delivery. The high levels of CRH in human pregnancies are of placental in origin. The exact mechanisms controlling the placental CRH production remain unknown. One of the proposed theories is that placental hypoxia and ischaemia are responsible. CRH is a potent vasodilator of fetoplacental circulation and has been suggested to be important in regulating fetoplacental vascular tone. Pregnancies complicated by pre-eclampsia and

intrauterine growth restriction are associated with insufficient uteroplacental blood flow. Reduced placental tension has been shown to cause placental production of many inflammatory cytokenes. It is reasonable to postulate that hypoxia also up-regulates the gene for CRH, resulting in increased CRH production by trophoblastic cells and release into maternal and fetal circulation. While CRH may have an important role in maintaining uteroplacental vasculature in pregnancy, low oxygen tension causes a compensatory rise in CRH secretion in an attempt to alleviate the effect of reduced placental blood supply. This project aims to mimic placental hypoxia *in-vitro* and to study its effect on CRH production in human placental tissues and trophoblastic cell lines. CRH production is measured by measurement of CRH peptides using RIA, by localisation in placental tissue via immunocytochemistry, and by examination of mRNA via Northern Blot analysis. (MD99046)

To Determine the Relationship between Umbilical Cord Artery Lipid Peroxide Concentrations and Morbid Neonatal Outcomes

✉ 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

☐ 1 December 1999

❖ Research Grants Council (Earmarked Grants)

The goals of this study are:

- (1) to compare the pattern of serial, neonatal urinary 8-isoprostane measurements (as a marker of perinatal oxidative stress) between neonates with poor and good outcomes;
- (2) to establish the concentrations of lipid peroxidation products in umbilical cord blood that are associated with significant neonatal morbidity and with continued oxidative stress; and
- (3) to clarify the relationship between oxidative stress associated with labour and significant short- and long-term neonatal morbidity. (CU99329)

Effect of Antenatal Corticosteroids Therapy on Material Bone Metabolism and Lipids Changes

✉ 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)

☐ 1 November 1999

❖ CUHK Research Committee Funding (Direct Grants)

Antenatal corticosteroid therapy before preterm delivery reduces the incidence of respiratory distress syndrome in the newborn. It also enhances the efficacy of neonatal surfactant therapy and thereby reduces the risk of intravascular haemorrhage, necrotising enterocolitis and neonatal death.

Corticosteroid therapy however is associated with the suppression of bone formation, resulting in a drop in both bone mass and bone mineral density. The development of specific and sensitive biochemical markers of bone formation and bone resorption allows a simple and non-invasive assessment of bone turnover. Markers of bone formation in serum include bone specific alkaline phosphatase, osteocalcin and carboxy terminal pro-peptide of type I pro-collagen (PICP). Bone resorption can be assessed by measuring serum cross-linked carboxy terminal telopeptide (ICTP) and urinary excretion of deoxypyridinoline and urinary calcium/creatinine ratio. By measuring serum PICP and ICTP, a single course of antenatal corticosteroid therapy is associated with a transient suppression of bone formation without affecting bone resorption. However, the cumulative effect of corticosteroid therapy and its long term effect on bone turnover are still unknown.

Corticosteroids also cause insulin resistance and impaired glucose tolerance, which lead to hypertriglyceridaemia and a reduction in high density lipoprotein (HDL) cholesterol. This combination of lipid abnormalities is often associated with small, dense low density lipoprotein (LDL) particles and their increased susceptibility to in vitro oxidation, which are new risk factors of atherosclerosis.

The aim of the study is to investigate the effects of repeated courses of antenatal corticosteroids on maternal bone metabolism and lipid changes, including the LDL particle size and oxidisability. (MD99047)

Gene Expression Profiles in Cervical Cancer Based on a cDNA Array Analysis

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

□ 2 January 2000

❖ CUHK Research Co mmittee Funding (Direct Grants)

The pathogenesis of squamous cell cervical cancer remains incompletely understood. Many genes and signalling pathways controlling cell proliferation, death and differentiation, as well as genomic integrity are involved in cancer development. A new technique, cDNA microarray, has made possible quantitative measurement of the expression profiles of thousands of genes simultaneously in the same cancer.

Recently the researchers have used a cDNA microarray containing 588 cDNAs to investigate the

gene expression profile of one cervical carcinoma. This showed an abundant expression of 5 genes that are related to tumour suppressor (1), oncogene (2), apoptosis (3), DNA synthesis (4) and cell invasion (5), respectively. This demonstrated the potential of cDNA microarray technology to elucidate tumour-specific gene expression profiles in cervical cancers as it has in other cancers.

The researchers propose to investigate the gene expression profiles in 40 cases of squamous cell cervical cancer using cDNA array technique. In addition, they will determine the presence of HPV infection and its HPV genotype. This study will allow a detailed evaluation of gene expression profiles and their correlation with clinico-pathologic features in these cancers, therefore, may help in the elucidation of cervical carcinogenesis, identify useful biomarkers for cervical cancer diagnosis and prognosis, and eventually lead to appropriate targeting for the rapeutic intervention.

This will be a collaborative study with Professor Khew-Voon Chin, The Cancer Institute of New Jersey, USA. His team is very renowned for the application of cDNA microarray technique, especially in the area of anticancer drug resistance. (MD99048)

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

✉ YIP Shing Kai Alexander • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research) • CHUNG Kwok Hung Tony • LEUNG Peter Ho Yin* • CHEON Cecilia* • LIU John Yu Sun* • WONG Thomas Hong Kwong*

□ 20 March 2000

❖ Pharmacia and Upjohn Limited

Objectives: This study aims to compare the tolerability, clinical efficacy, quality of life changes and cost expenditure imparted by tolterodine against oxybutynin treatment in Chinese women with overactive bladder.

Design: Multi-centre, randomized, evaluator blinded controlled clinical trial.

Setting: Sub-specialty outpatient clinics at two major regional hospitals.

Subjects: 354 Chinese women attending sub-specialty clinic with a urodynamically confirmed diagnosis of overactive bladder, excluding women with contraindication to medical treatment, psychiatric diseases or cognitive impairment.

Methods: Informed consent will be obtained from all participants. After their confirmatory urodynamic test, subjects will be asked to fill in a modified Urinary Dysfunction Prevalence (UDP)

Questionnaire, Visual Analogue Scale (VAS) for symptom severity and Xerostomia Questionnaire (XQ) for baseline assessment. The King's Health Questionnaire with (KHQ) and the Short Forms-36 (SF-36) will be completed for quality of life assessment before start of treatment. Subjects will then be randomized to take either oxybutynin 5 mg BD orally or tolterodine 2 mg BD orally which is blinded to the evaluator. A baseline urinary pad test and Dowell Brant Incontinence Cost Index (DBICI) will be performed and patients will be asked to keep a record of their expenditure related to their urinary problems. A urinary diary will be kept for one week before starting treatment, and before the next two outcome assessments. Outcome assessments will be performed at 4 and 10 weeks after the commencement of medical treatment by the XQ, VAS, KHQ and SF-36. A second urinary pad test and DBICI will be performed in week 11 and the study will be ended by a telephone follow-up or interview at week 13.

Outcome measures: The tolerability of treatment will be measured in terms of development of dry mouth by XQ scores. Subjective efficacy of treatment will be measured in terms of self-reported symptom severity and changes in mean VAS scores. Objective efficacy of treatment will be measured in terms of urinary diary and urinary pad weighing test findings. Quality of Life changes will be measured in terms of mean change of KHQ and SF-36 scores. Economic analysis will be measured in terms of cost-utility ratios.

(MD99094)

A Follow-up Study of Patients with Post-partum Urinary Retention

✉ YIP Shing Kai Alexander • CHUNG Kwok Hung Tony

☐ 1 June 2000

❖ CUHK Research Committee Funding (Direct Grants)

Post-partum urinary retention is a common phenomenon, and it has a prevalence of 14.6% at the Prince of Wales Hospital. It has been demonstrated that post-void residual bladder volume (PVRBV) has a positive correlation with duration of labour, with large PVRBV associated with long labour. One hypothesis for the association between post-partum urinary retention and duration of labour is that during protracted labour the presenting part of the fetus may exert pressure on the pelvic floor and the pelvic soft tissues, which include the pelvic nerve plexuses. This may subsequently lead to either urinary outflow obstruction by tissue oedema, or detrusor dysfunction due to pudendal neuropraxia. These pressure-related injury to the components of the voiding mechanisms may therefore lead to urinary retention in the post-partum period. However, these pelvic floor damages

may lead to urinary incontinence in the long run. This project sets out to follow up a cohort of women who had post-partum ultrasonographic examination for their PVRBV, and to compare the long term outcomes between women with and without post-partum urinary retention.

(MD99107)

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 | Characterization of the Up-Stream Regulators of Retinoblastoma Gene in Squamous Cell Carcinoma of Uterine Cervix (MD97052) ✉ CHANG Mang Z. Allan • CHEUNG Tak Hong • WONG Yick Fu |
| 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) |
| 1997-98 | Hypoxic-Ischemic Induction of Apoptosis in the Newborn Rat (MD96210) ✉ HAINES Christopher John • CHANG Mang Z. Allan • ROGERS Michael Scott |
| 1997-98 | Evidence of Oxidative Stress and Apoptosis after Perinatal Hypoxic-Ischaemic Insults on the Rat Brain (MD97053) |

- ✎ HAINES Christopher John • CHANG Mang Z. Allan • FISCUS Ronald Ray (Dept of Physiology) • JAMES Anthony Edward (Laboratory Animal Services Centre) • STADLIN Alfreda (Dept of Anatomy) • WONG Yick Fu
- 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
- 1997-98 Oxygen Free Radicals in Amniotic Fluid Sample in Second Trimester of Pregnancy (MD97119)
- ✎ LAU Tze Kin • FUNG Tak Yuen* • ROGERS Michael Scott
- 1997-98 Psychosexual Function after Childbirth in Hong Kong Chinese Women (MD97120)
- ✎ LEUNG Tse Ngong • LEE Tak Shing Dominic (Dept of Psychiatry) • TANG So Kum Catherine (Dept of Psychology) • CHUNG Kwok Hung Tony • YIP Shing Kai Alexander • LAU Tze Kin
- 1997-98 A Study of Actocardiogram in Patients with External Cephalic Version at Term (MD97148)
- ✎ LO Wing Kit • LAU Tze Kin • SAHOTA Daljit Singh • LEUNG Tak Yeung • ROGERS Michael Scott
- 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)
- 1997-98 Feasibility of a PCR-Based Technique of Whole Genome Amplification to Screen for Allelic Loss in Cervical Intraepithelial Neoplasia (MD97055)
- ✎ WONG Yick Fu • CHUNG Kwok Hung Tony • CHEUNG Tak Hong
- 1998-99 Is Bat Quasi-monomorphic Tract a Prognostic Indicator for Endometrial Cancer? A Translational Study of a Biomolecular Marker to Clinical Utility (MD98045)
- ✎ WONG Yick Fu • CHUNG Kwok Hung Tony • CHEUNG Tak Hong
- 1998-99 Effect of Antenatal Corticosteroids Therapy on Bone Metabolism and Lipids Changes (MD98016)
- ✎ YUEN Pong Mo • MAK Wing Lai Tony (Dept of Chemical Pathology) • NG Pui Shan • LEUNG Tse Ngong • LAM Wai Kei Christopher (Dept of Chemical Pathology) • CHANG Mang Z. Allan
- 1998-99 Effect of Antenatal Corticosteroids Therapy on Maternal Hypothalamic-Pituitary-Adrenal Suppression (MD98015)
- ✎ YUEN Pong Mo • MAK Wing Lai Tony (Dept of Chemical Pathology) • PANG Man Wah Selina • LEUNG Tse Ngong • LAM Wai Kei Christopher (Dept of Chemical Pathology) • CHANG Mang Z. Allan

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000026> **Lau, Tze Kin; Keith Wing Kit Lo; Tak Yeung Leung; Wing Yee Fok and Michael S. Rogers.** "Outcome of Labour After Successful External Cephalic Version at Term Complicated by Isolated Transient Fetal Bradycardia". *British Journal of Obstetrics and Gynaecology* vol.107, pp.401-405. UK, 2000.03.
- <P000032> **Lau, W. C.; W. H. Tam; W. K. Lo and P. M. Yuen.** "A Randomised Double-blind Placebo-controlled Trial of Transcervical Intrauterine Local Anaesthesia in Outpatient Hysteroscopy". *British Journal of Obstetrics and Gynaecology* vol.107, pp.610-613. UK, 2000.05.
- <P000033> **Pennell, C. E.; Turner A.; Ping Y.; Wang C. C.; Rogers M. S and Murray H. G.** "Lipid Peroxidation and Lactic Acid Production During Cord Occlusion in the Ovine Fetus". *The Perinatal Society of Australia & New Zealand 4th Annual Congress in Conjunction with the Australian Neonatal Nurses Association 7th Annual Conference* pp.112-243. Brisbane, Australia: The University of Queensland & Wyeth Australia Pty Limited, 2000.03.
- <P000034> **Yuen, P.M.** "Outpatient Thermal Balloon Endometrial Abation Under Patient Controlled Sedation". *Minimal Invasive Techniques in Gynecologic Diseases* p.71. Korea: I.B Yoon Multispecialty Endoscopic Research & Training Center, 2000.05.07.
- <P000038> **Yuen, P. M.** "Preliminary Experience with Microwave Endometrial Ablation". *Abstracts of the 52nd Annual Congress of the Japan Society of Obstetrics and Gynecology* p.42. Tokushima, Japan, 2000.04.03.
- <P000039> **Yim, S. F. and P. M. Yuen.** "A Prospective Randomized Double Blind Trial Comparing Radially Expanding Access System with Conventional Cutting Tip Trocars". *Abstracts of the 52nd Annual Congress of the Japan Society of Obstetrics and Gynecology* p.41. Tokushima, Japan, 2000.04.03.
- <P000040> **Tam, W. H.; Rogers M. S; Arumanayagam M. and Cockram C.S.** "The Use of 1,5 Anhydroglucitol in the Management of Gestational Diabetes". *Abstracts of the 52nd Annual Congress of the Japan Society of Obstetrics and Gynecology* p.52. Tokushima, Japan, 2000.04.03.
- <P000049> **Mak, T. W. L.; Pang M. W.; Lam C. W. K. and Yuen P. M.** "Repeated Courses of Antenatal Corticosteroid Suppresses Maternal Adrenal Function". Paper presented in the Chinese Congress of Clinical Chemistry & Laboratory Medicine 2000. Hong Kong, 2000.02.
- <P000050> **Strachan, Bryony K.; Willem J. Van Wijngaarden; Daljit Sahota; Allan Chang and David K. James.** "Cardiotocography Only Versus Cardiotocography Plus PR-Interval Analysis in Intrapartum Surveillance: A Randomised, Multicentre Trial". *The Lancet* vol.355 no.9202, pp.456-459. UK, 2000.02.05.
- <P000052> **Lau, W. C. and Yuen P.M.** "Paracervical Anaesthesia in Outpatient Hysteroscopy: A Randomised Double-blind Placebo Controlled Trial". *British Journal of Obstetrics and Gynaecology* vol.107, pp.143-144. UK, 2000.02.
- <P000055> **Wijngaarden, Willem J. Van; Bryony K. Strachan; Daljit S. Sahota and David K. James.** "Improving Intrapartum Surveillance: An Individualised T/QRS Ratio?". *European Journal of Obstetrics & Gynaecology and Reproductive Biology* vol.88, pp.43-48. Ireland, 2000.01.
- <P000056> **Chung, T. K. H.; T. H. Cheung; K. F. To and Y. F. Wong.** "Overexpression of P53 and HER-2/neu and C-Myc in Primary Fallopian Tube Carcinoma". *Gynecologic & Obstetric Investigation* vol.49, pp.47-51. Basel, 2000.01.
- <P000057> **Yip, Shing-Kai; Angel On-ki Tse; Christopher John Haines and Tony Kwok-hung Chung.** "Misoprostol's Effect on Uterine Arterial Blood Flow and Fetal Heart Rate in Early Pregnancy". *Obstetrics and Gynecology* vol.95 no.2, pp.232-235. USA, 2000.02.

- <P000058> **Cheung, T. H.; Lo W. K.; Lam C.; Lau W. C. and Lam P.** "A Cross Over Study of Triptorelin and Leuprolide Acetate in the Treatment of Endometriosis". Paper presented in the Scientific Symposium Highlights Treatment of Endometriosis: New Perspectives, organized by OGSHK. Hong Kong, 2000.01.01.
- <P000087> **Pang, M. W.; T. N. Leung; D. S. Sahota; T. K. Lau and Allan M. Z. Chang.** "Development of a Customised Birthweight Standard for Ethnic Chinese Subjects". *Australian & New Zealand Journal of Obstetrics & Gynaecology* vol.40 no.2, pp.161-164. Australia, 2000.06.
- <P000157> **Lau, Tze Kin; Tak Yeung Leung; Keith Wing Kit Lo; Wing Yee Fok and Michael S. Rogers.** "Effect of External Cephalic Version at Term on Fetal Circulation". *American Journal of Obstetrics & Gynaecology* vol.182, pp.1239-1242. USA, 2000.05.
- <P000158> **Rogers, M. S.; Yuen P. M. and Wang C. C.** "8-Isoprostane F_{2d} As an Indicator of Peritoneal Damage During Surgery". *Proceedings of the 11th International Conference on Advances in Prostaglandin and Leukotriene Research: Basic Science and New Clinical Applications* p.63. Florence, Italy: Fondazione, Giovanni Lorenzine, Milan, Italy, 2000.06.
- <P000159> **Rogers, M. S.; C. C. Wang; Y. Qin and H. Kuehn.** "8-Isoprostane F_{2d} in Feto-Maternal Medicine". *Proceedings of the 11th International Conference on Advances in Prostaglandin and Leukotriene Research: Basic Science and New Clinical Application* p.35. Florence, Italy: Fondazione, Giovanni Lorenzine, Milan, Italy, 2000.06.
- <P000309> **Leung, T. N.; T. K. H. Chung; G. Madsen; W. A. W. Walters and R. Smith.** "Prediction of Pre-Eclampsia by Mid-Trimester Maternal Corticotrophin-Releasing Hormone Levels". *Abstracts from the 12th World Congress of the International Society for the Study of Hypertension in Pregnancy* vol.19 suppl.1, p.53. USA: Dekker. Pubs, 2000.06.17.
- <P001613> 邵浩達、阮邦武、王益夫、張明仁。〈醫學調查研究的概念和設計〉。《中國實用婦科與產科雜誌》第16卷第3期,頁185-186.中國,2000.03.
- <P002201> **Leung, T.N.; Tony K.H. Chung; Gemma Madsen; C.W.K. Lam; Peggo K.W. Lam; William A.W. Walters and Roger Smith.** "Analysis of Mid-Trimester Corticotrophin-Releasing Hormone and α -Fetoprotein Concentrations for Predicting Pre-Eclampsia". *Human Reproduction* vol.15 no.8, pp.1813-1818. 2000.
- <P992226> **Yip, Shing-Kai.** "Recent Advances in the Management of Female Urinary Incontinence". *Proceedings of the Annual General Meeting and Scientific Meeting, Hong Kong Continence Society* p.4. Hong Kong, 1999.09.18.
- <P992227> **Lau, W.C. and M.S. Rogers.** "Fetus Papyraceous: An Unusual Cause of Obstructed Labour". *European Journal of Obstetrics & Gynaecology and Reproductive Biology* vol.86, pp.109-111. Holland, 1999.09.
- <P992233> **Rogers, M.S. and Wang C.C.** "A Role for Ultrasonography in the Prevention of Intrapartum Hypoxia-Reperfusion Injury". Paper presented in 2nd International Congress on New Technologies in Reproductive Medicine, Neonatology and Gynecology, organized by Institute of Obstetrics & Gynecology, University 'La Sapienza'. Italy, 1999.09.
- <P992234> **Wang, C.C.; Murray H.G. and Rogers M.S.** "The Effect of Recurrent Hypoxia-Reperfusion on Brain Lipid Peroxidation: A Path Analysis". Paper presented in the 2nd International Congress on New Technologies in Reproductive Medicine, Neonatology and Gynecology, organized by Institute of Obstetrics & Gynecology, University 'La Sapienza'. Italy, 1999.09.
- <P992301> **Yuen, P.M.; D.S. Sahota and W.H. Tam.** "Outpatient Hysteroscopy Database Version 2.0". Hong Kong: Prince of Wales Hospital, The Chinese University of Hong Kong, 1999.09.
- <P992313> **Yuen, P.M.** "Territory-Wide Audit in Obstetrics & Gynaecology Hong Kong College of Obstetricians and Gynaecologists Version 2.1". Hong Kong: Prince of Wales Hospital, The Chinese University of Hong Kong, 1999.07.

- <P992448> **Leung, T.N.; T.K.H. Chung; Gemma Madsen; Mark McLean; A.M.Z. Chang and Roger Smith.** "Elevated Mid-Trimester Maternal Corticotrophin-Releasing Hormone Levels in Pregnancies that Delivered Before 34 Weeks". *British Journal of Obstetrics and Gynaecology* vol.106, pp.1041-1046. UK, 1999.10.
- <P992817> **Cheung, T. H.; W. K. Lo; C. Lam; W. C. Lau and P. Lam.** "A Cross Over Study of Triptorelin and Leuprorelin Acetate in the Treatment of Endometriosis". *Abstracts of the 1st Congress on Controversies in Obstetrics Gynecology & Infertility* p.40. Czech Republic: The Czech Republic Society of Obstetrics and Gynecology, 1999.10.
- <P992818> **Lo, Keith Wing-Kit and Pong-Mo Yuen.** "Mortality Following Laparoscopic Surgery". *Gynecologic & Obstetric Investigation* vol.48 no.3, pp.203-204. Switzerland, 1999.10.
- <P993139> **Pennell, C. E.; Turner A.; Ping Y.; Wang C. C.; Rogers M. S. and Murray H. G.** "Lipid Peroxidation and Lactic Acid Production During Cord Occlusion in the Ovine Fetus". Paper presented in the Fetal and Neonatal Physiological Society 26th Annual Meeting, organized by University Hospital Maastricht and University Medical Center Utrecht. Vlieland, Netherlands, 1999.09.
- <P993141> **Cheung, T. H.; Y. F. Wong; T. K. H. Chung; P. Maimonis and A. M. Z. Chang.** "Clinical Use of Serum C-ErbB-2 in Patients with Ovarian Masses". *Gynecologic and Obstetric Investigation* vol.48 no.2, pp.133-137. Basel, 1999.12.
- <P993156> **Yip, Shing-Kai; Shu-Pong Wong; Tak-Yuen Fung and Christopher John Haines.** "Unassisted Conception with a Normal Pregnancy Outcome in a Woman with Active Mycobacterium Tuberculosis Infection of the Endometrium: A Case Report". *The Journal of Reproductive Medicine* vol.44 no.11, pp.974-976. Hong Kong, 1999.11.
- <P993157> **Rogers, Michael Scott and Chi Chiu Wang.** "A Comparison of Three Ultrasound Estimates of Intrapartum Oligohydramnions for Prediction of Fetal Hypoxia-Reperfusion Injury". *Early Human Development* vol.56 no.2, pp.117-126. Ireland, 1999.12.
- <P993158> **Rogers, Michael Scott; Max Mongelli; Ka Hung Tsang and Chi Chiu Wang.** "Fetal and Maternal Levels of Lipid Peroxides in Term Pregnancies". *Acta Obstetrica et Gynecologica Scandinavica* vol.78 no.2, pp.120-124. Denmark, 1999.02.
- <P993244> **McGrath, S; Leung Tn; Chung T.K.H.; Lam C.W.K.; Lewia T. and Smith R.** "Oestradiol Concentration in Human Pregnancy is Independently Associated with Gestational Age and Corticotrophin-Releasing Hormone Concentration". *Proceedings of the 42nd Annual Meeting of the Endocrine Society of Australia* vol.42, p.125. Melbourne, Australia, 1999.09.
- <P993245> **Chung, T.K.H.; D.S. Sahota; T.K. Lau; J.M. Mongelli; J.A.D. Spencer and C.J. Haines.** "Threatened Abortion: Prediction of Viability Based on Signs and Symptoms". *Aust NZ J Obstet Gynaecol* vol.39 no.4, pp.443-447. Australia, 1999.08.
- <P993246> **Yim, S.F. and Yuen P.M.** "A Prospective Randomized Double Blind Trial Comparing Radially Expanding Access System with Conventional Cutting Tip Trocars". *Abstracts of the 7th Annual Scientific Meeting of Hong Kong Society of Minimal Access Surgery and the Hong Kong Gynaecological Endoscopy Society* p.9. Hong Kong, 1999.11.27.
- <P993247> **Cheung, Tak Hong; Tony Kwok Hung Chung; Cho Sun Poon; Garrett M. Hampton; Vivian W. Wang and Yick Fu Wong.** "Allelic Loss on Chromosome 1 Is Associated with Tumor Progression of Cervical Carcinoma". *Cancer* vol.86 no.7, pp.1294-1298. USA, 1999.10.01.
- <P993248> **Chung, T.K.H. and Lee D.T.S.** "Postnatal Depression: A North and Southeast Asian Perspective". *Journal of Paediatrics, Obstetrics & Gynaecology* vol.25 no.6, pp.39-42. Hong Kong, 1999.11.

<P993250> **Kean, L.H.; C. Suwanrath; S.S. Gargari; D.S. Sahota and D.K. James.** "A Comparison of Fetal Behaviour in Breech and Cephalic Presentations at Term". *British Journal of Obstetrics and Gynaecology* vol.106, pp.1209-1213. UK, 1999.11.

see also <P000051>, <P000178>, <P000179>, <P000607>, <P000624>, <P000701>, <P000702>, <P000703>, <P000774>, <P002561>, <P985055>, <P985056>, <P985124>, <P990206>, <P991342>, <P992224>, <P992265>, <P992269>, <P992564>, <P992682>, <P993155>, <P993214>, <P994616>, <P994617>

RESEARCH PROJECTS

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

✉ LAM Shun Chiu Dennis • CHUA Kien Han John • THAM C Y Clement* • LAI Jimmy S. M.* • CHEW Paul* • CHOY Kan* • MVSCAT Nina*

☐ 28 February 2000

❖ Pharmacia and Upjohn Limited

A 12-week, multi-center, double-masked, parallel-group comparison of the IOP-reducing effect and safety of latanoprost 50 µg/ml to that of timolol 5 mg/ml in 32 patients with chronic angle-closure glaucoma.

The primary objective is to demonstrate that latanoprost is at least as effective in reducing IOP as timolol in patients with CACG.

The secondary objectives are to:

- (1) demonstrate that latanoprost has a better IOP-reducing effect than timolol;
- (2) compare the proportion of patients reaching specified IOP levels in the two groups;
- (3) describe the IOP development throughout the study period;
- (4) and follow safety variables in the two groups. (MD99088)

Mitochondrial Permeability Transition in Retinal Excitotoxicity

✉ LAM Tim Tak

☐ 1 June 2000

❖ CUHK Research Committee Funding (Direct Grants)

The overall objective of this study is to understand the pathway(s) of retinal excitotoxicity so that new therapeutic approaches to “excitotoxicity related diseases such as ischemia and glaucoma” can be study. The purpose of this study is to further characterize the pathway(s) of retinal neuronal death after exposure to the excitotoxin, N-methyl-D-aspartate (NMDA). The underlying hypothesis of this study is that excitotoxicity of retinal neurons involves activation of “mitochondrial permeability transition (MPT)” pore on the mitochondrial inner membrane resulting in the release of various intramembraneous proteins including cytochrome c with subsequent cell death either by apoptosis or necrosis. The researchers propose to examine the role of MPT in the loss of retinal neurons after exposure to N-methyl-D-aspartate (NMDA). Their goal is to acquire preliminary findings to form a basis

for further detail study of MPT in neuronal death in retinal excitotoxicity. The researchers plan to examine the effect of two inhibitors of MPT: “cyclosporin A (CsA) and N-methyl-Val-4-cyclosporin A (MeValCsA), and FK506,” also an immunosuppressant but without any effect on MPT, on N-methyl-D-aspartate induced loss of inner retinal elements. Immunohistochemistry of cytochrome c and Western blotting on cytoplasmic cytochrome c will be performed to examine the release of cytochrome c/the opening of MPT pores. (MD99108)

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 | Molecular Marker for Familial Adenomatous Polyposis (FAP) and Predictive Value of Congenital Hypertrophy of the Retinal Pigment Epithelium (CHRPE) in FAP (MD97062) ✉ LAM Shun Chiu Dennis • PANG Chi Pui Calvin • TANG Leung Sang Nelson (Dept of Chemical Pathology) • LAU Wan Yee Joseph (Dept of Surgery) |
| 1997-98 | Diagnostic Kits for Early Detection of Genetic Eye Diseases for Blindness Prevention and Genetic Counselling (MD97092) ✉ LAM Shun Chiu Dennis • PANG Chi Pui Calvin |
| 1998-99 | Epidemiology of School Myopia in Hong Kong: Prevalence, Incidence and Risk Factors Analysis (MD98004) ✉ LAM Shun Chiu Dennis • CHEW Sek Jin* • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research) • FAN Shu Ping Dorothy • CHENG Hong Ming* |
| 1995-96 | Apoptosis of Photoreceptor Cells (CU95628) |

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| <p>≈ LAM Tim Tak • TSO Mark On Man#</p> <p>1996-97 Neuronal Rescuers for Apoptotic Degeneration of Retinal Ganglion Cells (CU96673) ≈ LAM Tim Tak • TSO Mark On Man#</p> <p>1997-98 Ultrastructural Studies of Rod and Cone Degeneration in Transgenic Mouse and Pig Models of Retinitis Pigmentosa (MD97025) ≈ LAM Tim Tak • TSO Mark On Man# • WONG Fulton*</p> <p>1997-98 Therapeutics for Apoptotic Loss of Retinal Neurons in Glaucoma (CU97639) ≈ LAM Tim Tak • TSO Mark On Man#</p> <p>1998-99 Molecular Study of Poly-adenylribose-polymerase (PARP) in Apoptotic Cell Death of Retinal Neurons after Ischemia/Glaucomatous Insult (MD98046) ≈ LAM Tim Tak</p> <p>1997-98 Interactions between Smoking, Diabetes Mellitus and Genes Affecting Lipoprotein Coronary Heart Disease Risk Factors (MD97172)</p> | <p>≈ PANG Chi Pui Calvin • JANUS E.D.* • MASAREI J R L*</p> <p>1997-98 Study of the Enzymic Properties of Lipoprotein Lipase (LPL) Variants and their Effects on Hyperlipidaemia (MD97113) ≈ PANG Chi Pui Calvin • TOMLINSON Brian (Dept of Medicine & Therapeutics)</p> <p>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</p> <p>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)</p> |
|---|--|

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000170> **Lam, Dennis S. C.; John K. H. Chua; Alfred T. S. Leung; Dorothy S. P. Fan; Joan S. K. Ng and Srinivas K. Rao.** "Sutureless Pars Plana Anterior Vitrectomy Through Self-Sealing Sclerotomies in Children". *Arch Ophthalmol* vol.118 no.6, pp.850-851. 2000.
- <P000654> **Lam, Dennis S. C.; Yuk Fai Leung; John K. H. Chua; Larry Baum; Dorothy S. P. Fan; Kwong Wai Choy and Chi Pui Pang.** "Truncations in the *TIGR* Gene in Individuals With and Without Primary Open-Angle Glaucoma". *Invest Ophthalmol Vis Sci* vol.41 no.6, pp.1386-1391. 2000.
- <P000658> **Lam, Dennis S.C.; Alvin L. Young; Alfred T.S. Leung; Srinivas K. Rao; Dorothy S.P. Fan and Joan S.K. Ng.** "Scleral Fixation of a Capsular Tension Ring for Severe Ectopia Lentis". *J Cataract Refract Surg* vol.26 no.4, pp.609-612. 2000.
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RESEARCH PROJECTS

The Application of Verbascoside, A Purified Extract of Chinese Medicine on Recovery of Muscle Injury after Immobilization

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□ 1 August 1999

❖ CUHK Research Committee Funding (Direct Grants) • Research Grants Council (Earmarked Grants)

Immobilization is one of the most common clinical procedures in Orthopaedics. Even though the current trend focuses on an early and progressive mobilization after injury, there are evident benefits of stabilizing an injured limb during the healing of a fracture or severe soft tissue injury. On the other hand, it is well known that immobilization results in dysfunction of the limb caused by a cascade of local catabolic sequences in all immobilized tissues.

Few experimental studies have focused the catabolic mechanisms involved during immobilization and restoration/remobilization. In an animal model, the level of thiobarbituric acid reactive substance and oxidized glutathione were elevated during remobilization after an immobilization period, reflecting the local oxidative stress. The researchers hypothesize that this local oxidative stress might delay restoration of muscle properties and consequently impair functional performance. Oxidative damages caused by local free radicals are suggested to be a major factor. The use of antioxidants in reducing this oxidative stress has not been previously elucidated. Verbascoside is an antioxidant purified from a traditional Chinese medicine extract named *Smilax lebrunii*. In their previous studies, verbascoside was shown to decrease the oxidative stress from excessive endurance activities in an animal model.

The aims of this study are to explore the oxidative stress, defined as locally increased free radicals, and the antioxidant defense profile in rabbit hind limb muscles during immobilization and remobilization. Muscle damage is defined and evaluated by histomorphology and biochemistry parameters. Muscle blood supply will be monitored using Laser Doppler and evaluated histomorphometrically. Muscle function is assessed by electromyography and vibromyography. The effects of verbascoside on reducing the oxidative stress and muscle damage will also be evaluated.

(CU99344)

A New Approach to the Treatment of Skeletal Muscle Injury – Isolation and Cloning of A New Myogenic Factor

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□ 1 February 2000

❖ France/Hong Kong Joint Research Scheme

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

In previous studies, the researchers have identified and purified a myogenic protein fraction ranging from 5-7 kDa from rat muscle aqueous extract. The functional assay of this myogenic fraction demonstrated its effect in triggering and enhancing the proliferation and differentiation of the cultured myoblasts and muscle fibre regeneration in the rat model. A 6 kDa protein has been isolated from this 5-7 kDa fraction, which could significantly enhance the proliferation and differentiation of cultured myoblasts. A recent microsequencing of this protein has been unsuccessful due to the N-terminal block of this protein.

Therefore, in this present research, the researchers will further perform peptide mapping to create fresh N-termini of this 6 kDa protein, so that the fresh N-termini can be sequenced by Edman degradation method. After the sequencing data has been obtained, the molecular cloning of this new myogenic factor will be conducted. Furthermore, the gene coding for this myogenic factor will be transfected into myoblast cell line (C2C12). The effects of this gene overexpression on the proliferation and differentiation of cultured myoblast will be studied. (MD99082)

Active Living – the Way to Healthy Ageing

✉ CHAN Kai Ming • HA Sau Ching Amy (Dept of Sports Science & Physical Education)

□ 1 May 2000

❖ Health Care & Promotion Fund, Hospital Authority

Elderly generally lack confidence in their ability to be active despite substantial health benefits of physical activity. This project builds on the new concept of *Active Living* advocated by the World Health Organisation and aims to change the attitude of elderly in becoming more active in their daily living. It will include:

- (1) a video on how elderly may incorporate physical activity in their daily routines;
- (2) a "Health Passport" depicting recommendations of Active Living and a monthly progress chart;
- (3) a resource manual for workers in elderly services centre to increase provision of physical activities through modification of existing programmes; and
- (4) monthly health talks and counseling sessions, a 6-month pilot programme for 100 elderly in social centres in Shatin.

The project will last for 13 months from 1, May 2000 to 31, May 2001. An editorial board will oversee the project and a questionnaire survey is built in to evaluate the effectiveness.

(ED99033)

“Subacute Synovitis of the Hip in Children” A Distinct Entity? – A Follow up Study of 84 Cases

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

☐ 1 January 1999

❖ 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 PWH 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 synovitis different significantly from those with acute transient synovitis in terms of age of presentation & duration of symptoms before hospitalization. Moreover, patient having transient synovitis significantly differ from those with septic arthritis in terms of temperature on admission, ESR and White Cell Count.

(MD98168)

Percutaneous Intramedullary Kirschner Wiring for Displaced Diaphyseal Forearm Fractures in Children

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

☐ 1 January 1999

❖ CUHK Departmental Funding

This is to assess the results and pitfalls in treatment of children diaphyseal forearm fracture with percutaneous K-wire fixation with an average FU of 48 months.

The researchers have performed percutaneous Kirschner (K) wire fixation in 112 children with displaced forearm shaft fracture in the past 9 years, with 84 cases reviewed. 64 (76%) of them had both the radius and ulna fractured, and 10 (12%) the radius only and the other 10 (12%) the ulna only. In 60 (71%) patients the researchers performed close reduction, while in the remaining 24 (29%) close reduction failed and an open reduction through a small incision was required before K-wiring performed. The K-wire was inserted through the Radial styloid or the Lister tubercle for the radius, and through the tip of the olecranon for the ulna.

All the patients reviewed were found to have good functional results, none had non-union, deep infection or premature physal closure at a mean follow-up of 48 months. If initial pre-operative radiograph showed shortening or translation of the fracture, significant higher chance of open reduction was anticipated.

The researchers concluded that percutaneous K-wiring for forearm diaphyseal fracture in children is a convenient, effective and safe operation, with very minimal complications.

(MD98169)

Results of Treatment of Scoliosis Patients Undergoing Posterior Instrumentation and Fusion Using the ISOLA Segmental Spinal System

✉ CHENG Chun Yiu Jack • LEUNG Ping Chung • NG Kin Wah Bobby • LAM Tsz Ping

☐ 1 July 1999

❖ CUHK Departmental Funding

Although good surgical techniques are of prime importance, a good implant system will greatly enhance the success of posterior spinal surgery for scoliosis. ISOLA is one of the latest generation of 3D multiple purchase implant system. Unfortunately, only few reports on its clinical use are available.

The aim of the present study was to evaluate the effectiveness and safety profile of the ISOLA Spinal Implant System in the treatment of scoliosis.

The charts and radiographs of all patients undergoing surgery for scoliosis with the ISOLA implant from 1996 to 1999 were reviewed and analyzed retrospectively.

41 patients were recruited with 31 girls and 10 boys. The average age was 14.2 years old with an average follow-up of 26 months. There were 32 idiopathic scoliosis, 7 neuromuscular scoliosis and 2 miscellaneous types. The pre-operative Cobb's angle ranged from 54 to 82 degrees. An average of 12.3

levels was fused posteriorly. The average pre-operative Cobb's angle, apical vertebral rotation, apical vertebral translation and lumbar lordosis were 66 degrees, 2.2, 48mm and 40 degrees respectively. The corresponding post-operative data were 34 degrees (50% correction), 1.8, 23mm and 40 degrees respectively. There were 4 complications including transverse process hook dislodgment, superficial sacral sore, and partial pull-out of pedicle screw. One case with spinal muscular atrophy undergoing extensive fusion down to the ilium developed deep wound infection, which was treated with debridement and retention of the implants.

The ISOLA Spinal Implant System is an effective, safe and user-friendly posterior system that can be used in different types and patterns of scoliosis with low complication profiles compared favourably with that of other posterior spinal instrumentation systems. (MD99141)

Intestinal Calcium Absorption Measured by Stable Calcium Isotopes in Northern Chinese Adolescents with Sub-optimal Vitamin D Status

- ✉ CHENG Chun Yiu Jack • LEE Tak Keung Warren • Jiang Ji* • Hu Pei* • Hu Xiaopeng*
□ 1 July 1999
❖ CUHK Departmental Funding

Adequate calcium intake and serum vitamin-D status are important for bone mineralisation in adolescents. In North China, calcium intake and serum vitamin-D level of adolescents are low due to non-dairy-based diets and inadequate sunshine exposure respectively. This study aimed to evaluate nutritional adaptation, i.e. calcium absorption (CaAbn) and urinary calcium excretion (CaEx) among Northern Chinese adolescents under these adverse conditions.

Healthy adolescents (12 girls, 4 boys) aged from 9-17-year-old were recruited from Beijing during winter months. CaAbn was determined by a dual stable-isotope technique (^{44}Ca and ^{42}Ca) coupled with Thermal-Ionization-Mass-Spectrometry.

Mean \pm SD calcium intake, 24-h CaEx, serum 25-hydroxycholecalciferol and CaAbn were $603 \pm 158\text{mg/d}$, $87.5 \pm 59.2\text{mg/24-h}$, $13.7 \pm 4.8\text{ng/mL}$ and $57.4 \pm 15.4\%$ respectively. Mean serum 25-hydroxycholecalciferol was close to the lower normal-limit (11ng/mL). 24-h-CaEx ($<100\text{mg/d}$) reflected a higher renal calcium conservation. CaAbn was significantly higher than the U.S. counterparts (25-34%; Calcium intake: 925mg/d), $P<0.05$. However, CaAbn was comparable to a group of 7-year-old Hong Kong children (CaAbn: 54.8%, calcium intake: 862mg/d , serum 25-hydroxycholecalciferol: 33.3ng/mL).

The study indicated that growing adolescents with sub-optimal vitamin D status are still capable of enhancing calcium absorption and reducing urinary calcium excretion to maximise bone mineralisation.

(MD99142)

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

- ✉ CHENG Chun Yiu Jack • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • QIN Ling • GUO Xia
□ 1 December 1999
❖ Research Grants Council (Earmarked Grants)

Scoliosis is a serious deformity that can affect any parts of the spine. Among the various causes the most common group is Adolescent Idiopathic Scoliosis (AIS) which typically affects the growing adolescent girls of the age of 10 to 16. Scoliosis deformity when not treated or improperly treated may progress and deteriorate leading to significant cosmetic problems and functional disabilities and in severe cases mortality due to cardiopulmonary failure. The incidence of AIS in Hong Kong was found to be 2.7% of all adolescents out of which one-tenth would require treatment. Current methods of treatment of AIS are unsatisfactory and have to involve long time bracing or major destructive surgery with many complications. It would be more effective if we can treat the cause of AIS which unfortunately is not clear yet. The researchers' recent study has found alarmingly that 88% of AIS patients had lower bone mineral density. To look into more detail scientifically on the possible link of osteoporosis to AIS they proposed this study. The main objectives are to establish the baseline values in bone mineral density, bone turnover and osteoporosis genetic marker in AIS patients vs. normal age, sex and maturity matched controls and to correlate longitudinally the progression of scoliosis deformity with the rate of change in bone mineral density, bone turnover and other parameters.

The outcome of the study will shed light on the etiology and pathogenic mechanisms of osteoporosis in AIS. This may lead to a novel approach in the monitoring, prognostication, and treatment of AIS. In those AIS with osteoporosis, one may be able to alter the natural story of the scoliosis deformity by non-invasive interventions to improve the bone mineral status.

(CU99336)

The Loss of Synchronous Coupling of Endochondral and Membranous Ossification in Adolescent Idiopathic Scoliosis

- ✉ 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 Idiopathic Scoliosis (IS), the researchers hypothesize 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 degrees 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 proves the above mentioned hypothesis and suggests that scoliotic deformity of the spine is a result of disturbed synchronous coupling of endochondral and membranous ossification.

(MD99140)

Nutrition & Physical Activity as Possible Factors Affecting Bone Mineral Status in Adolescent Idiopathic Scoliosis (AIS) – Cross-sectional & Case-control Studies

✉ CHENG Chun Yiu Jack • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research) • HO CHAN Suzanne (Dept of Community and Family Medicine) • GUO Xia

☐ 1 January 2000

❖ Health Services Research Fund, Hospital Authority

Background: Scoliosis, a spinal deformity typically affecting the growing adolescent girls, was found in 2.7% of the school children (10 - 15 years of age) in Hong Kong, the researchers' previous research indicated a high prevalence of osteopenia (18%) in adolescent girls with adolescent idiopathic scoliosis (AIS). Life style factors such as dietary calcium intake and physical activity are proven as important factors affecting development of bones in healthy children. No similar study has been carried out for AIS.

Objectives: The primary objective of the study is to understand the relationship between two life style factors (dietary nutrients intake and physical activity) and bone mineral density (BMD) in adolescent girls with AIS. The secondary objective is to study the relationship between the two life style factors and AIS.

Design and Methodology: The primary objective will be achieved by a cross-sectional study of 600 AIS girls of age 10 to 15. The secondary objective will be achieved by an age-matched case-control study

consisting a 50% random sample (n = 300) from the AIS subjects and 300 age-matched healthy girls.

Outcome and Results: Validated BMD measurement and questionnaire on dietary nutrient intake and physical activity will be performed on the subjects. The results will provide the scientific data and basis for future controlled interventional studies of osteopenia in AIS patients.

(MD99018)

Association of Neuropathology with Adolescent Idiopathic Scoliosis – MRI and SEP Studies

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☐ 1 June 2000

❖ CUHK Research Committee Funding (Direct Grants)

Idiopathic scoliosis is a three dimensional structural deformity of the spine with unknown etiology. It is the most common form of spinal deformity in adolescent girls (AIS). The researchers have established a Scoliosis Clinic with a large pool of more than 3,000 AIS patients with an annual new patient intake of over 600. A database including scoliosis clinical characteristics, growth pattern, skeletal development, family history, lifestyle factors and MRI data of more than 100 AIS patients and 50 age-matched normal control subjects have been established. From their preliminary study, an association of neuropathology, such as tonsillar ectopia and syringomyelia with IS has been demonstrated, a finding quite similar to some sporadic reports in the literature. Detail data and more systematic studies of larger series of AIS patients and the reference information of normal adolescents are however, not available. *The overall objective of this study is to evaluate the possible association of neuropathology with AIS Vs matched normal control group by:*

- (1) Magnetic Resonance Imaging (MRI) to identify structural abnormalities of the neuraxis;
- (2) Somatosensory Evoked Potential (SEP) to identify functional abnormalities in the neuraxis;
- (3) Correlating the MRI and SEP findings with clinical characteristics and progression of the deformity in AIS patients.

Results of this study will provide important information on the relationship between possible neuropathology in the etiology of AIS and possibility of new strategy of diagnosis, prognosis and treatment for AIS.

(MD99109)

Repair of Large Peripheral Nerve Defects with Artificial Nerve Grafts Composing of Cultured Schwann Cells

- ✉ HUNG Leung Kim • KWONG Wing Hang (Dept of Anatomy) • WU Hay Tong • LUI Kong Kei Walter
- 1 June 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Large segmental peripheral nerve defect is a difficult condition to treat, and the results of nerve grafting has not been entirely satisfactory. There are the questions of availability of autologous nerve grafts in extensive injuries, and the need for additional biological support to the nerve grafts to improve regeneration. Silicone tubes have been used to study nerve regeneration and later used as bridging graft to repair a nerve defect. Neurotrophic factors and cultured Schwann cells have been added to the tubes. In the study by Lao (1999) silicone tubes containing cultured Schwann cells achieved as good a regeneration as autologous nerve grafting. Lundborg (1997) added artificial fibers into the silicone tube and reported improved nerve regeneration, whereas Suzuki et al (1998) demonstrated the preferential regeneration of sensory axons. In the present study, distribution of sensory and motor fibers inside such a composite artificial graft will be studied to establish whether a differential regeneration exists and how this differential regeneration can be altered to achieve better motor regeneration. Alginate fibers will be studied to see if it will be a suitable form of artificial fibers to be combined with the silicone tube and Schwann cells, to create a composite artificial nerve graft. (MD99110)

The Effect of Non-invasive Low Intensity Pulsed Ultrasound on the Consolidation of Osseous Tissue after Callotaxis - The Biological Basis and Its Potential Clinical Application

- ✉ LEUNG Kwok Sui • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • FUNG Kwok Pui (Biochemistry) • CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)
- 1 November 1999
- ❖ Research Grants Council (Earmarked 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:

- (1) The surgical procedure to break the bone and preparation for distraction with the application of external distractor;
- (2) The actual lengthening of the bone by distraction with the rate of one mm per day; and
- (3) The consolidation and remodeling of the newly formed bone to become normal bone.

Although the clinical results have been satisfactory, the complications are still common. Most of the complications are related to the prolonged applications of the external distraction device, the problem of consolidation of the newly formed bony tissue and the long duration of hospitalisation. In this project, the researchers study the effect of low intensity pulsed ultrasound on mineralisation, consolidation and remodeling of the newly formed bony tissue in the third phase. The aims are to shorten the duration of external fixation and to enhance bony remodeling and maturation. This investigation will employ rabbits as an animal. The results obtained will help us to modify clinical treatment protocol, which leads to a decrease in the complications. The information obtained will also improve our understanding of ossification and remodeling of the bony tissue in fracture healing and in the regeneration of bone by distraction osteogenesis. (CU99257)

Prevention of Osteoporotic Fractures among the "High Risk" Groups of Postmenopausal Women

- ✉ LEUNG Ping Chung • QIN Ling • AU Sze Ki
- 1 July 1999
- ❖ Health Care & Promotion Fund, Hospital Authority

The prevalence of osteoporosis among the elderly women in Hong Kong as evidenced by osteoporotic fractures is high. Indeed, osteoporotic fractures have become the 5th most common cause for hospital care in Hong Kong. It is difficult to prevent osteoporosis but to prevent osteoporotic fractures is necessary and the most cost-effective way to do so is to identify the high-risk subjects and to put them on an effective preventive program. The high-risk group is defined as those elderly women who have already developed one non-traumatic fracture and whose annual trabecular bone loss exceeds 3%.

The researchers propose to conduct a randomized controlled study to investigate the effects of standard exercises and two antiresorptive drugs: alendronate and calcitonin on the bone mineral density (BMD) among 200 postmenopausal women who are identified either as fast bone losers (n=100) or patients with at least one non-traumatic fracture (n=100). Supervised standard exercises will be performed 45 minutes for 3 days a week for the exercise group (standard exercise is specially designed for patients with non-traumatic fracture to practise) while standard drug treatments are given to the other groups. Capacity of both static and dynamic balance will be measured as a relevant and independent predictor for fall and fall induced fracture. BMD will be measured using the newly available and the most precise volumetric and high-resolution image pQCT (peripheral quantitative

computed tomography) and conventional areal DEXA (Dual-energy X-ray Absorptiometry). The percentage changes of BMD, bone metabolic markers, muscle strength and balance among the exercise group, alendronate and calcitonin treatment groups will be compared with controls at 6, 12 and 18 months after starting the interventions.

The outcome of this study is expected to provide relevant information for practical preventive programs to be launched by Health Service Organizations.
(MD99001)

An Evidence Based Study on the Clinical Effects of Two Herbal Preparations Recommended for the Treatment of Diabetic Ulcers

✉ LEUNG Ping Chung • YEW Tai Wai David (Dept of Anatomy) • BUT Pui Hay Paul (Dept of Biology) • WONG Wan Nar Margaret

☐ 9 September 1999

❖ CUHK Research Committee Funding (Direct Grants)

Elderly patients suffering from diabetes mellitus are prone to the development of ulcers in their feet. Many of such patients end up in amputation of the involved leg. Attempts to salvage the leg in the past had not been successful because of the complicated coexisting pathologies of impaired local circulation, infection and peripheral neuropathy. Amputation, on the other hand, is not a good solution, because of frequent stump problems, and poor compliance in prosthesis utilization.

Traditional Chinese Medicine (TCM) claims that there are herbal preparations which would heal diabetic ulcers. Indeed the Shanghai Research Institute on the treatment of vascular diseases using integrated Western Medicine and TCM claimed such successes in over 90% of patients suffering from diabetic ulcers. Preliminary observations on patient volunteers at the Prince of Wales Hospital in Hong Kong indicated a ten out of twelve success on limb salvage, using two of the herbal preparations supplied by the Shanghai Research Institute and simple surgery consisting of day by day debridement of necrotic tissues and split-skin grafting.

The investigators want to collect objective experimental, biochemical and clinical evidences on the effects of the two herbal preparations used. The experimental animal model is the diabetic rat. A controlled study on the healing of experimentally produced ulcers will give data on the effects of the herbal preparations on the local circulation, granulation formation and state of neuropathy.

A controlled clinical study on 20 + 20 volunteers suffering from diabetic ulcers will be conducted in the same period. Detailed data on the local circulation, granulation formation and ulcer healing will be taken. While the patients are monitored for

changes in haemopoietic state, liver and renal functions.

While the components of the two herbal preparations are known and found to be mainly non-toxic, they would be further studied at the Chinese Medicinal Material Research Center (CMMRC) for a better understanding of the biochemical nature and authentication.

This Research aims at a break-through on the barrier between modern practice and TCM. The evidence based study offers the only approach to further justification of TCM in the treatment of diabetic ulcers.
(MD99050)

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

✉ LEUNG Ping Chung

☐ 15 October 1999

❖ Merck Sharp & Dohme (Asia) Ltd

Patients suffering from osteoarthritis of the knee were recruited under the researcher's strict criteria. They were divided into two groups, one group taking the new NSAID MK-0966 while the control group was given Naproxem. The clinical states were carefully scrutinized for 10 weeks and the results of the two groups were carefully compared.
(MD99084)

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

✉ QIN Ling • MAK Arthur* • CHAN Kai Ming • ROLF Christer# • CHAN Pui Barbara • ZHANG Yuanting (Dept of Electronic Engineering)

☐ 1 November 1999

❖ CUHK Research Committee Funding (Direct Grants)

Immobilization is a common method in the management of musculo-skeletal injuries. The negative effects on various immobilized tissues are well known. The time for recovery of the affected tissues is disproportionately long. From the performance perspective, the negative impact is obvious in sports, because injured athletes strive to return to training and competition as early as possible. From the public health perspective, it may be stressed that some tissues never fully recover after immobilization, which may cause severe morbidity,

in particularly the elderly individuals. Consequently, prevention measures directed to the adverse effects of immobilization are of great importance in orthopaedic rehabilitation. Approach may be either by direct intervention during the immobilization period, or/and by an early mobilization and active rehabilitation after immobilization.

Electrical stimulation has been used clinically to decrease muscle atrophy during immobilization, and has been shown effective in the researchers' previous experimental studies. The effects of electrical stimulation on tissues other than muscles are lacking. Based on their established methodologies and research tools developed for their previous and on-going research projects, the researchers will systematically investigate whether electrical stimulation can reduce the adverse effects of limb immobilization simultaneously on muscle, tendon, cartilage and bone using a rabbit knee experimental model. They will also investigate the effects of an active mobilization after an immobilization period by using progressive treadmill running. A number of new non-invasive and technologies will be used, such as the most accurate and high resolution peripheral quantitative computed tomography (pQCT) to monitor bone density and muscle volume, vibromyography to evaluate muscle contraction force and fatigue, and cartilage elastography to detect pathological changes in the articular cartilage. The outcome of this study will provide the relevant information leading to a strategic planning of rehabilitation after immobilization of muscle skeletal injuries.

(MD99051)

Changes in Foot Shape with Age

✉ WONG Wan Nar Margaret • CHENG Chun Yiu Jack • GRIFFITH James Francis (Dept of Diagnostic Radiology & Organ Imaging) • TANG Y N

□ 1 July 1999

❖ CUHK Research Committee Funding (Direct Grants)

Foot has two principle functions -- propulsion and congruity support. In order to perform well, it depends highly on the shape of the bones, joint and stability, ligament tension and muscle balance. Any abnormalities of these factors will be reflected on the contour and performance of the foot (such as pes planus, pes cavus, clubfoot, hallux valgus, etc). However, human foot exhibits a wider range of structural variation. In order to assess such deformities and manage the patients successfully, it is necessary to have an accurate analogue -- that is the normal foot values. The researchers need to know the base line of these variations so as to diagnosis patient objectively. And they need to know the normal values so as to make an accurate treatment.

The researchers find that many foot deformities appeared in the elderly without an obvious underlying cause, so they postulate that even the "normal" foot values are changing with age. Therefore, it is valued to examine whether it is a normal phenomenon that everyone is involved. If it is true, then why some people develop the deformity early and the other later, what is the determining factor and the its rate.

(MD99003)

Deleterious Effect of Glucocorticoids on Human Tendon Fibroblast and Possible 'Rescue' with Platelet Derived Growth Factor Isoform B (PDGF_{BB})

✉ WONG Wan Nar Margaret • ROLF Christer# • CHAN Kai Ming • CHAN Pui Barbara

□ 1 October 1999

❖ CUHK Research Committee Funding (Direct Grants)

Glucocorticoid injections are used in a wide spectrum of soft tissue and tendon disorders. The anti-inflammatory action often gives rapid clinical response. In the majority of patients, the target for the anti-inflammatory effect is most often acute inflammatory disorders affecting tendon sheaths, paratenon, bursae etc., and also the tendon itself. There are reports on spontaneous tendon ruptures after glucocorticoid injection, but a cause-effect relationship cannot be confirmed. Previous studies using animal models to find the association of local steroid injection with tendon damages were non-conclusive, and the validity of extrapolating animal study result to human is in doubt. The full effect of glucocorticoid on tendon cells remains unrevealed.

The researchers postulate that glucocorticoid injection has a deleterious effect on tendon cells, disturbing its extra-cellular matrix, leading to eventual deterioration and weakening of the tendon structure, with ultimate rupture. They therefore propose to use human tendon fibroblast culture to study the effects of glucocorticoids on human tendon fibroblasts in a uniform environment, with specific reference to changes in their extra-cellular matrix metabolism. Their preliminary result has shown cytotoxic effect of dexamethasone on tendon fibroblast.

In their previous studies, platelet derived growth factor isoform B (PDGF_{BB}) had been shown to stimulate chemotaxis and cell proliferation in cultured patellar tendon fibroblast. It also promoted restoration of ultimate stress when delivered to an *in vivo* model of injured tendon. They will assess a possible 'rescue' effect of PDGF_{BB} on human tendon fibroblast treated with glucocorticoids.

The research outcome may clearly define the role of glucocorticoid in tendon ruptures, and may have a

significant influence on the use of glucocorticoid in tendon disorders.
(MD99052)

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 (School of Public Health)

1998-99 The Mechanims 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)

1997-98 Abormal Somatosensory Evoked Potential in Adolescent Idiopathic Scoliosis - Where is the Site of the Abnormality? (MD97140)
 ✎ CHENG Chun Yiu Jack • GUO Xia • SHER Hing Leung Andy (Lee Hysan Clinical Research Laboratories)#

1997-98 Correlation between Curve Severity, Somatosensory Evoked Potential and MRI in Adolescent Idiopathic Scoliosis (MD97141)
 ✎ CHENG Chun Yiu Jack • GUO Xia • SHER Hing Leung Andy (Lee Hysan Clinical Research Laboratories)# • CHAN Yu Leung (Dept of Diagnostic Radiology & Organ Imaging) • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging)

1997-98 Application of Bone Morphogenetic Protein-Hydroxyapatite Composite Implant in Un-Decorticated Posterior Spinal Fusion (CU97669)
 ✎ CHENG Chun Yiu Jack • GUO Xia • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • MAK Arthur K.F.* • ROSIER Randy N.*

1997-98 Outcome of Surgical Treatment of Congenital Muscular Torticollis (MD97182)
 ✎ CHENG Chun Yiu Jack • TANG S. P.* • NG B K W*

1997-98 Correction of Lower Limb Deformity in Children – An Early Outcome Analysis (MD97183)
 ✎ CHENG Chun Yiu Jack • NG B K W* • FUNG P W*

1997-98 Scoliosis and Abnormal Postural Balance (MD97137)
 ✎ CHENG Chun Yiu Jack • CHOW Hung Kay, Daniel*

1998-99 Enhancement of Spinal Fusion with Osteoinductive Growth Factors Proacted HA-TCP (MD98139)
 ✎ CHENG Chun Yiu Jack • GUO Xia • LAU L P* • QU S X* • ZHANG X D* • LI J*

1998-99 Molecular Cloning and Expression of Bone Morphogenetic Protein 2 (BMP-2) in Bacterial System (MD98135)
 ✎ CHENG Chun Yiu Jack • WONG Lai Man# • LI Ming (Dept of Medicine & Therapeutics) • PU Q*

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*

1998-99 Expression of Bone Morphogenetic Protein 4 (BMP-4) in Myoblasts Leading to Osteoblast Formation (MD98137)
 ✎ CHENG Chun Yiu Jack • WONG Lai Man# • LI Ming (Dept of Medicine & Therapeutics) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories)

- 1998-99 Evaluation of the Quality of Posterior Spinal Fusion with High Resolution 3D-QCT (MD98138)
 ✎ CHENG Chun Yiu Jack • GUO Xia • QIN Ling • KOLLER B* • Ruegsegger P*
- 1998-99 Study of the Mechanical Properties of Bone-Hydroxyapatite Tricalcium Phosphate (HATCP) Interface by Nanoindentation (MD98142)
 ✎ CHENG Chun Yiu Jack • GUO Xia • LEUNG Y* • GUO L H*
- 1998-99 Outcome of Treatment of Congenital Pseudarthrosis of the Tibia - PWH Experience (MD98134)
 ✎ CHENG Chun Yiu Jack • NG B K W* • LAM C Y*
- 1998-99 Correlation Study on Calcaneal Ultrasound with Bone Mineral Density, Structural and Strength Indices of Weight Bearing Distal Tibia and Non-Weight-Bearing Distal Radius (MD98140)
 ✎ CHENG Chun Yiu Jack • HUNG Wing Yin Vivian • QIN Ling • AU Sze Ki • CHOY Wing Yee • LEUNG Ping Chung
- 1998-99 Surgical Treatment of Recurrent Patella Dislocation in Children - PWH Experience (MD98141)
 ✎ CHENG Chun Yiu Jack • NG B K W* • MOK WY*
- 1998-99 The Use of Allograft in Posterior Spinal Fusion in Scoliosis Surgery (MD98143)
 ✎ CHENG Chun Yiu Jack • NG B K W* • FU LLK*
- 1998-99 Production of Recombinant Bone Morphogenetic Protein 4 for the Treatment of Bone Defects and Disorders (MD98091)
 ✎ CHENG Chun Yiu Jack • LI Ming (Dept of Medicine & Therapeutics)
- 1998-99 Osteopenia in Adolescent Idiopathic Scoliosis - A Study of the Genetic Markers, Bone Mineral Turnover and Their Correlation with the Severity and Progression of the Spinal Deformity (MD98106)
 ✎ CHENG Chun Yiu Jack • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • QIN Ling • GUO Xia
- 1993-94 Distraction Lengthening of Upper Limb Anomalies in Children (MD94145)
 ✎ HUNG Leung Kim • CHENG Chun Yiu Jack
- 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)
- 1996-97 A Study to Correlate the Hand Function with the Physical and Physiological Structure of the Cervical Spine in Cervical Myelopathy (MD96169)
 ✎ LEUNG Kwok Sui • LEE Yuen Lun
- 1997-98 A Study of Physeal Retardation to Osteosarcoma Growth: Its Significance in Clinical and Basic Studies in Tumour Spread (MD97059)
 ✎ LEUNG Kwok Sui • FUNG Kwok Pui (Biochemistry) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • CHAN Chun Wai (Lee Hysan Clinical Research Laboratories) • CHEUNG Wing Hoi
- 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)
- 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.*
- 1996-97 Cartilage Elastography (MD96128)
 ✎ QIN Ling • MOW Van C.* • MAK F. T. Arthur*

- 1998-99 A Study of the Effect of Cartilaginous Tissues on Endothelial Cells in Angiogenesis of Tumour (MD98109)
 ✎ QIN Ling • LEUNG Kwok Sui • FUNG Kwok Pui (Biochemistry) • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)
- 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)

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000068> **Leung, Kwok Sui.** "Callotasis - Biological Response to External Mechanical Stimulation". *Proceedings of the 26th Annual Meeting of Japanese Society of Fracture Repair* p.51. Tokyo, Japan, 2000.06.
- <P000103> **Hung, L.K.; Cheng J.C.Y.; Ho P.C. and Leung P.C.** "An Analysis of Complications of Correction of Upper Limb Deformity Using Distraction Lengthening and Callotasis Technique". *The 5th International Symposium on Congenital Differences of the Upper Limb* Poster 100. Kyoto, Japan, 2000.05.
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- <P000605> **Guo, X.; Cheng J.C.Y.; Law L.P.; Lee K.M.; Guo L.H.; Qu S.X.; Zhang X.D.; Mak A.T.F. and Rosier R.** "Porous HA/TCP Augemented with Rhbmp -R Induces Undecorticated Posterior Spinal Fusion". *Society International de Rechercren Orthopaedic et Traumatologie and Chinese Speaking Orthopaedic Society 2000* Shanghai-Beijing, China: SIROT/CSOS, 2000.05.

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RESEARCH PROJECTS

Study of Predisposition Genotypes in Chinese Children with Asthma

- ✉ LEUNG Ting Fan • TANG Leung Sang Nelson
(Dept of Chemical Pathology)
- ☐ 1 December 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

Atopy is an inherited condition characterized by the formation of immunoglobulin E(IgE) antibody in persons with a genetic predisposition, who respond with immediate hypersensitivity on exposure to specific allergens. Epidemiological studies show that the prevalence of atopy and asthma is increasing worldwide. Both genetic susceptibility and environmental factors play important roles in the development of allergic diseases. A number of atopy susceptibility genes have recently been identified. Some of these genes regulate the production or effector functions of IgE whereas other loci determine the responsiveness of asthmatics to bronchodilator treatment. The associations between different phenotypes of asthma and these susceptibility loci are well described in Caucasian societies. Nonetheless, this kind of important information is lacking in the Chinese population. In the present study, the degree of atopy in our asthmatic children is defined by their cutaneous responses to a number of allergenic extracts whereas severity of asthma is determined by pulmonary function studies. The technique of restriction fragment length polymorphism is used to characterize polymorphic markers, in four candidate genes for atopic diseases in Chinese children with asthma. The researchers will then determine the association between asthma and polymorphisms in these gene loci. Besides, their study will look into the possible correlation between clinical phenotypes of asthma and various proposed predisposition genotypes in the subjects.

(MD99053)

Study of Varicella-zoster Virus Immunization in Paediatric Haematopoietic Stem Cell Transplantation

- ✉ LEUNG Ting Fan • CHAN Kay Sheung Paul
(Dept of Microbiology) • LI Chi Kong*
- ☐ 1 June 2000
- ❖ Children's Cancer Foundation

Haematopoietic stem cell transplantation (HSCT) is now the treatment of choice for most of the advanced malignant diseases in children. Nonetheless, these patients are at high risk of having severe varicella-zoster virus (VZV) infection because of significant

and prolonged immunosuppression in the post-transplant period. The researchers' recent review showed that 27 (25%) of 108 children who received HSCT developed post-transplant herpes zoster (HZ). Twenty-two (81%) children developed HZ within one year after transplant. Three (11%) children were found to have HZ with visceral dissemination. The cumulative incidences of post-transplant HZ at one and five years were 24% and 34% respectively. This study is a clinical trial involving prospective follow-up of post-transplant children regarding the effect of immunization with a live, attenuated VZV vaccine on the occurrence of VZV infection following HSCT. This approach, if feasible, may be an inexpensive method of preventing post-transplant VZV reactivation and its complications such as severe neuralgia, secondary bacterial infection and the need of hospitalization for antiviral treatment. In addition, the researchers will investigate on the relative contribution of cell-mediated and humoral immunity in controlling VZV reactivation after HSCT. Lastly, little information is available on the immunogenicity and safety of VZV vaccine in post-transplant children. This study will try to evaluate on these important but uncertain areas of VZV infection.

(MD99087)

Effects of Interleukin -1 β on the Proliferation and Signal Transduction of the Megakaryocytic Lineage

- ✉ LI Kwai Har Karen • YANG Mo
- ☐ 1 October 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

IL-1 β , a highly pro-inflammatory cytokine, induces thrombocytosis in mice and the effect was suggested to be indirect and mediated by accessory cells and IL-6. In a preliminary study, the researchers established that IL-1 β stimulated murine and human megakaryocyte progenitor cell growth. They also detected the expression of IL-1 type I and II receptors on megakaryocytic cell lines by RT-PCR, strongly indicating that IL-1 β may exert a direct effect on this lineage. Their hypothesis is that IL-1 β exerts direct stimulatory effects on megakaryocytic cells via its receptors, the signal transduction pathways involving STAT5/JAK2 and the transcription factor NF-E2. Their approach is (1) to confirm mitogen effects of IL-1 β on the differentiation of cord blood CD34+ enriched cells to the megakaryocytic progenitors by colony assays (CFU-MK); (2) to identify IL-1 β receptors I and II and the receptor accessory protein RI AcP in megakaryocytic cell lines and primary CD61+/CD41+ cells from human bone marrow; and (3) to investigate the signal transduction mechanism of IL-1 β on the megakaryocytopoiesis by the expression of STAT5/JAK2 and the transcription

factor NF-E2. The direct involvement of IL-1 β on the megakaryocytic lineage is a new concept. If proven, it would provide an explanation for the phenomenon of thrombocytosis during inflammation. It also has significant implications on the role of platelets in physiological and pathological conditions. (MD99054)

Is Hypotension in Preterm very Low Birth Weight Infants due to Hypothalamic-pituitary Adrenal Insufficiency?

✉ NG Pak Cheung • LAM Wai Kei Christopher (Dept of Chemical Pathology) • FOK Tai Fai

☐ 1 November 1999

❖ CUHK Research Committee Funding (Direct Grants)

Hypotension is a common occurrence in preterm newborn infants and may result in increased morbidity and mortality. Recently, the researchers have observed that preterm, very low birth weight (VLBW) infants may experience profound hypotension which does not respond to volume expanders and inotropic agents, but reacts favourably to physiological doses of hydrocortisone or dexamethasone. It has, therefore, been postulated that a significant proportion of VLBW infants have decreased ability to produce a stress-induced release of glucocorticoid because of their 'immature' hypothalamic-pituitary-adrenal (HPA) axis. However, the relationship between hypotension and HPA axis insufficiency has not been systematically studied or proven, and the exact site of endocrine dysfunction has not been determined. The researchers propose in this study to investigate the association between the neonatal blood pressure and pituitary-adrenal function using the human corticotropin (hCRH) test in preterm, VLBW infants. They also hope to identify the principal site of endocrine dysfunction in the HPA axis. The result will enable them to decide whether corticosteroid replacement should be used as the preferred treatment as opposed to plasma expanders or inotropic agents in this situation. (MD99055)

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 Controlled Study of Obstructive Sleep Apnea Syndrome in Obese Children in Hong Kong (MD97002)
 ✉ FOK Tai Fai • WING Yun Kwok (Dept of Psychiatry) • LEUNG Suk Fong Sophie# • HUI Hon Lam Stephen • CHEN Char Nie (Dept of

Psychiatry) • HO Kwok Wah Crover (Dept of Psychiatry)

1997-98 Determination of Local Oxygen Consumption by Healthy and Diseased Lungs in a Rabbit Model (MD97064)
 ✉ FOK Tai Fai • GU Jia Shi • XU Feng# • YIN Ai Tsang Jane

1997-98 To Provide Gestational Age-Specific Standards of Physical Measurements for Local Chinese Newborns (MD97086)
 ✉ FOK Tai Fai • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research) • NG Pak Cheung • CHANG Mang Z. Allan (Dept of Obstetrics & Gynaecology) • LEE Wai Hong* • CHOW Chun Bong*

1998-99 Randomized Comparison of Cefpodoxime Versus Cefuroxime Axetil as Follow on Treatment of Pneumonia (MD98127C)
 ✉ FOK Tai Fai • SUNG Yn Tz Rita • YU Chung Wah

1998-99 Effects of Oxygen Toxicity on Megakaryocytopoiesis (MD98047)
 ✉ FOK Tai Fai • LI Kwai Har Karen • YANG Mo • XU Feng

1998-99 Novel Molecular Defense-mechanism Against Tuberculosis: Enhanced Expression of the Inflammation-associated Gene *PML* (MD98048)
 ✉ HUI Hon Lam Stephen • CHAN Yeuk Hon John (Dept of Clinical Oncology)# • CHOW Louis Tsun Cheung (Dept of Anatomical & Cellular Pathology)*

1997-98 Vincristine Neurotoxicity in Children with Acute Lymphoblastic Leukaemia (MD97016)
 ✉ LEUNG Ting Fan • YEUNG Wai Lan • CHIK Ki Wai

1998-99 Effect of Interleukin-13 on Eosinophil Activation, Degranulation and Survival in Chinese Patients with Multitransfused Thalassaemia (MD98049)
 ✉ LEUNG Ting Fan • LI Kwai Har Karen • CHIK Ki Wai • 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 Anatomical & Cellular Pathology) • TSANG Kam Sze Kent (Dept of Anatomical & Cellular Pathology)*
- 1998-99 WHO/GSTF Maternity Advice Study (MD98123)
- ✎ NELSON Edmund Anthony Severn • COWAN S.* • MANGIATERRA V.* • CAFFERATA M.*
- 1997-98 The Pituitary-Adrenal Response in Preterm Very Low Birth Weight Infants after Treatment with Multiple Courses of Antenatal Corticosteroids (MD97024)
- ✎ NG Pak Cheung • LAM Wai Kei Christopher (Dept of Chemical Pathology) • WONG Wing Kin Gary • FOK Tai Fai • LEE Cheuk Hon
- 1998-99 The Effect of Postnatal Systemic Corticosteroids on Serum Leptin Concentration in Preterm, Very Low Birth Weight Infants (MD98050)
- ✎ NG Pak Cheung • LAM Wai Kei Christopher (Dept of Chemical Pathology) • FOK Tai Fai • WONG Wing Kin Gary
- 1995-96 The Epidemiology of Childhood Diabetes in Hong Kong (MD90205)
- ✎ WONG Wing Kin Gary • LEUNG Suk Fong Sophie# • OPPENHEIMER Stephen James#
- 1997-98 Bone and Collagen Turnover in Preterm Neonates with Dexamethasone Treatment (MD97065)
- ✎ WONG Wing Kin Gary • NG Pak Cheung • LAM Wai Kei Christopher (Dept of Chemical Pathology) • FOK Tai Fai
- 1998-99 CTLA-4 Gene Polymorphism in Childhood Graves' Disease (MD98051)
- ✎ WONG Wing Kin Gary • LI Kwai Har Karen
- 1996-97 The Correlation between Graft-versus-Host Disease and Cytokine Profiles in Bone Marrow and Peripheral Blood Stem Cell Transplantation (CU96663)
- ✎ YUEN Man Pan Patrick • CHIK Ki Wai • LI Kwai Har Karen • PONG Nga Hin Henry

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000017> **Li, Chi Kong; Rita Y. T. Sung; Ka Li Kwok; Ting Fan Leung; Matthew Ming Kong Shing; Ki Wai Chik; Chung Wah Yu; Man Ching Yam and Patrick M. P. Yuen.** "A Longitudinal Study of Cardiac Function in Children with Cancer Over 40 Months". *Pediatric Hematology and Oncology* vol.17, pp.77-83. USA, 2000.
- <P000111> **Lee, V.; C. K. Li; M. M. K. Shing; K. W. Chik; K. Li; K. S. Tsang; D. C. Zhao; D. H. Lai; A. Wong and P. M. P. Yuen.** "Single vs Twice Daily G-CSF Dose for Peripheral Blood Stem Cells Harvest in Normal Donors and Children with Non-Malignant Diseases". *Bone Marrow Transplantation* vol.25, pp.931-935. 2000.
- <P000145> **Leung, T. F.; P. C. Ng; T. F. Fok; M. C. K. Wong; W. Wong; K. L. Cheung and K. W. So.** "Pneumocystis Carinii Pneumonia in an Immunocompetent Infant with Congenital Cytomegalovirus Infection". *Infection* vol.28 no.3, pp.184-186. Germany, 2000.05.
- <P000289> **Li, C. K.** "Role of Radiology in Paediatric Oncology". *Journal of the Hong Kong College of Radiologists* vol.3 no.3, pp.197-200. Hong Kong, 2000.
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- <P000684> **Hui, J.; W.L. Yeung; N. Tang; K.W. Chik; M.K. Shing; C.K. Li; P.M.P. Yuen and T.F. Fok.** "4 Chinese Families with Adrenoleukodystrophy-Clinical Presentation and Treatment". *Proceedings of the 10th Asian Congress of Pediatrics* p.148. Taipei, Taiwan: The Chinese Taipei Pediatric Association, 2000.03.
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- <P000702> **Chan, S.M.; Nelson E.A.S.; Leung S.S.F.; Ip P.; Wu C. and Li C.Y.** "Breastfeeding in Hong Kong". *Abstracts of the 10th Asian Congress of Pediatrics* Abstracts no.033. Taipei, Taiwan: The Chinese Taipei Pediatric Association, 2000.03.26.
- <P000703> **Chan, S.M.; Nelson E.A.S.; Leung S.S.F. and Li C.Y.** "Diet of Hong Kong Chinese Lactating and Non-Lactating Women in the First Six Weeks Postpartum". *Abstracts of the 10th Asian Congress of Pediatrics* Abstracts no.FP6.5. Taipei, Taiwan: The Chinese Taipei Pediatric Association, 2000.03.26.
- <P000718> **Su, R.J.; K. Li; M. Yang; C.M.Y. Chiu and P.M.P. Yuen.** "Effects of PDGF on the Expansion of CD34+ Cells in Umbilical Cord Blood to the Megakaryocytic Lineage". *Hong Kong Society of Flow Cytometry 5th Annual Symposium* p.4. Hong Kong: Hong Kong Society of Flow Cytometry, 2000.01.08.
- <P000809> **Li, A.M. and T.F. Fok.** "Erythromycin-Induced Carbamazepine Toxicity: An Avoidable Problem". *Hong Kong Journal of Paediatrics (New Series)* vol.5, pp.43-44. Hong Kong, 2000.
- <P000810> **Xu, F.; T.F. Fok; E. Yung; J.A. Yin and K.F. To.** "Antioxidant Enzyme Activities and Antioxidant Enzyme Gene Expression in Hyperoxia-Induced Lung Injury in Premature Rat". *Hong Kong Journal of Paediatrics (New Series)* vol.5, pp.3-7. Hong Kong, 2000.
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RESEARCH PROJECTS

Delineation of the Second Messenger Pathways Involved in α_3 -adrenoceptors-mediated Relaxation of Rat Isolated Pulmonary Artery

- ✉ KWAN Yiu Wa
- 1 June 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

The autonomic nervous system can modify pulmonary blood flow under physiological conditions and may be involved in the pathophysiology of pulmonary vascular disease e.g. pulmonary hypertension. Adult pulmonary artery is a low-resistance, low-pressure system. In comparison to the excitatory α -adrenoceptors, the roles of the β -adrenoceptors in the regulation of the tone of pulmonary circulation received relatively little attention, especially under diseased conditions. Before the development of the selective subtype β_1 -adrenoceptor agonists and antagonists, it was generally believed that there are only two subtypes of β -adrenoceptors, β_1 - and β_2 -adrenoceptors, found in the blood vessels of various species including man. Recently, it has been demonstrated that other subtypes of β -adrenoceptors, namely β_3 - and the putative β_4 -adrenoceptors, exist in the cardiovascular system. The physiological functions of these two "newly" identified β -adrenoceptors (β_3 - and β_4), however, have not been examined in detail especially in the pulmonary circulation. In their preliminary study using a range of selective β_3 -adrenoceptor agonists and antagonists, the researchers have positively identified the presence of functional β_3 -adrenoceptors. The pulmonary artery relaxation elicited by β_3 -adrenoceptor activation was markedly attenuated in SHR rats, compared to normotensive WKY rats. However, the underlying mechanism(s) (e.g. type of ion channels and the cellular second messenger pathways) responsible for the attenuation of β_3 -adrenoceptor-mediated relaxation is not known at present. In addition, the importance of the endothelial cells in modulating the vascular responses of pulmonary artery to β_3 -adrenoceptors challenge will also be evaluated. (MD99111)

Role of Sensory Neuropeptides in Chronic Arthritis

- ✉ LAM Fu Yuen
- 1 May 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

The number of possible mediators in inflammatory joint diseases is vast. Conventional drug therapy for inflammatory diseases normally employs either glucocorticoids or non-steroidal anti-inflammatory drugs (NSAIDs) for their modulatory effects on cells and mediators involved in inflammatory processes. These treatments can merely provide partial relief for patients as the drugs are effective in inhibiting only some of the inflammatory mediators involved. An important group of inflammatory mediators that has been neglected in current anti-arthritis therapy is the neuropeptides that originate from nerves innervating the joint. There is substantial evidence supporting a role for sensory neuropeptides, particularly substance P (SP), in provoking inflammatory reactions in normal joints. However, few studies have been performed on the actions of neuropeptides in inflamed joints. In this study, the inflammatory actions of sensory neuropeptides will be characterised in normal and inflamed rat knee joints. Furthermore, the effectiveness of sensory neuropeptide antagonists in inhibiting joint inflammation will be assessed. (MD99112)

Investigation into Human *in vitro* Metabolism of Pyrrolizidine Alkaloids and Role of Their Toxic Pyrrolic Metabolites in Inducing Hepatotoxicity

- ✉ LIN Ge
- 1 April 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

More than 200 pyrrolizidine alkaloids (PAs) have been found in about 7,500 different plant species. Many of these plants are used for herbal medicinal products, and PA-containing traditional Chinese medicines are widely used in Hong Kong, Mainland China, and other Chinese Communities worldwide. However, PAs are almost invariably hepatotoxic, causing a serious natural product poisonings in human and animals. Investigations on the mechanism of PA-induced hepatotoxicity in laboratory animals have been extensively conducted. Biotransformation of PAs to the reactive pyrrolic esters mediated by hepatic cytochrome P450 enzymes and covalent binding of such toxic metabolites with tissue macromolecules have been demonstrated to play a key role in inducing PA intoxication. However, little information is known on the mechanism of PA-induced hepatotoxicity in man. The present research is to investigate the formation of toxic pyrrolic metabolites of PAs in man by using *in vitro* human microsomal metabolic study and the hepatic enzyme(s) mediating such formations. The results will enable the establishment of the relationship between the formation of toxic pyrrolic metabolites and PA induced hepatotoxicity and also

significantly contribute to a better understanding towards the mechanism of PA intoxication in man. (MD99056)

An Investigation into the Multiple Coupling Capacity of Prostacyclin Receptors

✉ WISE Helen • WONG Yung Hou*

☐ 1 August 1999

❖ Research Grants Council (Earmarked Grants)

The classical approach to drug design relies on an understanding of how agonists and antagonists work, and an accompanying search for receptor subtypes to improve the selectivity of drug action. In addition to a dependence on the discovery of receptor subtypes, an alternative approach is to examine the ability of agonist drugs to selectively target receptor signalling toward a specific G-protein. This phenomenon, known as agonist trafficking, is relevant to G-protein-coupled receptors that possess the capacity to couple to multiple G-proteins. The prostacyclin (IP)-receptor is one such receptor, capable of coupling to G_s and G_i in a variety of cells types. However, for endogenously expressed IP-receptors and the current range of IP agonists, it is often difficult to unambiguously demonstrate if IP agonists that activate multiple signalling cascades do so by interacting with IP-receptor subtypes or with a single IP-receptor capable of coupling to multiple G-proteins. By co-transfecting cells with the cDNAs of the IP-receptor and different G α subunits, the researchers propose to assess the full capacity of the IP-receptor for multiple signalling and relate this information to responses of endogenous IP-receptors. Not only will this work increase our knowledge concerning the behaviour of IP-receptors in different cellular environments, but it also has importance in increasing our understanding of receptor theory in general, and the mechanism of action of agonists in particular. (CU99253)

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

Edition Title/Investigators

1997-98 Mechanisms of the Contractile Action of Prostanoid EP₃-receptor Agonists on Vascular Smooth Muscle (MD97068)
 ✉ JONES Robert Leslie • KWAN Yiu Wa

1998-99 Cellular Mechanisms Involved in the Excitatory Actions of Prostanoid EP₃-and IP-Receptor Agonists (BL98001)

✉ JONES Robert Leslie • GURNEY A. M.* • KWAN Yiu Wa • KENNEDY C.* • SNEDDON P.*

1998-99 Characterization of Muscarinic Receptors in Rat Isolated Pulmonary Artery and Thoracic Aorta (MD98052)

✉ KWAN Yiu Wa

1996-97 Evaluation of Anti-inflammatory Agents in Animal Models of Arthritis (MD96088)

✉ LAM Fu Yuen

1998-99 Studies on Anti-inflammatory Neuropeptides in Rat Knee Joints (MD98053)

✉ LAM Fu Yuen

1998-99 Functional Characterisation of Mast Cells Cultured from Human Cord Blood (MD98054)

✉ LAU Hang Yung Alaster • OBATA Toru* • NAGAKURA Toshikazu*

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*

1998-99 Neuropharmacological Investigations into the Role of Prostaglandin-Receptors in the Emetic Reflex (MD98055)

✉ RUDD John Anthony • JONES Robert Leslie

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

1997-98 Effects of Polysaccharide Peptide (PSP) on Glutathione-Related Enzymes in the Mouse (MD97071)

✉ YEUNG Hok Keung John

1998-99 Metabolic Studies of a Series of Drugs in Horses (MD98082)

✉ YEUNG Hok Keung John • WONG Nai Ching Henry (Dept of Chemistry)

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- <P993445> **Kwan, Y.W.; T.C. Yeung and K.S. Lee.** "Characterization of Subtype of Muscarinic Receptors in Rat Isolated Pulmonary Artery and Thoracic Aorta". *Abstracts of the 8th Southeast Asian-Western Pacific Regional Meeting of Pharmacologists* p.86. Taipei, Taiwan: The Pharmacological Society, Taipei, 1999.11.
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see also <P000125>, <P000255>, <P992140>, <P992882>, <P993336>, <P993427>, <P999830>

RESEARCH PROJECTS

Project on Effect of Isoflavones on Bone Density in Chinese Early Postmenopausal Women

✉ HO Suk San Susan • HO Yee Ping • CHOW Hee Lum Albert • HO CHAN Suzanne (Dept of Community and Family Medicine)

☐ 5 June 2000

❖ Donation from SoyLife Nederland BV

A study was designed to measure the effects of isoflavones and calcium supplementation on bone density and serum lipids in Chinese early postmenopausal women. This project aimed at developing, formulating and manufacturing suitable dosage forms for the supplements used in the study. Various physical and chemical techniques (including HPLC analysis) will be used to assess the quality of the final products.
(MD99143)

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

✉ 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)

☐ 1 September 1999

❖ Donation from Roche Pharmaceutical

The study aimed to evaluate the potential cost savings following orlistat treatment, compared with dietary control, in patients with impaired glucose tolerance (IGT) or type 2 diabetes mellitus, in the setting of a diabetes clinic in Hong Kong. A decision-tree analysis model will be used to compare the effects of orlistat to dietary control on the direct medical costs associated with the management of IGT and type 2 diabetes mellitus with coexisting obesity over a 1-year period. The results of the study will provide important cost-related information to the decision-makers of health care systems as well as practitioners in the management of IGT and type 2 diabetes in Hong Kong.
(MD99145)

A Cost-effectiveness Analysis of High-dose Omeprazole Infusion as Adjuvant Therapy to Endoscopic Haemostasis for Bleeding Peptic Ulcers

✉ 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)

☐ 1 December 1999

❖ CUHK Departmental Funding

The study was designed to investigate the cost-effectiveness of high dose IV omeprazole as an adjuvant therapy to endoscopic hemostasis for prevention of early ulcer rebleeding from a hospital perspective. A randomized, placebo-controlled clinical trial was conducted previously in a local hospital to study the effects of high dose IV omeprazole infusion on patient outcomes after endoscopic ulcer hemostasis. Although the interim data suggested that IV omeprazole significantly decreased the rate of early rebleeding that occurred 72 hours after therapy, the cost implication of this therapy has not been examined. The data of the 157 patients who completed the above study will be analyzed.
(MD99148)

Cost Analysis of Losartan-to-candesartan Switch in Specific Patient Groups

✉ LEE Kwing Chin Kenneth • YOU Hoi Sze Joyce

☐ 1 May 2000

❖ CUHK Departmental Funding

The benefits of angiotensin-converting-enzyme-inhibitors (ACEIs) therapy in congestive heart failure patients and hypertensive patients with diabetes mellitus (DM) are well documented. Whereas ACEIs are well tolerated in general, a dry cough may develop requiring treatment withdrawal. The reported prevalence of cough with ACEIs in Chinese population is relatively high comparing to the prevalence reported overseas. The current general practice is to treat patients who cannot tolerate ACEIs with antiangiotensin II inhibitors instead.

The study aims to analyse the cost implication if losartan is replaced by candesartan for treatment in 3 specific groups of patients when they are intolerable to the side effects of ACEIs:

- (1) DM patients with hypertension;
 - (2) Patients with congestive heart failure;
 - (3) Hypertensive patients with concurrent hyperlipidaemia.
- (MD99147)

Quantification of the Hepato- and Entero-cytic Autoinduction Effects of Rifamycins: Significance for Drug Interactions

✉ RAYMOND Kenneth • CHIU Chi Keung Francis #

☐ 1 January 2000

- ❖ CUHK Research Committee Funding (Direct Grants)

The rifamycins are effective anti-tuberculosis agents. They are also one of the most fascinating group of drugs to study from a drug metabolism and drug interaction point of view. For example, not only does rifampicin have some very important drug interactions with many other drugs (e.g. it will interfere with the metabolic oxidation and detoxification of many drugs, e.g. cyclosporin A, warfarin, theophylline etc, which leads to decreased blood levels of these interacting drugs when they are co-administered with the rifampicin) it will also affect its own metabolism (auto induction). This means that the metabolism of rifampicin is increased as it is used initially by the patient. The amazing fact is that the mechanisms of the autoinduction and rifampicin's metabolism are quite distinct from its effects on the metabolism of other drugs. For example, rifampicin is metabolised by general non-specific esterase and by hydrolysis into 2 major compounds. This metabolic pathway is not well understood, even less so is its autoinduction processes. As for drug metabolism interactions, it is well known that hepatic metabolism reactions involve cytochrome p450 subtypes, particularly CYP3A. However, we have previously found that as well as CYP3A having effects in the hepatocytes, it also may have marked effects on the metabolism of the drug before it is absorbed and passes to the liver. That is, gut wall metabolism involving drug-metabolising enzymes such as CYP3A4 in the gut wall (enterocytes). Hence this project, building on data already collected will quantify this gut wall metabolism and will elucidate the total picture of rifampicin's metabolic fate. Once the full picture is known, the mechanisms of the drug metabolism and the rifamycins' clinically significant drug interactions will then be researched in more detail. (MD99057)

Economic Analysis of Four Triple Regimens for the Treatment of Helicobacter Pylori-related Peptic Ulcer Disease in Inpatient and Outpatient Settings in Hong Kong

- ✉ YOU Hoi Sze Joyce • LEE Kwing Chin Kenneth • HO Suk San Susan • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • KUNG Nam Shing Nelson (Dept of Medicine & Therapeutics) • CHAN YUNG Man Yee (Dept of Surgery) • LEE Chi Wai • Yee Gary C*
- 1 October 1999
- ❖ Chung Chi College Student Work Fund

Peptic ulcer disease is a common and life threatening condition with a mortality rate of 5-10%. The association between Helicobacter pylori and peptic ulcer disease is well established. Different regimens

have been studied and used in clinical practice. Although most of the studied regimens have high eradication rates and ulcer healing rates in excess of 80%, the total direct cost of care affected by the choice of triple regimen has not been examined. The researchers plan to conduct an economic analysis of four different triple regimens for the treatment of Helicobacter pylori-related peptic ulcer disease from a hospital perspective. (MD99146)

Healthcare Resources Utilization Associated with Nonsteroidal Anti-inflammatory Drug-induced Gastrointestinal Complications

- ✉ YOU Hoi Sze Joyce • LEE Kwing Chin Kenneth • KUNG Nam Shing Nelson (Dept of Medicine & Therapeutics) • CHAN Ka Leung Francis (Dept of Medicine & Therapeutics)
- 27 October 1999
- ❖ United Board for Christian Higher Education in Asia Faculty Research Gr.

Gastrointestinal (GI) complications related to nonsteroidal anti-inflammatory drugs (NSAIDs) are well documented in numerous reports. The severe GI complications, such as symptomatic ulcer, GI bleeding, severe dyspepsia and abdominal pain, associated with NSAIDs often cause hospitalization and usually require various surgical procedures and pharmacotherapies. The health care resource consumption associated with NSAID-induced GI complications would serve as a benchmark for the evaluation of the new NSAID agents, such as cyclooxygenase-2 inhibitors. The study is to estimate the cost of illness for management of GI events associated with NSAID therapy from the perspective of the Hospital Authority using the prevalence-based approach. (MD99149)

Eradication of Helicobacter Pylori to Prevent Peptic Ulcers Prior to NSAID Therapy – A Cost-effectiveness Analysis

- ✉ 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)
- 1 June 2000
- ❖ CUHK Departmental Funding

The objective is to study the cost-effectiveness of Helicobacter pylori eradication therapy on patients receiving NSAID treatment for musculoskeletal pain from the perspective of a public health organization. A decision tree was designed to analyse the cost-

effectiveness of *H. pylori* eradication in the prevention of NSAID-induced peptic ulcers. (MD99150)

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

Edition Title/Investigators

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)

1997-98 Hygroscopic Growth of Pharmaceutical Aerosols (MD97134)

✉ CHOW Hee Lum Albert • CHAN Chak Keung* • CHEN Guo Hua*

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

1996-97 Assessing the Pharmacokinetics and Pharmacodynamics of Drugs with Non-linear, Input Rate-dependent Dispositions (MD96087)

✉ RAYMOND Kenneth • LI Chi Keung Ronald#

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RESEARCH PROJECTS

Involvement of CFTR in Mediating Neurohormonal-regulated HCO₃⁻ and Cl Secretion by the Endometrial Epithelium

- ✉ CHAN Hsiao Chang
- ☐ 1 April 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

It is believed that the endometrial epithelium lining the lumen of the uterus has electrolyte transport activities which provide a suitable fluid environment for sperm movement and capacitation, embryo development and implantation. The endometrial epithelium is among the various epithelia expressing cystic fibrosis transmembrane conductance regulator (CFTR), mutation of which has been found to be responsible for the disease of cystic fibrosis (CF), the most common genetic disease associated with defective electrolyte transport and reduced fertility in male and female. This project aims to elucidate the functional role of CFTR in uterine transport of both Cl⁻ and HCO₃⁻. The expression of CFTR in a recently established culture of mouse endometrial cells will be examined at different levels, mRNA by RT-PCR and northern blot analysis, protein by western blot analysis and localization by immunohistochemistry. The patch-clamp techniques, both single-channel and whole-cell recordings, will be employed to analyze the anion conductance activated by a number of uterine regulatory factors known to evoke cAMP. The electrophysiological properties of the cAMP-activated anion conductance will be compared to that reported for CFTR. Antibodies or antisense oligodeoxynucleotides against CFTR will be used to confirm the involvement of CFTR. The results of project should shed new light on the understanding of the functional role of CFTR in uterine function. An improved understanding of endometrial transport mechanisms may, thus, provide an explanation for some cases of menstrual dysfunction or "unexplained" infertility. (MD99058)

The Cloning of Two Rat Epididymis-specific Novel mRNAs and Their Potential Roles in Sperm Maturation

- ✉ CHAN Hsiao Chang
- ☐ 1 May 2000
- ❖ The Rockefeller Foundation

The epididymis is an integrate part of the male reproductive system, which is responsible for sperm maturation, storage and protection. However, the molecular mechanisms underlying these processes have not been fully elucidated. The present project

aims to clone two rat epididymis-specific novel mRNAs and study their role in sperm maturation. Molecular biological and physiological approaches will be employed. The full length of cDNA will be cloned and sequenced. Expression patterns and regulation will also be examined. Functional assays will be conducted in cultured epididymal epithelial cells as well as sperm collected from the epididymis. The results of the project should shed light to the understanding of molecular mechanisms governing sperm maturation process and may provide new ground for development of contraceptives. (MD99124)

Innovation Development of Chinese Medicine-based Health Care Products for Women of All Ages

- ✉ CHAN Hsiao Chang • BUT Pui Hay Paul (Dept of Biology)
- ☐ 1 June 2000
- ❖ Eu Yan Sang (Hong Kong) Ltd. • University-Industry Collaboration Prog.: Matching Grant for Joint Research, ITF, Innovation & Tech. Commission

The project aims to innovatively develop Chinese medicine-based health care products for women of all ages. While keeping the tradition, the researchers aim to apply modern scientific methodology to investigate the pharmacological action mechanisms of the time-tested, most venerable traditional Bai Feng Pills of the company, to analyze their active ingredients and quantify their bioefficacy using the latest technology. By optimizing the beneficial ingredients, they will develop quality-controlled new therapeutic formulations and innovative formulas to treat gynecological disorders, and formulate dietary supplements or food products to enhance overall body functions of women of all ages. This will not only open up a much bigger market for the company but also have a significant impact on TCM (Traditional Chinese Medicines) development in Hong Kong. (MD99127)

Nitric Oxide (NO) Enhancement of Adrenomedullin- and CGRP-induced Vasodilation and Delayed Vasodepression via NO Synthase (iNOS) Gene Expression: Involvement in Endotoxin Shock

- ✉ FISCUS Ronald Ray
- ☐ 1 September 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

The life-threatening hypotension of endotoxin shock is thought to be mediated in part by the vascular

actions of calcitonin gene-related peptide (CGRP) and nitric oxide (NO). The researchers' laboratory has shown that endotoxin triggers the release of CGRP from perivascular nerves, that NO synergistically enhances the immediate vasorelaxant effects of CGRP and that prolonged exposure to CGRP causes induction of iNOS and delayed vasodepression. Adrenomedullin (ADM), a recently-discovered peptide produced by vascular endothelial and smooth muscle cells during inflammation, can activate CGRP receptors as well as its own receptors and has been proposed to contribute to the hypotension of endotoxin shock. The hypotheses to be tested in this project are:

- (1) immediate vasodilation induced by ADM, like that of CGRP, is enhanced by NO via a mechanism involving cGMP-mediated inhibition of type III phosphodiesterase (PDE3);
- (2) delayed vasodepression via iNOS gene expression in smooth muscle cells induced by either ADM or CGRP is enhanced by endothelium-derived NO via cGMP-mediated inhibition of PDE3; and
- (3) these responses play an important role in the early and late stages of hypotension during endotoxin shock.

Both *in vitro* and *in vivo* experimental models will be used to test these interactions and cellular mechanisms of ADM, CGRP and NO. The results should provide valuable new information about the signal transduction mechanism of two important bioactive peptides, ADM and CGRP, and their biological interactions with NO and involvement in the pathogenesis of endotoxin shock. This new information should help the development of new, more efficacious therapies for the treatment of the life-threatening hypotension of endotoxin shock. (MD99059)

Electrophysiological and Molecular Studies of Epithelial Potassium Channels

- ✉ HUANG Yu • WILSON Stuart M.*
☐ 1 July 1999
❖ UK/Hong Kong Joint Research Scheme, the British Council

Activation of potassium channels is an important part of the mechanism that allows hormones and neurotransmitters to evoke epithelial ion transport, and so the study of these channels has become an important aspect of modern, cellular physiology. However, means by which hormones and transmitters control the activity of these channels is not fully understood. To a large extent this is because many epithelial cells can express a number of different potassium channel species; it is, therefore, extremely difficult to assess the contribution that these make to the overall potassium permeability of the cell

membrane. In the present study the researchers therefore propose to:

- (1) record potassium currents in single epithelial cells held under voltage clamp in the "whole cell" recording configuration;
- (2) develop a technique using antisense oligonucleotides that will allow the selective disruption of genes encoding particular potassium channels; and
- (3) explore the effects of this disruption upon the electrophysiological properties of the cells.

Completion of these experiments would thus allow us to assess the contribution that the different channel species make to the overall control of potassium permeability. (MD99002)

Studies on Cellular and Molecular Mechanisms Involved in Estrogen-induced Beneficial Effects on Coronary Vasculature

- ✉ HUANG Yu • YAO Xiaoqiang • LAU Chi Wai • CHEUNG Wing Tai (Biochemistry) • CHAN H Y
☐ 1 August 1999
❖ CUHK Research Committee Funding (Direct Grants)

Women experience a dramatic increase in the incidence of coronary heart disease following the onset of menopause. Physiological levels of estrogen clearly exert cardioprotective effects since postmenopausal women receiving estrogen replacement therapy are two to three times less likely to develop heart disease. The beneficial effects of estrogen include lowering of low-density lipoprotein cholesterol and decreased vascular reactivity. However, the precise pathways, and the cellular and molecular mechanisms by which estrogen influences coronary 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, may play important roles in the effects of estrogen on the coronary vasculature. The researchers' hypotheses propose that (1) estrogen-induced endothelium-dependent relaxation of female rat coronary arteries is mediated through increased production of endothelium-derived vasodilators, (2) an estrogen-induced increase in release of nitric oxide (a potent vasodilator) attenuates coronary constriction through enhanced expression of potassium channels and non-selective cation channels in the endothelial cells; (3) an estrogen-induced decrease in vascular reactivity is partly mediated through enhanced expression of potassium channels or reduced expression of calcium channels in vascular smooth muscle. The primary objective of this study is to investigate their hypotheses, presenting the cellular and molecular

mechanisms linking the estrogen-induced effects in endothelium and vascular smooth muscle to decreased coronary reactivity. The study should provide new insight into the molecular mechanisms underlying the protective effects of estrogen against coronary heart disease.
(MD99060)

The Pancreatic Renin-angiotensin System: Its Role and the Effect of Chronic Hypoxia on Pancreatic Ductal Secretion and Blood Flow

- ✉ LEUNG Po Sing
- ☐ 1 February 2000
- ❖ CUHK Research Committee Funding (Direct Grants)

Although the renin-angiotensin system (RAS) is primarily considered to be a circulating endocrine system, its presence in a variety of tissues acting as paracrine or autocrine system has been recently documented. Using immunocytochemical approach, key RAS components, notably angiotensin, angiotensinogen and angiotensin receptor subtypes were localized coincidentally in the endothelial cells of pancreatic blood vessels and the epithelial cells of pancreatic ducts. The data suggest the notion for the existence of an intrinsic RAS in the pancreas, with possible paracrine or autocrine roles in the regulation of pancreatic functions. It is known that the expression of local RAS components is finely regulated by physiological and pathological conditions so as to reflect its diverse role in mediating tissue functions. In the pancreas, changes of angiotensin levels and pancreatic blood flow in acclimatizing to long-term deprivation of oxygen (chronic hypoxia) have been implicated. Moreover, some clinical pancreatic problems, such as pancreatitis, alcoholism and transplantation are associated with hypoxia. It is the goal of the present study to demonstrate solid evidence for the existence of an intrinsic RAS and study the effects of chronic hypoxia and pancreatitis on the expression of RAS in the rat pancreas. More importantly, the role of an intrinsic RAS and the effect of chronic hypoxia on regulation of pancreatic functions in the rat pancreas will be elucidated. Its possible effects on pancreatic ductal secretion and local blood flow will be elucidated *in vivo* and *in vitro* conditions. The results of the research should provide useful data on the role of pancreatic RAS. The significance of changes in expression of pancreatic RAS by chronic hypoxia and its effects on the pancreatic functions may shed light on the understanding of physiological and pathophysiological aspects of the pancreas.
(MD99061)

Changes in the Expression of Renin-angiotensin System in Patients with Idiopathic Dilated Cardiomyopathy

- ✉ LEUNG Po Sing • Dr. Gerd Wallukat*
- ☐ 15 June 2000
- ❖ Germany/Hong Kong Joint Research Scheme

Recent findings of cardiac research have greatly improved the treatment of diseases causing reduced performance of the heart (heart failure), such as enlargement of the heart (cardiomyopathies). However, the pathogenesis of idiopathic dilated cardiomyopathy (DCM) is yet clearly understood. Interestingly, activation of local cardiac renin-angiotensin system (RAS) has been shown to trigger the pathogenesis of cardiac function. The present study is therefore aimed at studying the changes in the expression of cardiac RAS in patients with DCM and compare it with those in normal and in patients with DCM, who were implanted with cardiac assist devices showing an improved cardiac function. The significance of expression changes of RAS in DCM patients and in DCM patients with implanted cardiac assist device when compared with that in normal subject may have implications of cardiac RAS in DCM. The researchers hypothesize that there is a significant difference in expression pattern of RAS between DCM patients who have shown significant improvement under the cardiac assist device and DCM patients who have not been implanted with the devices. In addition, they are planning to investigate the effect of autoantibodies against the β -adrenoceptor in patients with DCM and the effect of autoantibodies against the angiotensin receptor in patients with preeclampsia on the regulation and expression of RAS using bioassay systems in cardiomyocyte, endothelial and smooth muscle culture cells.
(MD99090)

To Investigate the Chloride Channel Blocking Effects of Lonidamine and Its Derivatives

- ✉ WONG Patrick Yee Ding
- ☐ 1 July 1999
- ❖ Population Council

It has been established in the researchers' laboratory that the epithelial cells lining the epididymis secrete chloride and bicarbonate (and secondarily water) when stimulated by physiological neurohumoral stimuli. These transport processes determine the fluidity of the luminal environment in which spermatozoa undergo maturational changes. A correct fluid environment is essential to the normal development and full expression of sperm fertilizing capacity. It is known that an anion channel encoded by the cystic fibrosis transmembrane conductance regulator (CFTR) gene plays a pivotal role in anion secretion hence the formation of epididymal fluid environment. In the genetic disease cystic fibrosis,

mutation of the CFTR gene has led to abnormal luminal environment associated with blockage or agenesis of the epididymis/vas. In the mildest form of the disease, male infertility appears to be the only disease manifestation without loss of lung and pancreatic functions (non-clinical CF). This may imply that the epididymis is highly dependent on CFTR for its normal function and consequently most vulnerable to modest loss of CFTR. Through collaboration with the Population Council, it has been found that lonidamine and its analogues inhibited anion secretion by cultured rat epididymal epithelia in the micromolar concentration range. This study is undertaken to investigate the feasibility of using these new chloride channel blockers as potential male contraceptives.
(MD99004C)

Characterization of Transport Properties of the Rat Efferent Duct with Particular Reference to the Role of Estrogen

- ✉ WONG Patrick Yee Ding
- 1 July 1999
- ❖ CUHK Research Committee Funding (Direct Grants) • Population Council

It is well known that the Sertoli cells of the testis secretes fluid which is reabsorbed by the excurrent ductal system. Micropuncture studies of the male reproductive tract have indicated that the efferent duct reabsorbs about 90% of the rete testis fluid. The more distal part of the male tract viz, ductus epididymidis is also engaged in tonic fluid reabsorption. However, the epithelial cells there can also secrete electrolytes and fluid under neurohumoral influences. The dual function of the ductus epididymidis provides a way for fine 'tuning' of the tonicity of the epididymal fluid. In this regard, the male reproductive tract has many features in common with the mammalian kidney. The efferent duct can be likened to the proximal tubule where bulk reabsorption of the glomerular filtrate occurs and the distal epididymis resembles the distal nephron where fine adjustment of the tonicity and volume of the urine takes place. Whilst a lot is known about the mechanisms and regulation of electrolyte transport processes in the epididymis, little attention has been paid to the efferent duct. This project undertakes to characterize the transport properties of the rat efferent duct. Attention will be focussed on the role of estrogens in the regulation of fluid absorption.
(MD99006C)

To Investigate the Feasibility of Blocking Epididymal Anion Channels as a Novel Method for Male Fertility Regulation

- ✉ WONG Patrick Yee Ding
- 1 September 1999

❖ The Rockefeller Foundation

The exponential growth of the world population and the associated threat to the planet and human health has led to calls for increased availability of methods for family planning. In contrast to the various methods available for women, men have only three choices, viz withdrawal, vasectomy and the condom, each having problems of inconvenience, low efficacy and/or irreversibility. There is a need for better methods for men. The researchers propose a new initiative for a male method based on interference with epididymal sperm through inhibition of the formation of the sperm microenvironment. The concept underpinning this approach is built on our own work which showed that the epididymal environment is formed by fluid secretion by the epididymal cells. In this process, an integral membrane protein, CFTR (which acts as a cAMP-activated chloride channel) plays a pivotal role. Recently, the researchers discovered a new class of indazole derivatives which are powerful blockers of CFTR in the epididymis. They propose to screen a number of novel indazole compounds for their effects on blocking epididymal CFTR and fertility in rats. It is hoped that this study will provide information on the feasibility of blocking epididymal CFTR and fertility in rats. It is hoped that this study will provide information on the feasibility of blocking epididymal anion channels as a novel method for male contraception.
(MD99014)

Patch Clamp Study of Ca-permeable Nonselective Cation Channel in Vascular Endothelial Cells

- ✉ YAO Xiaoqiang • KWAN Hiu Yee
- 1 October 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

Ca²⁺ entry into vascular endothelial cells is a key signal triggering the formation of NO, which subsequently act on neighboring smooth muscle cells and cause vasorelaxation and a decrease in blood pressure. Since voltage-gated calcium channels are not present in vascular endothelium, Ca²⁺ permeable NSC channels are believed to be the sole Ca²⁺ entry pathway in the vascular endothelium. With the use of confocal Ca²⁺ imaging study, the researchers have recently demonstrated the existence of cGMP-sensitive Ca²⁺ entry pathway in cultured vascular endothelial cells. These data suggest an important role of a cGMP sensitive nonselective cation channel in vascular endothelial cells.

In this study, the researchers plan to identify the putative cGMP sensitive nonselective cation channel by patch clamp technique. They will study whether the effect of cGMP is directly on the channel or is mediated by protein kinase G. Their research could

reveal the basic electrophysiological and pharmacological properties of endothelial Ca^{2+} -permeable channel. (MD99063)

Isolation and Characterization of An Endothelial Cyclic Nucleotide-gated Cation Channel (CNG)

- ✉ YAO Xiaoqiang • HUANG Yu
- 1 December 1999
- ❖ Research Grants Council (Earmarked Grants)

Ca^{2+} entry into vascular endothelium triggers the formation of vasoactive substances. These substances subsequently act on neighboring smooth muscle cells and cause vasorelaxation and a decrease in blood pressure. Ca^{2+} -permeable nonselective cation (NSC) channels are believed to be the sole Ca^{2+} entry pathway in the vascular endothelium. The researchers have recently cloned three partial cDNAs of cyclic nucleotide-gated (CNG) nonselective cation channel from guinea pig mesenteric arteries and cultured human vascular endothelial cells. With the use of northern blot and *in situ* hybridization, they found that CNG mRNA was abundantly expressed in the vascular endothelium of large, medium, and small arteries. Confocal laser Ca^{2+} imaging study demonstrated the existence of cGMP-sensitive Ca^{2+} entry pathway in cultured vascular endothelial cells. These data suggest an important role of endothelial CNG channel in Ca^{2+} entry in vascular endothelium and therefore implicate a possible involvement of the channel in regulating arterial tone blood pressure. However, the endothelial CNG channel has not been cloned and they know virtually nothing about the molecular structure and electrophysiological/pharmacological properties of this channel.

The researchers propose here to isolate full-length cDNA of endothelial CNG channel and then to characterize electrophysiological properties of the cloned channel. Their research should potentially reveal the molecular identity of the main Ca^{2+} entry pathway in vascular endothelial cells. It aims to identify a channel protein in which an abnormal regulation could possibly cause hypertension. (CU99259)

Cannabinoid Modulation of Synaptic Functions in the Basal Ganglia: An Electrophysiological Study

- ✉ YUNG Wing Ho
- 1 September 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

Cannabinoids are a group of highly-abused psychoactive compounds derived from marijuana. Although the effects of the naturally occurring and

synthetic cannabinoids have been well described, their mechanisms of actions are just beginning to be known. Studies from specific binding of ligands suggest that cannabinoid receptors are differentially distributed in the central nervous system. Notably, the basal ganglia, a brain circuit important for the control of movement and cognitive functions, could be important in mediating the motor effects of cannabinoids such as a decrease in motor activity. The purpose of the study is to advance our understanding of the cellular actions of cannabinoids in the rat basal ganglia output nuclei. Electrophysiological recording techniques will be applied to test whether cannabinoids have any effect on the synaptic functions in these areas by examining (1) the effects and mechanisms of cannabinoid agonists and antagonists on the release of transmitters; (2) the possibility that cannabinoids may act as an inhibitor of neurotransmitter, uptake and (3) the direct effect of cannabinoids on the excitability of the postsynaptic membrane. Information derived from the project will not only help us better define the action of cannabinoids in discrete brain regions but could also have implication in the search of therapeutic actions of cannabinomimetics that are free from psychoactive side-effects. (MD99064)

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 |
| 1998-99 | Modulation of Sperm Ca^{++} -Activated K^+ Channels by Angiotensin II Receptors (MD98110) ✉ CHAN Hsiao Chang |
| 1998-99 | Ultrastructural Identification of Apoptotic Cells by Direct Immunogold |

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|---------|---|---------|--|
| | Detection of Digoxigenin-labeled Genomic DNA in Semithin Sections (MD98056) ✍ CHEW CHENG Siew Boon | 1998-99 | Ca ²⁺ Signaling in Polarized Epithelial Cells (MD98118) ✍ KO Wing Hung • Jens LEIPZIGER* |
| 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 | 1998-99 | The Function of Merkel Cell as a Touch Sensory Receptor (MD98111) ✍ LEUNG Man Sing |
| | | 1997-98 | Testicular Hormone-Regulated Expression of the Renin-Angiotensin II System in the Rat Epididymis (CU97621) ✍ LEUNG Po Sing • CHAN Hsiao Chang |
| 1997-98 | Study on Mechanisms of Vasodilator Effects of Green Tea Epicatechin Isomers in Spontaneously Hypertensive Rats and Normotensive Rats (CU97609) ✍ HUANG Yu • CHEN Zhen Yu (Biochemistry) | 1997-98 | Expression and Localization of the Pancreatic Renin-Angiotensin System in the Rat (MD97073) ✍ LEUNG Po Sing |
| 1997-98 | Interaction between G Protein and K ⁺ Channels in Rat Pituitary GH3 Cells (MD97101) ✍ HUANG Yu • HESCHELER Jurgen* | 1998-99 | Changes in the Localization and Expression of Angiotensin Receptors in the Chronic Hypoxic Rat Carotid Body (MD98112) ✍ LEUNG Po Sing |
| 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 | Internalization and Routing of Trichosanthin (CU98243) ✍ TAM Michael S C • SHAW Pang Chui (Biochemistry) • CHAN Wood Yee (Dept of Anatomy) |
| 1998-99 | Study on Mechanisms of Vasodilator Action of Berberine (MD98058) ✍ HUANG Yu | 1998-99 | Study of CNG1 Channel in Vascular Endothelial Cells (MD98060) ✍ YAO Xiaoqiang • KWAN Hiu Yee |
| 1998-99 | Study on Calcium Sparks in Smooth Muscle Cells (MD98117) ✍ HUANG Yu • GOLLASCH Maik* | 1998-99 | Rod-Type Nonselective Cation Channel in Vascular Endothelial Cells (MD98090) ✍ YAO Xiaoqiang • GARLAND Christopher* |
| 1997-98 | Electrolyte Transport Mechanisms Underlying the Formation of Seminiferous Tubular Fluid by Rat Sertoli Cells (CU97640) ✍ KO Wing Hung • CHAN Hsiao Chang | 1998-99 | Property and Role of Endothelial CNG Channel (MD98122) ✍ YAO Xiaoqiang • KWAN Hiu Yee |
| 1998-99 | Simultaneous Measurements of Intracellular pH and ATP-evoked Anion Secretion in Cultured Equine Sweat Gland Epithelia (MD98059) ✍ KO Wing Hung | 1997-98 | The Nigral GABAergic Inhibitory Pathway as an Endogenous Control System of Epileptic Seizures: An Electrophysiological Study (CU97626) ✍ YUNG Wing Ho |

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000125> **Sam, S. W.; S. W. Chan; J. A. Rudd and J. H. K. Yeung.** "Action of Corticosteroids and Metyrapone to Modify Cisplatin-Induced Emesis in the Ferret". *Abstracts of the 11th International Conference on Advances in Prostaglandin and Leukotriene Research: Basic Science and New Clinical Applications* p.42. Florence, Italy: Giovanni Lorenzini Medical Foundation, 2000.06.
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RESEARCH PROJECTS

A Clinical Trial of the Motivational Strategy for Engaging Early Drug Abusers

✉ CHEUNG Kin Leung Ben • TANG Jinling (Dept of Community and Family Medicine) • CHAN Shiu Yee Cynthia (Dept of Community and Family Medicine)

☐ 1 February 2000

❖ Narcotics Division, HKSAR Government

Objectives:

- (1) To explore the strength and weakness of various existing methods of persuading drug abusers;
- (2) To study the demographic characteristics and drug abuse patterns in early drug abusers;
- (3) To identify factors affecting the engagement of early drug abusers in treatment; and
- (4) To test the hypothesis that motivational interviewing in the form of "free body check-up" followed by personalized feedback will be an effective strategy to attract early addicts, and that such early and brief intervention will produce significant and lasting results.

(MD99118)

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

✉ 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*

☐ 1 November 1999

❖ Social Welfare Department, HKSAR Government

This project will evaluate the effectiveness of pilot projects of day care centres for elderly with dementia as well as specific dementia units in residential homes. The study will examine benefits of these facilities on the elderly with dementia, the formal and informal carers, as well as their cost-effectiveness. (MD99071)

Duplication of the *CYP2D6* Gene in Hong Kong Chinese

✉ CHOW Lok Yee • CHIU Fung Kum Helen • UNGVARI Gabor Sandor • GARCIA BARCELO Maria Mercedes#

☐ 15 June 2000

❖ CUHK Research Committee Funding (Direct Grants)

The cytochrome P450 *CYP2D6* enzyme debrisoquine 4-hydroxylase metabolizes many different classes of commonly used drugs in psychopharmacotherapy such as tricyclic antidepressants and neuroleptics. This enzyme presents inter-individual and cross-ethnic variations regarding their metabolic activity leading to variations in drug response to practically all cases of psychotropic medication. These variations are genetically determined by polymorphisms on the *CYP2D6* gene. Caucasian and Oriental populations differ greatly regarding the *CYP2D6* gene alterations responsible for lower/absent enzymatic activity. Both populations have been exhaustively studied. In particular, we genotyped Hong Kong Chinese to obtain information on the constitution of *CYP2D6* gene in our population. The duplication or multiplication of an active *CYP2D6* gene results in an increment of the *CYP2D6* enzyme activity, which accounts for the ultrarapid metabolizer phenotype (UM). UM individuals metabolize drugs at ultrarapid rate, hence, requiring more than average dosages of drugs to reach therapeutic plasma concentration. Ultrarapid *CYP2D6* enzymatic activity leads to drug inefficacy, implying lack of response to acute treatment or relapse during continuing therapy. The occurrence of *CYP2D6* gene duplication varies also among populations and little is known about its prevalence in our population and its therapeutic implications. Polymerase chain reaction (PCR) and restriction fragment polymorphism analysis (RFLP) techniques are being applied to screen for *CYP2D6* gene duplication. These tests have been designed based on the *CYP2D6* gene structure found for Caucasians, which it is different from that in Orientals. (MD99113)

Attitudes Toward and Social Meanings of Suicide in Contemporary Chinese Society

✉ LEE Sing • PHILLIPS Michael* • KLEINMAN Arthur*

☐ 1 November 1999

❖ CUHK Research Committee Funding (Direct Grants)

Suicide remains a major cause of death and economic loss in both Hong Kong and mainland China. According to the World Bank's Global Burden of Disease study, China has 21% of the world's population but accounts for 44% of all reported suicides worldwide (over 300,000 suicides each year) and for an astounding 56% of all female suicides worldwide. Moreover, the rate of suicide in China is unique: it is more common in females than males, three times more frequent in rural than urban areas, and exhibits less connection with psychiatric

disorders. In contrast, Hong Kong is also a "Chinese" society, but its rate (10.6/100,000/year) and pattern of suicide are more similar to those of Western countries, and the rate is likely to rise following the recent economic downturn. The rates in women are relatively high and those of the elderly are very high. Previous research in the Chinese, being predominantly statistical and/or clinical in approach, is not sufficient for understanding these disparate patterns of suicide, which may reflect major social, economic and historical differences. The current project takes advantage of the expertise of three bilingual researchers with a strong track record in health research in Chinese society. It is a comparative study that aims to assess a comprehensive range of cultural attitudes toward suicide among respondents in Hong Kong and urban and rural Beijing. The results are essential to the development of effective public campaigns, programs, and policies for reducing suicides in the increasingly inter-connected societies of Hong Kong and China. (SS99004)

The Outcome of Postnatal Depression among Chinese Women in Hong Kong

- ✉ LEE Tak Shing Dominic • YIP Shing Kai Alexander (Dept of Obstetrics & Gynaecology) • CHUNG Kwok Hung Tony (Dept of Obstetrics & Gynaecology)
- 1 September 1999
- ❖ Research Grants Council (Earmarked Grants)

Postnatal depression (PND) is a common and potentially fatal disorder. It affects 10 to 20 per cent of recently delivered women, causing a host of complications to the mother, family and children. There are still significant gaps of knowledge in relation to the outcome of postnatal depression that require investigation. Although postnatal depression makes multidimensional impact, most outcome studies of PND have focused on short-term and traditional outcome measures, such as symptom level and rate of recurrence. Few studies have examined the medium term (1 to 3 years) effect of postnatal depression and even fewer have looked into the domains of social functioning and quality of life. Recurrent and brief depressive spells are not uncommon among new mothers but the course and outcomes of such subthreshold disorders are largely unknown. To the best of our knowledge, there is as yet no study of prognostic indicators of postnatal depression and almost all outcome studies of PND have been conducted in western countries. Whilst clinical experience suggests superficial resemblance between outcomes in Western and Chinese societies, the course and outcomes of PND among Chinese women is largely unknown. A systematic outcome study is needed to clarify the situation. The relevance of cultural factors in outcome of postnatal depression

also deserves investigation. This study proposes to study the short and medium term outcomes of postnatal depression among Chinese women, and to identify factors, including indigenous cultural ones, that shape its outcome. (CU99294)

Development of a Local Drug Abuse Treatment Outcomes Measure

- ✉ LEE Tak Shing Dominic
- 1 June 2000
- ❖ Beat Drugs Fund Association

Objective: This proposed project aims to develop a drug abuse outcome measure and user-friendly data entry and analysis software for local treatment and rehabilitation agencies to measure the outcomes of their services. It will also collect benchmark normative treatment outcomes data for future reference.

Method: The research version of the Chinese Addiction Treatment Outcome Measure (CATOM), which has been used in two previous government consultancies, will be modified according to the needs of all local treatment agencies. Data entry and analysis software will be constructed. Following a short pilot and revision, the final product will be disseminated to interested treatment agencies via training seminars and technology transfer package. A six-month service support will be provided to help the drug abuse workers and supervisors to familiarize themselves with the CATOM and software.

Results: All local treatment agencies that are interested in measuring the outcomes of their services will have a suitable instrument that is tailor-made for local needs. Future agencies may also learn this package using training videos and manuals.

Potential values: This research team has been approached by treatment agencies and government departments for appropriate benchmark indicators to monitoring the effectiveness of treatment programs. This project will yield both the instrument and the benchmark normative reference that the HKSAR government departments should be equipped. This project therefore goes hand-in-hand with the HKSAR government's continuing efforts to consolidate the drug abuse treatment and rehabilitation services in Hong Kong. (MD99119)

Psychiatric Morbidity in Stroke: A Pilot Study

- ✉ UNGVARI Gabor Sandor • SZE Kai Hoi Frank* • TANG Wai Kwong
- 1 November 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

Over the past two decades it has been established that stroke is associated with significant psychiatric morbidity which has far-reaching implications for post-stroke management and the outcome of rehabilitation. There is a paucity of data concerning post-stroke psychiatric morbidity in Chinese patients. The main objectives of the present study are:

- (1) to explore the most suitable rating instruments for screening psychiatric morbidity following stroke;
- (2) to find out the most efficient ways of carrying out such a screening process; and
- (3) to estimate the magnitude of the total psychiatric morbidity following stroke including depression, anxiety disorders, apathy, pathological emotional reactions and psychosis.

Four weeks after their first stroke while undergoing rehabilitation, 80 consenting subjects will be assessed with several rating scales covering the whole spectrum of psychiatric morbidity. The rating scales will be administered by a research assistant and various staff members (nurses, OT, PT). Subjects will also be examined by a research psychiatrist using a standardized psychiatric interview. Based on the number of admissions to the rehabilitation facility, the expected duration of the study is 7-8 months. (MD99065)

An Open-label Pilot Study to Assess the Effect of Venlafaxine-XR in the Treatment of Chinese Patients in Hong Kong with Neurasthenia

✉ WING Yun Kwok • LEE Sing • LEE Tak Shing Dominic • CHAN Shiu Yee Cynthia (Dept of Community and Family Medicine)

☐ 1 March 2000

❖ Wyeth (HK) Ltd

Objectives: (1) To evaluate the effect of Venlafaxine-XR in the treatment of Chinese patients with neurasthenia; (2) To generate local clinical experience of Venlafaxine-XR in Chinese patients with Neurasthenia.

Study design: Open-labeled, non-comparative, single center study in Chinese patients with Neurasthenia.

Duration of study: Each subject will be treated for eight weeks. Enrolment will be completed in 10 months; the entire study will last approximately 12 months.

Number of patients: Approximately 30 patients will be enrolled in this study.

(MD99126)

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

Edition Title/Investigators

1998-99 Cytochrome P450 2D6 Genotyping and Movement Disorders in Schizophrenia (MD98061)

✉ LAM Chiu Wa • WAYE Mary Miu Yee (Biochemistry) • UNGVARI Gabor Sandor • CHIU Fung Kum Helen

1998-99 Outcome and Cultural Context of Anorexia Nervosa in Hong Kong (CU98029)

✉ LEE Sing • HSU L. K. George*

1997-98 A Study on Factors Affecting Drug Abuse Trend in Hong Kong (MD97091)

✉ LEE Tak Shing Dominic • LAU Tai Shing (Dept of Statistics) • SO Man Pui* • LEE Albert (Dept of Community and Family Medicine) • TANG Leung Sang Nelson (Dept of Chemical Pathology)

1998-99 A Randomised, Controlled Trial of Educational Counselling on the Management of Women Who Suffered Suboptimal Outcomes During Childbirth (MD98002)

✉ LEE Tak Shing Dominic • CHUNG Kwok Hung Tony (Dept of Obstetrics & Gynaecology) • CHIU Fung Kum Helen • CHEUNG Lai Ping* • TAM Wing Hung (Dept of Obstetrics & Gynaecology) • LEE Albert (Dept of Community and Family Medicine)

1998-99 A Study to Look into the Risk and Protective Factors for Drug Related Deaths in Hong Kong (MD98079)

✉ LEE Tak Shing Dominic • LAU Tai Shing (Dept of Statistics) • YIP Paul* • HALLIDAY Peter* • CHAN Kong Hei* • CHAN Choi Ha*

1997-98 The Effectiveness of Piracetam on ECT-Induced Memory Disturbances (MD97124)

✉ UNGVARI Gabor Sandor • LEUNG Chi Ming • CHUNG Wai Sau Dicky • TANG Wai Kwong* • LEUNG Yip Shing Tony

1997-98 An Epidemiological Study of Narcolepsy in Hong Kong Chinese (CU97675)

✉ WING Yun Kwok • CHEN Char Nie • HO Kwok Wah Crover • LEUNG Yip Shing Tony • LI Kam Tao Philip (Dept of Medicine & Therapeutics)

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- <P000945> **Garcia-Barcelo, Merce; Lok Yee Chow; Helen Fung Kum Chiu; Yun Kowk Wing; Dominic Tak Shing Lee; Kwok Lim Lam and Mary Miu Yee Waye.** "Genetic Analysis of the *CYP2D6* Locus in a Hong Kong Chinese Population". *Clinical Chemistry* vol.46 no.1, pp.18-23. USA, 2000.01.
- <P000954> **Ungvari, G.S. and W.K. Tang.** "Comments on the Clinical Heterogeneity of Schizophrenic Psychoses". *Progress in Differentiated Psychopathology* ed. by Ernst Franzek, Gabor S. Ungvari, Eckart Ruther and Helmut Beckmann. pp.78-81. Wurzburg Germany: International Wernicke-Kleist-Leonhard Society, 2000.04.
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- <P994273> **Lee, Sing.** "Fat, Fatigue and the Feminine: The Changing Culture Experience of Women in Hong Kong". *Culture, Medicine & Psychiatry* vol.23, pp.51-73. 1999.
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- <P994617> **李德誠、張麗冰、韓英士、鐘國衡.** <流產後抑郁障礙調查>. 《上海精神醫學》第 11 期 第 3 期, 頁 132-134. 1999.

see also <P000364>, <P001812>, <P985125>, <P993188>, <P993248>, <P993704>, <P994245>

RESEARCH PROJECTS

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

Edition Title/Investigators

1998-99 “Health Schools” and “Health Society”:
Quality Education for Children and
Teachers (MD98068)
✉ LEE Shiu Hung • LEE Albert (Dept
of Community and Family Medicine)
• TO Cho Yee (Dept of Community
and Family Medicine)

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000678> 李紹鴻. <健康城市>. 《社聯季刊》第 152 期, 頁 11-12. 香港, 2000.02.
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- <P981448> **Lee, S.H.** *Comments on Review of District Organization - Consultation Document.* Paper submitted to the HKSAR, 8 pgs. Hong Kong, 1998.07.03.
- <P992946> 李紹鴻. <迎接 21 世紀疾病雙重挑戰>. 《第四屆粵港澳預防醫學學術交流會議論文匯編》. 頁 11-15. 深圳, 中國, 1999.12.12.
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RESEARCH PROJECTS

Does Acid Suppression Reduce Rebleeding in Peptic Ulcers after Endoscopic Haemostasis - A Double Blind Placebo-controlled Randomized Trial

✉ CHUNG Sheung Chee Sydney • SUNG Joseph Jao Yiu (Dept of Medicine & Therapeutics) • LEE Kwing Chin Kenneth (School of Pharmacy) • LAU Yun Wong James

☐ 1 July 1999

❖ Research Grants Council (Earmarked Grants)

Bleeding peptic ulcer is a common medical emergency. Endoscopic hemostasis is now the first treatment of choice. While endoscopic hemostasis is successful in the majority of bleeding ulcers, recurrent bleeding occurs in about 15 per cent of them. In these patients, mortality approaches 30 per cent. A high-dose infusion of proton pump inhibitor (PPI) can consistently maintain a high intra-gastric pH, which is essential for maintaining clot stability in the stomach. The adjunctive use of high-dose PPI infusion can theoretically reduce recurrent bleeding after initial endoscopic control of bleeding and thereby improve patients' outcome. A double-blind placebo-controlled randomized trial is conducted to evaluate PPI in such a clinical setting. In this trial, patients with actively bleeding ulcers and ulcers with major stigmata of bleeding are recruited. They are treated by adrenaline injection and heater probe thermo-coagulation to the vessels. Following hemostasis, they are randomized to receive high-dose PPI or its placebo. The principal outcome parameter is the rate of recurrent bleeding.

(CU99315)

Coronary Endothelial Function Related to Open Heart Surgery and Its Protection

✉ HE Guo Wei

☐ 1 September 1997

❖ Research Grants Council (Earmarked Grants)

During open heart surgery, the heart is arrested and ischemia-reperfusion injury is the main cause of subsequent alteration of the heart function. Little has been known about which component of the endothelium-derived relaxing factors (EDRFs) is altered and what role cardioplegic solutions play on the EDRFs. The effect of ischemia and hyperkalemic cardioplegic (or organ preservation) solutions on the EDHF-mediated relaxation and hyperpolarization is unknown. Therefore, the researchers propose this study to examine the effect of ischemia (hypoxia) and hyperkalemic cardioplegia on coronary endothelial function with focus on the EDHF-mediated function. This will be studied at the level of large vessels

(conductance vessels, diameter > 1.5 mm) as well as small (micro) vessels ("proximal" resistance vessels, diameter between 100-500 μ M) by using organ baths (for large vessels) and myograph (for micro vessels). Pigs will be used as an animal model. Some results will be confirmed in the human coronary artery obtained from heart transplant. Isometric tension changes will be recorded through a transducer and a recorder. In some experiments, membrane potential will be directly measured by microelectrodes to determine whether hyperpolarization induced by EDHF is altered by ischemia (hypoxia) and cardioplegia. The well-controlled setting of the laboratory allows the researchers systematically to study the endothelial function mediated by EDHF. The results derived from these studies will provide important knowledge for prevention and treatment of cardiac complications related to the change of coronary circulation and for development of new cardioplegic (or organ preservation) solutions, and therefore have strong clinical implications.

(CU97280)

Protection of Coronary Endothelium-smooth Muscle Function During Cardiac Surgery

✉ HE Guo Wei

☐ 1 September 1999

❖ Research Grants Council (Earmarked Grants)

EDNO and EDHF are the major regulators for the coronary flow. EDHF is particularly important in the micro-circulation. During cardiac surgery, the heart is arrested and ischemia-reperfusion injury is the main cause of subsequent alteration of the heart function. The researchers demonstrated that the endothelial function may be partially or fully restored by the hyperpolarizing cardioplegia using potassium channel opener aprikalim. However, little has been known about (1) whether this is true in the coronary resistance (micro) arteries (diameter less than 500 μ M) and if it is, what the mechanism is; (2) the interaction between EDNO and EDHF during cardioplegic arrest in both large and micro coronary arteries; and (3) whether these altered functions may be restored by pharmacological agents. Therefore, the researchers propose this study to answer the above questions. The study will be conducted at the level of large vessels (conductance vessels, diameter > 1.5 mm) as well as small (micro) vessels ("proximal" resistance vessels, diameter between 100-500 μ M) by using organ baths (for large vessels) and myograph (for micro vessels). The endothelium-smooth muscle function will be studied by (1) isometric tension changes; (2) electrophysiological measurement (membrane potential in the single smooth muscle cell); and (3) direct measurement of EDNO electrochemically by using a porphyrinic

microsensor. The results derived from these studies will provide important knowledge for prevention and treatment of intra-and post-operative complications in cardiac surgery related to the alteration in the coronary endothelium-smooth muscle function and to the development of new method to protect the heart. (CU99246)

Evaluation of Swallowing Problems in Patients with Nasopharyngeal Carcinoma after Radiotherapy – A Phase I Prospective Study

✉ 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*

□ 1 October 1999

❖ CUHK Research Committee Funding (Direct Grants)

Nasopharyngeal carcinoma (NPC) is endemic in Southern China. The mainstay of treatment is external radiotherapy as the tumour cells are highly responsive to irradiation. Complications related to radiotherapy especially intracranial and otological have been well documented. Swallowing problems that we often encounter in the specialist Ear, Nose and Throat Clinic have seldom been reported in literature. This present group of researchers has been solely responsible for the publication of a descriptive analysis showing a significant prevalence in swallowing disorders in NPC patients after radiotherapy. A prospective study to evaluate the effect of NPC and its treatment on the swallowing function of these patients is conducted aiming at revealing the incidence and the type of swallowing dysfunction in those patients suffering from NPC before and after radiotherapy. A comparison between fiberoptic endoscopic examination of swallowing and videofluoroscopy in evaluating the swallowing pathology is made. (MD99066)

A Preliminary Study on Thallium-201 Single Photon Emission Computed Tomography (Tl-201 SPECT) in Evaluating Primary and Post-Radiotherapy Nasopharyngeal Carcinoma

✉ 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)

□ 1 May 2000

❖ CUHK Research Committee Funding (Direct Grants)

Nasopharyngeal carcinoma (NPC) is common in Southern China. The mainstay treatment for primary NPC is external beam irradiation (or simply radiotherapy) and a good survival with early-stage disease is expected. Depending on the initial staging, 19% to 56% of patients have recurrences or relapses within 5 years of initial radiotherapy. Accurate staging of the disease is of vital importance in planning the radiotherapy and the detection of post-irradiation recurrences and hence the prognosis of the patients. Current diagnostic and staging tools for nasopharyngeal carcinoma include magnetic resonance imaging (MRI), computed tomography (CT) and ultrasonography (US) giving a high sensitivity but low specificity in detecting loco-regional disease. These imaging techniques are unable to monitor the immediate tumour response nor to detect distant metastases. An imaging technique which give a high sensitivity and specificity in detecting loco-regional nasopharyngeal tumours, distant metastasis and the treatment response would therefore be extremely useful. Thallium-201 SPECT scan has been used in detecting head and neck squamous cell carcinoma with favourable results. Therefore, a study on the use of Thallium-201 single photon emission computed tomography (Tl-201 SPECT) is conducted to evaluate primary and post-radiotherapy nasopharyngeal carcinoma. (MD99114)

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

✉ YIM Ping Chuen Anthony • IZZAT Mohammad Bashir# • WAN Song

□ 1 October 1999

❖ Research Grants Council (Earmarked Grants)

The saphenous vein from the leg is the most commonly used conduit for bypassing blocked coronary arteries. Unfortunately in a large number of cases, these vein grafts undergo a process of "furring" due to multiplication of cells from the vessel wall and migration into the lumen where they continue to secrete fibrotic proteins, therefore gradually reducing lumen size. This process results in blockage of more than 50% of all grafts within 10 years. To date, no pharmacological or surgical intervention has proved successful in ameliorating this problem in man. However, in a porcine model of bypass surgery, the researchers have recently shown that supporting the vein externally by placement of a tube-like "stent" around a vein graft prevents thickening and closure of the graft. The mechanisms underlying this effect are

not yet well-defined and such knowledge is crucial to the future development of this form of surgical intervention. From their previous experiments the researchers have observed that the stent material appeared to encourage the growth of cells and small blood vessels in the space between the stent and the vein graft. These events have two effects:

- (1) provision of the graft with oxygen which is known to reduce cell proliferation; and
- (2) the release of substances that inhibit cell division in the graft.

The objective of this study therefore, is to test this hypothesis in a porcine model of vein graft (stented and unstented) surgery using immunocytochemistry, autoradiography and histological techniques. (CU99310)

Novel Strategies for the Treatment of Vein Graft Failure: Investigation Using a Pig Model

✉ YIM Ping Chuen Anthony • WAN Song* • JEREMY Jamie*

☐ 1 June 2000

❖ UK/Hong Kong Joint Research Scheme, the British Council

Although coronary artery bypass graft surgery (CABG) has revolutionised the treatment of patients with coronary arterial disease there is a relatively high incidence of failure following CABG which is caused by excess thickening of the graft. This process involves the proliferation and migration of vascular smooth muscle cells (VSMCs) to the lumen of the graft where they continue to proliferate forming a "neointima". Neointima formation, which usually occurs within one month, is susceptible to the development atheroma which ultimately increases the risk of occlusion. To date no pharmacological intervention has proved successful in ameliorating vein graft failure. However, the researchers have established that there is an upregulation of ET-1 receptors and its subtypes (ETA and ETB) but a decrease in nitric oxide (NO) synthase and NO-linked cyclic GMP formation in porcine vein grafts. Since ET-1 promotes and NO inhibits replication and migration of VSMCs, they proposed that these changes are involved in vein graft thickening. Other studies have demonstrated that the administration of inhibition of ET receptor antagonists and NO donors inhibit neointima formation following balloon injury. No studies have been carried out in vein grafts, however. The objective of this project, therefore, is to investigate the effect of drugs that block ET-1 receptor and modulate NO formation using a porcine model of vein graft thickening. (MD99089)

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 intragastric 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 |
| 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 ³¹ P Magnetic Resonance Spectroscopy Study (CU98214) ✉ LAU Wan Yee Joseph • Darren Vivian MANN • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • HJELM Nils Magnus (Dept of Chemical Pathology)# • LAM Wai Man Wynn (Dept of Diagnostic Radiology & Organ Imaging) |
| 1998-99 | Linezolid for the Treatment of MRSA Infections: An Evaluator – Blinded Trial |

- Comparing Linezolid with Vancomycin (MD98083)
 ✎ LEUNG Ka Lau • LAU Wan Yee Joseph • LYON Donald James (Dept of Microbiology) • LEUNG Chi Hang Bertrand
- 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 timer (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 Haemostasis Following Trauma (MD97109)
 ✎ Robert Anthony COCKS • LAM Yuk Lan (Accident and Emergency Medicine academic unit) • RAINER Timothy Hudson (Accident and Emergency Medicine academic unit) • NG Heung Ling Margaret (Dept of Anatomical & Cellular Pathology) • MAYCOCK Paula*
- 1998-99 Predicting Severe Cerebral Ischaemia (SCI) During Carotid Endarterectomy (CEA) with Preoperative Stable Xenon-Enhanced Computed Tomography (XeCT) Cerebral Blood Flow Measurement (MD98062)
 ✎ Ronald BOET • POON Wai Sang • LAM Wai Man Wynn timer (Dept of Diagnostic Radiology & Organ Imaging) • METREWELI Constantine (Dept of Diagnostic Radiology & Organ Imaging) • WONG Ka Sing Lawrence (Dept of Medicine & Therapeutics) • KAY Li Chi Richard (Dept of Medicine & Therapeutics) • LAM J.M.K.*
- 1997-98 Development of a New Hyaluronic Acid Membrane Delivery System for Using the Cultured Keratinocytes as a Permanent Wound Cover (MD97126)
 ✎ TO Wai Hei Edward • KING Wing Keung Walter • LAM Ping Kuen • CHAN Sun Yin Eric#
- 1997-98 An Open Clinical Trial of Dysport in Bilateral Masseteric Hypertrophy (MD97142)
 ✎ TO Wai Hei Edward • HO Wai Sun*
- 1994-95 Investigations into the Aetiology and Management of Nasopharyngeal Carcinoma (MD94071)
 ✎ VAN HASSELT Charles Andrew • LEE Chuen Kwun Joseph (School of Chinese Medicine)
- 1997-98 Neonatal Hearing Screening Using Distortion Product Otoacoustic Emissions (DPOAEs), Steady State Evoked Potentials (SSEPs) and Impedance Audiometry - A Preliminary Study (MD97076)
 ✎ VAN HASSELT Charles Andrew • TONG Chi Fai Michael • WONG Terrence K. C.* • LEUNG Eric K. C.* • FOK Tai Fai (Dept of Paediatrics) • McPHERSON B.*
- 1997-98 The Effect of Indoor Pollution on the Development of Rhinitis in Office Workers in Hong Kong (MD97019)
 ✎ VAN HASSELT Charles Andrew • TONG Chi Fai Michael • TSANG King Yin Raymond* • WOO Kong Sang John • LAU Tak Fai Joseph (Centre for Clin. Trials & Epidemiological Research) • WONG Ming Chung (Centre for Clin. Trials & Epidemiological Research) • NG Heung Ling Margaret (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*
- 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) • Charles David GOMERSALL (Dept of Anaesthesia & Intensive Care) • FOK Tai Fai (Dept of Paediatrics) • LAU Wan Yee Joseph
- 1998-99 Appraisal of Microchimerism, Graft Tolerance and Rejection by Plasma and Urinary DNA Following Solid Organ Transplantation (MD98064)
 ✎ YEUNG Chung Kwong • LO Yuk Ming Dennis (Dept of Chemical Pathology) • PANG Chi Pui Calvin (Dept of Ophthalmology and Visual Sciences) • 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 • John Elsby SANDERSON (Dept of Medicine & Therapeutics) • CHOW Tsun Cheung Louis (Dept of Anatomical & Cellular Pathology)
- 1997-98 Effect of Short Term Exposure of Saphenous Vein Grafts to Thapsigargin on Medial and Intimal Thickening in a Porcine Arterio-Venous Bypass Graft Model (MD97079)
 ✎ YIM Ping Chuen Anthony • HO Chin Ho Kenny#
- 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)

RESEARCH OUTPUTS AND PUBLICATIONS

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- <P000019> **Wang, J. C. Y. and E. W. H. To.** "Application of Dermal Substitute (Integra) to Donor Site Defect of Forehead Flap". *British Journal of Plastic Surgery* vol.53, pp.70-72. UK, 2000.01.
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- <P000216> **Burd, Andrew and Anil Ahuja.** "Cervical Lymph Node Biopsy When Is It Necessary?". *Abstracts of the 2000 International & 6th National Head Neck Cancer Congress* p.70. Shanghai, China: China Society for H & N Tumor Surgery Tianjin/Shanghai 2nd Medical University/Affiliated 9th People's Hospital, Shanghai/CUHK, Hong Kong, 2000.06.
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RESEARCH PROJECTS

A Cost-effectiveness Analysis of the Treatment of Pain Following Limb Injury in an Emergency Department: A Comparison Between Intravenous Ketorolac Tromethamine & Morphine Sulphate

✉ RAINER Timothy Hudson • Robert Anthony COCKS (Dept of Surgery) • CHEUNG Nai Kwong • LAM Kwok Wai (Centre for Clin. Trials & Epidemiological Research) • JACOBS Philip* • NG Ying Chu*

☐ 1 May 2000

❖ Health Services Research Fund, Hospital Authority

Background: Painful limb injuries present commonly to emergency departments. The current gold standard for the treatment of such pain is intravenous (iv) morphine titrated according to the patient's requirements. Although it is a cheap and effective analgesic, iv morphine causes significant adverse effects and is regarded as a 'dangerous' drug with significant risk of dependence. These effects require close monitoring, additional treatment and result in delays to discharge/disposal, all of which have an

additional 'cost.' Recent studies suggest that the non-steroidal anti-inflammatory drug, ketorolac, may be as effective an analgesic as morphine but with less adverse effects. Consequently, although ketorolac is more expensive than morphine, it is associated with less 'additional' costs and may be a more cost-effective option. Therefore, in the management of blunt limb injury in Emergency Departments (ED) a cost-effectiveness analysis (CEA) of ketorolac and morphine has important financial implications in the management of pain.

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

Design: Prospective double blind randomised study.

Participants: 240 subjects having sustained isolated blunt limb injury presenting to The Prince of Wales Hospital.

Main outcome measures: Cost effectiveness ratio (CER) of relative pain relief per dollar saved, CER of relative number of adverse effects per dollar saved, and total resources (costs) saving at ED. (MD99095)

RESEARCH OUTPUTS AND PUBLICATIONS

<P000177> **Rainer, T. H.** "The Role of Plasma DNA in Trauma". *Abstract Book, Chinese Congress of Clinical Chemistry & Laboratory Medicine 2000* p.25. Hong Kong: Hong Kong Society of Clinical Chemistry and Chinese Society of Clinical Chemistry, 2000.06.

<P000450> **Rainer, T.H.; K.L. Law; J.F. Griffith; C. Metreweli and R.A. Cocks.** "Does Ultrasound Have a Role in the Clinical Diagnosis and Management of Fractured Ribs?". *Journal of Accident and Emergency Medicine* vol.17 no.1, p.68. UK: BMJ Publishing Group, 2000.01.

<P000491> **Mitchell, R.G.; U.M. Guly; T.H. Rainer and C.E. Robertson.** "Paramedic Activities, Drug Administration and Survival From Out of Hospital Cardiac Arrest". *Resuscitation* vol.43 no.2, pp.95-100. UK, 2000.01.

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- <P001367> **Tam, M.M.K.; T.H. Rainer; P. Jacobs; Y.C. Ng; N.K. Cheung; P.K.W. Lam; W.S. Ng; R. Wong and R.A. Cocks.** "Cost Effectiveness Analysis of Titrated Intravenous Doses of Ketorolac Tromethamine Versus Morphine Sulphate in the Management of Pain after Blunt Limb Injuries". *Journal of Accident and Emergency Medicine* vol.17 no.1, pp.58-59. UK: BMJ Publishing Group, 2000.01.
- <P001373> **Tam, M.K.; Lam P.; Ho H.F.; Cocks R.A. and Cheung W.L.** "Observer Variability in Injury Coding and Its Effect on Subsequent Trauma Outcome Analysis". *Annals of Emergency Medicine* vol.35 no.5, p.S9. USA: American College of Emergency Physicians, 2000.05.
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- <P993332> **Rainer, T.H.; K.L. Law; J.F. Griffith; C. Metreweli and R.A. Cocks.** "Does Ultrasound have a Role in the Clinical Diagnosis and Management of Fractured Ribs?". *Abstracts Book, Annual Scientific Meeting of the Faculty of Accident and Emergency Medicine* p.11. UK: Faculty of Accident & Emergency Medicine, Royal College of Physicians London, 1999.12.
- <P993538> **Rainer, T.H.; L.Y.S. Chan; N.M. Hjelm; R.A. Cocks and Y.M.D. Lo.** "Plasma DNA as a Marker for the Early Prediction of Post-Traumatic Complications". *Abstract Book, Annual Scientific Meeting of the Faculty of Accident and Emergency Medicine* p.2. UK: Faculty of Accident & Emergency Medicine, Royal College of Physicians, London, 1999.12.
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RESEARCH PROJECTS

Enhancing Children's Emotional Intelligence

- ✉ LAU Tak Fai Joseph • CHAN Kam Kuen
- ☐ 1 June 1999
- ❖ Christian Family Services Centre of Funding from Quality Education Fund

This project is targeted to equip educators and parents of the nurseries and kindergartens with skills to enhance the emotional intelligence of students. An intensive curriculum, with seminars, workshops and group affect state/trait, teaching/parenting style and emotional responses is administered to both teachers and parents in a pre- and post- training format. Teachers and parents are also requested to fill in Rutter A and Rutter B Scales to assess the mental health condition of the kindergarten children. Process evaluation will also be conducted up, supervisions was designed to train the participating educators to be trainers in their own schools to promote the concept of emotional intelligence. A series of seminars was also designed for parents with children studying in nurseries and kindergartens thus to promote home-school co-operation. The outcomes of these activities will be measured for evaluative purposes. A series of standardized questionnaires on coping strategies, affect state/trait, teaching/parenting style and emotional responses is administered to both teachers and parents in a pre- and post- training format. (ED98037)

Emotional Education for Primary School Students

- ✉ LAU Tak Fai Joseph • CHAN Kam Kuen
- ☐ 1 June 1999
- ❖ Holy Carpenter Primary School of Funding from Quality Education Fund

This project is an evaluation on an education project about emotional intelligence funded by the Quality Education Fund. This study targeted to equip educators, parents and students of 13 primary schools with skills to enhance the emotional intelligence. An intensive curriculum, with seminars, workshops and group supervisions, was designed to train the participating educators with comprehensive knowledge and skill to enhance their own emotional well-being and growth as well as the students. Separate series of seminars was also designed for parents as well as the students. The outcomes of these activities will be measured for evaluative purposes in several ways. A series of standardized questionnaires on coping strategies, personality, general health condition, affect state/trait, teaching/parenting style and emotional responses is administered to both teachers and parents in a pre-

and post-training format. Teachers and parents are also requested to fill in Rutter A2 and Rutter B2 Scales to assess the mental health condition of the primary children. Students are also requested to fill in the Junior Eysenck Personality Questionnaire, the Hong Kong Student Information Form and the affect state/trait questionnaire. Process evaluation will also be conducted at the very end of the program. (ED99058)

Behavioural Surveillance of the Sexually-related Behaviours of the Chinese Female General Population in Hong Kong

- ✉ LAU Tak Fai Joseph • SIAH Poh Chua • BROW Tin*
- ☐ 1 August 1999
- ❖ Council for the AIDS Trust Fund

It has been documented that a high proportion of male adults in Hong Kong frequently practised high risk behaviours but did not use condom with their spouse or their regular sex partners, and that most of the HIV-infected women in Hong Kong got the infection from their spouse/regular sex partners, it is therefore important to understand the related behaviours practised by the women in Hong Kong. The information in this respect is however rare, as most of the research of risk behaviours in Hong Kong has been male-biased, and also that a few study carried out to study women's behaviour in Hong Kong was not based on a random territory-wide sample. The main objective of this study is therefore to set up a behavioural surveillance research project to understand the related behaviours practised by the women in Hong Kong. It is believed that the results of this study will not only improve the understanding of the reasons of using or not using condom from the female perspective and facilitate better empowerment projects to be done, but will also offer an objective yardstick to monitor and evaluate the outcomes of relevant education programs in Hong Kong. (SS99005)

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 | 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* |

| | |
|--|--|
| <p>1997-98 The Development of Indicators to Track Awareness, Attitude and Behaviours (MD97129) ✉ LAU Tak Fai Joseph • LEE Shiu Hung (School of Public Health)</p> | <p>1998-99 Evaluation of a program for Frequent Travellers Crossing the China-Hong Kong Border (MD98147) ✉ LAU Tak Fai Joseph • SIAH Poh Chua</p> |
|--|--|

RESEARCH OUTPUTS AND PUBLICATIONS

- <P001308> **Sze, Kai-Hoi; Wong E.; Lo R. and Woo J.** "Do Pain and Disability Differ in Depressed Cancer Patients?". *Palliative Medicine* vol.14 no.1, pp.11-17. USA, 2000.01.
- <P001309> **Easterbrook, Philippa J.; Ly Me Yu; Els Goetghebeur; Fiona Boag; Ken Mclean and Brian Gazzard.** "Ten-Year Trends in CD4 Cell Counts at HIV and AIDS Diagnosis in a London HIV Clinic". *AIDS* vol.14, pp.561-571. UK, 2000.03.
- <P001311> **Wong, Eric Ming-Chung; Chetwyn Chan; Sing-Kai Lo; Bobby Ng and Leonard Li.** "Rasch Analysis of the Functional Independence Measure for Chinese Stroke Patients Aged 80 Years and Above in Hong Kong". Paper presented in the 3rd International Outcomes Measurement Conference, organized by MESA Psychometric Laboratory, University of Chicago. Chicago, USA, 2000.06.
- <P001312> **Wong, Eric Ming-Chung; Chetwyn Chan and Sing-Kai Lo.** "E-Psychometric: An On-Screen Web Book for Measurement Theory". Paper presented in the 3rd International Outcomes Measurement Conference, organized by MESA Psychometric Laboratory, University of Chicago. Chicago, USA, 2000.06.
- <P001313> **Fung, Adrian Y.P.; Paul C.N. Look; Lai-Yin Chong; Paul P.H. But and Eric Wong.** "A Controlled Trial of Traditional Chinese Herbal Medicine in Chinese Patients with Recalcitrant Atopic Dermatitis". *International Journal of Dermatology* vol.38 no.5, pp.387-392. 2000.05.
- <P992890> **Lau, Joseph T. F.; Joseph L. Y. Liu; Aaron Yu and C. K. Wong.** "Conceptualization, Reporting and Underreporting of Child Abuse in Hong Kong". *Child Abuse & Neglect* vol.23 no.11, pp.1159-1174. USA, 1999.
- <P993366> **Lau, Joseph Tak-Fai and Chau-Kiu Cheung.** "Discriminatory Attitudes to People with Intellectual Disability or Mental Health Difficulty". *International Social Work* vol.42 no.4, pp.431-444. 1999.

see also <P000025>, <P000058>, <P000617>, <P001186>, <P001234>, <P001235>, <P001367>, <P001368>, <P001369>, <P001373>, <P001447>, <P002081>, <P002201>, <P985111>, <P992396>, <P992509>, <P992555>, <P993824>, <P993937>, <P993938>

RESEARCH PROJECTS

Functional Analysis of a Novel Gene that Modulates Life and Death

- ✉ CHUI Yiu Loon • CHAN Yeuk Hon John (Dept of Clinical Oncology)#
- ☐ 1 November 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

This research is aimed at elucidating the function of a new gene *BRE* that the researchers have found to induce cell death (apoptosis). Enhanced expression of *BRE* was also found in embryonic cells that were undergoing apoptosis. In addition, they have identified that *BRE* binds to the tumor necrosis factor receptor (TNFR1) and inhibits some of the functions of TNF- α . *BRE* may act by blocking the survival pathway of TNF, thereby facilitating cell death. The researchers propose to: (1) determine if the *BRE* gene could induce apoptosis in different cell-types; (2) raise antibodies against *BRE*, and to determine the expression of *BRE* during maturation and/or apoptosis of hemopoietic cells. As a modulator of cytokine and transcriptional factor, this *BRE* gene may enhance the efficacy of TNF and other cytotoxic agents in cancer therapy and immunotherapy. Alternatively, the antisense-cDNA of *BRE* could be used in anti-senescence and anti aging approaches. Since many of the cytokines are being used clinically, this research will not only enhance our understanding of apoptosis, but could also have application potentials soon.
(MD99030)

Production of Recombinant Human Telomerase and Anti-telomerase Antibody and RNA Probes to Examine their Diagnostic Utility in Autoimmune Disease and Cancer

- ✉ LIM Pak Leong • LEUNG Tze Ming
- ☐ 20 November 1999
- ❖ CUHK Research Committee Funding (Direct Grants)

The cloning of the human enzyme, telomerase, last year was exciting because this can hopefully lead to a cure for cancer and ailments linked to ageing. The enzyme apparently helps to prevent the normal process of cell senescence by adding back bits of DNA (telomeres) to chromosomes which are lost during cell division. It is absent in most normal cells but abounds in cancerous cells and may thus be important in cancer development. The researchers hope to exploit this discovery as immunologists rather than as cell biologists and study this enzyme in areas of medicine not examined previously. They intend to produce the enzyme in their laboratory by

re-cloning the gene and expressing this as a recombinant protein, and then make monoclonal antibodies to it. [The researchers have performed similar work with other proteins (and antibodies) previously.] They will use both the enzyme and antibodies produced as immunological reagents to see if these can help in the diagnosis of important local cancers, for example, in the form of a simple blood test. So far, there are very few blood tests available for this purpose. [They have developed various diagnostic tests previously, including that for typhoid fever.] They also plan to use the reagents to see whether patients with autoimmune disease such as lupus (a common disease in Hong Kong) produce antibodies to telomerase as some of them do with other enzymes in the body. Nothing is known about this. If they do, this may be diagnostically or biologically important. The researchers have researched for many years on antibodies directed to other self-proteins such as DNA. The reagents produced will not only be useful in medicine but also for biotechnology, where, hopefully, these can help to bolster the local industry.
(MD99031)

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> |
|----------------|---|
| 1996-97 | Molecular Mechanism of Immunoglobulin Gene Hypermutation: Does It Resemble the Transcription-DNA Repair System? (CU96664) ✉ CHUI Yiu Loon • LIM Pak Leong |
| 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 Anatomical & Cellular Pathology) • CHEUNG Siu Tim (Dept of Anatomical & Cellular Pathology)# • LO Kwok Wai (Dept of Anatomical & Cellular Pathology) |
| 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) |

RESEARCH OUTPUTS AND PUBLICATIONS

- <P000413> **Tam, F.C.H.; Chui Y.L. and Lim P.L.** "Dissection of the Fine Specificity of Antibodies with Peptide Surrogates of the Antigen". *The 2nd Congress of the Federation of Immunological Societies of Asia-Oceania (FIMSA) (Proceedings)* p.119. Bangkok, Thailand: The Allergy and Immunology Society of Thailand and The Faculty of Science Mahidol University, 2000.01.23.
- <P000419> **Wun, K.H.L.; Chui Y.L. and Lim P.L.** "Another Look at Antiidiotypic and Anti-DNA Antibodies in Autoimmunity". *The 2nd Congress of the Federation of Immunological Societies of Asia-Oceania (FIMSA) (Proceedings)* p.98. Bangkok, Thailand: The Allergy and Immunology Society of Thailand and the Faculty of Science, Mahidol University, 2000.01.23.
- <P000542> **Chan, K.W.; P.L. Lim; F.C.H. Tam; E.T.S. Li and B.L. Lim.** "Isolation of Leptin-Binding Peptides from a Random Peptide Phage Library". *Journal of Peptide Research* vol.55, pp.318-324. USA, 2000.04.
- <P993295> **Wun, K.H.L.; Leung D.T.M.; Chui Y.L. and Lim P.L.** "Induction of Antiidiotypic Antibodies to A Transgene-Encoded Antibody". *Scandinavian Journal of Immunology* vol.50, p.116. UK: Blackwell Science, 1999.07.

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RESEARCH OUTPUTS AND PUBLICATIONS

- <P001240> **James, Anthony E.** "Comparison of Animal Experimentation Legislation in the Asia-Pacific Region". *Australian and New Zealand Society for Laboratory Animal Science Newsletter* 2000.
- <P985116> **James, Anthony E.** "Occupational Health and Safety in the Animal House and Associated Laboratory Facilities". *Australian & New Zealand Council for the Care of Animals in Research and Teaching Newsletter* vol.11 no.3. Australia, 1998.09.
- <P985142> **James, Anthony.** "A Comparison Between the Effect of Percutaneous and Oral 17- Oestradiol on Atheroma Formation in Cholesterol-fed Rabbits (Master of Science Thesis)". p.153. Monash University, Australia, 1998.06.
- <P994252> **James, Anthony.** "Biomedical Research in Hong Kong and the Use of Laboratory Animals: Outdated legislation and Ethical Concerns". *Animal Technology: Journal of the Institute of Animal Technology (I.A.T.)* vol.50 no.3, pp.165-172. UK, 1999.12.

see also <P002063>

RESEARCH OUTPUTS AND PUBLICATIONS

<P994469> 劉明菊、李靜先、李廣文、秦嶺、陳啟明、盧景芬. <毛蕊花苷在解固定體骼肌氧化損傷中的作用 ESR 研究>. 《中國運動醫學學術會議論文摘要》 265 頁. 中國廣州: 中國體育科學學會運動醫學專業委員會, 1999.11.

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RESEARCH PROJECTS

Web-based Medical Education Development (Web-MED)

- ≈ Clarke Blaine HAZLETT • CHANG Mang Z. Allan (Dept of Obstetrics & Gynaecology) • CHEAM Teo Seng • YIP Pak Yiu Simon • NICHOLLS John* • LAU Y L*
- 1 September 1999
- ❖ 2nd Tranche Teaching Development Grants 1998-2001, RGC

The use of Web-based educational resources (for teaching in Medicine) in conjunction with evidence-based medicine protocols (for searching and evaluating electronic medical information databases) are uniquely suitable aids for achieving the principal goal of any medical school. That goal is to produce graduates whose clinical reasoning and decision making are based on the best available evidence, and

who are able to maintain such skill throughout their professional careers (because they can efficiently find available information and correctly evaluate its level of evidence and applicability to their own clinical practice).

The educational advantages of these aids are not realized unless medical educators are able to use, develop and incorporate these same educational technologies in their repertoire of teaching skills. This grant proposes to address this need by providing the enabling mechanisms for medical educators at The Chinese University of Hong Kong and The University of Hong Kong to successfully adopt these pedagogical technologies by (1) conducting appropriate medical teacher training workshops and, (2) expanding the access to resources by establishing a cohort of medical schools that contribute to and share their Web-based learning resources with Hong Kong's medical schools.

(MD99136)

RESEARCH OUTPUTS AND PUBLICATIONS

<P000412> **Hjelm, N.M. and C.B. Hazlett.** "Theory of Telemedicine: The Expressivity of the Virtual Patient". *Journal of Telemedicine and Telecare* vol.6, pp.119-120. 2000.

see also <P993461>