Faculty of

Medicine

The Effect of Syntocinon on the Gravid Uterus During Early Pregnancy

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- □ 1 May 1997
- CUHK Departmental Funding

A double-blind randomized placebo controlled study to determine the effect of syntocinon on the gravid uterus and the associated blood loss during early pregnancy suction currettage. (MD96205)

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

Edition Title/Investigators

- 1995-96 Hepatic Venous Saturation Monitoring in the Management of Severe Sepsis (CU95663)
 - GOMERSALL Charles OH Teik
 E.* STEWART Ian Edward Tam
 (Diagnostic Radiology & Organ
 Imaging)**
- 1996-97 Effect of Pregnancy on the Concentrations of Propofol Required for Hypnosis and Anaesthesia (MD96107)
 - ✓ JOYNT Gavin Matthew MORLEY Andrew P.

RESEARCH OUTPUTS AND PUBLICATIONS

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

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- □ 1 August 1997
- * Research Grants Council

Till now, on the two highly prevalent gastric cancers, lymphomas and adenocarcinomas, only scattered genomic analysis data have been available. The use of CGH (comparative genomic hybridization) seeks to redress this serious deficiency by analysis of the complete genome. It will also provide rare information on the ploidy status of a relatively large number of tumors by retrospective analysis on paraffin embedded tissue. Together with molecular analysis, the researchers aim to produce the most comprehensive and coherent outline of the genomic aberrations of the gastric cancers to date. combined structured study will set a precedent for studies of other tumors. This is more comprehensive than blindly choosing targets for gene and microsatellite loci analysis both in terms of economy and relevance. Objectives of the project: (1) To delineate the genomic imbalances, ploidy status, onogene/ Oncosuppressor gene mutations and microsatellite instability in gastric adenocarcinomas and lymphomas. (2) To compare the Helicobacter positive tumors with their Helicobacter negative counterparts. (3) To compare the genomic abnormalities of Helicobacter positive carcinomas with Helicobacter positive lymphomas and thus possible common paths carcinogenesis with particular emphasis on early stage tumors. (CU97624)

Tumor-**Isolation** and Characterization of Gastric **Infiltrating** Lymphocytes in Adenocarcinoma: A Comparative Study on **Tumors** with and without Helicobacter Association

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- □ 1 September 1997
- CUHK Research Committee Funding

Gastric adenocarcinoma is the third most important cause of cancer deaths in Hong Kong. These tumors have extremely poor prognosis. Less than 10% of the patients with advanced stage gastric carcinoma survive 5 years. Chemotherapy and surgery

advancement have not improved the outcome. One of the characteristics of gastric carcinomas is the diffuse spread of tumor cells especially in the signet ring type tumors. If a group of cells with the ability to target these tumor cells can be utilized to either deliver cytotoxic agents to them or can themselves be augmented to carry out tumor lysis, this will undoubtedly result in a major breakthrough in therapy for gastric cancers. Tumor infiltrating lymphocytes (TIL) are the most likely candidate for this task, they appear to recognize and interact with their autologous tumor cells. Before the researchers carry out more ambitious studies immunotherapy with these TILs, it is mandatory to understand their characteristics, phenotypes and cell surface antigens/receptors. Armed with these basic information, they can perform further in vitro experiments to augment their cytotoxic functions and introduce cytotoxic drugs producing genes into them. This study is thus designed to be the first of a major project on immunotherapy for gastric cancer.

The aims of this study are:

- (1) To isolate TILs from gastric adenocarcinomas with and without Helicobacter pylori.
- (2) To determine the immunophenotypes, adhesion molecules and cytokines expressed by these TILs.
- (3) To evaluate the significance of Helicobacter on the characteristics of TILs.

(MD97027)

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

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- 1 November 1997
- CUHK Research Committee Funding

Epstein Barr Virus (EBV) is known to be present in carcinomas and lymphomas of the nasopharynx/nose and stomach. In each location there is a predominant variant common to both types of tumors. The predominant variants found in the 2 locations differ slightly in deletions and codon changes found in the LMP-1 gene. Though a few cases of EBV-positive colorectal carcinomas and lymphomas have been reported in the literature, no large-scaled study has been previously performed. As the researchers have found a much higher rate of EBV-positive gastric carcinomas and lymphomas than reported in the literature, the same type of systematic survey should be performed for the even more prevalent colorectal tumors, which bear great morphological and/or clinical similarity to their gastric counterparts. A large number of archival paraffin blocks are available for study. Initial screening for EBV by the sensitive

method of *in situ* hybridization for EBV encoded small nuclear RNA (EBER) shall be followed by analysis of the N terminus of the LMP-1 gene in the positive cases by Polymerase Chain Reaction (PCR)-Restriction Fragment Length Polymorphism (RFLP) and the C-terminus by PCR-Single Strand Conformation Polymorphism (SSCP). (MD97029)

Cloning and Characterizing of the Aberrant DNA Methylation Sequences in Nasopharyngeal Carcinoma (NPS)

- □ 1 September 1997
- **❖** CUHK Research Committee Funding

Alterations in the DNA methylation are among the most common genetic changes associated with neoplasia and may have a causative role in the development of human cancers. Aberrant methylation of the cancer-related genes may contribute to tumorigenesis either by generating point mutation at the CpG sites or by altering gene expression. Recent evidence also suggested that altered methylation may directly influence genomic instability in cancer.

In NPC, silencing of the tumor suppressor gene p16 by de novo methylation of the 5'CpG island has recently been demonstrated by the researchers. It is possible that other genes involved in the tumorigenesis of NPC may also be influenced by this type of epigenetic change. In order to understand the role of DNA methylation in the tumorigenesis of NPC, a genome-wide search for the abnormally hypermethylated and hypomethylated sequences in the NPC tumor cells will be carried out by the methylation-sensitive restriction fingerprinting (MSRF) analysis. The differentially methylated sequences in the NPC tumor cells will be cloned and confirmed by the southern blotting analysis. In addition to the identification of the chromosomal location, the sequence of the isolated DNA fragments will be analyzed and searched for homology to the known sequence. For the DNA fragments containing novel expressed sequences, full length cDNA will be isolated. Cloning and characterization of these sequences may lead to the identification of the specific tumor suppressor genes and oncogenes involving in the development of NPC. (MD97028)

A Comparative Investigation of Telomerase Activity in Human Liver with Hepatocellular Carcinoma, Chronic Viral B Hepatitis, Cirrhosis, and Nomal Liver

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- □ 1 November 1997

Research Grants Council

Telomeres are specialized structures located at the end of chromosomes that appear to function in chromosome protection, positioning and replication. Telomeres shorten after each cycle of cell replication and contribute to genetic instability. This could be a mechanism in cell aging, senescence and tumorigeneses. The re-expression of telomerase, the enzyme that maintains telomeres and prevents their shortening, occurs in many tumors. Telomere shortening and telomerase activity are detected in many common cancers and some reports indicate that telomerase activity could have prognostic values for cancers.

In Hong Kong hepatocellular carcinoma (HCC) is the second and fourth most common cancer cause of death in male and female respectively. In this investigation, the researchers will assay, determine and compare telomerase activity in human livers with various disease states such as HCC, chronic hepatitis, biliary atresia and metastatic cancer in the liver. The telomerase activity in these tissue samples will be correlated with the demographic data, clinical parameters, laboratory results and tumor recurrence. Finally, they will determine the value of assaying telomerase activity in HCC and the possible application of the results of these studies in the clinical management of patients with HCC. (CU97677)

Studies on the Molecular Genetics of CNS Tumors

- NG Ho Keung HUANG POON Wai Sin Dolly
 LAM Yeng Po[#] LO Kwok Wai PANG Chung Sean POON Wai Sang (Surgery)
- ☐ 1 January 1998
- * Research Grants Council

The overall objective of this research is to further understand the molecular genetic events leading to the development of CNS tumors, especially malignant astrocytomas and meningiomas. researchers aim to provide information which helps correlate conventional morphology abnormalities of tumor suppressor genes including p53, p16, p19, epidermal growth factor receptor (EGFR) gene, in the paradigm of malignant progression of CNS tumors. It has been proposed by some authors that the malignant progression of astrocytomas involves two distinct clinical and molecular pathways, one arising de novo and the other from pre-existing low-grade tumors. On the other hand, in some de novo malignant astrocytomas, morphologically low-grade and high-grade areas occur side by side. They want to define the genetic alterations of these subpopulations of cells by microdissection and genetic analysis. Results will be compared to similar examination of astrocytomas which progress to a malignant form over the years.

Such information may also provide an adjunct to conventional morphological diagnosis and prognostication, in problems relating to sampling, infiltrating margins, etc.. As regards meningiomas, they are generally benign with a small proportion of atypical / malignant cases. The researchers plan to continue their present work on abnormalities of p16 gene and its expression as a major molecular event of malignant progression. (CU97671)

Preliminary Evaluation of Antisense Epidermal Growth Factor Receptor (EGFR) RNA in the Treatment of Malignant Gliomas

- MG Ho Keung PANG Chung Sean CHEN Jie*
- ☐ 1 April 1998
- CUHK Research Committee Funding

Malignant gliomas are the commonest primary tumors of the brain and the prognosis is less than one year despite aggressive therapy. In this study, the researchers propose to develop the antisense technology against the epidermal growth factor receptor (EGFR) gene as adjuvant therapy for malignant gliomas. The antisense technology utilizes synthetic segments of DNA called oligonucleotides to inhibit translation of the targeted mRNA and production of disease-related protein, in this case EGFR. In gliomas, the EGFR gene is amplified or overexpressed in 50% of cases, often in late-stage malignant transformation. They hypothesize that down-regulation of the EGFR gene, the key gene for malignant transformation in gliomas, by the antisense strategy would inhibit production of the EGFR protein with resultant arrest of cellular proliferation and abolishment of tumorigenecity of glioma cells. (MD97110)

"Telomerase Activity in Urinary Bladder Cancer" Does It Correlate with the Biological Behavior?

- ∠ TO Ka Fai LO Kwok Wai
- □ 1 November 1997
- CUHK Research Committee Funding

Urinary bladder cancer is a significant health care issue. In Hong Kong, more than 600 new cases and nearly 200 cancer death per year. It is the sixth most commonest cancer in men. Various attempts have been tried to disclose the patho-biology and search for factors predicting the patient outcome. The conventional prognostic factors include histological grading and clinopathological staging. However, these factors alone may not be able to predict the outcome of individual patient. Searching for useful prognostic factor(s) remains a challenge.

Recently, detection of telomerase activity in tumors has become a feasible method and may be of prognostic value. With every somatic cell division, the chromosomal ends, or telomeres, progressively shorten. Eventually, the chromosomes with truncated ends become unstable, fused or even disappear during mitosis. Telomere shortening appears to be nature's timing mechanism leads to cell senescence and death. It appears that a variety of tumors also express the telomerase activity which repairs the chromosomal ends, and contribute to the unlimited growth of tumor cells.

Only a few studies have been performed in bladder cancer. These suggested that almost all bladder cancer samples express the telomerase activity. However, the prognostic significance of telomerase activity is controversial. The researchers propose to investigate the expression of telomerase activity in the local population, to identify the rate of expression of telomerase activity and the potential prognostic value. These may enhance then understanding of the patho-biology and disclose the potential diagnostic and prognostic factor in bladder cancer. (MD97030)

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

Edition Title/Investigators

- 1993-94 The Investigation of Tumour Marker Expression in Cytology Specimens (MD94033)
 - CHANG Alexander Russell
- 1994-95 An Investigation on the Use of Exfoliative Cytology for the Detection of Nasopharyngeal Carcinoma and Precursor Lesions; A Potential Technique for Mass Screening (MD95026)
 - CHANG Alexander Russell CHAN Kwok Mei May
- 1993-94 Sinonasal T Cell Lymphomas: A Study in Formalin-Fixed Tissue and Peripheral Blood using Antibody against Cytolytic Granule Associated Protein (TIA-1) (MD93086)
 - ∠ CHOW John Hei-sing CHAN Wing Yee*
- 1994-95 Expansion of the Large Granular Lymphocyte (LGL) Compartment in Decidual Tissue and Its Relationship with First-Trimester Spontaneous Abortion (MD94112)
 - ∠ CHOW John Hei-sing CHAN Wing Yee* LAU Woon Chung* (Obstetrics & Gynaecology)

- 1995-96 Cytogenetics and Florescence *in situ* Hybridization (FISH) of Sinonasal T-cell Lymphoma (SNTCL) (MD95164)
 - ∠ CHOW John Hei-sing ◆ WONG Nathalie (Clinical Oncology)
- 1996-97 Application of Comparative Genomic Hybridization to the Detection of DNA Imbalances in Sinonasal T-cell Lymphoma (MD96010)
 - CHOW John Hei-sing WONGNathalie (Clinical Oncology) •WOO Kong Sang John (Surgery)
- 1996-97 Correlation of the Expression of c-myc and bc1-2 Oncoproteins with the Expression of Epstein-Barr Encoded EBER mRNA, LMP-1 and bc1-2 Homologue, BHRF1 in Primary Gastric Lymphoma (MD96029)
- 1995-96 Epstein-Barr Virus (EBV) specific Latent Membrane Protein (LMP1) Gene and Its Variants in the Hong Kong Chinese Population: Molecular Epidemiology and Pathogenetic Significance in Nasopharyngeal Carcinoma (NPC) (CU95617)
 - HUANG POON Wai Sin Dolly •
 TAM Siu Lun John (Microbiology) •
 NG Ho Keung LEUNG Sing Fai
 (Clinical Oncology) FOK Tai Fai
 (Paediatrics) VAN HASSELT
 Charles Andrew (Surgery) LEE
 Joseph C. K.
- 1994-95 Apoptosis in CNS Tumours Pilot Studies with *in situ* Labelling and Expression of Oncogenes and Tumour Suppressor Genes (MD95050)
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 - ∠ LEE Joseph C. K. HUANG POON
 Wai Sin Dolly TO Ka Fai LO
 Kwok Wai LEUNG Sing Fai
 (Clinical Oncology)
- 1996-97 Detection and Clinical Relevance of Genetic Abnormalities (E2A/PBX1 and BCR/ABL) in Pediatric Acute Lymphoblastic Leukemia by Multiplex Polymerase Chain Reaction (MD96030)
 - ∠ LEE Joseph C. K.

 NG Heung Ling Margaret

- 1995-96 The Investigation of Genomic Instability by Polymerase Chain Reaction to Detect Microsatellite Polymorphisms on Chromosomes 1, 2, 3, 4, 6, 7, 11, 16, 17 and 18 in Hepatocellular Carcinoma (CU95661)
 - LIEW Choong Tsek LEE Joseph C.K. LAU Wan Yee Joseph (Surgery)
- 1995-96 Study on the Interactions of EBV Latent Proteins and the Common Cellular Tumour Suppressors by Yeast Two-Hybrid System (MD95118)
 - ∠ LO Kwok Wai HUANG POON
 Wai Sin Dolly WAYE Mary Miu
 Yee (Biochemistry)
- 1993-94 In Situ Hybridization of Estrogen Receptor Gene and Immunohistochemical Studies of Estrogen Receptor Level in Carcinoma of Prostate (MD93087)
 - Mac-MOUNE LAI Fernand ◆
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 Foon Peter (Surgery)
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 Thrombophilia (ATIII, Protein C or
 Protein S Deficiencies) in Idiopathic
 Young Stroke Patients Among Hong
 Kong Chinese (MD95119)
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 Ka Sing Lawrence (Medicine &
 Therapeutics)
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 - NG Ho Keung
- 1995-96 Studies on the Genetic Alterations of CNS Tumours (CU95614)
 - ✓ NG Ho Keung HUANG POON
 Wai Sin Dolly POON Wai Sang
 (Surgery) WONG Nathalie
 (Clinical Oncology)
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Kwok Wai • PANG Chi Pui Calvin (Ophthalmology & Visual Sciences) • POON Wai Sang (Surgery) • TO Ka Fai Intratumoral Heterogeneity of DNA Content (MD95166)

▼ TO Ka Fai • Mac-MOUNE LAI Fernand • TSOI Wai Chiu*

1996-97 Correlation between Apolipoprotein E
Genotype and β-Amyloid Deposition in
Chinese Brains (MD96031)

× NG Ho Keung

"Recurrent Urinary Bladder Cancer":
True Recurrence or New *de novo* Cancer?
Application of Microsatellite Analysis (MD96032)

**TO Ka Fai • LO Kwok Wai

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A Study of Prostatic Secretory Protein of 94 Amino Acids Expression in Normal, Castrated and Hormone-Treated Rat and Mouse Prostate Glands

- ∠ CHAN Leung Franky XUAN Jim W.*
- □ 1 October 1997
- CUHK Research Committee Funding

The prostatic secretory protein of 94 amino acids (PSP94), also named as ß-microseminoprotein, is one of the major proteins secreted by the human prostate gland, in addition to prostatic acid phosphatase (PAP) and prostatic-specific antigen (PSA). It is a small, nonglycosylated protein, rich in cysteine residues and has a molecular weight of 10.7 kDa Research interests on this protein stems from its potential use as a diagnostic marker as it can be measured in the serum of prostate cancer patients and also its expression pattern is correlated to two established tumor markers, PAP and PSA and thus may be useful to monitor prostate cancer. However, its function in the reproductive biology as well as its regulation of synthesis is still unclear ever since its first isolation from the human seminal plasma in 1984. This protein is reported to have an inhibin activity as shown by its inhibitory effect on the secretion of follicle stimulating hormone by the pituitary cells and thus it is also called ß-inhibin, however, this is proved later to be untrue. It is also shown to be identical to a sperm motility inhibitor and have a weak inhibitory effect on N⁺, K⁺ATPase. Homologous proteins as well as its cDNAs and genes have also been identified and cloned in other animal species including rhesus monkey, baboon and pig. Similar studies of this homologous protein in small experimental animals such as rat and mouse are absent so far. The main difficulty is that its homologus protein or gene is not identified until recently PSP94 has been identified and its cDNAs have been cloned in rat and mouse prostates. The present study is to investigate the expression of PSP94 and its alternative transcripts in normal, aging. castrated and hormone-treated rat and mouse prostates. It is hoped that through this study, it will help to provide more important information on its possible functional role and its regulation of synthesis in the prostate gland. (MD97035)

Mechanism of Glutamate Induced Neurotoxicity in Retina

- ∠ CHAN Sun On LAM Tim Tak (Ophthalmology & Visual Sciences)
- ☐ 1 October 1997
- CUHK Research Committee Funding

Glutamate induced neurotoxicity has been implicated to the neuronal damage in central nervous system. Neuronal loss in retina after ischaemia/reperfusion injury and during glaucome has also been linked to exposure of excess glutamate. In order to understand the mechanism of glutamate neurotoxicity to retinal neurons, the researchers look at the dose dependent toxicity of glutamate to explant culture of adult rat retina. The mechanism of glutamate induced neuronal damage in retina is then determined using blockers of specific glutamate receptor subtypes: NMDA and AMPA/kainate receptors. Drugs which selectively block functions of these receptors will be added simultaneously with glutamate to see whether they can reduce the neuronal loss in the retina. Results of this study will further our understanding of glutamate toxicity to retinal neurons and will form the basis of further studies on therapeutic intervention of neuronal cell death in retinal diseases related to glutamate toxicity.

(MD97032)

The Role of SPARC, an Extracellular Matrix-Associated Protein, in Ovarian Tumor Growth and Invasion

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- □ 1 November 1997
- Research Grants Council

Although ovarian cancer is the most common cause of death among all gynecological malignancies, little is known about the pathogenesis of the cancer. Using a fingerprinting approach, the researchers have identified a cDNA which is present in all normal human ovarian cell cultures but is consistently absent in ovarian carcinoma cell lines. The cDNA was then characterized and identified as a coding region of an extracellular matrix-associated protein known as SPARC. SPARC is a secreted protein which is acidic and rich in cysteine. Analyses on mRNA (Northern blot) and protein (Western blot) expression in fresh human ovarian tumor tissues and carcinoma cell lines showed that SPARC was down-regulated by as much as ten-fold in the ovarian cancer when compared to normal tissues. The preliminary results on ovarian carcinoma cell lines showed that SPARC can inhibit cell growth. In order to characterize the biological role of SPARC in ovarian tumor growth and invasion, the researchers propose: (1) to establish the expression pattern of SPARC in the normal ovary and ovarian carcinomas; (2) to examine the effect of exogenous SPARC on the tumor growth and tumor invasion; (3) to alter the expression of SPARC in both normal ovarian cells and carcinoma cells. Results obtained from the present study will provide information on the role of SPARC during ovarian carcinogenesis. (CU97610)

The Role of Endothelin-1 in the Development of the Mouse Embryo

- ∠ CHAN Wood Yee
- □ 1 November 1997
- CUHK Research Committee Funding

Endothelin-1 (ET-1) is a potent vasoconstrictor and has been implicated in a wide variety of functions involving vascular and non-vascular systems. Studies on knock-out mice and in situ hybridization showed that it also plays an important role in embryogenesis. ET-1 mRNA is expressed in a restricted set of embryonic tissues and mouse embryos with abnormal expression of ET-1 have severe defects in the craniofacial and cardiovascular structures. However, the expression of ET-1 peptide in normal mouse development has not been studied and the functional role of ET-1 during embryogenesis is still unclear. To establish the role of ET-1 in embryonic development, this study is proposed to examine (1) ET-1 expression pattern in mouse embryos at different developmental stages; (2) Effects of ET-1 depletion and excess ET-1 on organogenesis; and (3) Effects of ET-1 depletion and excess ET-1 on craniofacial and cardiovascular development. (MD97033)

Development of a Novel Diagnostic Kit for Early Detection of Human Cervical Cancer: Identification and Generation of a Monoclonal Antibody

- □ 1 July 1997
- Industrial Support Fund, Industry & Technology Development Council

Carcinoma of the uterine cervix is one of the commonest cancers in woman. In Hong Kong, cervical cancer is the fifth commonest cancer in Chinese women with a mortality rate of 5 per 100,000 women. The PAP smear is a common method used in clinical laboratories to detect this cancer. However, the method suffers an estimation of 25% false negatives. In this study, the researchers intend to produce a more sensitive and specific diagnostic kit for early diagnosis of cervical cancer in women. (MD97003)

Application for Development of a Novel Nuclear Matrix Laboratory for Both Research and Teaching at Prince of Wales Hospital

- CHEW Eng Ching
- □ 1 October 1997

CUHK Strategic Research Program

Structural changes of cells and tissues have always been used by pathologists for the diagnosis of malignant tumors. Among these, the alterations in nuclear size and shape are commonly being used. These architectural changes of the nucleus may be associated with the reconstruction of the internal nuclear scaffold, the nuclear matrix. In addition, the nuclear matrix is involved in gene localization and in the control of replication and transcription.

In view of the important roles played by the nuclear matrix in normal and abnormal cellular functions, a Nuclear Matrix Laboratory was established in 1997. This laboratory is located at the Sir Y K Pao Centre for Cancer, Prince of Wales Hospital. researcher's recent studies have confirmed the presence of cell-type-specific nuclear matrix proteins in several different tumors. He has identified several cervical cancer specific nuclear matrix proteins and has also shown that HPV 16DNA is bound to different nuclear matrix and chromosomal proteins in normal and cervical cancers. He also discovered that dexmethasone inhibited the growth of cervical carcinoma cells in vitro and altered their nuclear matrix protein profiles. Currently, the researcher is focusing on the identification and purification of nuclear matrix proteins in common Hong Kong hepatocellular such carcinoma, nasopharyngeal carcinoma, cervical and lung cancers. (MD97008)

Effect of All-Trans-Retinoic Acid on the Nuclear Matrix of Nasopharyngeal Carcinoma Cells in vitro

- CHEW Eng Ching
- ☐ 1 October 1997
- CUHK Research Committee Funding

Nasopharyngeal carcinomas (NPC) are relatively rare in most of the geographical regions. In certain areas, however, NPC occurs commonly. The areas in which this tumor is commonly found are North Africa and the province of Guangdong in Southern China, including Hong Kong. Nuclear matrix is a scaffoldlike structure of the nucleus after sequential treatments with detergents, DNase, and high salt buffers. Its involvement in various cellular activities has been emphasised in various studies. Retinoids are effective inhibitors of neoplastic development in several experimental models of carcinogenesis, suggesting their clinical application as both cancer chemo-preventive and anticancer agents. Among all retinoids, all retinoids, all-trans-retinoic acid seems to be the more active natural isomer. The purpose of this study is to assess the effect of all-trans-retinoic acid on the nuclear matrix of human normal and NPC cell lines in vitro, and to evaluate the ability of this drug to induce cell differentiation.

(MD97034)

Bmp2 and Alk6 Gene Interaction During Programme Cell Death in the Limbs of Mouse **Embryos**

- ∠ LEE Ka Ho Kenneth MUNEOKA Kenneth* NGO-MULLER Valerie*
- □ 1 November 1997
- CUHK Research Committee Funding

Worldwide, deformities of the limb (e.g. club foot, meromelia, polydactyly, syndactyly) are the second most common category of congenital abnormalities observed in human. It is crucial that we understand how some of these abnormalities arise, at the molecular and cellular level, if we are to develop a potential treatment for these conditions. In this propose study, the researchers will examine bmp2 and its receptor AKL-6 to determine how these 2 genes interact in the transduction pathway to induce apoptosis in the developing limb. Apoptosis is essential to limb development because it eliminates excess tissue from the limb, helping to separate the chondrogenic elements from each other and it also help to establish the joints between articulating cartilage. They will first establish by in situ hybridization the expression pattern of bmp2and ALK-6 in 12-5 -14.5 day embryonic limbs. Using TUNEL techniques, they will also determine the corresponding apoptotic pattern in the limb. To ascertain whether bmp2 can induce apoptosis in the limb, they will generate a cell line that can secrete human recombinant Bmp2 protein. These cells will be transplanted into the various regions of the limb to determine whether it can induce ectopic cell death. The researchers will also examine whether the procedure can up-regulate ALK-6 gene expression to understand the transduction pathway of Bmp2's action. The results obtained from this study, will provide valuable information on the molecular mechanism that regulates programme cell death in the limb. It may also help explain how congenital abnormalities, such as syndactyly (characterized by the presence of webbed fingers), are formed in human. (MD97036)

The Effect of Mushroom Extract on the Tumor Vascular System in Inbred Mice - A Scanning **Electron Microscopic Study**

- ∠ LIU Wing Keung Ken KONERDING Moritz*
- ☐ 1 June 1998
- Germany/Hong Kong Joint Research Scheme

The blood vessels are present in all the tissues of the body for replenishing nutrients and carrying off waste products. Their number and size are constant because

they are under stringent growth control. However, persistent and unregulated new blood vessel formation occurs in neoplastic tissues because tumor cells can stimulate neovascularization that brings fresh nutrients and growth factors into the expanding tumor mass. This is a crucial step when a small group of benign mutated cells transforms to a large and malignant mass. The structural change of the tumor vasculature can hardly be studied unless a replica of the vascular system is formed and observed under a powerful microscope. The scanning electron microscopy of vascular corrosion casts is a widely used method through which the 3-dimensional arrangement of tumor vasculature morphometrically analysed. It is anticipated that the change of vascular pattern in the tumor mass will provide an insight into the anti-tumor and antineovascular activities of the mushroom extract in a tumor-bearing animal model.

(MD97102)

A Study of the Molecular Basis of Diabetic Embryopathy and Interaction of Maternal Diabetic Milieu with Genetic or Environmental **Factors**

- □ 1 October 1997
- Research Grants Council

Infants of diabetic mothers have a higher incidence of congenital anomalies than infants of non-diabetic mothers. The increased prevalence is thought to arise from the teratogenic effect of the maternal milieu on the developing embryo. However, the fundamental mechanisms that are disturbed during development of many of these malformations remain unclear. The present proposal will focus on studying the cellular and molecular bases of two spinal defects, caudal agenesis and spina bifida, which are strongly associated with maternal diabetes mellitus. Moreover, two hypotheses are under investigation: the findings that embryos of diabetic mothers are more prone to congenital malformations may not be solely due to the teratogenic action of the maternal diabetic milieu, but also (1) arise as a result of interaction with other environmental factors such as drugs taken during pregnancy, or (2) result from the concurrent action of independent genetic suceptibility factors. hypotheses will be studied by treating diabetic mice with a vitamin A metabolite, retinoic acid, which is known to induce caudal agenesis in the embryo and also by determining the effect of inducing diabetes in a mouse mutant, curly tail, genetically predisposed to spina bifida.

(CU97691)

The Role of Wilms' Tumor Gene (WT1) and Apoptosis in the Development of Renal Agenesis

- ✓ SHUM Sau Wun Alisa HASTIE Nicholas D.*
 TSE K. W. Herman* MENKE Aswin*
- ☐ 10 February 1998
- ❖ UK/Hong Kong Joint Research Scheme, the British Council

Renal agenesis is a clinically significant birth defect which arises as a result of abnormalities in the early stages of kidney formation. The main aim of this study is to obtain information on the cellular and molecular basis of development of this defect. The strategy involves the use of a mouse model recently set up in the researchers' laboratory, in which renal agenesis in the offspring is induced by maternal exposure to retinoic acid, an active metabolite of vitamin A. Preliminary data showed that the kidney underwent rudiments massive apoptosis (programmed cell death) and also failed to express the Wilms' tumor gene (WTI) which is a gene crucial for kidney development. Subsequently, the kidney rudiments degenerated completely. The specific objectives in this study are to: (1) determine the temporal and spatial expression patterns of apoptotic cells in the kidney rudiments; (2) determine whether deregulation of WT1 is accompanied by misregulated expression of genes associated with cell death; (3) determine whether the kidney rudiments can be rescued from degeneration by addition of exogenous growth factors in an organ culture system.

Results of these studies will provide not only important information on the pathogenic mechanisms of renal agenesis, but also contribute to the first step towards deriving methods for early detection, prevention and treatment of the defect *in utero*. (MD97106)

Oxygen Free Radicals as Mediators of Methamphetamine-Induced Neurotoxicity

- ☐ 1 October 1997
- CUHK Research Committee Funding

Methamphetamine (METH), a central nervous system (CNS) stimulant and drug of abuse has been shown to have long-lasting neurotoxic effects on the dopamine (DA) and forebrain serotonin systems in the CNS. It was reported that METH would induce the release of DA and caused the loss of DA terminals within the striatum as well as result in extensive astrogliosis. The mechanisms of this release and subsequent neurotoxicity are not well defined. Some evidence to date have shown that oxygen free radicals may play an important role in the manifestations of METH-induced neurotoxicity in the dopaminergic system.

The aim of this study is to examine the role of oxygen free radicals in mediating METH-induced neurotoxicity using an in vitro system. DA neurons obtained from C57BL/6 mice midbrain will be cocultured with retrovirally transfected primary cultured astrocytes over-expressing the gene for antioxidant glutathione peroxidase (GSH-Px). Cells will be treated with 4mM METH for 0, 4, 8, 12, 24, and 48 hrs. The amount of oxygen free radicals production will be measured using a non-fluorescent probe 2',7'-dichlorofluorescin diacetate (DCFH-DA). which in the presence of free radicals, will be oxidized highly fluorescent to dichlorofluorescein (DCF). Cell viability will be assessed using the fluorescent probes, Calceinacetoxymethyl ester (Calcein, AM) and ethidium homodimer-1 (EthD-1) as indicators of living and dead cells, respectively. Change in DCF, Calcein AM and EthD-1 and will be examined under a confocal microscope. Cell viability and free radical production in DA neurons co-cultured with GSH-Px transfected astrocytes will be compared to neurons co-cultured with non-transfected astrocytes as an index of free radical mediated toxicity. (MD97031)

Limbal Stem Cell Identification in a Rabbit Model

- ∠ YEW David Tai Wai AU Yue Kong (Ophthalmology & Visual Sciences)[#]
- □ 1 November 1997
- ❖ CUHK Research Committee Funding

Limbal stem cells (LSC) are undifferentiated cells located at the peripheral cornea. LSC are essential for maintenance of the normal cell mass of the corneal epithelium under normal conditions. They are also responsible for corneal wound healing after injury of the corneal epithelium. Clinically, limbal stem cell transplantation is an established method for treatments of serious ocular surface diseases, including alkaline and thermal burns. However, little is known about factors modulating the metabolic and proliferative behavior of these cells.

In the present study, investigators would like to achieve the following objectives: (1) to delineate the proliferative and metabolic behavior of the LSC under normal and pathological conditions & (2) to identify any cell-cell or cell-substrate interaction of the LSC with the other part of the cornea.

Experiments will be done in a rabbit model. In some animals, a demand stress of corneal epithelium is created by making a 50% central corneal abrasion. Laboratory techniques used include:

- (1) cytochrome oxidase localization with histochemical technique,
- calcium binding protein localization with immunohistochemical techniques, and

(3) Epidermal growth factor (GF) and EGF receptor localization with immunohistochemical technique.

(BL97007)

Microglial Reaction Pattern in Normal and SCID (Severe Combined Immunodeficient) Mice

- ∠ YEW David Tai Wai SCHUMACHER U.* •
 LORKE D. E.*
- ☐ 1 April 1998
- Germany/Hong Kong Joint Research Scheme

A study of the reaction pattern of microglial cells after traumatic lesion of the central nervous system will be compared in the SCID and normal mice. The SCID mice (severe combined immunodeficient) mice is a BALB/c inbred strain deficient in the V(D)J joining gene and thus lacks B & T lymphacytes. As a consequence, all defence mechanisms involving antigan-antibody reactions are completely absent. However, NK cells and monocytes/macrophages function does not seen to be impaired, the researchers are establishing facial nerve and spinal cord lesion models in these animals and will evaluate the microglia responses after lesion. The results also demonstrate the extent of lymphocyte participation in CNS injury and repair. These findings will be compared with the normal mice and will add to the understanding of the CNS reactions immunodeficient conditions. (MD97103)

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

Edition	Title/Investigators		
1995-96	A Study of Glycoproteins and Extracellular Matrix of the Normal, Dysplastic and Neoplastic Prostates of the Noble Rat (CU95622) ∠ CHAN Leung Franky • HO Shuk Mei*		
1996-97	Identification of Up- and Down-regulated cDNAs that are Differentially Expressed between Normal and Dysplastic Prostates of Noble Rat (MD96033) CHAN Leung Franky		
1995-96	Axon Guidance in the Development of Mammalian Retinofugal Pathways (CU94643) CHAN Sun On • YUNG Wing Ho (Physiology)		
1995-96	Investigations of the Cellular Mechanisms Underlying the Turning of		

Uncrossed Retinal Axons at the Midline of the Optic Chiasm (MD95110)

∠ CHAN Sun On

- 1996-97 Identification of the Molecular Determinants in the Retina that Govern Axon Pathfinding in the Chiasm of Mammals (CU96623)
 - ∠ CHAN Sun On CHENG Shuk Han
 (Orthopaedics & Traumatology)
- 1996-97 Embryological Basis of Congenital Heart Defects: A Study Using a Mouse Mutant and a Transgenic Marker (MD96034)

 © CHAN Wood Yee COPP A. J.*
- 1995-96 The Role of Nuclear Matrix Proteins in Cancer: A Morphological and Molecular Biological Approach (MD95055)

 © CHEW Eng Ching
- 1996-97 Long Term Culture of the Whole Retina of Adult Hamsters as a Model to Study Regeneration of Retinal Ganglion Cells (CU96632)

 © CHO Yu Pang Eric
- 1995-96 Physiology of the Ampullary Gland and Ventral Prostate: A Possible Regulatory Role in Mammalian Fertility (CU94358)
 - ∠ CHOW Pak Ham Patricia CHENG Lydia Yuk Luen*
- 1996-97 The Ampullary Gland, Ventral Prostate and Embryogenesis (BL96033)
 - ∠ CHOW Pak Ham Patricia O Wai Sum*
- 1996-97 Male Accessory Sex Glands and Fertility: The Role of Apoptosis and Angiogenesis During Early Development (BL96031)
 - ∠ CHOW Pak Ham Patricia

 ✓ YI
 Xianjin[#]
- 1995-96 Histological, Histochemical and Immunohistochemical Studies of the Ureterovesical Junction in Patients with Acute and Chronic Vesicoureteral Reflux (CU95602)
- 1994-95 Apoptosis in the Developing, Diseased and Aging Nervous Systems (MD95061)

	GOSLING John Arthur • CHAN Wood Yee • CHO Yu Pang Eric • DIXON John Stuart • LEUNG Ping Chung (Orthopaedics & Traumatology) • SHUM Sau Wun Alisa • YEW David Tai Wai • YU Mang Chung	1996-97	Mechanisms Underlying the Immunomodulatory and Antitumor Activities of Selected Lectins (CU96667) ∠ LIU Wing Keung Ken • NG Tzi Bun (Biochemistry) • OOI Vincent E. C. (Biology) • CHANG Shu Ting (Biology)
1992-93	Neural Influence on Muscle Regeneration (MD92048)	1995-96	The Mechanisms of Transition from Primary to Secondary Neurulation (CU95662)
1994-95	Neuronal Death Caused by Trichosanthin (MD94075)		SHUM Sau Wun Alisa
	★ KWONG Wing Hang • NG Tzi Bun (Biochemistry)	1995-96	To Study the Pathogenesis of Renal Agenesis (MD95111) SHUM Sau Wun Alisa • GOSLING
1996-97	Neurotoxicity of Type I Ribosome- inactivating Proteins (BL96032)		John Arthur • WOOLF Adrian S.*
	 × KWONG Wing Hang • WONG Jianbin[#] • SHEN Wei Zai* 	1996-97	To Study the Relationship of Maternal Diabetes Mellitus, Insulin and Caudal Agenesis in Offspring Using an Animal
1995-96	Role of Retinoic Acid on Limb Development in Transgenic Mouse Embryos (MD95107)		Model (MD96037)
	∠ LEE Ka Ho Kenneth • EDE Donald* • PAULIN Denise*	1996-97	The Effects of Prenatal Heroin Exposure on Postnatal Brain Development and Behavior in Rats (CU96615)
1996-97	Role of Growth Arrest Specific Gene in Mouse Embryonic Development		
	(MD96036)	1995-96	Aging Changes in the Human Central Nervous System (MD95185) X YEW David Tai Wai
1996-97	The Role of BMP and MSX Genes in the Control of Programme Cell Death in the Limbs of Normal and Hammertoe Mutant Embryos (MD96122) LEE Ka Ho Kenneth • MUNEOKA Kenneth*	1996-97	An Animal Model of Proliferative Vitreoretinopathy (MD96038) X YEW David Tai Wai

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Oligonucleotide Combinatorial Library: Application in Diagnostic and Therapeutic Drug Development

- ∠ CHEUNG Wing Tai HO Walter K. K. WAN David Chi Cheong
- □ 1 August 1997
- CUHK Strategic Research Program

Recent development in the generation of large libraries of random sequences of single-stranded oligonucleotides offers the opportunity in searching ligands with selective affinity for any defined targets. For instance, Systematic Evoluation of Ligands by Exponential Enrichment (SELEX) is a technology which aims to create and select high affinity oligonucleotides from a large random sequence pool by utilising their capacity to bind to a target molecule, with the subsequent amplification of the selected oligonucleotides by PCR to enrich those sequences in the pool specific for the target. SELEX-drived oligonucleotides are (1) small in size and not complex, (2) highly specific, (3) chemically consistent, (4) easy to manufacture, (5) can be chemically or radioactively labelled without affecting affinity or specificity, (6) can be scaled up for production. The present project aims at exploring the SELEX technology in the following areas: (1) development of diagnostic reagents, (2) evaluation of its application in therapeutic drug development, and (3) recombinant antibody engineering. (BL97005)

Establishment of a Hong Kong Bioinformatics Centre

- ▼ FUNG Kwok Pui LEE Cheuk Yu WAYE Mary Miu Yee TSUI Kwok Wing SMITH David Keith* XUE Hong* ZHU Guang*
- □ 1 July 1997
- Industrial Support Fund, Industry & Technology Development Council

A Hong Kong Bioinformatics Centre which is to be available to the Hong Kong bioinformatics community will be established in The Chinese University of Hong Kong. This centre will contain the computer hardware required to hold and provide access to the biotechnology related databases and the software appropriate for database searching and molecular biology research. An annotated non-redundant database of the human heart expressed sequence tags (ESTs) will also be established and maintained for the public access. Staff of the Centre are competent in Bioinformatics and will provide advice to the user community on the use of and interpretation of the results of the softwares used. In

addition, training course and workshops in Bioinformatics will be conducted. From the work of the Centre it is expected that collaborations will be fostered among academic groups and between industry and academic groups. The Centre will also provide the foundation for University courses in Bioinformatics.

(BL97001)

Low density lipoprotein as carrier for targeted delivery of antitumoral drugs

- □ 15 September 1997
- Research Grants Council

Antitumoral drugs always exhibit toxic side effects on normal cells in the treated hosts. It has been an urgent need to search for carriers which can target the cytotoxic drugs towards the tumour cells. The aim of present project is to examine whether human low density lipoprotein (LDL) can serve as a carrier for antitumoral drugs such as vincristine and doxorubicin. Cultured liver tumour cells and leukemia cells which have been found to possess high density of LDL receptors on the cell membrane, and mice bearing these tumours will be used as experimental models. Approaches to be investigated involve downregulation of LDL receptors in normal cells: this treatment may lower the side effects of LDLdrug complexes on normal cells; (2) upregulation of LDL receptors in tumour cells: this treatment may enhance the uptake rate of LDL-drug complexes into the tumour cells and therefore increase the drug efficacy; (3) circumvention of multidrug resistance in tumour cells by LDL-drug complexes; (4) dual functions of oxidized or acetylated LDL as a cytotoxic agent and a drug carrier; (5) antitumoral effect of combined treatment of LDL-drug complexes with cytokines and hyperthermia. It is hoped that from these work a better understanding of the mechanism regulating drugs targeting and uptake via the LDL receptors on the tumour cells will accrue which might lead to the development of new therapeutic modes in tumour therapy. (CU97309)

Discovery of Traditional Chinese Medicine (TCM) - Derived Saponins with Anti-Tumour and Cardiotonic Activities for Use as Health Food Supplements or Therapeutics

- FUNG Kwok Pui ◆ WONG Nai Ching Henry (Chemistry) ◆ CHANG Yen (Chemistry) [#] ◆ HUI Yongzheng ^{*} ◆ YU Biao ^{*}
- ☐ 15 December 1997
- Industrial Support Fund, Industry & Technology Development Council

Cancer and heart disease are the two leading causes of death in Hong Kong and China. Search for effective drugs for therapy are urgently needed to ameliorate the medical, economic and social sequences of these diseases. The aim of this project is to make use of advanced screening techniques to search TCM-derived saponins with anti-tumour cardiotonic activities. Saponins carbohydrate-containing compounds of steroids or They are non-toxic components triterpenes. commonly found in tonic TCM. Saponins from various TCM known to be effective in treating cancer or coronary heart diseases, such as Di'ao and Maidong, will be synthesized and stepwisely modified. The structures of these products will be characterized by analytical methods. In present project, toxicity of the saponins and their synthetic derivatives will be tested by a brine shrimp lethality bioassay which is more efficient than the conventional toxicity tests on mice. For screening anti-tumour activities, their effects on killing cultured tumour cells and/or stimulating immune cellular systems will be recorded. Non-toxic saponins which are effective in cultured tumour and/or immune cells will then be tested in animals. A tumour-bearing mouse model will be used to screen for anti-tumour To test the anticoagulation effect of saponins, their anti-platelets-aggregation properties will be studied. For screening antioxidant-based saponins, their effects on the protection of oxidantmediated damage of erythrocytes will be monitored. Ischemia-reperfusion models including isolated rat heart model and in vivo rabbit model will then be used to screen for saponins for coronary heart disease therapy. It is expected that upon the conclusion of this project, some non-toxic and highly effective saponins to prevent and treat cancer and cardiovascular diseases will be discovered. These agents should be of value for further development into health food supplements or therapeutics by companies in Hong Kong and the Mainland. (MD97085)

Effect of Glucose Transporter Antisense Nucleic Acids on Human Tumour Cells

- FUNG Kwok Pui
- ☐ 15 March 1998
- CUHK Research Committee Funding

The researchers observed that during tumour development, the mRNA levels of glucose transporter 1(GLUT-1) and GLUT-3 increase progressively in the tumour cells; however, there are no changes observable in mRNA levels of GLUTs of all types in the brain, liver and heart of the host mice (J. Cell. Biochem. 67: 131-135, 1997). These findings suggest that tumour may augment its glucose transport mechanism relative to other tissues in the host in response to its unique growth needs. It is conceivable

that suppression of glucose transport system in tumour cells should result in tumour regression. They will test the possibility of employing glucose transport system of tumour cells as an anti-tumour target. Human tumour cells including hepatoma, breast tumour, leukemia, glioma and colon tumour cells will be used. The incidence of these tumours especially hepatoma is high in Hong Kong, and the findings may be of clinical importance in designing treatment for local patients in future. Normal human cells will be used as control. The researchers seek answers to test whether GLUT antisense nucleic acids suppress tumour growth and at the same time suppress the expression of GLUTs' mRNA and inhibit glucose uptake in the cells. They will also test whether GLUT antisense nucleic acids reverse the multidrug resistance in resistant tumour cells. The researchers will further examine whether suppressing glucose transport system in tumour cells by GLUT antisense nucleic acid may result in ATP depletion and/or change in intracellular pH which may affect the p-glycoprotein-mediated drug extrusion in the resistant tumour cells. Through examination of the effects of GLUT antisense nucleic acid which suppress the glucose transport system in tumour cells. They expect to gain insight into the possible employment of glucose transporter in tumour cells as an anti-tumour target.

(MD97111)

Gain of Function by p53 Mutation: Induction of Drug Resistance

- KWOK Tim Tak
- □ 1 October 1997
- CUHK Research Committee Funding

p53 is frequently mutated in cancer and the mutation correlates with poor prognosis for patients. DNA damaging agents induce wild type p53 and subsequently cell cycle block and apoptosis in cells. It is hypothesized that mutant p53 can interact with DNA damaging agents and effect the sensitivity of cells to anticancer drugs. The hypothesis is based on the results from p53-273 mutant (mutation at codon 273). P53-273 can be induced by doxorubicin, a DNA damaging agent, its expression correlates with drug resistance. The experiments will be carried out in cells transfected with different p53 mutants. The sensitivity of mutant p53 transfectant to a panel of common anticancer drugs will be measured. Possible mechanisms will include drug resistant genes, cell cycle block, apoptosis and DNA damage repair. If the specific mutant is regulated by drugs, the level of regulation will be investigated. The studies will provide insight in drug resistance mechanisms related to p53, and basic mechanisms for DNA damage related gene regulation. The information obtained may be useful in designing new drugs or strategies for cancer therapy.

(BL97022)

Atherosclerosis Genes

- ∠ LEE Cheuk Yu WAYE Mary Miu Yee FUNG Kwok Pui
- □ 1 October 1997
- CUHK Research Committee Funding

Atherosclerosis is recognised to be a multifactorial disease, but apart from the now well established link between cholesterol disorder and atherogenesis, relatively little progress has been made on identifying the primary factors which predispose the vascular endothelium to thrombotic, inflammatory and vasospastic complications. Most of the genes that can improve or worsen the atherosclerotic condition remain obscure. The researchers have, in projects supported by the Research Grants Council, sequenced over 20,000 clones from several human heart cDNA libraries and have at the disposal a catalogue of genes active in the cardiovascular system. Inasmuch as the heart contains a vast vascular bed, this catalogue will serve as a frame of reference against which genes of the atherosclerotic arteries can be viewed. By comparing cDNA clones from normal and diseased hearts and noting the different profiles and levels of expression, they hope to mark genes in atherosclerosis and delineate the molecular basis for the atherosclerotic state. Knowing the genes in atherosclerogenesis and understanding how they work will pave the way for better diagnosis, management and design of palliative and therapeutic measures for the disease. (MD97037)

Natural Products with Anti-Human Immunodeficiency Virus Activity

- ☐ 1 October 1997
- Research Grants Council

In order to combat the human immunodeficiency virus (HIV), the causative agent of the debilitating disease AIDS, colossal amounts of money, manpower, time and energy have been dedicated to research on compounds which can be developed as therapeutic agents. The chemotherapeutic strategies have been focused on the development of inhibitors of retroviral enzymes. The efficacy of these HIV enzyme inhibitors is limited by the development of HIV resistance to these drugs, and an attempt has been made to circumvent this problem by using a combination of drugs. Nevertheless, drug toxicity and a need for more potent antiretroviral activity necessitate a search for more and better drugs. In the proposed project on isolation of HIV enzyme

inhibitors, the researchers would like to use as the starting material medicinal herbs, which have been proven to be effective against HIV, in view of the finding that compounds derived from plant sources like the well-known antimalarial drug qinhaosu may have different chemical structures and different mechanisms of action from the Western drugs and may also possess the advantage of reduced toxicity. They will use different extraction methods and chromatographic procedures for the isolation of various compounds. These compounds will be tested for ability to inhibit the activities of the HIV enzymes. It may turn out that chemically different compounds are present in the extracts of herbs previously demonstrated to possess anti-HIV activity, and that these compounds may inhibit one or more of the HIV enzymes.

(CU97688)

Biological Activities of Milk Proteins

- NG Tzi Bun
- □ 1 October 1997
- CUHK Research Committee Funding

Lactoferrin is a glycoprotein present in human and bovine milk, in other secretions such as tears, plasma, semen and synovial fluid and also in the reproductive tract. It is a member of the family of iron-binding proteins including transferrin. Evidence has been presented that it plays a role in iron absorption during infancy (Davidson LA and lonnerdahl B., Am. J. Physiol., 254: G580-585, 988), as a growth factor resulting in cell differentiation (Nichols B L et al. Pediatr. Res. 27: 525-528, 1990) and as a modulator of immune response in infections (Crouch SPM et al Blood 80: 235-240, 1992). Lactoferrin is expected to be useful as a functionally active component for use in food, drugs and cosmetics, and the thermostability of the milk protein is important because heat treatment may be involved in the production of these products. The importance of lactoferrin is attested to by the production of the recombinant form of the milk protein. Consumption of milk by infants and adults explains the importance of research on milk proteins and investigators from a variety of disciplines are engaged in this type of research.

The aims of the present investigation are to elucidate the contribution of the glycan moiety and histidine residues to the various biological activities (antimicrobial, DNase RNase etc) of lactoferrin, to uncover additional biological activities of lactoferrin, to determine if lactoferricin (lactoferrin fragment) possesses the biological activities of lactoferrin in addition to the demonstrated antimicrobial activity, and to isolate minor whey proteins and ascertain their biological activities.

(MD97038)

Proteins that Screening for Interact with **Trichosanthin**

- SHAW Pang Chui
- □ 1 September 1997
- CUHK Research Committee Funding

Screening of human placenta cDNA library:

Yeast two hybrid system has been employed to find proteins that interact with trichosanthin (TCS). By screening a human placenta cDNA library, nine putative positive clones that interact with TCS were obtained and partially sequenced. Eight of them were found to be ribosomal protein P0 and one P1. Further confirmation of their interaction is being verified by a mammalian two-hybrid system.

Passing of human cell extract through TCSimmobilized column:

An alternative approach to screen for proteins that interact with TCS is to pass the cell extract through a TCS column. Proteins having affinity with TCS will be retained and can be eluted by high concentration of salt or low pH. The researcher has already immobilized TCS to an N-hyadroxy-succinimideactivated Hi-Trap column and has just obtained the human choriocarcinoma Jar cell one from ATCC. This cell line has been reported to be highly sensitive to TCS. The researcher is going to test if any protein from this cell line can be retained by the TCSimmobilized column.

Generation of C-terminal deleted TCS mutants:

The last nine amino acid residues of TCS have been systematically deleted, the mutants expressed and ribosome-inactivating activity and conformation stability assayed. These mutants will facilitate the investigation of whether the C-terminal region of TCS interacts with other proteins in the future. (MD97039)

Studies on the Terminal Differentiation of Cardiac Myocytes

- TSUI Kwok Wing
- □ 1 November 1997
- CUHK Research Committee Funding

In the course of postnatal myocardial development, cardiac myocytes convert from hyperplastic to hypertrophic growth. In the rat, myocytes lose their capacity to replicate after about two weeks, and myocardial growth from this point forward is primarily due to hypertrophy of existing myocytes. In contrast to the relatively well characterized possess that control myocyte hypertrophy, investigations focused on determining the mechanisms regulating the loss of myocyte proliferation during postnatal myocardial development are limited. Studies in the skeletal muscle system have provided a model where muscle lineage termination gene directly interacts

with retinoblastoma susceptibility gene product to produce and maintain the terminally differentiated state. This interaction provided the critical components for the lock in cell cycle arrest in skeletal muscle cell. Cardiac muscle appears on the surface very similar to skeletal muscle especially since they share large number of structural and contractile proteins. However, it is clear that cardiac muscle cells are distinct biologically at the regulatory level. To study the mechanism of the terminal differentiation of cardiac myocytes, the researcher plans to construct a rat heart two-hybrid cDNA library, which is enriched with cell-cycle related genes. Afterward, differential screening of the rat heart cDNA library will be performed to identify differential regulated genes in the terminal differentiation of cardiac myocyte. The results of this project might shed light on the understanding of the mechanism of the terminal differentiation of cardiac myocyte and might provide information in designing treatment of by cardiac cardiovascular diseases myocyte regeneration. (BL97024)

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

- TSUI Kwok Wing
- □ 14 November 1997
- ❖ Lee Hysan Foundation Research Grant (under United College) CUHK

14-3-3 proteins belong to a highly conserved multigene family of small acidic proteins that associated with cell and cell death regulators, oncogenes, and signaling molecules. A number of functions have been proposed for 14-3-3 proteins, including inhibition of protein kinase C (PKC), activation of Raf-1 protein kinase, regulation of the biosynthesis of neurotransmitters and determination of the timing of cell division. Since 14-3-3 proteins associate with a number of proto-oncogenes and oncogenes, they might play an important role in tumor development. Recently, the researchers found that the epsilon isoform of human 14-3-3 proteins (h1433ɛ) can interact with calmodulin, which is a calcium-binding protein that participates the signal transduction pathway through the interaction with CaM kinase. They have also mapped the h1433E gene to human chromosome 17p13, which contains a number of cancer-related loci and a common hot spot for translocation and mutation in breast cancer. In this project, they plan to study the structure, functions and precise chromosomal location of h1433ε. The minimal domains, calcium and phosphorylation dependency of the interaction between h1433ɛ and calmodulin will be examined. The effect of h1433ɛ on the activity of CaM kinase will be determined. The h1433 ϵ gene will be fine-mapped using radiation

hybrid panel to determine whether it is located within any well-established cancer loci. These studies should provide useful information on the role of 14-3-3 proteins in tumor development and cell regulation mediated by calmodulin and CaM kinase. (BL97041)

Molecular and Immunological Characterization of Endothelin Coverting Enzymes

- MAN David Chi Cheong
- ☐ 16 October 1997
- Research Grants Council

Endothelins (ETs) are highly homologous 21 amino acid vasoconstrictive polypeptides that are originally isolated from the human and bovine endothelial cells. structurally related isoforms termed endothelin-1 (ET-1), ET-2 and ET-3 are synthesized as larger preproforms which are processed firstly by dibasic amino acid endopeptidase to 38-39 residue corresponding Big endothelins (big ET). Big ETs are then proteolytically cleaved by highly specific endothelin converting enzyme (ECE) to form the bioactive ETs. Pathological increases in ET release and synthesis have been shown to be associated with a wide variety of pathological states including hypertension, myocardial infarction, ischemia and bronchial asthma. Although the role of endothelins in the pathogenesis of diseases in not well established, it has generally been proposed that inhibition the synthesis of ETs has great potential for therapy. Recent studies have demonstrated that there are multiple forms of ECEs that may be involved in the processing of different isoforms of ETs. The regulation of gene expression of ECEs is at present not very well examined. The main objective of this project is to characterize the expression of ECE isforms in cultured cell lines as well as in the rat brain, where ET isopeptides are differentially produced in different brain regions. Information obtained from this study should provide significant insight into the roles of different forms of ECE in various pathophysiological conditions. (CU97320)

Cloning of the Mouse FHL2 Gene

- WAYE Mary Miu Yee
- □ 1 October 1997
- CUHK Research Committee Funding

LIM domain protein family is an important new family of proteins which carries a cysteine-rich zinc-binding domain called the LIM domain. This protein family is found in mammals, amphibians, flies, worms and plants, and they may be involved in cell identity, differentiation, growth control and developmental regulation. While the researchers

sequenced more than 7000 ESTs from a human heart cDNA library, they have cloned and characterized five cDNAs coding for novel LIM-only proteins. One of them - FHL2 is of particular interest because it is expressed specifically in the human heart (unpublished results from our laboratory, Chan et al). The researchers have used a yeast two-hybrid system and discovered two interesting protein partners that interact with FHL2. They plan to clone the mouse gene coding for FHL2 and characterize the mouse FHL2. In particular they will study the promoter region and find out the sequences that are responsible for heart specificity. The mouse FHL2 gene will be useful for future transgenic knock-out mice experiments. (BL97011)

Sequence Analysis of the SLIM1(FHL1) Gene

- WAYE Mary Miu Yee BENTLEY David R.*
 ROSS Mark*
- 1 March 1998
- UK/Hong Kong Joint Research Scheme, the British Council

LIM domain proteins are a class of proteins that are defined by the possession of a highly conserved double zinc finger motif. The function of LIM-domain remains unclear, although a number of LIM-proteins have been associated with key points of development and differentiation. The researchers' laboratory has cloned and sequenced a cDNA that codes for SLIM1. They plan to use this cDNA as a probe to screen for the genomic clone from a human genomic (PAC) library and the sequence encoding the SLIM1 gene will be analysed by automatic DNA sequencing techniques. SLIM1 is expressed in skeletal muscle and has been mapped to human chromosome Xq27.2. (BL97017)

Study on the Expression of HSP 27L in Animal & Model Systems

- □ 31 March 1998
- Germany/Hong Kong Joint Research Scheme

The researchers have previously isolated a novel protein that is a member of the small heat shock protein family, and have named it HSPL27 (for Heat Shock Protein Like) protein. They plan to express the HSPL27 in mammalian cells and to see its effect in protection of the cells against stress such as heat, and to study the expression of HSPL27 in animal model systems of ischemia and/or reperfusion in porcine myocardium and rabbit hindlimb. (BL97015)

Please refer to previous issues of this publication for more details of the following ongoing research at the department:		1995-96	Molecular and Biochemical Characterization of the Drosophila Exuperantia Protein: Identification of Structural/Functional Domains
Edition	Title/Investigators		(CU94322) ∠ LUK Ka Shing Sandy
1996-97	Biochemical Characterisation of Mas Oncogene: An Antibody Approach (BL96025) CHEUNG Wing Tai	1996-97	The Role of Phosphorylation in the Functions of the Exuperantia Protein during Oogenesis in <i>Drosophila</i> (CU96322)
1995-96	Purification and Enzymatic Characterization of Fish Alcohol Dehydrogenases (BL95031) FONG Wing Ping	1996-97	Molecular Dissection of the Transforming Growth Factor Signal Transduction Pathway (BL96027)
1995-96	Mechanism of Combination Treatment of Tumour Necrosis Factor-α and Hyperthermia on Tumour Cells (CU95316)		LUK Ka Shing Sandy CHEUNG Wing Tai TSANG David Sau Cheuk WAN David Chi Cheong
	FUNG Kwok Pui	1995-96	Investigation of the Relationship Among the Diverse Enzymic and
1996-97	Formulation of Preservation Solution for Transplantation of Heart and Other Organs (MD96002) FUNG Kwok Pui		Pharmacological Activities of Antiviral Proteins (CU95325)
1996-97	Search for Treatment Strategies to Enhance the Cytotoxic Effect of Free-radical-mediated Antitumour Drugs on Tumour Cells and to Lower Their Adverse Side Effects on the Host (CU96311) FUNG Kwok Pui	1995-96	Isolation and Characterization of Compounds with Anti-human Immunodeficiency Virus, Anti-lymphoma and Immunostimulatory Activities from Medicinal Herbs (BL95020) NG Tzi Bun • FONG Wing Ping •
1996-97	Tumour Necrosis Factor-α: Biological Activities and Action Mechanism in Health and Diseases (MD96127)	1996-97	WAN David Chi Cheong An Investigation of the Purification and Biological Activities of Mammalian Carbohydrate-binding Proteins (BL96024) MG Tzi Bun
1996-97	LEUNG Kwok Nam • WAN David Chi Cheong Mechanistic Studies on the Regulation of	1995-96	Trichosanthin Derivatives with Reduced Immunogenicity and Nephrotoxicity and Long Plasma Half-life (CU95324)
1990-97	Glucose Transporter Expression in Tumour Cells (MD96040)		C. (Physiology)
	FUNG Kwok Pui	1996-97	Transcriptional Regulation of Human Glycogen Synthase Kinase- 3α and -3β -
1996-97	Growth Factor and Drug Sensitivity (BL96005)		cloning and Analysis of Their Promoters (CU96305)
1995-96	Sequence Analysis of Human Heart cDNA Clones (CU95642)	1995-96	Characterization of Brain Specific Endothelin Converting Enzyme(s) and Its Role in Cerebral Ischemia (BL95027) WAN David Chi Cheong

1996-97	Characterization of Isoforms of	1995-96	Sequence Analysis of Human Heart
	Endothelin Converting Enzyme in		cDNA Clones (CU93303)
	Cultured Endothelial Cells (BL96008)		
	WAN David Chi Cheong		Yu
1995-96	Molecular Characterisation of Natural	1996-97	Molecular Cloning and Characterization
	Heterozygosity and Mutation Process in		of Human Heart cDNAs Coding for LIM
	Candida Albicans (CU95313)		Domain Containing Proteins (CU96313)
	Lakshman Perera*		Yu • FUNG Kwok Pui

RESEARCH OUTPUTS AND PUBLICATIONS

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<P974173>, <P974174>, <P974280>, <P974291>, <P974309>, <P974548>, <P974722>, <P980035>,
<P980742>, <P980786>, <P981095>, <P981444>, <P981445>, <P981446>, <P981494>, <P981495>,
<P981739>, <P982167>, <P982267>, <P982279>

Combined Effects of Thyroid Hormone and Insulin on Na⁺,K⁺-ATPase Isoform Expression in Rat Skeletal Muscle: A Possible Animal Model for Thyrotoxic Hypokalaemic Periodic Paralysis

- ARUMANAYAGAM Manoharan COCKRAM Clive Stewart (Medicine & Therapeutics)
- □ 1 November 1997
- CUHK Research Committee Funding

Thyrotoxic periodic paralysis (TPP) is the most common form skeletal muscle paralysis in Hong Kong and the Far East. Typically attacks occur after a heavy carbohydrate meal and paralysis is associated with hypokalaemia. The mechanism of hypokalaemia is not known but Na+,K+-ATPase, an important regulator of potassium homeostasis has been implicated in this disease. It is well known that thyroid hormones increase the Na+,K+-ATPase activity in various tissues including muscle. Insulin is another factor that increases Na+,K+-ATPase activity. In early studies, the researchers have shown that Na+,K+-ATPase activity of platelets was higher in patients with TPP compared to thyrotoxic patients without paralysis. They have also shown that insulin and glucose responses are higher in TPP Patients compared those without paralysis in response to oral glucose load. Furthermore, hyperinsulinaemia was found at the time of the attack. The reason why paralysis occurs after a heavy carbohydrate meal may be explained on the basis of hyperinsulinaemia leading to further activation of Na+,K+-ATPase.

 Na^+,K^+ -ATPase consists of 2 subunits α & β ; for each subunit, three isoforms have been demonstrated. The thyroid hormone responsive Na^+,K^+ -ATPase is the α_2 : β_2 dimer whilst for insulin it is the α_2 : β_1 dimer. This research plan is to study the isoform expression and membrane characterisation of Na^+,K^+ -ATPase in skeletal muscle by both, thyroid hormone and insulin. Long term significance of the project is the understanding of the disease process/the mechanism of TPP. (MD97045)

Telemedicine Project

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 ← HJELM Nils Magnus LEE Joseph C. K.
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 Қау (Information Engineering) TSUI Hung Tat
 (Electronic Engineering) ZHANG Yuanting
 (Electronic Engineering)
- □ 6 May 1997
- ❖ One-time Support, CUHK

Telemedicine is defined as the use of electronic information and communication technology to provide and support health care when distance separates the participants (i.e. patients and doctors or other health professionals). The task of determining the efficacy and more importantly the effectiveness of telemedical procedures by randomized controlled trials is an important area of medical research.

The University's project in telemedicine was established to facilitate such research with the following outcomes:

- (1) installation of extensive communications system (including broad-based ATM-LAN) in the University's teaching hospital (Prince of Wales Hospital) for teleconsultations and tele-education within the hospital itself and with other hospitals in the local area and overseas;
- (2) testing of the technical infrastructure in a series of teleconferences and teleconsultations;
- (3) initiation of a series of randomized controlled trials in teleradiology, telegeriatrics, tele-endocrinology, telepathology, teledermatology and telepsychiatry;
- (4) documentation of outcomes in an initial series of publications.

As a result, the technological infrastructure for telemedicine is now well established, providing the basis for extensive internal and external clinical trials and the introduction of tested telemedical procedures into clinical routine. (MD96202)

Trafficking of Nucleated Cells between Fetus and Mother

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 CHANG Mang Z. Allan (Obstetrics &
 Gynaecology)
- □ 1 September 1997
- * Research Grants Council

This project aims to use molecular biological techniques to study the two-way trafficking of nucleated cells between fetus and mother during human pregnancy. The strategy is based on the use of polymorphic genetic markers which can differentiate the fetus from the mother, and vice versa. The presence of fetal cells in maternal blood and maternal cells in fetal blood will then be detected using very sensitive polymerase chain reaction (PCR)-based techniques. Categories of subjects studied will include babies delivered by normal vaginal delivery, babies delivered by Caesarean section and pregnancies complicated by preeclampsia. Gestational age-related parameters of feto-maternal cell trafficking will also be studied in a longitudinal cohort. These data will improve our understanding of the physiology of feto-maternal cell trafficking, the development of the fetal immune system and may have clinical implications in the use

of cord blood in bone marrow transplantation, the vertical transmission of infectious agents during pregnancy and the use of fetal cells in maternal blood for non-invasive prenatal diagnosis. (CU97670)

Mutation Screening of a New Oncogene: The Human Smoothened (SMO) in Sporadic Basal Cell Carcinoma

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 - YUEN W. F.* LEE K. C.*
- ☐ 1 April 1998
- CUHK Research Committee Funding

Basal cell carcinomas (BCC) are the commonest cutaneous malignant tumours. The incidence is about 180 in 100 000 of the general population. Recent insight into their genesis came from identification of mutations in the PATCHED (*PTCH*) gene in patients with the basal cell nevus syndrome (BCNS, a hereditary disease characterized by multiple BCCs and by developmental abnormalities). The binding of Sonic hedgehog (SHH), a protein involved in human development, to its receptor PTCH prevents the latter's normal inhibition of Smoothened (SMO), a seven-pass transmembrane protein.

According to this model, the inhibition of SMO signalling is removed following mutational inactivation of PTCH in BCNS. Very recently, the researchers report the identification of activating somatic missense mutations in the SMO gene itself in sporadic BCCs from three patients. Mutant SMO, unlike wild type, can cooperate with a viral oncoprotein, adenovirus E1A, to transform rat embryonic fibroblast cells in culture. Furthermore, skin abnormalities similar to BCCs developed in transgenic murine skin overexpressing mutant SMO. These findings support the role of SMO as a signalling component of the SHH-receptor complex and provide direct evidence that mutated SMO can function as an oncogene in BCCs. By identifying more functional domains in the SMO protein by mutation mapping, they hope that this can provide fundamental information for the pharmacological inhibition of SMO, and possibly a new treatment for BCCs.

(MD97112)

Activation of Eosinophils in Allergy

- LAM Wai Kei Christopher HJELM Nils Magnus
- □ 1 October 1997
- CUHK Research Committee Funding

- 1. The researchers have established and maintained a human eosinophilic leukaemia cell line, EoL-1, in their laboratory.
- 2. They were able to induce differentiation of EoL-1 cells using dibuty1 cyclic AMP (dbc AMP) and L929 conditioned medium.
- 3. EoL-1 cells were shown to express cell surfure IL-3 and GM-CSF receptors, CD95 and CD94d.
- Treatment with dbc AMP could elevate CD116 but decrease CD95 expression. L929 medium could down-regulate the expression of GM-CSF receptor α.
- 5. Differentiated EoL-1 cells also up-regulated ECP synthesis.

(MD97043)

Development of a Rapid and Accurate Molecular Assay for the Diagnosis of Chromosomal Aneuploidies

- ∠ LO Yuk Ming, Dennis HJELM Nils Magnus LAM Ching Wan
- □ 1 September 1997
- CUHK Research Committee Funding

The purpose of the project is to develop a novel method for the rapid and accurate diagnosis of chromosomal aneuploidies such as Down's syndrome. Conventional karyotyping requires time-consuming cell culture and chromosome preparation which has a turnaround time of 2-3 weeks. This new method can reduce this time to just 2-3 hours, thus contributing significantly to reducing patient anxiety and facilitating clinical decision-making. The strategy is based on a new technology called real time quantitative PCR which offers unprecedented accuracy and efficiency. This work is based on preliminary results obtained by Dr. Y.M.D. Lo, previously of Oxford University and who has recently joined the Department of Chemical Pathology since January 1997. Over the last few months, this technology has been set up in the department whereby accurate quantitation chromosome 11 copy number can be performed with a dynamic range of at least 100,000 orders of magnitude. The next phase of the project is to develop this system for Down's syndrome, by the quanitation of chromosome 21 copy number, using the above-mentioned chromosome 11 system as an internal reference standard. This system has the potential to be extended to other chromosome aneuploidies (e.g. trisomy 18 and Turner's syndrome) and also for diagnosing these conditions during pregnancy using maternal blood, without employing invasive procedures such as amniocentesis. This technology may also have implications for other medical specialties such as oncology for rapidly detecting and quantifying oncogene amplification in cancer which may have diagnostic and prognostic implications.

(MD97044)

The Role of Androgen Receptor and Vitamin D Receptor Genotypes on the Risk of Prostate Carcinoma and Patient Prognosis in Chinese Patients

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 Cellular Pathology)
- □ 1 October 1997
- CUHK Research Committee Funding

Two steroid hormone receptors, androgen receptor (AR) and vitamin D receptor (VDR) show a regulatory role in prostate epithelial proliferation. Their transactivating ability is influenced by their genotypes which are revealed by trinucleotides repeats, restriction polymorphism and micro-satellite polymorphism. Recently, genotypes of the two steroid receptor genes are associated with risk of prostate cancer. In a case control study, an odd ratio of 4.6 was associated with a particular VDR genotypes among American patients with prostate carcinoma. The researchers propose to study the genotypes on archival tissue from local Chinese patients in a case control study. The collection of genotypes data on the AR and VDR genes will help to clarify their role in tumorigenesis. These genes are also likely to be regulatory elements of cellular proliferation, their genotypes may also be significant factors for prognosis. As the incidence of prostate cancer in Chinese is lower than those in Western populations, the local genotype data will strengthen any association between these genes and prostate cancer when data from multiple ethnic groups are analysed with the corresponding incidence of prostate cancer. (MD97046)

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

Edition Title/Investigators

1995-96 Serum Proinsulin, Insulin and C-peptide Concentrations in Healthy Chinese Subjects, Those with Non-Insulin Dependent Diabetes (NIDDM) and Impaired Glucose Tolerance (IGT) (MD95227)

- ARUMANAYAGAM Manoharan COCKRAM Clive Stewart (Medicine & Therapeutics)
- 1996-97 Clinical Usefulness of a Novel Serum Marker, 1,5-anhydroglucitol in

Monitoring Glycaemic Control (MD96111)

- ARUMANAYAGAM Manoharan COCKRAM Clive Stewart (Medicine & Therapeutics)
- 1995-96 The Application of Mass Spectrometry to the Analysis of Alpha-fetoprotein (AFP) Variants in the Serum of Patients with Hepatitis, Cirrhosis and/or Hepatocellular Carcinoma (HCC) (MD95108)
 - HJELM Nils Magnus JOHNSON
 Philip James (Clinical Oncology) •
 LANE Trevor (Clinical Oncology)#
- 1996-97 Development and Application of an *in situ* PCR Method for the Detection of Mutations and DNA Polymorphisms in Single Intact Cells (MD96052)
 - HJELM Nils Magnus LO Yuk Ming, Dennis
- 1996-97 Molecular Epidemiology of Diabetes Mellitus: Detection and Prevalence of a Mutation in Mitochondrial DNA (MD96109)
 - ∠ LAM Ching Wan PANG Chi Pui Calvin (Ophthalmology & Visual Sciences) • TSANG M. W.* • HJELM Nils Magnus
- 1995-96 Identification of Environmental Risk Factors for Asthma and Allergic Rhinitis in Adults in Hong Kong (MD95173)
 - ∠ LAM Wai Kei Christopher LEUNG Chung Chuen Roland (Medicine & Therapeutics) WOO Kong Sang John (Surgery) HJELM Nils Magnus LAI Kar Neng (Medicine & Therapeutics) VAN HASSELT Charles Andrew (Surgery)
- 1995-96 Role of Human Chorionic Gonadotropin in the Aetiology of Hyperemesis Gravidarum (MD00112)
 - ∠ PANESAR Nirmal Singh ◆ LI Chi Yin (Obstetrics & Gynaecology)
- 1996-97 Detection of Tumor Cells and Tumor DNA in Peripheral Circulation in Patients with Breast Carcinoma (MD96110)

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<P974314>, <P974431>, <P980071>, <P980231>, <P980310>, <P980390>, <P980500>, <P980649>,
<P980784>, <P980845>, <P980854>, <P980875>, <P981136>, <P981313>, <P981313>, <P981327>,
<P981364>, <P981564>, <P981567>, <P981742>, <P981745>, <P982086>

RESEARCH PROJECTS

Detection, Purification and Identification of Isoforms of Serum Glycoproteins: Use as Diagnostic and Dedifferentiation Markers in Cancer

- Philip James • LANE Trevor* • HJELM Nils Magnus (Chemical Pathology) • HO Chung Shun (Chemical Pathology)
- □ 1 November 1997
- Research Grants Council

The researchers have recently identified glycoprotein isoforms of the tumour marker alphafetoprotein, which appear to be highly specific for hepatocellular carcinoma (HCC) and non-seminomatous germ cell tumour (NSGCT), by using the technique of isoelectric focusing (IEF). Preliminary analysis using mass spectrometry, after purification of the protein by affinity chromatography, has helped to elucidate the structural changes in the carbohydrate moieties which are responsible for these tumour specific isoforms. Further investigations suggest that AFP from NSGCT has a similar pattern on IEF to that derived form early fetal blood (when AFP is made by the yolk sac), and that AFP from HCC has a similar pattern to that derived from fetal liver. The aim of the proposed study is to determine if the changes detailed above are specific to AFP or whether similar changes will be seen in four other glycoproteins whose levels are raised in HCC, namely thyroxine binding globulin, alpha l-antitrypsin, alpha 2-macroglobulin and transferrin. IEF, affinity chromatography and mass spectrometry will be performed on each protein from stored sera from patients with different cancers, such as HCC and NSGCT. The identification of cancerspecific isoforms of these glycoproteins may be useful in improving the specificity of present diagnostic tests or in the earlier detection of individual tumours. In addition, the study of the glycosylation state in different proteins and at different stages of cellular differentiation will provide information on the events taking part in dedifferentiation and cancer development. (CU97654)

The Role of Biological Markers as Prognosticators in Undifferentiated Nasopharyngeal Carcinoma

- CHAN Anthony Tak Cheung HO King Wah Stephen* • TEO Man Lung Peter • CHIU Kwok Wing • JOHNSON Philip James
- ☐ 1 April 1998
- CUHK Research Committee Funding

Nasopharyngeal Carcinoma (NPC) is endemic in Hong Kong. Despite effective local control with radiotherapy (RT), the rate of relapse with distant metastasis is high resulting in a 5 year overall survival rate of only 52%. The aim of this proposal is to measure biological markers including p53, Ki-67, C-erb B-2 and degrees of tumour angiogenesis (as measured by microvessel density) in NPC patients present for treatment at the Prince of Wales Hospital. The prognostic significance of the markers will be defined by correlation with the clinical outcome of the patients. If these markers can predict, before treatment which patients are likely to do worse with RT alone, then the use of more intensive therapy including hyperfractionated RT and concurrent chemotherapy-RT may be indicated in this sub-group of patients.

(MD97114)

Functional Analysis of a New Gene (BRE) Responsive to DNA Damage and Retinoic Acid, and its Interactions with the TNF Receptor

- CHAN Yeuk Hon John
- □ 1 September 1997
- Research Grants Council

The researchers have previously published on the cloning of a novel gene from human cells using the subtractive hybridization technique (BBRC 206:764-774, 1995). This new gene is apparently responsive to DNA damage and retinoic acid (RA) treatment, and it is highly expressed in brain and reproductive organs (BRE). Decrease in BRE mRNA was also observed in a squamous carcinoma cell, 1483, that showed X-ray resistance and has a more aggressive tumorigenic phenotype. Recent findings also indicated that BRE may interact with the p55 TNF They propose to: (1) determine the receptor. interaction between the p55 TNF receptor and BRE by immunoprecipitating the protein complex in cells that were co-transfected with the expression vectors for BRE and TNF receptor; (2) determine if the decreased expressions of BRE after UV and RA treatment of cells are associated with the alterations in expression and translocation of the TNF receptor; (3) transfect the sense and/or the antisense cDNA of BRE into HeLa or the SCC 1483 cells which expressed low levels of the BRE mRNA, and to determine the alterations in cell behavior including cell adhesion and TNF receptor function. (CU97672)

Aberrant Telomerase Activity in Malignant **Tumors**

- CHAN Yeuk Hon John
- 1 October 1997
- CUHK Research Committee Funding

The researchers have analyzed the telomerase activity from various types of cancers using the Telomeric Repeat Amplification Protocol (TRAP) assay, and found that increased telomerase activity was present in a majority of hepatocellular carcinomas and cirrhotic tissues (manuscript submitted). Similarly, increased telomerase activity was found in both benign breast tumors (fibroadenoma) and malignant tumors (infiltrating ductal carcinoma). Telomerase activity was present in the cell extracts from both fibroadenoma and infiltrating ductal carcinoma. These results are in accordance with the notion that activation of telomerase is often an early event and is associated with the development of neoplasia for different types of tumors. However, whether telomerase may play a role in the conversion of benign dysplasia to malignancy is still unknown. Their hypothesis is that different isozymes of telomerase may have a differential response to heat or chemical treatment. Telomerases from different tissues were subjected to heat-treatment with increasing time, and the remaining activities were then determined. It was found that malignant breast tumor (infiltrating ductal carcinoma of the breast tumor (infiltrating ductal carcinoma of the breast) contained a heat resistant form of telomerase as compared to the benign form of breast tumor (fibroadenoma). When cell extract from a single sample of benign tumor was heated at 40°C for increasing time at 5-min intervals, the activity of telomerase was inactivated quite substantially, only 5-10% of the original telomerase activity was detected. In contrast, the cell extract from a single sample of the malignant tumor retained 90% of the original activity of unheated sample after 40 min of These data indicate that the heat treatment. malignant tumor contains a heat-resistant form of telomerase as compared to the benign tumor. These results were found in 2 out of 5 pairs of samples The presence of this aberrant form of telomerase in malignant tumor could be the result of increased genomic instability and increased mutation rate during the multi-hit multi-stage process of oncogenesis. It could be important for the pathologic increase of telomeres in cancer cells which may contribute to the loss of growth control and the malignant transformed-phenotypes of breast cancer. (MD97041)

A Pilot Study of 5-Azacytidine in Patients with Relapsed and/or Refractory EBV-Associated Malignancies

- ✓ JOHNSON Philip James AMBINDER R* WICKHAM Nicholas[#] LEUNG Wai Tong Thomas CHAN Anthony Tak Cheung MOK Shu Kam CHOW John Hei-sing (Anatomical & Cellular Pathology) FLINN I* MANN R*
- □ 1 July 1997
- National Cancer Institute

EBV-associated malignant disease including nasopharyngeal carcinoma represents a special problem for Chinese populations. 5-Azacytidine has been demonstrated to lead to demethylation of viral transcription regulatory elements and expression of the full spectrum of latency antigens in EBV lymphoma cell lines in vitro and in animal models. This study aims to test the null hypothesis that treatment with 5-Azacytidine will not be associated with altered viral gene expression in EBV-associated malignancies with limited antigen expression, and to monitor the therapeutic activity of 5-azacytidine when administered to patients with EBVmalignancies. (MD97011)

T-Cell Immunotherapy for Advanced Nasopharyngeal Carcinoma: A Pilot Study of Immunisation with LMP2 Peptide Epitopes Presented on Autologous Dendritic Cells in Patients with Metastatic or Locally Recurrent Nasopharyngeal Carcinoma

- ✓ JOHNSON Philip James CHAN Anthony Tak Cheung • RICKINSON Alan B.* • LEE Steven P.*
- □ 1 July 1997
- Cancer Research Campaign

The objectives of this trial are to determine the safety and toxicity of synthetic LMP2 peptide immunisation together with autologous dendritic cells in patients with locally recurrent or metastatic Epstein-Barr virus (EBV)-related Nasopharyngeal Carcinoma (NPC), to determine whether immunisation with such peptideloaded autologous dendritic cells evokes a significant cytotoxic T lymphocyte (CTL) response to LMP2 in patients with advanced NPC, and to document tumour the above-mentioned responses to immunisation and to correlate any such responses with evidence of vaccine-associated immunologic modulation. (MD97144)

The Prognostic Significance of Serum Levels of Soluble ICAM-1 in Patients with Primary Extranodal Non-Hodgkin's Lymphomas

- ✓ JOHNSON Philip James LEI Ieng-Kit Kenny*
- ☐ 1 November 1997
- CUHK Research Committee Funding

Primary extra-nodal non-Hodgkin's lymphomas are a heterogeneous group of diseases occurring commonly Asian populations. The prognosis varies depending on the interplay of various clinical and laboratory parameters, including age, stage, performance status, the primary site of involvement, tumor bulk, histologic features of the tumor, serum lactate

dehydrogenase level, and the modality of treatment being given. The intercellular adhesion molecule-1 ICAM-1, a member of the immunoglobulin superfamily, is the ligand for the integrin lymphocyte function-associated antigen 1 (LFA-1). Increased cellular expression of ICAM-1 on malignant melanoma cells has been shown to correlate with the metastatic potential. An elevated level of the soluble form of ICAM-1 (sICAM-1) in the serum has been shown to correlate with metastasis, tumor spread and poor prognosis in melanoma, gastrointestinal cancers, and Hodgkin's disease. In non-Hodgkin's lymphomas, increased level of Sicam-1 has recently been found to be related to a poorer survival rate. These findings suggest that Sicam-1 could also be a useful prognostic marker for primary extra-nodal lymphomas. The researchers therefore propose to evaluate the serum levels of Sicam-1 and their prognostic significance in patients with primary extranodal lymphomas, using a commercially available enzyme-linked immunoassay. Stored serum samples collected from patients with primary extranodal lymphoma will be retrieved, analyzed for Sicam-1 and compared with those from normal subjects. Results will be correlated with treatment outcome and survival. In Hong Kong we are in a unique position to undertake this study since primary extranodal lyumphomas are more common than in the West. A better understanding of pathobiology of metastasis in extranodal lymphomas should be forthcoming. (MD97040)

Alterations of the Growth and Transformation-Suppressor PML in Hepatocellular Carcinoma and Nasopharyngeal Carcinoma

- ∠ LEUNG Sing Fai CHAN Yeuk Hon John CHAN Anthony Tak Cheung LIEW Choong Tsek (Anatomical & Cellular Pathology) JOHNSON Philip James
- ☐ 1 September 1997
- * Research Grants Council

Tumor and growth suppressor genes are known to play important roles in regulating cell growth and cell cycle progression. Since many of the tumor suppressor genes are mutated or abnormally expressed in a variety of human cancers, they are implicated in the loss of growth-control during the multi-stage and multi-hit process of oncogenesis. The purpose of this project is to elucidate the role of altered expression of a growth and transformation suppressor PML (promyelocytic leukemia) in the tumorigenesis of two of the major cancers in Hong Kong, the hepatocellular carcinoma (HCC) and the nasopharyngeal carcinoma (NPC). The researchers propose to: (1) determine the frequency of aberrant localization and over-expression of the PML Oncogenic Domain (POD) structure as well as the

levels of the PML protein and mRNA in HCC and NPC; (2) determine if such alterations are due to mutations in the PML gene or modification of the PML protein in HCC and NPC. Identifying the genomic alterations in growth and tumor suppressor genes including PML in HCC and NPC will have great ramification for the diagnosis and treatment of these common cancers in Hong Kong. (CU97653)

A Two Stage Phase II Safety and Efficacy Study of Intradose (Cisplatin/Epinephrine) Injectable Gel (MPF 5010) Administered to Patients with Unresectable Primary Hepatocellular Carcinoma

- ∠ LEUNG Wai Tong Thomas JOHNSON Philip James YU S.* LAU Wan Yee Joseph (Surgery) CHAN Anthony Tak Cheung MOK Shu Kam YEO Winnie
- □ 1 July 1997
- Matrix Pharmaceutical Inc.

IntraDose is a new novel compound composed of cisplatin and epinephine mixed with an injectable gel. It has activity in local solitary tumour through intralesional injection. This phase II study is going to study its effect on inoperable hepatocellular carcinoma. (MD97013)

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

- ∠ LEUNG Wai Tong Thomas

 CHAN Anthony
 Tak Cheung

 CHAN Anthony

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- ☐ 1 November 1997
- ❖ Ares-Serono International

The primary objective of this trial is to assess the survival of patients with advanced colorectal cancer treated with the combination of r-hIFN β 1a and 5-FU as compared to the standard treatment of 5-FU plus leucovorin. Secondary objective is to assess tumour control, quality of life and safety and tolerability of the treatment.

(MD97145)

Phase I/II Study of Topotecan and Oral Etoposide in Treatment of Small Cell Lung Cancer

- MOK Shu Kam CHAN Anthony Tak Cheung
 YEO Winnie YIM Ping Chuen Anthony
 (Surgery) JOHNSON Philip James
- □ 1 August 1997
- Smith Kline Beecham

Topotecan is a novel chemotherapeutic drug with proven efficacy as single agent in treatment of small cell lung cancer. The drug is a Topoisomerase I inhibitor and in theory it should work synergistically with etoposide, a Topoisomerase II inhibitor. The purpose of the project is to study the clinical efficacy of this new combination and examine the sequence of administration. (MD97012)

Molecular Prognostication of Therapeutic Response of Liver and Lung Cancers

- □ 1 October 1997
- **❖** CUHK Research Committee Funding

Resistance to therapeutic treatment is a major obstacle in modern oncology. This project is aimed at establishing an accurate correlation with the radiation-and chemo-therapeutic response of patients of liver and lung cancers at the Prince of Wales Hospital, The Chinese University with the altered expressions and/or mutations of the isoforms of multi-drug resistant gene mdr and the tumor suppressor p53. The status of these radiation-and drug-associated changes will be analyzed with respect to clinical parameters, and with the choice of therapy. The combination analysis of these two molecular diagnostics would be considered as new, comprehensive markers for the choice of treatment, the prediction of outcome and the relapse-free survival. (MD97082)

The Application of Comparative Genomic Hybridization to the Analysis of Genetic Changes During Development and Progression of Hepatocellular Carcinoma

- WONG Nathalie

 JOHNSON Philip James
- □ 1 September 1997
- ❖ CUHK Research Committee Funding

Comparative Genomic Hybridization (CGH) was applied to the study of genomic aberrations in 67 surgically resected samples of HCC, 3 of adenomatous hyperplasis (AH) and 12 of nontumorous cirrhotic liver surrounding the tumors. CGH analysis of the HCC samples revealed frequent copy number gain of 1q (48/67 cases; 72%), 8q (32/67 cases; 48%), 17q (20/67 cases; 30%) and 20q (25/67 cases; 37%), 13q (25/67 cases; 37%) and 16q (20/67 cases; 30%). The researchers' finding of a high incidence of 1q gain strongly suggested this aberration was associated with the development of HCC. Genomic abnormalities were detected in 1 of the 3 AH specimens but absent in all 12 cirrhotic tissues surrounding the tumor. Clinical staging

classified 3/67 HCC cases as T1, 53 cases as T2 and 11 cases as T3. No significant difference in the pattern of genomic imbalances was detected between stages T2 and T3. A significant copy number loss of 4q11-q23 was, however, identified in those tumors larger than 3cm in diameter. Of particular interest was the identification of 8q copy number gain in all 12 cases of HCC which arose in a non-cirrhotic liver, compared to only 20/55 cases in HCC arising in a cirrhotic liver. The researchers suggest that 8q overrepresentation is likely associated with growth advantage and proliferative stimulation that have encourage malignant changes in the non-cirrhotic human liver. (MD97042)

High Dose Adjuvant Chemotherapy and Peripheral Stem Cell Transplant for High Risk Breast Cancer Patients

- □ 1 October 1995
- CUHK Departmental Funding

As one of the centre of the International Breast Cancer Study Group, this is a phase III prospective randomized study to compare conventional versus high dose adjuvant chemotherapy in breast cancer patients.

(MD95266)

Adjuvant Tamoxifen - Longer Against Short (ATLAS)

- ∠ YEO Winnie KWAN W. H.* LEUNG C. M.*
- □ 1 July 1996
- CUHK Departmental Funding

As one of the centre of this study, which is headed by the Clinical Trial Service Unit and Imperial Cancer Research Fund Studies Unit in University of Oxford, UK, this trial is designed to assess the optimal duration of adjuvant tamoxifer therapy after surgery is breast cancer patients. (MD96216) Detection and Characterization of Circulating Hepatocellular (HCC) Cells for Predicting HCC Metastasis and Monitoring Treatment of HCC Patients

- ✓ YEO Winnie WONG Hing Nam (Anatomical & Cellular Pathology) JOHNSON Philip James
 LEUNG Wai Tong Thomas LAU Wan Yee Joseph (Surgery) HO King Wah Stephen* CHAN Sai Yu Michael (Diagnostic Radiology & Organ Imaging)[#]
- □ 1 July 1997
- * Research Grants Council

Hepatocellular carcinoma (HCC) is one of the most common malignancies in Hong Kong and is the second major cause of cancer death locally. While 10% of the patients are candidates for surgical resection with curative intent, the majority of patients are only amenable to palliative forms of treatment due, to amongst other factors, to the presence of multiple intra-hepatic metastases, gross vascular involvement or extra-hepatic metastases. Even for patients who have undergone apparently successful surgery only half maintain long term survival, due to the presence of pre-existing micrometastases, already present at the time of surgery. It has been suggested that the presence of HCC cells in the circulation of patients could be inferred if mRNAs of hepatocyte-specific genes such as albumin and alpha-fetoprotein can be detected. The reverse transcription-polymerase chain reaction (RT-PCR) is sufficiently sensitive for such detection. In the preliminary studies, levels of mRNAs of albumin, and alpha-fetoprotein detected in the peripheral blood of HCC patients and normal subjects were quantitated by comparison with a standard curved developed with reference to HepG2 (a hepatoblastoma cell line) cells. These two mRNA markers detected by RT-PCR may potentially enable the prediction of the occurrence of metastasis, and aid clinicians in the pre-treatment assessments and treatment-planning. The levels of the serum markers of individual HCC patients may also serve as prognosticators and for monitoring their treatment outcome. In this study, the researchers propose to confirm their initial findings by assessing the extent to which the laboratory findings of quantitative RT-PCR technique in peripheral blood of HCC patients reflect the clinical status of these patients. Once these are verified, they will proceed to investigate the process of tumour dissemination during and after HCC resection, and also to longitudinally follow-up of those HCC patients who have undergone interventional therapy. Further plans would involve the applying of laboratory findings in deciding the clinical sequence of treatment necessary for HCC patients. (CU97656)

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

- ✓ YEO Winnie KWAN W. H.* MOK Shu Kam CHAN Anthony Tak Cheung LEUNG Wai Tong Thomas JOHNSON Philip James
- □ 1 May 1998
- ❖ Novaritis Pharmaceutical Ltd

This is a phase II study to determine the efficacy and tolerability of Fermara in postmenopausal Chinese breast cancer patients who have previously failed tamoxifen.
(MD97165)

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

- ∠ YEO Winnie JOHNSON Philip James LEUNG Wai Tong Thomas
- □ 1 May 1998
- Glaxo Wellcome Research Development

Multicentre prospective randomized trial to compare FU/776C85/5 and FU/FA regime in advanced colorectal cancer. (MD97166)

Randomized Trial of Tamoxifen Versus Placebo for the Treatment of Inoperable Hepatocellular Carcinoma

- □ 1 May 1998
- CUHK Departmental Funding

This is a phase III randomized controlled study to determine the efficacy of tamoxifen in patients with inoperable hepatocellular carcinoma.

The research centre is one of the study centre of Asia Pacific Hepatocellular Carcinoma Trials Group. (MD97169)

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

Edition Title/Investigators

1995-96 Determination of Cell Kinetic Parameters of Nasopharyngeal Carcinoma by *in vivo*

- Bromodeoxyuridine Labelling and Flow Cytometric Analysis (MD95159)
- ∠ CHAN Anthony Tak Cheung HO
 King Wah Stephen* TEO Man
 Lung Peter TSANG Kam Sze
 Kent* (Anatomical & Cellular
 Pathology) JOHNSON Philip
 James
- 1995-96 Hepatocellular Carcinoma Health Care Services (MD95174)
 - CHAN Anthony Tak Cheung YEO
 Winnie JOHNSON Philip James •
 HAZLETT Clarke Blaine (Office of Educational Services)
- 1996-97 A Phase II Study of Temozolamide (Temodal SCH 52365) in the Treatment of Patients with Advanced Nasopharyngeal Carcinoma (MD96153)
 - CHAN Anthony Tak CheungLEUNG Wai Tong ThomasJOHNSON Philip James
- 1996-97 Cell Kinetic Studies in Undifferentiated Nasopharyngeal Carcinoma and the Implications for Clinical Management (CU96636)
 - ∠
 ∠
 CHAN Anthony Tak Cheung TEO
 Man Lung Peter LEUNG Wai
 Tong Thomas CHANG Alexander
 Russell (Anatomical & Cellular
 Pathology) JOHNSON Philip
 James
- 1996-97 Functional Analysis of a New Gene that Response to DNA Damage and Retinoic Acid, and Interact with the TNF-Receptor (MD96043)
 - CHAN Yeuk Hon John
- 1996-97 Isolation, Purification and Structural Elucidation of Disease-specific Isoforms of Glycoproteins and Glycopeptide Hormones (CU96633)
 - ✓ JOHNSON Philip James HJELM Nils Magnus (Chemical Pathology) LAWSON Alexander M.*
- 1996-97 The Pathophysiology of Hepatitis B Reactivation in Lymphoma Patients (MD96046)
 - ✓ JOHNSON Philip James WICKHAM Nicholas[#] •
 STEINBERG Joyce LEUNG Wai Yee Nancy (Medicine & Therapeutics) TAM Siu Lun John (Microbiology) CHAN Kay Sheung Paul (Microbiology)

- 1996-97 Novel Mutations in HBV PreS2/S Gene in Hepatocellular Carcinomas: Potential Induction of the Transactivator Function During Oncogenesis (MD96044)
- 1996-97 The Application of Comparative Genomic Hybridisation for the Detection of Genomic Imbalances in Nasopharyngeal Carcinoma (CU96637)
 - ∠ LEUNG Sing Fai WONG Nathalie
 HUANG POON Wai Sin Dolly
 (Anatomical & Cellular Pathology) •
 TSAO George* JOHNSON Philip James
- 1996-97 Randomised Trial of Radiotherapy Alone Versus Concomitant Radiotherapy and Chemotherapy in Locoregional Advanced Nasopharyngeal Carcinoma (MD96152)
 - ∠ LEUNG Wai Tong Thomas CHAN Anthony Tak Cheung TEO Man Lung Peter LEUNG Sing Fai
- 1996-97 A Phase II/III Randomized Controlled Study of Thymitaq (AG337) Versus Doxorubicin in Patients Having Hepatocellular Carcinoma (MD96155)
 - ∠ LEUNG Wai Tong Thomas JOHNSON Philip James LAU
 Wan Yee Joseph (Surgery) CHAN
 Anthony Tak Cheung YEO Winnie
 MOK Shu Kam
- 1996-97 A Molecular Approach to Delinate Antiestrogenic Drug Effects on Breast Cancer Cell Lines (MD96108)
 - ∠ LEUNG Wai Tong Thomas CHUI Chung Hin
- 1996-97 An Open Label Phase II Study to Evaluate a 28 Days Regimen of Oral 5-Fluorouracil (5FU) Plus 776C85 in Patients with Inoperable Hepatocellular Carcinoma (MD96156)
 - ∠ LEUNG Wai Tong Thomas •
 JOHNSON Philip James LAU
 Wan Yee Joseph (Surgery) MOK
 Shu Kam CHAN Anthony Tak
 Cheung YEO Winnie LAM Shun
 Chiu Dennis (Ophthalmology &
 Visual Sciences)
- 1996-97 Phase III Randomised Trial of ⁹⁰Yttrium-Microspheres Selective Internal Radiation Versus Systemic Doxorubicin in the Treatment of Inoperable Hepatocellular Carcinoma (MD96157)

- ∠ LEUNG Wai Tong Thomas LAU
 Wan Yee Joseph (Surgery) •
 JOHNSON Philip James HO S.* •
 CHAN M.* CHAN Anthony Tak
 Cheung YEO Winnie MOK Shu
 Kam LEUNG Nancy*
- 1996-97 Investigation of Possible Subtypes of Prostatic Specific Antigen Related to Prostatic Cancer and Benign Prostatic Hypertrophy by Isoelectric Focusing Technique (MD96045)
 - MOK Shu Kam LEUNG Wai Tong Thomas HO Stephen K. W.*
 CHAN Siu Foon Peter (Surgery) JOHNSON Philip James

- Ping Chuen Anthony (Surgery) ◆ HUI P.* ◆ JOHNSON Philip James
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 - WONG Nathalie NG Heung Ling Margaret (Anatomical & Cellular Pathology)
- 1996-97 Application of Reverse Transcriptase Polymerase Chain Reaction in the Detection of Circulating Tumour Cells in Peripheral Blood (MD96048)
 - ✓ YEO Winnie WONG Hing Nam (Anatomical & Cellular Pathology) JOHNSON Philip James

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RESEARCH PROJECTS

Interactive Multimedia Health Web Pages

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- □ 1 October 1997
- Health Care & Promotion Fund, Hospital Authority

Health organizations in Hong Kong have created health promotional web pages to educate the public for the past year. Owing to the lack of relevant programming expertise, these pages have been limited to mostly plain texts plus some still pictures. This project exploits modern Internet programming software to incorporate more actions and effective features such as animation, sound effects, and interaction with the users. As the programming language is object-oriented, another key benefit is the programming products developed from this project can be downloaded and redeployed by interested health services Web authors. (MD97167)

Computer-Assisted Interactive Tutorials of Clinical Problem Solving in Family Medicine

- CHAN Shiu Yee Cynthia WUN Yuk Tsan CHAN Keith*
- ☐ 1 December 1997
- ❖ Action Learning Project Fund

The project develops interactive computer-assisted tutorials on clinical problem solving for medical and para-medical students. Each tutorial consists of a series of videotaped vignettes of patient(s) presenting to the family physician with one or more problems. During the tutorial, the student will be asked to input the working diagnostic hypothesis and answer questions on how to solve these problems. The same scenario may have development of different outcomes and levels of difficulties. The complexity and degree of difficulty may be adjusted to suit students of various learning stages.

The tutorials are installed in the computer network sever of the Department and is accessible by students within the Department via intranet or outside via internet. A student may send queries to the teaching staff by leaving messages at the end of the tutorial or e-mail them to a teaching staff who may discuss with the students through e-mails or in face-to-face tutorials later. A debriefing session will be arranged afterwards to discuss the lessons learnt and the queries raised.

Students are divided into two groups: One with traditional tutorials and one with computer-assisted tutorials. The project is evaluated with students' feedback, their problem solving skills at formative assessment by tutors blind to the project and their

performance at summative assessment at end of the attachment to the Department. (MD97022)

Qualitative Study of HIV/AIDS Risk Behaviour among Hong Kong's Teenage "Street Roamers" and Approaches for Harm Reduction

- CHAN Shiu Yee Cynthia TANG Shao Fen
- □ 1 April 1998
- Council for the AIDS Trust Fund

HIV/AIDS is a growing public health problem in Hong Kong. The number of HIV cases has been steadily increasing since 1994, with 51 new cases reported in the last quarter of 1997. The Department of Health of Hong Kong and non-governmental organisations such as the Family Planning Association have published and unpublished reports on the HIV/AIDS and safe sex knowledge, attitudes and practices surveys on certain known higher risk groups such as commercial sex workers, intravenous drug users and cross border truck drivers; as well as youth surveys. The youth surveyed have been mainly in-school youth or sampled from established formal youth groups such as the YMCA, or young offenders in correctional institutions. However, a gap in knowledge exists for the HIV risk of marginalised youth who "hang around" the streets in the evenings but may not have been arrested. This study aims to ascertain the HIV risk behaviours of these young people and their motivating factors. As these teenagers are disenfranchised, they are less likely to participate in school or other mainstream organised social activities; this makes them difficult to enumerate and survey. Therefore, a qualitative approach is used with specific introduction into their culture and in-depth interviews and field observations in order to gain insight into their reasoning and actions. The results of the study will be used to enhance HIV/AIDS prevention specifically targeted at these young people. (MD97094)

Developing Problem Based Learning Tutorials in Family Medicine

- CHAN Shiu Yee Cynthia WUN Yuk Tsan DICKINSON James
- □ 15 May 1998
- Problem Based Learning Management Committee

Aims of the Project:

(1) To develop problem-based learning (PBL) in Family Medicine at The Chinese University of Hong Kong (CUHK) to encourage self-directed learning, critical thinking and problem solving by medical students.

- (2) To study the feasibility of implementing PBL and its acceptance by medical students at CUHK.
- (3) To develop the departmental staff in the process of PBL.
- (4) To use results of the study to promote PBL in the rest of the Medical Faculty at CUHK.

Description of the Project:

A Series of PBL tutorials will be developed and implemented for fourth year medical students during their term in Family Medicine.

Evaluation will be made of the process of implementation of PBL. It will concentrate on 4 areas:

- (1) Evaluation of students' learning methods and how self-study and group discussion affected their understanding of and interest in the subject.
- (2) Evaluation of student and staff acceptance of PBI.
- (3) Evaluation of students' problem solving and critical appraisal skills by formative and summative assessments.
- (4) Evaluation of the content of self learning resources and approaches used.

(MD97130)

A Randomized, Parallel-group Study to Compare the Effects on Bone Density of Oral Alendronate or Placebo in Postmenopausal Women with Osteoporosis

- ∠ LAU Edith Ming Chu WOO Jean (Medicine & Therapeutics)
 LEUNG Suk Fong Sophie (Paediatrics)[#]
- □ 11 July 1997
- Merck Sharp & Dohme (Asia) Ltd

This is a triple-blind, randomized, parallel-group study to compare the effects on bone density of daily Alendronate (Fosamax) 10mg to those of placebo in 100 postmenopausal southern Chinese women with osteoporosis. Two groups of patients will receive either daily oral treatment with Alendronate (Fosamas) 10mg/day or matching oral placebo. Treatment will be continued for one year. The study will be divided into two periods: (1) Pretreatment -Potential patients will be recruited, informed consent will be obtained, and potential patients screened according to the inclusion and exclusion criteria, including the presence of osteoporosis (lumber spinal bone mineral density at least two standard deviations below the mean for normal premonopausal women). Baseline clinical, and bone density measurements will be made. (2) Treatment - Oral Alendronate (Fosamax) 10mg or placebo will each be administered daily for one year. Patients will be monitored for safety with clinic visits every three months. A follow up monitoring will also be done by the research nurse through telephone one month after receiving the treatment. Laboratory hematology will

be done before and after treatment to ensure a normal renal function of the patient.

The primary efficacy endpoint is the change in lumbar vertebral bone content assessed as the computed change (percent change) from baseline in bone mineral density (BMD) of the posterior-anterior lumbar spine (mean of L1L4) determined by dual-energy X-ray densitometry.

The result of the study will have a major impact on the treatment for osteoporosis in Chinese. (MD97009)

A Randomized, Parallel-Group Study to Compare the Effects on Bone Density of Oral Alendronate or Placebo in Elderly Chinese Men and Women with Vertebral Fractures

- ∠ LAU Edith Ming Chu LEUNG Ping Chung (Orthopaedics & Traumatology) CHAN W. S.*
- ☐ 1 October 1997
- Merck Sharp & Dohme (Asia) Ltd

This is a double-blind, randomized, parallel-group study to compare the effects on bone density of daily Alendronate 10mg to those of placebo in elderly Chinese men and women with vertebral fracture. Two groups of patients will receive either daily oral treatment with Alendronate 10mg/day and 500mg calcium carbonate or 500mg calcium carbonate only. Treatment will be continued for one year.

The primary efficacy endpoint is the change in hip bone mineral density assessed as the computed change (percent change) from baseline in bone mineral density of the hip as determined by dualenergy x-ray densitometry. This will be measured at 0 month, 6 months and 12 months. (MD97099)

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

- ∠ LAU Edith Ming Chu WOO Jean (Medicine & Therapeutics) LAI Kei Wai Christopher (Medicine & Therapeutics)
- ☐ 1 November 1997
- Merck Sharp & Dohme (Asia) Ltd

This is a double-blind, randomized, parallel-group study to compare the effects on bone density of daily Alendronate (Fosamax) 10mg and 500mg calcium carbonate to those of calcium carbonate only in Chinese men and women on inhaled steroids. Two groups of patients will receive either daily oral treatment with Alendronate 10mg/day or calcium carbonate only. Treatment will be continued for one year.

The primary efficacy endpoints are the change in lumbar and hip bone content assessed as the computed change from baseline in bone mineral density of the posterior-anterior lumbar spine and hip determined by dual-energy x-ray densitometry. (MD97098)

The Prevalence of Patient's Non-Compliance with Chronic Medications and its Determinants with Particular Emphasis on Patients' Satisfaction with Therapy in Both the Hospital and GP Settings Using Anti-Hypertensive Drugs as an Example

- ∠ LEE Albert CHAN Chung Ngor Juliana (Medicine & Therapeutics) CHANG Sophie (Pharmacy) CHAN Man Chi (Medicine & Therapeutics) LO Siu Chee Amelia CRITCHLEY Julian A.J.H. (Medicine & Therapeutics) HUNG Chung Wing (Pharmacy)[#]
- □ 1 September 1997
- Merck Sharp & Dohme (Asia) Ltd

In many Western countries, the pattern of illnesses has changed from a predominance of acute infectious diseases to high prevalence of chronic degenerative diseases. A recent Dutch national survey of general practice also shows that hypertension, diabetes mellitus and angina pectoris were among the 20 most prevalent diagnoses in general practice, with hypertension ranking the first.

In this survey, approximately 60 adjunct clinical tutors / lecturers of Department of Community and Family Medicine of The Chinese University of Hong Kong were invited to participate. Each GP will recruit 10 to 12 consecutive patients. The total number of patients from the GP setting will be 600. A total of 600 patients attending the hypertension, diabetes and general medical clinics at the Prince of Wales Hospital will be identified by the research pharmacists. The researchers aim to examine the pattern of drug-taking behaviours amongst patients taking long-term antihypertensive treatments in both GP and hospital setting. Phone interview will be performed for all the patients by the research assistants. The reasons for non-compliance, the incidence and pattern of perceived side effects of drugs and their impacts on daily lives will be evaluated.

The attitudes of the GPs towards treatment and hypertension and their rationale for therapy will be examined. Furthermore, their methods to monitor patient compliance and satisfaction will be addressed. (MD97097)

Social Costs of Drug Abuse in Hong Kong

∠ LEE Albert • CHEUNG Yuet Wah (Sociology)
 • CHIN James M N* • LEE Shiu Hung • LAM K C*

- ☐ 1 February 1998
- ❖ Action Committee Against Narcotics

The past decade has witnessed a deteriorating drug problem in Hong Kong and the growing concern of the public over the problem. The government has responded by allocating increasing amounts of resources to drug treatment, drug prevention, and research. This study assesses the social and economic costs due to drug abuse. Findings of the study will contribute to the making of informed decisions regarding the allocation of resources to programmes and services for the reduction of drug abuse in Hong Kong. (SS97030)

A Survey of Patients' Knowledge, Attitude and Behaviour on Drug Prescriptions

- WUN Yuk Tsan ◆ CHAN Shiu Yee Cynthia ◆
 DICKINSON James
- ☐ 1 June 1998
- **❖** CUHK Research Committee Funding

Prescription is the result of the combined effects of disease nature, doctor preference, and patient expectation. In primary care, the interaction of doctor- and patient-factors plays an important role. Patients' knowledge, attitude and behaviour towards medication may influence doctors' prescribing behaviour. A good understanding of patient factors in prescription will guide better patient education and effect positive changes in doctor's management.

A validated 21-item questionnaire in Chinese is used to explore patients' knowledge, attitude and behaviour towards medication in general practice. The researchers' hypothesis is that these are associated with a patient's age, gender, education, seeing a regular doctor, frequency of visits to the doctor, time taken during the consultation, seeing a doctor with higher qualifications, e.g. in family medicine, practice of seeing a herbalist, and health belief. Three groups of primary care doctors will be selected at random: (1) those with no secondary qualifications, (2) those with qualification in family medicine, and (3) those with secondary qualification in other specialties. Adult patients (or accompanying adults in case of children) are systematically recruited from each doctor's surgery and requested to answer the questionnaire.

Scores from the questionnaire will be compared among the different groups and any association with the hypothesised parameters are analysed. The results will be discussed with the doctors for better understanding of patient factors in prescribing and for means of improving quality of care. (MD97115)

Conducting a Review of the Situation Regarding Occupational Health Research and Occupational Health Services in Hong Kong

- □ 1 September 1997
- Occupational Safety and Health Council Research Grant

The objectives of this research are (1) to collect and collate information about studies that have been done or being undertaken in Hong Kong in the field of occupational health; (2) to review the situation of occupational health including services available to industries in Hong Kong, sources of information, and needs for training and research; and (3) to make recommendations on the future application of the information collected. (MD97007)

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

Edition Title/Investigators

- 1995-96 A Study of Bone Mass and Bone Loss in Chinese Perimenopausal Women (MD95065)
 - ∠ HO Chan Suzanne WOO Jean (Medicine & Therapeutics) CHAN Shiu Yee Cynthia LEUNG Ping Chung (Orthopaedics & Traumatology) CHAN Sieu Gaen
 ∠ Traumatology CHAN Sieu Gaen
 ∠ Trauma
- 1996-97 A Population Based Case-control Study of Risk Factors for Low Back Pain in Hong Kong Perimenopausal Women (MD96008)
- 1996-97 Habitual Physical Activity, Health Fitness and Behaviour among Adult Population in Hong Kong (MD96011)
 - HO Chan Suzanne ◆ LEE Shiu Hung
 ◆ CHAN Sieu Gaen#
- 1996-97 The Relationship between Sex Hormones and Bone Mass in Chinese Perimenopausal Women (MD96041)
 - Man Simon (Lee Hysan Clinical Research Laboratories) WOO Jean (Medicine & Therapeutics) CHAN Shiu Yee Cynthia CHAN Sieu Gaen#

- 1995-96 Risk Factors for Primary Osteoarthritis of the Hip and Knee in Chinese - A Case-Control Study (MD95176)
 - ∠ LAU Edith Ming Chu CHAN V. L.

 H.* KUMTA Shekhar Madhukar

 (Orthopaedics & Traumatology) •

 LAM D. T. K.*

 ∠ LAU Edith Ming Chu CHAN V. L.

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- 1996-97 The Vitamin D Receptor Gene, Lifestyle Factors and the Aetiology of Osteoporosis in Chinese (CU96626)
 - LAU Edith Ming Chu YOUNG Robert P. (Medicine & Therapeutics)* HO Chan Suzanne
 CRITCHLEY Julian A.J.H. (Medicine & Therapeutics) WOO Jean (Medicine & Therapeutics)
- 1996-97 Asian Osteoporosis Study (AOS) (MD96193)
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- 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)
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 - ∠ LEE Albert LAU Fei Lung* •

 HAZLETT Clarke Blaine (Office of Educational Services)
- 1996-97 Systematic Review of Effectiveness of Traditional Chinese Medicine: A Preliminary Study (MD96042)

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 AU Kin Kwok Dennis*
- 1995-96 Standardised Proportional Mortality Ratio Study among Food-service Workers in Hong Kong (MD95200)
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RESEARCH PROJECTS

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

Edition Title/Investigators

1996-97 Magnetic Resonance as a Single Examination to Replace Ultrasound, Radioisotope Scintigraphy, and Intraarterial Digital Subtraction Antigiography in the Evaluation of

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

> KEW Jacqueline • KUMTA Shekhar Madhukar (Orthopaedics & Traumatology) • GRIFFITH James • METREWELI Constantine • LEUNG Ping Chung (Orthopaedics & Traumatology)

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RESEARCH PROJECTS

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

- ∠ CHAN Chung Ngor Juliana LEE Shing Cheung (Pharmacy) CHANG Sophie (Pharmacy) CRITCHLEY Julian A.J.H.
- □ 1 August 1997
- Health Care & Promotion Fund, Hospital Authority

Due to the escalating drug costs, pharmacist intervention to provide cost-effective, rational use of drug has been well-recognized as a major function of clinical pharmacy services in other countries. Unfortunately, this type of services is still not being practised in Hong Kong probably due to lack of manpower, resources and proven "cost-effectiveness". Therefore, there is a need for some benchmark programme to be initiated in Hong Kong to prove its significance and efficacy. Recent data has shown that despite the availability of cheaper therapeutic alternatives, high cost agents are still being used extensively in Hong Kong. The researchers hope that with their initiation of an intervention mechanism in the in-patient and out-patient hospital settings, other hospitals in Hong Kong can use it as a guideline in setting up their own programme, expanding to the drugs that need control and ultimately improving patient outcome. (MD96023)

- A Multicentre Study to Examine the Renoprotective Effects of Losartan, an Angiotensin II Antagonist Versus Placebo in Type 2 Diabetic Patients
- CHAN Chung Ngor Juliana COCKRAM Clive Stewart • CRITCHLEY Julian A.J.H.
- □ 1 November 1997
- Merck Sharp & Dohme (Asia) Ltd

Type 2 diabetes in a leading cause of renal failure worldwide and locally. Based on the United States figure, 30% of patients with end stage renal disease (ESRD) requiring dialysis have diabetes. Amongst these diabetic patients, more than 60% have type 2 diabetes. The 5-year survival of patients, with ESRD averages 50% and this is reduced to less than 20% in diabetic patients. In Hong Kong, the annual mortality rate of diabetic patient is 3% per year. Renal failure and cardiovascular diseases including stroke and ischaemic heart disease are the leading causes of death in Type 2 diabetic patients. Over 50% of patients have increased albuminuria, which is a powerful predictor for death and renal disease.

Angiotensin II has potent effects on tissue growth and haemodynamics. Inhibition of the renin angiotensin system by angiotensin converting enzyme inhibitor (ACEI) is associated with cardioprotective and antiproteinuric effects in both Type 1 and Type 2 diabetic patients. In Type 1 and normotensive Type 2 diabetic patients, this class of agents reduces the rate of deterioration in renal function. However, the renal effects of this class of drugs in the majority hypertensive Type 2 diabetic patients remain uncertain.

In this multicentre study involving more than 1300 Type 2 diabetic patients with macroalbuminuria and renal impairment, the effects of losartan, a nonpeptide angiotensin II (AII) antagnoist, versus placebo, on progression of renal function will be examined over a 3.5 year period. The centre at CUHK–PWH has enrolled 55 patients and together with studies on similar theme, their group will be in an unique position to examine the effects of these agents on hormonal changes as well as its interactions with genetic markers for nephropathy in Chinese Type 2 diabetic patients. (MD97168)

Phenotypic and Genotypic Characterisation of NIDDM (Type 2 Diabetes Mellitus) and their Interactions with Environmental Factors

- CHAN Chung Ngor Juliana CHENG Shuk Han (Orthopaedics & Traumatology) YEUNG Tok Fai Vincent CHOW Chun Chung Francis
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- 1 January 1998
- * Research Grants Council

Type 2 diabetes is a heterogeneous disease with both genetic and environmental determinants. This study aims to examine the phenotypes including blood pressure, body mass index, waist to hip ratio, metabolic indices, insulin secretion and in vivo action in 1600 family members of 400 index diabetic cases. The latter will include 150 patients with young onset of disease (<35 years) and 250 patients with late onset of disease (≥35 years). The researchers have previously shown in a model that reduced growth hormone (GH) and increased stress hormones explained much of the heterogeneity of NIDDM. These changes are compatible with the known effects of psychosocial stress, physical inactivity and ageing on hormonal changes. Much of the effects of GH are mediated by IGF and may be expected to be reduced with ageing as well as with physical inactivity. Serum cortisol will be used as a marker of psychosocial stress. The relationships between these hormones, obesity and insulin resistance will be examined. Recently, mutations of the hepatic nuclear factor (HNF) have been reported in a large number of Type 2 patients with young onset of disease and their

families. The researchers will also examine some of these mutations in the index cases. These results will provide the future directions in their search for genetic and environmental causes in the affected family members of these index cases. (CU97682)

NSAID-Induced Peptic Ulcer Bleeding: Protection at a Lower Cost?

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 Yiu
- □ 3 July 1997
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Non-steroidal anti-inflammatory drug (NSAID)induced peptic ulcer bleeding is a common condition in Hong Kong. The use of expensive anti-ulcer drugs for long-term prophylaxis has caused a major burden to the health care budget. Among patients who present with NSAID related ulcer bleeding, about 50% are also associated with *H. pylori* infection. While eradication of *H. pylori* has markedly reduced the recurrence of non-NSAID related ulcers, the role of H.pylori in NSAID related ulcers remains unknown. Furthermore, the safety of newer NSAIDs that claim to have low ulcerogenic risk is not known. The researchers propose two prospective randomized controlled trials which sought to address the following questions: (1) for patients who are infected by H. pylori, does eradication of the infection prevent NSAID-induced ulcer bleeding? and (2) for *H. pylori* negative patients, can the use of (safer) NSAIDs replace prophylactic therapy in preventing ulcer bleeding. The ultimate goal is to reduce the risks of NSAID-induced ulcer bleeding with an affordable regimen. (MD97004)

Helicobacter Pylori Infection, Cyclo-Oxygenase, and Gastric Carcinogenesis

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- □ 1 May 1998
- ❖ CUHK Research Committee Funding

Background:

Cyclo-oxygenase-2 (COX-2) is an enzyme which is found at areas of inflammation or abnormal cellular proliferation. Overexpression of this enzyme contributes to the pathogenesis of colonic cancer by inhibiting apoptosis. Recent data also suggests an increased expression of COX-2 in gastric cancer. While *Helicobacter pylori* infection is an important factor in gastric carcinogenesis, any relationship between *H. pylori* and COX-2 expression is entirely

unknown. The preliminary data has shown a significant increase in the gastric mucosal expression of COX-2 in patients with *H. pylori*-associated gastritis.

Hypothesis & Objectives:

The researchers hypothesize that *H. pylori* infection predisposes to gastric carcinogenesis through an overexpression of COX-2 in the gastric mucosa. This study aims at: (1) correlating the mucosal COX-2 activity with different stages of precancerous gastric lesions in *H. pylori* infected patients; and (2) studying the effect of *H. pylori* eradication on COX-2 expression.

Methods:

Biopsy specimens of the gastric antrum (x 9) are obtained by endoscopy to document the presence of *H. pylori* infection and the severity of gastritis by histology. COX-2 activity is determined by using immunostaining, reverse transcriptase polymerase chain reaction (RT-PCR) and Northern blotting. Follow-up endoscopy is performed at 8 and 24 weeks after anti-*H. pylori* therapy is given.

Outcome Measures:

(1) the mucosal distribution and activity of COX-2 in relation to the different stages of gastritis and precancerous gastric lesions; (2) the change in the severity of gastritis and mucosal expression of COX-2 after eradication of *H. pylori*.

Significance:

To better define the mechanisms of *H. pylori*-induced gastric carcinogenesis. Eradication of *H. pylori* and selective inhibition of COX-2 expression may prevent gastric cancer in the future.

(MD97116)

The Effects of an Education Programme on the Compliance with Nasal CPAP in the Treatment of Obstructive Sleep Apnoea

- ∠ LAI Kei Wai Christopher HUI Shu Cheong LEUNG Chung Chuen Roland CHAN Ka Wing, Joseph*
- □ 1 August 1997
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Obstructive sleep apnoea (OSA) is a common disease in our community associated with significant morbidity and mortality due to its adverse cardiovascular consequences and symptoms of daytime sleepiness. Although nasal continuous airway pressure (CPAP) can effectively treat OSA and reduce mortality the compliance rate is often suboptimal, and it is virtually unknown in the local Hong Kong population. This study will determine prospectively the compliance rate of CPAP use in unselected patients with OSA and the predictive factors that may influence compliance including an intensive education and follow-up programme. The results will provide valuable information on the

extent of suboptimal CPAP use in our community and help identify ways to improve CPAP compliance, which in turn, would be cost-effective by significantly decreasing long-term cardiovascular morbidity and mortality among the many partial CPAP users in the community. (MD97006)

Matrix-Metalloproteinases (MMPs) and their Specific Inhibitors (TIMPs) in Tuberculous Pleural Effusions

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 HOHEISEL Gerhard*
- □ 1 November 1997
- Germany/Hong Kong Joint Research Scheme

Matrix-metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) play a role in inflammatory processes. The researchers hypothesise that a pattern of MMPs and TIMPs specific to tuberculous pleural effusions might contribute to the pathophysiological changes observed in tuberculous pleurisy, in particular, fibrosis of the pleural space. Patients with tuberculous pleurisy, congestive heart failure, and malignancy will be examined. MMP-1, -2, -3, -9, TIMP-1, and -2 will be determined in pleural effusion fluid using enzyme-linked immunosorbent assays (EIA), zymogram, and Western blot techniques. The degree of fibrosis in patients with tuberculous pleurisy will be evaluated by chest roentgenograms. The expected findings might contribute to the understanding of pathophysiological aspects and to the development of new therapeutic options in prevention of unfavourable sequelae of matrix remodeling in tuberculous pleurisy. (MD97132)

The Non-Invasive Assessment of Left and Right Ventricular Diastolic Function with Two Dimensional and Doppler Echocardiography. Colour Doppler Myocardial Imaging (CDMI) and Atrio-Ventricular Plane Displacement

- □ 1 March 1998
- ❖ CUHK Research Committee Funding

The non-invasive assessment of ventricular diastolic function remains a problem despite considerable advances in Doppler echocardiography over the past decade. Currently the most widely used methods involve measurement of mitral valve inflow velocities and isovolumic relaxation time. These techniques do provide useful clinical information and the previous work has demonstrated their value. However, mitral inflow velocities are dependent on many other factors independent of diastolic function

such as cardiac mechanics, ultrasound bean alignment etc. Colour Doppler Myocardial Imaging (CDMI) is a new imaging modality, which allows real time acquisition of tissue velocities. The myocardial velocity gradient can assess ventricular wall motion directly. Furthermore, it should be possible to measure myocardial velocities at predetermined positions across the myocardium. This may give useful information on the collagen content and fibrosis within the myocardium. These techniques therefore have potential for clinical and research applications. Most of the current work is focused on systole and little attention has been paid to the use of these techniques in the assessment of diastolic function, the researchers wish to extend their previous studies by assessing the usefulness of this new modality by comparison with standard techniques. If this new technique can give a better functional measurement of diastolic dysfunction and also an indirect measurement of tissue collagen and fibrosis then it will prove to be an extremely useful research tool in particular for the assessment of drug therapy on the reversal of myocardial collagen and fibrosis, and overall diastolic function. (MD97117)

The Use of Endosonography and MR Angiography in Predicting the Risk of Variceal Bleeding in Portal Hypertension

- □ 1 July 1997

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* Research Grants Council

Massive bleeding from oesophageal varices is the most important complication of portal hypertension causing an in-hospital mortality of about 50%. The standard treatment for prevention of variceal haemorrhage is the use of β-adrenergic blockade for patients with no previous history of bleeding and the use of endoscopic therapy to obliterate varices for those who presented with clinical bleeding. However, the response to β -blockers is variable and recurrence of bleeding after endoscopic therapy is common. Study in haemodynamics of the portal system provides important information on the risk of bleeding from varices. Until recently, these studies involve invasive procedures and are mainly confined experimental investigations. With the development of endoscopic ultrasonography (EUS) with Doppler capability and magnetic resonance angiography (MRA), non-invasive haemodynamic assessment has been made possible. The researchers resolve to use these 2 techniques to (1) compare the haemodynamics of portal venous system in cirrhotic patients with different degrees of hepatic dysfunction,

(2) study the changes of haemodynamics after receiving β -blocker and (3) study the changes in haemodynamics after endoscopic therapy for variceal bleeding. The results of these studies will provide important information that may guide the management of variceal bleeding in the future. (CU97657)

The Effects of Different Doses of Vitamin E on Atheroma Formation and Indices of antioxidant Activity and Oxidative Stress in Cholesterol-Fed Rabbits

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- □ 1 November 1997
- **&** CUHK Research Committee Funding

There is increasing interest in the use of antioxidants in the prevention of cardiovascular disease in addition to controlling the major risk factors of hypertension, diabetes, hyperlipideaemia, cigarette smoking and obesity. Potential benefits of certain foods and nutritional supplements are often attributed to antioxidant properties. Vitamin E is probably the best-established antioxidant which may protect against progression or development of cardiovascular disease, but even with this, opinions are divided on recommendations for its usage.

Assessment of potential for preventing atheroma in animal models and measurement of the effects on antioxidant levels and lipid peroxidation are essential steps in the assessment of any antioxidant. This study will examine a wide range of doses of vitamin E in a cholesterol-fed rabbit model of atheroma to determine if a dose-response relationship can be demonstrated for the protection against atheroma development and whether this can be correlated with changes in antioxidant levels or lipid peroxidation. The results will establish if certain doses and blood levels of vitamin E are protective and these can be extrapolated into further clinical studies in patients at risk from atheromatous disease. Establishment of the model with positive and negative controls will facilitate subsequent studies to examine other potentially useful substances. (MD97047)

A Prospective Study of Asymptomatic Patients with Middle Cerebral Artery Stenosis

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- Yu Leung (Diagnostic Radiology & Organ Imaging) KAY Li Chi Richard
- □ 1 September 1997
- * Research Grants Council

Stroke is one of the top three killer diseases in Hong Kong and most stroke is due to cerebral infarction. In Chinese, the commonest found vascular lesion is intracranial large artery stenosis, in particular middle cerebral artery stenosis. Unfortunately, the determinants and the natural history of asymptomatic middle cerebral artery stenosis is unknown. Without such basic background information, it is difficult to formulate preventive strategy. With recent development of transcranial Doppler ultrasonography, it is now possible to screen large number of patients safely. In addition, magnetic resonance angiography is a non-invasive and reliable method to grade the severity of middle cerebral artery stenosis. researchers propose to use these two methods to investigate the frequency and the determinants of middle cerebral artery stenosis in patients with high vascular risk like diabetes and hypertension. They will follow these patients for up to 2 years initially in order to document the prognosis of different grades of middle cerebral artery stenosis. understanding of the risk factors and prognosis of asymptomatic middle cerebral artery stenosis will guide them on the best strategy to prevent stroke in these patients who are in the asymptomatic stage. (CU97673)

Provision of Health Services - Elderly Residents in Nursing Homes Using Telemedicine

- WOO Jean HJELM Nils Magnus (Chemical Pathology) TSUI Hung Tat (Electronic Engineering) ZHANG Yuanting (Electronic Engineering)
- 1 November 1997
- ❖ S K Yee Medical Foundation

The aim of this project is to pilot the use of telemedicine in strengthening health services support to the elderly living in nursing homes, where currently significant deficits exist which are unlikely to be met by any existing organizations in the near future. The target population are elderly residents with multiple problems including chronic diseases, functional or cognitive impairment, which form a large proportion of those residing in nursing homes. They require services from different health care professionals, which may be provided through the community geriatric outreach team. Such teams reduce the time taken for consultation with different health care professionals in different places outside the home, and enable preventive measures to be taken. However, the number of homes to be supported are too numerous for existing teams, and the application

of telemedicine would increase the efficiency of such teams in supporting a larger number of homes in an effective way.
(MD97005)

A Nutrition Manual for Carers in Elderly Residential Homes

- WOO Jean

 GULDAN Georgia (Biochemistry)
- ☐ 1 January 1998
- Health Care & Promotion Fund, Hospital Authority

There is increasing prevalence of malnutrition with age, with consequent increased morbidity and mortality. Undernutrition is also more common among elderly people residing in institutions, and is associated with cognitive impairment, poor functional status, immune deficiency, and delayed wound healing and recovery from illness. Among the Hong Kong elderly, nutritional status of those living in residential homes is poorer compared with community living subjects. There is also a need for nutritional information among carers of elderly residential homes, as documented by community geriatric outreach teams. The nutrition manual will provide nutritional education for carers, to enable them to carry out simple nutritional screening to detect undernutrition, and to seek professional advice appropriate, to provide an optimum environment for dietary intake, to provide suitable diets for different chromic diseases, to promote healthy eating habits for maintenance of optimum health, and to summarize principles of food hygiene. (MD97026)

An Investigation of the Roles of C-Type Natriuretic Peptide in Central Haemodynamic and Endocrine Control Using a Gene-Targeting Approach

- ✓ YEUNG Tok Fai Vincent CHUI Yiu Loon (Clinical Immunology Unit) • LEE Susanna Sau Tuen (Biochemistry) • COCKRAM Clive Stewart
- □ 1 September 1997
- CUHK Research Committee Funding

C-type natriuretic peptide (CNP) is the most recently discovered member of the natriuretic peptide family. It is also the most abundant natriuretic peptide present in the central nervous system (CNS). Recent evidence suggests that CNP could play important roles in the central control of blood pressure, fluid and electrolyte homeostasis and pituitary hormone secretion. The research group has established the presence of CNP receptors on astrocytes. They have also shown that CNP inhibits astrocyte proliferation,

and it could potentially modulate communication between neurons and astrocytes.

The researchers intend to generate mice which lack CNP by targeted disruption of the CNP gene. This work requires the construction of CNP-targeting vectors and the use of which to generate the embryonic stem (ES) cell clones containing the disrupted CNP gene. These ES cells are then ready to be developed into CNP gene-knockout mice upon injection into blastocysts. They propose to achieve the step of generating the targeted ES cells in 18 months. Further funding will then be sought from the next round of RGC Earmarked Grant for subsequent generation and phenotypic characterization of the CNP-deficient mice. The ultimate objective of this work is to enhance the knowledge of the roles of CNP in circulatory and fluid balance, and control of pituitary hormone secretion. This may have relevance to the pathophysiology of hypertension, fluid balance disorders and endocrine disturbances and allow development of new therapeutic concepts for these diseases.

(MD97048)

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

Edition Title/Investigators

- 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)
- 1995-96 A Study of the Cellular Mechanisms of Actions of Adrenomedullin and Interactions with Other Vasoactive Peptides in Cultured Astrocytes (MD95202)
 - ∠ COCKRAM Clive Stewart

 YEUNG Tok Fai Vincent

 ✓ Cockram

 ✓
- 1996-97 A Study of Gastrointestinal Motility
 Disorders (GMD) in Chinese Patients
 with Non-insulin-dependent Diabetes
 Mellitus (NIDDM): Its Characteristics
 and Response to Cisapride (MD96054)

- 1996-97 Pilot Study of Clomethiazole in the Treatment of Intracerebral Haemorrhage (MD96055)
 - KAY Li Chi Richard WONG Ka
 Sing Lawrence AHUJA Anil
 Tejbhan (Diagnostic Radiology & Organ Imaging)
- 1995-96 Cytokine Profile of CD4+ and CD8+ T Lymphocytes in Asthma (CU95608) ∠ LAI Kei Wai Christopher
- 1995-96 The Development of Allergen Sensitisation, Bronchial Hyperresponsiveness, Asthma and Allergic Rhinitis in Hong Kong Migrants Living in Australia - A Prospective Study (MD95109)
 - ∠ LAI Kei Wai Christopher LEUNG Chung Chuen Roland
- 1996-97 Relationship between Air Quality and Hospital Admissions for Respiratory Disease in Hong Kong (MD96056)
 - ∠ LAI Kei Wai Christopher LAU Tai Shing (Statistics) LEUNG Chung Chuen Roland WONG Wing Kin Gary (Paediatrics) YAM Loretta*
- 1996-97 Prevalence of Sleep Disorder Breathing in Young Adults in Hong Kong (MD96057)
 - ∠ LEUNG Chung Chuen Roland LAI Kei Wai Christopher
- 1994-95 Effect of Treatment with Cyclosporin A on the Immunological Profile of Severe Lupus Nephritis (MD94098)
 - ∠ LI Kwok Ming Edmund LUI Siu Fai WONG Kong Chiu
- 1995-96 A Comparison of the Efficacy and Tolerability of Carvedilol and Metoprolol in Chronic Heart Failure (MD95256)
 - ∠ SANDERSON John Elsby YU
 Cheuk Man* CHAN Wai Man
 Wilson RAYMOND Kenneth
 (Pharmacy) CHAN Kam Wing
 (Diagnostic Radiology & Organ
 Imaging) WOO Kam Sang
- 1996-97 The Role of Cytokine Growth Factors in the Control of Myocardial Collagen Turnover and the Development of Left Ventricular Diastolic Dysfunction in Patients with Heart Failure (CU96670)
 - ≤ SANDERSON John Elsby CHOW
 Tsun Cheung (Anatomical &
 Cellular Pathology) WOO Kam
 Sang

- 1996-97 Does Progesterone Attenuate the Estrogen Induced Increase in Coronary Blood Flow? (MD96139)
 - ✓ SANDERSON John Elsby •
 HAINES Christopher John
 (Obstetrics & Gynaecology) •
 CHAN Wai Man Wilson WOO
 Kam Sang WOO Jean
- 1995-96 Immunological Defences in Biliary Tract Infection (CU94604)
 - SUNG Joseph Jao Yiu LAI Kar Neng# • CHUNG Sheung Chee Sydney (Surgery)
- 1995-96 Eradication of Helicobacter Pylori and Recurrence of Bleeding Peptic Ulcers (MD95064)
 - SUNG Joseph Jao Yiu CHUNG Sheung Chee Sydney (Surgery)
- 1995-96 *Helicobacter pylori:* Mode of Transmission and Carcinogenesis (MD95255)
 - ∑ SUNG Joseph Jao Yiu CHUNG Sheung Chee Sydney (Surgery) TO Ka Fai (Anatomical & Cellular Pathology) CHENG Fun Bun Augustine (Microbiology) LIN Sar-ren*
- 1996-97 Does Eradication of *Helicobacter pylori* Prevents NSAID-related Ulcers and Complications (CU96604)
 - ✓ SUNG Joseph Jao Yiu CHAN Ka
 Leung Francis CHUNG Sheung
 Chee Sydney (Surgery) LING Kin
 Wah Thomas (Microbiology) •
 CHENG Fun Bun Augustine
 (Microbiology)
- 1995-96 Identification of Risk Factors for Atheroma in Chinese Patients with Overt Peripheral Vascular Disease and Diabetic Patients with Asymptomatic Peripheral Vascular Disease (CU95649)
 - ▼ TOMLINSON Brian KING Walter Wing Keung (Surgery)[#] LI Arthur K. C. (Surgery) LAM Wai Kei Christopher (Chemical Pathology) LOLIN Yvette Ivanka (Chemical Pathology)[#] CHAN Chung Ngor Juliana CRITCHLEY Julian A.J.H. YOUNG Robert P. F COCKRAM Clive Stewart
- 1995-96 Thiazide Diuretic Antihypertensive Therapy and Cardiac Arrhythmias: The Influence of Concomitant Left

Ventricular Hypertrophy, ACE Gene Polymorphisms and Additional Therapy with ACE Inhibitors or Calcium Channel Blockers (CU95650)

- ▼ TOMLINSON Brian SANDERSON John Elsby WOO Kam Sang WOO Jean CHAN Yan Keung Thomas CRITCHLEY Julian A.J.H.
- 1996-97 Investigation of the Genetic Region of the Lipoprotein Lipase Gene in Families of Dyslipidaemic Patients and Relation to Blood Pressure and Insulin Resistance (MD96050)
 - ★ TOMLINSON Brian CHENG Shuk Han (Orthopaedics & Traumatology) CRITCHLEY Julian A.J.H. YOUNG Robert P.#
- 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 P.* PANG Chi Pui Calvin (Ophthalmology & Visual Sciences) ARUMANAYAGAM Manoharan (Chemical Pathology) CHAN Yu Leung (Diagnostic Radiology & Organ Imaging) CHAN Yan Keung Thomas SANDERSON John Elsby COCKRAM Clive Stewart YEUNG Tok Fai Vincent CHOW C. C.*
- 1996-97 Effects of Pretreatment with Vasodilatings β -Blockers on Experimental Cardiac Failure-Induced Changes in mRNA Levels for Types I and III Collagen and TGF β 1 (MD96058)
 - WEI Shan SANDERSON John Elsby SHUM Oi Ling Irene* CHOW Tsun Cheung (Anatomical & Cellular Pathology)

- 1996-97 A Prospective Study of Patients with Middle Cerebral Artery Stenosis Diagnosed After First Ever Ischemic Stroke (CU96605)
 - ∠ WONG Ka Sing Lawrence KAY
 Li Chi Richard AHUJA Anil
 Tejbhan (Diagnostic Radiology &
 Organ Imaging)
- 1996-97 Regress of Cerebral Artery Stenosis Study (MD96059)
 - WONG Ka Sing Lawrence LAM
 Wai Man Wynnie (Diagnostic
 Radiology & Organ Imaging) •
 CHAN Yu Leung (Diagnostic
 Radiology & Organ Imaging) •
 KAY Li Chi Richard
- 1995-96 Identification of the Role of Genetic and Environmental Factors in Parkinson's Disease in a Chinese Population (CU95601)
 - WOO Jean PANG Chi Pui Calvin (Ophthalmology & Visual Sciences)
 HO Chan Suzanne (Community & Family Medicine) CHAN Kam Yin Daniel*
- 1996-97 Domiciliary Pulmonary Rehabilitation Program: A Randomised Controlled Clinical Trial (MD96017)
 - WOO Jean ◆ LUM Christopher* ◆ HUI E.* ◆ LEUNG Chung Chuen Roland
- 1996-97 Transgenic Expression of C-type Natriuretic Peptide in Mouse Astrocytes to Study its Roles in Central Haemodynamic and Endocrine Control (MD96060)
 - YEUNG Tok Fai Vincent CHUI Yiu Loon (Clinical Immunology Unit) ● COCKRAM Clive Stewart
- 1996-97 Biocompatibility of 1-Lactate/Pyruvate Buffered PDS: Its Effects on the Host Defense Mechanism and Viability of the Peritoneal Mesothelial Cells (CU96621)

 YU Wai Yin Alex LAI Kar Neng

RESEARCH OUTPUTS AND PUBLICATIONS

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RESEARCH PROJECTS

Association of Human Herpesvirus Types 6 and 7 with Cervical Cancer

- ∠ CHAN Kay Sheung Paul CHAN May* LI W.

 H.* CHENG Fun Bun Augustine
- □ 15 September 1997
- CUHK Research Committee Funding

Cervical cancer is the commonest female genital tract malignancy world-wide. It is appreciated that infection with certain types of human papillomavirus is strongly associated with cervical cancer. However papillomaviruses by themselves are neither essential nor sufficient, thus contribution of other co-factors, in particular sexually transmitted viral infections, may be important in the oncogenic pathway. The two novel herpesviruses, human herpesvirus types 6 and 7 (HHV-6 and HHV-7) may be important in development of cervical cancer since they have been detected in cervixes of healthy women and their oncogenic potential has been demonstrated *in vitro*.

This study aims at: (1) defining the prevalence of HHV-6 and HHV-7 in cervixes of women with abnormal cervical cytology results; (2) elucidating the association between HHV-6 and HHV-7 and the progression of cervical lesions from premalignant to malignant stages; (3) assessing the value of HHV-6 and HHV-7 DNA detection in prediction and management of women with abnormal cervical cytology results; (4) providing preliminary data to support further in-depth study on the oncogenic role of HHV-6 and HHV-7.

Three hundred women with abnormal cervical cytology will be included. Total DNA will be extracted from exfoliated cervical cells and subjected to HHV-6 and HHV-7 DNA detection by nested polymerase chain reaction (PCR). PCR results will be confirmed by hybridisation and further differentiated into individual subtypes by restriction fragment length polymorphism. Results of HHV-6 and HHV-7 detection will be correlated with findings on cytology and histology. (MD97050)

In-vitro Activity of Tazocin in Comparison with Other Commonly Used Antibiotics against

∠ CHENG Fun Bun Augustine

LING Kin Wah
Thomas

□ 1 June 1998

Clinical Isolates

❖ Wyeth (HK) Ltd

Piperacillin/tazobactam is a new β -lactam in combination with β -lactamase inhibitor which demonstrates potent antimicrobial activity against

Gram-negative bacteria. Its in-vitro activity profile is extended towards both Gram-positive and anaerobic organisms. Piperacillin/tazobactam will be used to compare with eight antimicrobial agents including piperacillin, ciprofloxacin, amikacin, cefuroxime, ceftazidime, ceftriaxone, cefotaxime, and cefepime. Minimum inhibitory concentrations (MICs) of antimicrobial agents were determined by the agar dilution method. A total of about 1,000 clinical isolates will be included in this study. The Prince of Wales Hospital, Hong Kong has a large and welldocumented collection of bacterial strains which reflect the clinical isolates of the hospital of this region. It is proposed to undertake the study in order ascertain likely efficiency the piperacillin/tazobactam in Hong Kong. The other part of the study will be a multicenter study in collaboration with Union Hospital, Beijing. result will be very useful to compare the antibiotic resistance rate from these two major cities of China. (MD97147)

Acinetobacter Genospecies: Their Distribution in Hong Kong and Evaluation of PCR Identification Methods

- - PITT Tyrone Leslie*
- ☐ 1 October 1997
- * Research Grants Council

Acinetobacters are versatile bacteria, readily isolated from the environment. They are economically important in the food industry and potentially useful in biotechnology. Problems in their classification over past decades have impeded our understanding of their ecological and clinical roles. A. baumannii has become the main genospecies associated with increasing incidences of endemic and epidemic infections in hospitals in Hong Kong and elsewhere. It is inherently resistant to antibiotics and also to desiccation, important features for an opportunistic pathogen. Very little is known about other genospecies, particularly in hot, humid areas. Recently, 17-19 genospecies (DNA groups) have been recognized by the laborious DNA-DNA hybridization method. Several rapid species identification methods based on polymerase chain reaction (PCR) have been reported, but there are discrepancies. The researchers intend to study the distribution of the Acinetobacter genospecies in collections of isolates obtained from foods, soil, clinical specimens and from people. The precise characterization of a large numbers of acinetobacters from various sources should improve our knowledge of the ecological and pathogenic roles of different genospecies. Such data would also clarify confusion in present day genospecies classification. Studies of desiccation resistance and antimicrobial susceptibilities of different genospecies will help us

to determine their potential role as hospital-acquired pathogens. (CU97625)

The Study of Antimicrobial Resistance in Acinetobacter

- HOUANG Ting Sou Elizabeth IP Margaret CHU Yiu Wai
- ☐ 15 October 1997
- CUHK Mainline Research Scheme

Species of the genus Acinetobacter are recognised as important pathogen associated with a growing number of endemic and epidemic infections in hospitals world-wide. The researchers have established a research program on Acinetobacter and obtained 3 external grants to study the epidemiology, clinical significance and genospeciation of the genus in Hong Kong. Now, they wish to study the genetic basis and mechanisms of antimicrobial resistance of the genus. Similar to A.baumanii, Pseudomonas aeruginosa and enterococci are intrinsically resistant to many commonly used antimicrobials. intrinsic resistance of these two species may involve two different mechanisms: (1) an energy independent, passive mechanism which is based on structural alterations, or reduced expression of the outer membrane proteins responsible for the passage of the agents across cell membranes, and (2) an energyrequiring, active efflux mechanism. mechanisms may provide means for multiple antibiotic resistance (MAR). To date, no information on the multiple antibiotic resistance system(s) in Acinetobacter has been published. This area of research is state of the art and new to The Chinese University of Hong Kong. Their interests will initially be focused on the genetic basis of fluoroquinolone resistance and the role played by multiple antibiotic resistance (MAR) mechanisms. The purpose of this Mainline Research application is to establish research link with one of the worldrecognised group headed by Dr. Laura Piddock, University of Birmingham, UK; so that relevant methodologies may be set up locally and joint studies carried out. (MD97010)

Molecular Epidemiology of Penicillin- and Multidrug-Resistant Streptococcus pneumoniae

- ☐ 1 October 1997
- * Research Grants Council

Clinical resistance to penicillin and other antimicrobial agents in *Streptococcus pneumoniae* have emerged rapidly in recent years in many parts of

the world. Resistance to β -lactam antibiotics is due to alteration in the genes for high molecular weight penicillin binding proteins 1a, 2b and 2x. Spread of resistance genes is due to dissemination of resistant pneumococcal clones or horizontal spread of resistance determinants leading to altered (mosaic) pbp genes. The relative importance of these two processes in the worldwide dissemination of resistance in pneumococci has not been clearly defined. Knowledge of the genetic basis of resistance is essential for further epidemiological study and development of effective control strategies for the prevention of drug resistant *S. pneumoniae*. The aims of the present study are to develop methods for the molecular fingerprinting of S. pneumoniae, to apply these methods in determining the relatedness of clinical isolates from Hong Kong, and to investigate the likely origins and patterns of dissemination of antibiotic resistance determinants. (CU97607)

Study of the Colonisation and Role of Spread of (Drug-Resistant) Streptococcus Pneumoniae in Elderly Day Care Centres and Residential Homes

- ✓ IP Margaret HUI Elsie (Medicine & Therapeutics) LYON Donald James WOO Jean (Medicine & Therapeutics) CHENG Fun Bun Augustine
- □ 1 November 1997
- Health Services Research Fund, Hospital Authority

Streptococcus pneumoniae is the leading cause of community-acquired bacterial pneumonia and a major cause of sepsis at the extremes of age. The local epidemiology of S. pneumoniae in Chinese children has been well established but that in the elderly population is lacking. Preliminary data obtained from the Prince of Wales Hospital revealed that 60% of the isolates of *S. pneumoniae* were from hospitalized patients aged ≥65 (unpublished data). Superimposed with this concern is the rapid emergence of penicillin-resistant pneumococci from <10% in 1993 to >35% in 1995 (ranging 18-55%) in Hong Kong. This has complicated the treatment of such infections. The aims of the present study are to investigate the nasopharyngeal carriage rate of S. pneumoniae in elderly day care centres and residential homes; to identify the antibiotic resistance pattern of these isolates and to study the risk factors associated with carriage and the role of spread of S. pneumoniae, in particular, the drug-resistant strains in this setting. (MD97017)

Identification of Genes of Extended-Spectrum β -Lactamases by Polymerase Chain Reaction and Oligotyping

- LING Mei Lun Julia
- ☐ 1 April 1998
- CUHK Research Committee Funding

ß-Lactams are one of the most important group of antibiotics in the treatment of bacterial infections. Resistance to these drugs soon emerged after their widespread use. Such resistance was most often due to enzymes produced by resistant bacteria which hydrolyzed the drugs (ß-lactamases), the commonest being TEM-1. These enzymes attack penicillins such as ampicillin and ticarcillin. Cephalosporins, especially the third generation cephalosporins, stable to the enzymes were subsequently developed during the 1980s. They were extremely effective in treating Gram-negative bacterial infections when first introduced but had led to the selection of new enzymes. Molecular analysis of the structural gene of the first such enzyme indicated that it evolved from that of TEM-1 in enterobacteria by point mutation, resulting in amino acid substitution, thereby extending the enzyme substrate range. Subsequently may more enzymes which were TEM-type mutants had been isolated. The previous study showed that different B-lactamases, mostly of the group of extended-spectrum ß-lactamases, were responsible for resistance to third generation cephalosporins klebsiellae Escherichia coli, enterobacters isolated in the Prince of Wales Hospital. This study aims to use polymerase chain reaction (PCR) and oligotyping to characterize these enzymes. Oligotyping is the detection of point mutations by DNA-DNA hybridization with selected oligonucleotide probes giving a hybridization profile known as "oligotype". From this study, the researchers will be able to know the types of ßlactamases responsible for resistance to thirdgeneration cephalosporins prevalent in the Prince of Wales Hospital, Hong Kong and whether novel types of ß-lactamases have evolved. Such information is important in the understanding of the rapid development of antibiotic resistance amongst our isolates and will help in the design of rational antibiotic policies. (MD97118)

Cloning and Characterization of Epstein-Barr Virus (EBV) Latent Membrane Antigen 2 (LMP-2) Genes Associated with Nasopharyngeal Carcinoma

- □ 1 October 1997
- CUHK Research Committee Funding

Nasopharyngeal carcinoma (NPC) is common among southern Chinese and had been shown to be closely associated with the Epstein-Barr virus (EBV). In viro EBV latent infection is characterized by the expression of EBV nuclear antigens (EBNA1, EBNA2, EBNA3A, EBNA3C AND EBNALP) and latent membrane proteins (LMP1, LMP2A and LMP2B). LMP2 is consistently expressed in NPC and other EBV-related malignancies. The main objective of this project is to study the DNA sequence variability's of the LMP2 gene of EBV in NPC cells in relation to the standard EBV strain derived from B95-8 cell (a marmoset lymphocytic cell line infected with human EBV from infectious cDNA of EBV LMP2-specific mononucleosis). mRNA isolated from B95-8 cells and NPC biopsies will be amplified by a RT-PCR protocol and cloned into plasimd vector for DNA sequencing. The DNA sequences of LMP2 genes from B85-8 and NPC cells will be compared to elucidate genomic variability's among these EBV isolates derived from different diseases. Such information may be important in studied relating to the carcinogenesis of EBV and the pathogenetic role of latent membrane proteins of EBHV in NPC. (MD97049)

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

Edition Title/Investigators

1994-95 Evaluation of the Relative Frequencies of Different Resistance Mechanisms to Quinolones in Clinical Isolates of Gram Negative Bacteria at the Prince of Wales Hospital, Hong Kong (MD95054)

∠ ADEYEMI-DORO Folorunso
LYON Donald James
CHENG Fun
Bun Augustine
LING K. W.
Thomas*

1996-97 A Survey of the Presence of Human Herpesviruses 6 and 7 in Normal and Neoplastic Brain Tissues (MD96061)

 ∠ CHAN Kay Sheung Paul • NG Ho Keung (Anatomical & Cellular Pathology) • TAM Siu Lun John • CHENG Fun Bun Augustine • FUNG Sau Chun Kitty

1995-96 A Study of Extended-spectrum β -lactamases in Hong Kong Isolates of

	Enterobacteriaceae-characteristics and Prevalence (MD95249) CHENG Fun Bun Augustine • LYON Donald James • SCHEEL Olaf* • ADEYEMI-DORO Folorunso • LING Kin Wah Thomas	1996-97	A Comparison of Acinetobacter spp Distribution in Humans and in Raw Vegetables in Hong Kong and London (MD96019) HOUANG Ting Sou Elizabeth PITT Tyrone Leslie*
1996-97	An <i>in-vitro</i> Antimicrobial Susceptibility of Trovafloxacin (MD96137)	1996-97	Molecular and Seroepidemiology of Acute Hepatitis E Infection in Hong Kong (MD96063) ✓ IP Margaret • TAM Siu Lun John • CHAN Tak Shing (Accident and
1996-97	An <i>in-vitro</i> Antimicrobial Susceptibility of Meropenem (MD96138)		Emergency Medicine Academic Unit) • CHENG Fun Bun Augustine
	Kin Wah Thomas	1995-96	Molecular Genotyping of <i>Salmonella</i> Typhimurium and <i>S</i> Derby in Hong Kong
1996-97	The Development of a GLC Procedure for the Analysis of Ethambutol in Clinical Specimens (MD96112)		(CU95605)
	CHENG Fun Bun Augustine	1996-97	Detection of Virulence Genes in Salmonella typhimurium by an
1996-97	A Comparison of <i>Acinetobacter spp</i> Distribution in Humans and in Raw Vegetables in Hong Kong and London		Amplication Technique (MD96064) LING Mei Lun Julia
	(MD96062)	1996-97	Extended-spectrum β-lactamases in Clinical Resistance in Hong Kong (MD96125) ∠ LING Mei Lun Julia • LIVERMORE D M*
1996-97	Nosocomial (Hospital-acquired) Colonization of Hospital Employees (MD96013) MHOUANG Ting Sou Elizabeth • LYON Donald James	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)
1996-97	Ulcerative Keratitis and Contact Lens Related Infection in Hong Kong		∠ ∠ ∠ ∠ ∠ ← ∠ ←
	(MD96015)	1996-97	Molecular Epidemiology and Genomic Diversity of Small Round Structured viruses (SRSVs) Associated with Acute Infectious Gastroenteritis (MD96065)

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RESEARCH PROJECTS

Developing Equivalent, Reliable and Valid Chinese Measures of Variables that may Predict Exercise in Young Chinese People: A Pilot Investigation

- CALLAGHAN Patrick CHAN Kwan Shing Darius (Psychology)
- □ 1 March 1998
- Health Care & Promotion Fund, Hospital Authority

Objective: This study is designed to establish the psychometric properties of measures of some important psychosocial variables that may predict exercise behaviour among young Chinese people in Hong Kong.

Design: It will be a test-re-test survey, with all the materials presented in a questionnaire format in Chinese.

Subjects: A random selection of 130 Form 4 and Form 5 Chinese males and females attending public secondary schools in Hong Kong will be recruited.

Main outcome measures: Attitudes towards exercising, control over exercising, social support, self-efficacy, and the influence of others on their exercise levels will be measured and their relations to frequency of exercise will be assessed.

Conclusion: To our best knowledge, very little has been done to examine factors that affect exercise behaviour among young Chinese people in Hong Kong. Results of the proposed study may provide an important information base for future large-scale health promotion interventions designed to encourage these people to improve their levels of exercise. (MD97087)

Promoting Independent Learning and Clinical Competence through Implementing Contract Learning in a Clinical Context

- □ 1 October 1997
- ❖ Action Learning Project Fund

The purpose of this study is to enhance students' learning in clinical areas by implementing contract learning. Contract learning will be introduced in the "mental health nursing" clinical placement in the Bachelor of Nursing degree programme. The process of drawing up the learning contract include identifying individual learning objectives in line with the general objectives of this placement, proposing the learning strategies and resources, identifying evidence of accomplishment and evaluating their performance. Students have to discuss their learning contracts with their clinical instructor before the placement. The objectives to be achieved will be

negotiated and agreed between students and their clinical instructors.

The effectiveness of contract learning will be assessed through a triangulation of methods:

- (1) Clinical instructors will take observations notes on students' performance during clinical placement and post-clinical conference to assess their clinical competence and the ability to integrate theory in practice.
- (2) At the end of the clinical placement, a questionnaire will be used to obtain students views on the benefits of contract learning.
- (3) Semi-structured interviews will be conducted with 20% of students selected by random method at the end of the placement. The interviews are to obtain in-depth feedback about the benefit and difficulties of using contract learning in clinical learning.

This project will be able to suggest innovative strategy in enhancing clinical learning in terms of increasing students' motivation and autonomy. The findings of this study can be used in developing teaching and learning strategies that can be applied in other clinical areas, e.g. medical and surgical units. (ED97001)

A Pilot Study on the Use of Critical Pathway in Caring for In-Patients in a Mental Hospital in Hong Kong

- CHAN Wai Chi Sally
- ☐ 1 October 1997
- CUHK Departmental Funding

To provide quality health care and at the same time, to control cost, health care institutions have to depend upon a delivery system that focused on appropriate use of resources and controlling length of stay while monitoring clinical progress toward identified outcomes. Literature suggests that using critical pathway as a tool for managing resources, continuous quality improvement and increased collaborative practice can enhance the professional practice environment and benefit for patient care. The aim of this project is to develop a critical pathway for the care of schizophrenic patients and evaluate its use. Data was collected by variance record and semistructured interview. Through the use of critical pathway, it is hoped that the quality of care be increased. The critical pathway provides a framework for health care provider to determine the cost of treatment for the schizophrenic patient populations. If the result of this study is favourable, critical pathways can be developed for other patient groups to co-ordinate care. The critical pathway developed in this project will be integrated into case management service as well. (MD97143)

An Evaluation of the Implementation of Case Management in the Community Psychiatric Nursing Service

- □ 1 November 1997
- Health Services Research Fund, Hospital Authority

The purpose of this study is to compare the outcomes of case management service with the conventional practice of Community Psychiatric Nursing Service (CPNS) in the care of chronic schizophrenic clients. A matched, randomised pre-post case-control group The process of case design will be used. management implementation will be described. The impact of case management service on clients' clinical status, functional level, readmission rate and satisfaction will be measured and compared with the conventional CPNS. Cost-effective analysis will be performed. If it is found that the case management service model can improve the clinical outcomes, reduce readmission rate for chronic schizophrenic clients, and also cost-effective, the planning of care for these types of clients will be addressed in a helpful manner. In addition, the study may illustrate a means for evaluating health services in Hong Kong such that health care resources can be more efficiently used in the care of at least some mentally ill clients. (MD97084)

Exploring Oncology Nurses' and Clients' Perspectives toward Oral Care in Hong Kong

- ∠ CHAN YIP Carmen Wing Han TSANG W.F. June*
- ☐ 1 December 1997
- Student Campus Work Scheme, Shaw College, CUHK

The aim of this study is to seek understanding of the perceptions and practice of oncology nurses and cancer clients towards oral health.

Purposive sampling and qualitative approach was used for this study. Semi-structured interviews were conducted with 8 nurses and 8 patients. Each interview lasted about half to one hour. An open approach was adopted in the interviews to encourage clients and staff to raise their own issues and to explore comments.

Verbatim records of interviews in Cantonese were transcribed and translated into English by the research team. All data collected were considered and analysis commenced during transcription. Themes that emerge consistently in the data formed an interpretive plan and a coding protocol. Each

interview was then coded using that protocol. Issues identified included knowledge of oral care, attitude and feeling towards oral care, and barriers/facilitators of care. Findings showed the need of education program for both nurses and patients. (MD97173)

Understanding Fatigue in Cancer Patients Undergoing Chemotherapy and Radiotherapy in Hong Kong

- ∠ CHAN YIP Carmen Wing Han

 MOLASIOTIS
 Alexandros
- ☐ 1 April 1998
- CUHK Departmental Funding

The aims of this study are to gain initial understanding of the experience of fatigue of Chinese cancer patients in Hong Kong and assess the way they perceive & define fatigue. It also aims to investigate the association between febrile neutropenia and the onset of fatigue. Sixty-nine cancer patients were asked to record their experience of the intensity of fatigue and their oral temperature using a diary format. They also completed the Chinese version of fatigue sub-scale on admission, by the end of the first week, and by the end of the second week post-treatment. A semi-structured interview was conducted by the end of the second week after chemoradiation.

The mean score for fatigue sub-scale ranged from 3.65 to 9.60 with a maximum of 28. According to the diary, the fatigue levels were generally high on Day 2-4 post-chemotherapy and on Day 7-8 post-radiotherapy. There was a link between fatigue and febrile illness on post-chemotherapy patients, but this link was not evident on patients undergoing radiotherapy. Major themes identified including definition and understanding of fatigue, factors that trigger fatigue, the impact of fatigue on their daily living, and ways to handling fatigue. (MD97174)

Promoting Students' Critical Thinking: The Use of Videotaped Vignettes in a Baccalaureate Nursing Programme

- □ 1 October 1997
- Action Learning Project Fund

Critical thinking is a pre-requisite for graduation from a baccalaureate nursing programme. Such thinking indicates a person who is constantly questioning and analyzing situations while also facilitating the development of problem solving and decision making skills. Critical thinking is important

not only for acquiring theoretical knowledge but also for gaining and applying procedural knowledge. The focus in this project is on the development of critical thinking ability when learning the skills required for proficient, high quality nursing practice. In the past, the emphasis has been on promoting learning of the nursing skills alone with less attention paid to facilitating students' critical thinking. This project aims to develop videotaped vignettes that simulate clinical situations as part of a problem-based teaching approach for developing students' critical thinking. Such a teaching method aims to provide a realistic experience for students to learn and analyse complex clinical skills in a safe environment without the threat of harming the patient. The benefits of this new approach to teaching nursing skills will be evaluated and the findings will contribute to the continued refinement of the learning-teaching process. (MD97020)

Assessment of Psychosocial Adjustment, Attitudes and Motivation towards Unrelated Bone Marrow Donation

- MOLASIOTIS Alexandros
 HOLROYD Eleanor
- ☐ 15 October 1997
- ❖ CUHK Research Committee Funding

The study aimed to assess the psychosocial adjustment (in terms of self-esteem, mood states and anxiety) of unrelated bone marrow donors, their perceptions of the experience of donation, their motivation to donate bone marrow and their expectations from donation. The total population of unrelated marrow donors was approached and 37 donors participated in a semi-structured interview whereas 27 of them also completed a series of Questionnaire data was further questionnaires. compared with data from 99 volunteers who had not donated bone marrow. Self-esteem was generally low and donors did not see themselves as a better person after the donation. The majority believed that they were not prepared well for the experience and 40% found the experience emotionally less positive. A number of donors (10.5%) found the experience physically stressful with pain being the main problem reported post-donation. However about three quarters of the sample would donate again. From the qualitative data thematic analysis found the following categories that families had posed barriers to their decision to donate; their expectations are different from the reality of donation; religious beliefs played an important role in their decision to donate as well as generosity and altruism; and the donation was linked mainly to bad fortune but also good fortune at

(MD97051)

A Pilot Study to Assess the Effectiveness of Group Cognitive-Behavioral and Peer Support / Counselling in Symptomatic HIV Patients

- □ 1 May 1998
- Council for the AIDS Trust Fund

This is an RCT assessing the effectiveness of group cognitive-behavioral and peer support/counselling intervention in symptomatic HIV patients in terms of symptom distress, quality of life and uncertainty to illness; exploring the experiences of patients from their participation in such groups in relation to needs and expectations; assessing the influence of coping style in the management of illness; and assessing the contribution of such interventions in health promotion behaviors. 60 HIV patients will be randomised in 3 groups: one will receive cognitive behavioral interventions, the second support/counselling and the third will be the control group. The intervention will be carried out for 12 session, once a week. Three months after the end of the intervention the subjects will be reassessed in terms of quality of life, psychological status and mouth promotion behaviors and these data will be compared with the baseline data. The project is expected to be completed within 12 months. (MD97093)

The Fear of Hypoglycaemia among Patients Who are Working and Insulin-Treated

- □ 1 January 1997
- United Board for Christian Higher Education in Asia Research Grant

This study aims to examine fear of hypoglycaemia among insulin-treated patients of working age (18-65 years of age). The study employed a cross-sectional descriptive design. The entire population of the insulin-treated patients of working age attending a diabetes clinic in one of the regional hospitals over a period of eleven clinic days in early 1997 provided the sampling frame. Structured-interview guided by a questionnaire, that was developed from the work of Richmond and the Fear of Hypoglycaemia Survey, was adopted as the data collection method. From a possible total of 181 patients, 120 were successfully interviewed. This gives a response rate of 66.7%. The mean age was 46.58 and the mean year since insulintreated was 4.9. Results indicated that the mean fear of hypoglycaemia was low, however, 8.3% of respondents suffered from high fear. It is important to note that the majority of respondents (86.7%) had the experience of hypoglycaemic attacks in the preceding year and 16% of the respondents experienced

hospitalisation due to hypoglycaemia. Moreover, approximately half of them had the experience of hypoglycaemia influencing their work life, 21.7% had the experience of hypoglycaemia influencing their social life and 10.1% had the experience of hypoglycaemia influencing their personal life. Results also demonstrated that fear of hypoglycaemia correlated positively with the frequency of hospitalisation due to hypoglycaemia, the frequency of hypoglycaemia affecting work, social and personal life, and time since insulin-treated. However the fear correlated negatively with age. (MD97135)

The Lived Experience of Insulin-Treated Patients Who Worry about Diabetes Complications and Hypoglycaemia

- SHIU Tak Ying
- ☐ 1 January 1998
- United Board for Christian Higher Education in Asia Research Grant

The aim of this study is to explore the lived experience of insulin-treated diabetes patients who worry about diabetes complications and hypoglycaemic attacks. The study will employ a case study design using qualitative method of data collection. A previous study conducted by the author earlier last year in a diabetes clinic of a regional hospital identified 18 patients from the study sample who demonstrate worry about diabetes complications and hypoglycaemic attacks. They will be invited as participants.

(MD97136)

Perception of Caring Behaviours among Hong Kong Nurses

- YAM Man Chung
- □ 22 February 1997
- CUHK Departmental Funding

Ten registered nurses in Hong Kong were interviewed to collect their perceptions of caring behaviours in their clinical setting, the barriers to caring, and possible solutions to improve the situation. These nurses valued the importance of expressive behaviours and interpersonal communication skills in providing holistic patient care. They felt constrained by institutional and personal variables such as manpower shortages, limited skills and lack of appropriate training. It was thought that better staff education and facilitation of a caring culture in the ward environment could improve the situation. Some of these issues were acknowledged and addressed by the Hospital Authority, the major employer of nurses in Hong Kong. It is recommended that interpersonal skills and psychosocial care be integrated in the

nursing curriculum, and further research on caring among staff and patients would be useful. (MD96218)

Telling Stories: A Strategy to Enhance Ethical Decision Making

- YUNG Ha Ping Hilary
- □ 1 September 1997
- ❖ Action Learning Project Fund

The aim of this project is to enhance the ethical decision making skill of nurses and the application of ethical theories to practice using story telling. The story telling approach will be implemented in an ethics course which is a required first year course for registered nurses undertaking the Bachelor of Nursing programme offered by the Department of Nursing at The Chinese University of Hong Kong. An active student-centred approach to learning and assessment will be adopted. Students will have dialogue in small groups to reflect on their experience. They will be grouped into experiential small groups and share a story of dilemma which they personally encountered in practice with their peers within the small group. A pre-post experimental design with a control group is adopted for evaluating the effectiveness of the story telling approach to the teaching of ethics. The project will be conducted in two course cycles. It is expected that the students will be better prepared to recognize the ethical dimensions of clinical situations so that they are able to fulfill their professional roles. The innovative strategy will also contribute to the teaching of other professional human services courses where moral education is involved.

(MD97021)

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

Edition	Title/Investigators
1996-97	Being a Mature Age Nursing Student on Campus (ED96061)
1996-97	A Pilot Study on the Use of Critical Pathway in Caring for Clients in the Community Psychiatric Nursing Service in Hong Kong (MD96144) CHAN Wai Chi Sally
1994-95	Exploring Perception of Health Care and Service Provision for Hong Kong's Elderly: Implication for Families and Community Nurses (MD94170)

HOLROYD Eleanor

- 1996-97 How Chinese Elders Adjust to Residential Home Life (MD96179) LEE Tze Fan Diana
- 1996-97 Hospital Readmission Among Elderly
 Patients: A Preliminary Study (MD96178)

 ∠ LEE Tze Fan Diana MACKENZIE

 Ann LEE Fung Kam CHAN YIP

 Carmen Wing Han

- 1996-97 Hong Kong High School Students' Attitudes Towards Nursing Profession (MD96172)
 - ROSSITER Joh Chin FOONG Lai Sun[#] CHAN Po Tai
- 1996-97 Increasing Women's Knowledge of the Prevention of Cervical Cancer and the Uptake of Cervical Screening: the Implementation of a Nurse Led Community Outreach Programme (MD96026)
 - ▼ TWINN Sheila Frances MAK Mui Hing June[#]

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- <P973170> **Ip, Wan Yim.** "The Effect of the Husband's Presence During Labour in Hong Kong". *Journal of Clinical Nursing* vol.6, pp.169-170. Britain, 1997.
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see also <P972858>

RESEARCH PROJECTS

Characterization of the Up-Stream Regulators of Retinoblastoma Gene in Squamous Cell Carcinoma of Uterine Cervix

- - WONG Yick Fu
- □ 1 September 1997
- CUHK Research Committee Funding

Retinoblastoma (Rb) protein inhibits the G1-S transition. Activation and inhibition of the pRb is under intricate control of the cyclin-dependent kinases (CDK) 4 and 6, cyclins such as cyclin D1 and inhibitors of cyclin/CDK 4 complex such as p16 and p15. This p16-cyclin D1/CDK4-Rb pathway is believed to be one of the key pathways in preventing uncontrolled cell growth. Alteration of various components through different mechanisms along this regulatory axis have been shown to contribute to the development of many human cancers. It is apparent that the relative importance of different alternations varies in different malignancies.

Carcinoma of cervix is the most common gynaecological malignancies in Hong Kong and majority of them are of squamous cell type. The researchers have studied the deletion and mutation of p16 and p15 and the under-expression of pRb in this squamous cell cancer and the role of hypermethylation of the 5' CpG island in inactivating the p16 gene is being investigated.

The genetic alternations of the starting point and the end point of p16-cyclin D1-CDK-pRb pathway in carcinoma of cervix are known to us. The researchers would like to investigate in the same tumour samples the genetic alternations of cyclin D1 and cyclin-dependent kinases (CDK 4) to get a complete picture and understanding of this pathway. By correlating their findings with clinicopathologic variables, it is possible that subgroups of patients with different prognostic outcome can be identified. (MD97052)

Psychological Distress and Self-Esteem in Infertile Chinese Couples for Assisted Reproduction - A Prospective Study

- ∠ CHEUNG Lai Ping CHUNG Wai Sau Dicky (Psychiatry) LO Wing Kit LEUNG Tak Yeung HAINES Christopher John LOONG Ping Leung E.
- □ 28 May 1997
- CUHK Departmental Funding

The study is designed to evaluate the psychological state and self-esteem of infertile couples of different causes requiring assisted reproduction; the psychological impact of failed procedure of assisted reproduction; the association between personality traits, psychological state and success rate of assisted reproduction; and the common disbelieves concerning infertility and remedial methods to help fertility among these subjects. (MD96211)

Postnatal Depression - Epidemiology

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- ☐ 1 January 1997
- CUHK Departmental Funding

Recruitment of a cohort of pregnancies which are screened for signs of postnatal depression in order to establish prevalence and identify predictive factors. (MD96206)

Intratype Variation of Human Papillomavirus Infection in Cervical Cancer: A Regional Perspective in China

- ∠ CHUNG Kwok Hung Tony WONG Yick Fu CHEUNG Tak Hong
 ∠
- □ 1 November 1997
- **❖** CUHK Research Committee Funding

There is a substantial body of evidence which has linked HPV infection with the pathogenesis of cervical cancer. Among more than 70 genotypes of HPV isolated to date, types 16, 18, 31 and 33 have been identified as "high-risk" of causing cervical cancer while types 6 and 11 are known as the "low-risk" groups.

In USA, there are geographic and ethnic variations in the HPV genotypes detected in cervical cancers. However, there is no information whether there are similar HPV genotype variation in China. A large-scale epidemiological survey on the prevalence and incidence of different genotypes of HPV in cervical cancer would be important to assess the diagnostic and prognostic significance of HPV detection in this cancer. In addition, immunization to prevent HPV infection and thus cervical cancer is a potential future prospect.

The researchers propose a collaborative multi-centre study of HPV infection in cervical cancers in three geographic regions of China: Hong Kong, Shanghai and Guangdong Province. Polymerase chain reaction (PCR) – based HPV assays that afford the specific detection of 12 different HPV genotypes will be used. This proposal is to perform a pilot study to determine feasibility of a major nationwide survey of HPV genotypes and cervical cancers in China. The data obtained from this pilot study and the subsequent nationwide survey will also provide valuable information pertinent to the development of HPV diagnostic probes and development of vaccination strategies in the future.

This is to be a collaborative study with Professor H. zur Hausen, Germany who was the first person to show a clear link between HPV infection and cervical cancer.

(MD97054)

Hypoxic-Ischemic Induction of Apoptosis in the Newborn Rat

- ∠ HAINES Christopher John CHANG Mang Z. Allan ROGERS Michael Scott
- □ 1 May 1997
- CUHK Departmental Funding

This project is an indirect study of the effect of perinatal asphyxia on the brain of premature infants. The researchers are using 3-day-old rat model to characterize the site and nature of neuronal cell death after minor hypoxic-ischaemic insults. The results of this study will provide information which may be used in strategies to prevent brain damage in premature infants. (MD96210)

A Comparison of Two Stimulation Protocols for Poor Responders in IVF

- HAINES Christopher John CHEUNG Lai Ping
 LEUNG Tak Yeung LOONG Ping Leung E.
- □ 1 August 1997
- CUHK Departmental Funding

Success rates for treatment with *in vitro* fertilization are due in part to the manner in which the ovaries respond to hyperstimulation. A proportion of women is resistant to treatment with standard protocols of hyperstimulation. This study will compare a new treatment protocol with the standard protocol in women who have previously responded poorly to hyperstimulation. (MD97155)

The Effect of Sex Steroids on Neuronal Apoptosis

- □ 9 August 1997
- CUHK Departmental Funding

Postmenopausal women have an increased risk of developing Alzheimer's Disease. The lesions which cause this disease are thought to result indirectly from cell death due to apoptosis (programmed cell death) rather than from necrosis. This study will examine the ability of oestrogen to protect against apoptosis using a pc12 cell culture in which apoptosis is induced by the removal of nerve growth factor. The results of this study will provide information which

may explain the means by which oestrogen protects against Alzheimer's Disease. (MD97156)

Evidence of Oxidative Stress and Apoptosis after Perinatal Hypoxic-Ischaemic Insults on the Rat Brain

- HAINES Christopher John CHANG Mang Z.
 Allan FISCUS Ronald R. (Physiology) •
 JAMES Anthony (Laboratory Animal Services Centre) STADLIN Alfreda (Anatomy) •
 WONG Yick Fu
- □ 1 September 1997
- CUHK Research Committee Funding

If a foetus is exposed to a severe perinatal insult, evidence of brain damage is usually evident at the time of, or soon after birth. However the researchers propose that a foetus subjected to less severe hypoxic-ischaemic insults may suffer more subtle brain injury which is not detectable at birth, but which may cause developmental problems later in life. Such minor insults are likely to cause apoptotic cell death, mediated through the release of oxygen free radicals. Nitric oxide (NO) is a free redical which has several important messenger functions within the brain. However, excessive production of NO is neurotoxic. NO is capable of reacting with the superoxide free radical (O2) to form the highly reactive peroxynitrite (ONOO). ONOO can elicit DNA strand breaks which lead to cell death.

During perinatal hypoxic-ischaemic insults, the temporal relationship between the generation of NO and the development of apoptosis has not been established. This study aims to use a perinatal hypoxic-ischaemic rat model to correlate the degree of apoptotic cell death with the production of NO and ONOO as an index for early detection of perinatal hypoxic-ischaemic injury.

In this study, postnatal day 7 Sprague-Dawley rats will undergo a unilateral common carotid artery ligation followed by exposure to an 8% oxygen environment for a time interval ranging from 15-120 min. This will constitute the hypoxic-ischaemic insult. To measure the level of NO produced, cellular cGMP concentrations in different regions of the brain will be determined. ONOO formation will be determined immunocytochemically using the antibody to nitrotyrosine. Apoptotic cell death will be determined using the TUNEL method and DNA laddering.

The clinical application of this research is that it may become possible to predict the development of subtle perinatal brain damage due to apoptotic cell death by measuring the production of free radicals in utero. This early detection is critical for the implementation of a prophylactic treatment regime. (MD97053)

Circulating Vaso-Active Factors in Pre-Eclampsia and Normal Pregnancy

- KESBY John Gregory ◆ LEUNG Tse Ngong ◆
 TAM Wing Hung ◆ ARUMANAYAGAM
 Manoharan (Chemical Pathology)
- □ 1 May 1998
- CUHK Departmental Funding

A study of the uteroplacental production of vaso-active peptides in pre-eclampsia. (MD97159)

Leptin Levels in Multiple Pregnancy

- KESBY John Gregory LAU Tze Kin •
 LEUNG Tse Ngong FUNG Tak Yuen •
 WONG Yick Fu LAU Woon Chung
- ☐ 1 June 1998
- CUHK Departmental Funding

Determination of leptin levels in maternal serum, amniotic fluid, and arterial and venous cord blood in multiple pregnancy. Determination of the correlation of these levels with cord blood insulin levels, birth weight and placental weight. (MD97158)

Two Way Cell Trafficking: Elective LSCS

- ∠ LAU Tze Kin FUNG Tak Yuen CHANG Mang Z. Allan LO Yuk Ming, Dennis (Chemical Pathology)
- □ 1 May 1997
- CUHK Departmental Funding

To study the transplacental transfer of fetal and maternal cells between the fetal-maternal compartments in women undergoing elective caesarean section.
(MD96209)

Oxygen Free Radicals in Amniotic Fluid Sample in Second Trimester of Pregnancy

- ∠ LAU Tze Kin FUNG Tak Yuen* ROGERS Michael Scott
- □ 1 June 1998
- CUHK Research Committee Funding

Intra-uterine growth retardation (IUGR) and hypertensive disorders (or preeclampsia) are common and serious obstetric complications. Both conditions are major causes of perinatal morbidity and mortality while the latter also contribute to maternal morbidity and mortality. Both conditions are thought to be due to or mediated through placental pathology which can be detected as early as second trimester and result in

growth retardation, or preeclampsia due to abnormal maternal and fetal response. If this is true, there should be evidence of cellular hypoxia from early second trimester. Organic hydroperoxides (OHP) and malondialdehyde (MDA) are sensitive markers for hypoxic cellular and tissue damage.

The objective of the current study is to construct a normal range for MDA and OHP concentration in amniotic fluid in early second trimester, and to test the hypothesis that those pregnancies with higher MDA and OHP levels are at risk of IUGR and hypertensive disorders of pregnancy.

400 patients with singleton pregnancy undergoing amniocentesis for karyotyping are invited to participate into the study. Maternal venous blood sample (1 ml) and amniotic fluid (1 ml) will be collected and measured for OHP and MDA concentration. The relationship between OHP and MDA concentrations and the occurrence of obstetric complications will be analysed.

The finding of this study will provide further information as to the pathogenesis of these 2 common obstetric complications, namely IUGR and preeclampsia.

(MD97119)

Randomised Trial on the Use of Topical Anaesthesia in Outpatient Hysteroscopy

- ∠ LAU Woon Chung YUEN Pong Mo TAM Wing Hung LO Wing Kit
- □ 1 May 1997
- CUHK Departmental Funding

The objective of this project is to evaluate the efficacy and safety of paracervica and intracervical anaesthesia in reducing pain in women attending outpatient hysteroscopy. This is a prospective randomised placebo-controlled double blind study. (MD96204)

Randomized Trial of I/V Oxytocon vs I/M Oxytocin+Ergometrine in 3rd Stage

- ∠ LAU Woon Chung CHANG Mang Z. Allan YUEN Pong Mo
- □ 1 July 1997
- CUHK Departmental Funding

Primary post-partum haemorrhage is a serious condition and this can be prevented by the active management of the third stage of labour. The objective is to compare the effect of intravenous oxytocin alone and intramuscular oxytocin and ergometrine (Syntometrine) in the management of the third stage of labour. It is a prospective randomized study.

(MD97149)

Placental Apoptosis in Normal Pregnancy and Pregnancies Complicated with Preterm Labour, Pre-Eclampsia, or Intrauterine Growth Retardation

- ∠ LEUNG Tse Ngong TO Ka Fai (Anatomical & Cellular Pathology) SAHOTA Daljit CHANG Mang Z. Allan
- ☐ 1 February 1998
- CUHK Departmental Funding

This is a prospective collaborative project between the Department of Obstetrics & Gynaecology and the Department of Anatomical & Cellular Pathology. The aims of this study are: (1) using leing microscopy H&E staining and TUNEL method, to quantify the incidence of apoptosis in placental tissue obtained from (i) first trimester pregnancy termination, (ii) normal third trimester pregnancies, pregnancies complicated by (iii) pre-eclampsia, (iv) intrauterine growth retardation, (v) idiopathic preterm labour; (2) to perform electron microscopy examination in a random selection off samples from each group to verify the presence of apoptosis; (3) to identify the relative frequency of apoptosis in different types of cells in the placenta; (4) to apply neural network technique to quantify the incidence of d placental apoptosis among different groups. (MD97152)

Psychosexual Function after Childbirth in Hong Kong Chinese Women

- ∠ LEUNG Tse Ngong LEE Tak Shing Dominic
 (Psychiatry) TANG So Kum Catherine
 (Psychology) CHUNG Kwok Hung Tony •
 YIP Shing Kai LAU Tze Kin
- □ 1 April 1998
- CUHK Research Committee Funding

Profound physiological, psychological and social changes occur after childbirth and all these can lead significant maternal morbidity. However, postpartum care of women is concentrated on physical conditions and the psychological impact of childbirth is only now being investigated systematically in Hong Kong. There is a paucity of information on the psychosexual aspects of women in the postpartum period. Consequently, knowledge amongst health care professions is lacking hence limiting the quality of care to those with problems. This proposed longitudinal survey is a collaborative project of three departments of The Chinese University of Hong Kong, Obstetrics & Gynaecology, Psychiatry and Psychology. The purpose is to assess the psychosexual function after childbirth in the first year of motherhood. Hong Kong Chinese women

who have delivered in the Prince of Wales Hospital

are to be recruited in the hospital before discharge.

Interviews are conducted in the immediate postpartum period, 6-8 weeks, 3 months and 12 months after delivery using structured questionnaire with rating scales. Attention is paid to time to re-start intercourse, the frequency, satisfaction and interest of sex, marital relationship, and the source of advice sought in cases where problems are encountered. Gynaecological problems such as menstrual disorder, pelvic pain or perineal pain, and problems with contraception are also recorded. The information obtained from this project will facilitate better understanding of the problems that local Chinese women face in the first year after childbirth, in particular psychosexual and gynaecological problems. (MD97120)

A Study of Feto-Maternal Haemorrhage after External Cephalic Version at Term Using PCR Method

- ∠ LO Wing Kit LAU Tze Kin LO Yuk Ming,
 Dennis (Chemical Pathology) ROGERS
 Michael Scott
- □ 1 June 1997
- CUHK Departmental Funding

External cephalic version has been shown to be safe and effective in reducing the incidence of breech presentation at term and caesarean section rate. Although clinical abruption associated with ECV is now rarely reported, the incidence of subclinical fetal-maternal haemorrhage (FMH) has been reported to range from 0-28%. Sensitive polymerase chain reaction (PCR) technique has been newly developed to detect subclinical FMH. (MD96203)

Comparative Study of GnRHa (Enantone vs Decapeptyl) in Treatment of Endometriosis

- ∠ LO Wing Kit CHEUNG Tak Hong LAU Woon Chung
- □ 1 August 1997
- CUHK Departmental Funding

Endometriosis is found in approximately 5% of women in reproductive age. The presentation varies from asymptomatic to severe pelvic pain, dysmenorrhea, dyspareunia, irregular menstruation or urinary and bowel symptoms. For those symptomatic women, GnRH analogue is proven to be effective medical therapy. The study is to compare the clinical efficacy of the 2 preparations in the treatment of endometriosis.

(MD97154)

A Study of Actocardiogram in Patients with External Cephalic Version at Term

- ∠ LO Wing Kit LAU Tze Kin SAHOTA Daljit
 LEUNG Tak Yeung ROGERS Michael Scott
- □ 21 March 1998
- CUHK Departmental Funding

External cephalic version has been shown to be safe and effective in reducing the incidence of breech presentation at term and caesarean section rate. However, there is still concern over the safety of ECV, although evidence so far suggested that the risk is low. In order to improve the safety, actocardiogram is now used to ensure the fetal wellbeing before and after the procedure. (MD97148)

To Establish Reference Values of MDA and OHP in Cord Blood Following Elective Caesarean Delivery

- ☐ 1 January 1997
- CUHK Departmental Funding

To determine the difference in cord lipid peroxide levels between patients undergoing labour and those delivered by elective caesarean section. (MD96215)

Lipid Peroxidation in Prenancy: Comparison of Maternal and Umbilical Cord Concentrations

- ☐ 1 June 1997
- CUHK Departmental Funding

To compare maternal and fetal blood lipid peroxide concentrations following delivery in order to determine placental transfer.
(MD96214)

Lipid Peroxidation in Fetal Sheep: Relationship between Peroxides, Anti-Oxidants and Purine Metabolism

- □ 1 January 1998
- CUHK Departmental Funding

Joint research with University of Sydney to elucidate the effects on ATP depletion and purine degradation following severe hypoxia-reperfusion. (MD97160)

Lipid Peroxidation in Fetal Sheep: Identification of Unique Marker of Neurological Hypoxia-Reperfusion Injury

- ☐ 1 January 1998
- CUHK Departmental Funding

Joint research with University of Sydney to isolate a unique peroxidation product indicative of neural damage from severe hypoxia reperfusion. (MD97163)

Comparison of Cadherin, Catenin and Integrin Expression in Endometrium, and in Invasive and Non-Invasive Endometriosis

- ROGERS Michael Scott YUEN Pong Mo LIEW Choong Tsek (Anatomical & Cellular Pathology)
- ☐ 1 February 1998
- CUHK Departmental Funding

Prospective study of cell surface proteins in deep infiltrative endometriosis compared to ovarian endometriosis. (MD97161)

Lipid Peroxidation in Fetal Sheep: Development of a Hypoxia Reperfusion Model

- ☐ 18 February 1998
- CUHK Departmental Funding

Joint research with University of Sydney to determine the effects of recurrent cord occlusion on fetal lipid peroxidation. (MD97164)

A Study of Changes in Lipid Peroxidation, Purine Degradation and Antioxidant Status Following Variable Hypoxic Insults in the Acutely Exteriorised Fetal Sheep

- ☐ 1 April 1998
- CUHK Research Committee Funding

The researchers have established that lipid peroxidation assays provide a measure of cumulative hypoxic cellular damage in the fetus during labour in humans but, at present, they are unable to determine what levels of lipid peroxidation in the fetus reflect permanent, irreversible cell damage to somatic or neural tissues.

The researchers have established an acute hypoxiareperfusion model in the fetal lamb and have shown that lipid peroxidation is induced in neural tissue by 60-second total cord occlusions every 2-3 minutes, with minimal alteration of acid base balance. In contrast 30-second occlusions only produce peroxidation in somatic tissues.

The researchers propose to compare paired HPLC spectra in jugular venous plasma samples (already collected) following 30- and 60-second cord occlusions, to evaluate the relationships between lipid peroxidation, antioxidant activity and rates of purine degradation. (MD97121)

A Prospective Randomised Controlled Study of Using Oral Misoprostol and Vaginal Prostaglandin E_2 for Induction of Labour in Patients with Unfavourable Cervix

- ☐ 1 April 1998
- ❖ CUHK Research Committee Funding

Induction of labour in women with an unfavourable cervix is associated with a high failure and caesarean section rate. To increase the probability of a successful induction and vaginal delivery, cervical ripening agents are often employed. Prostaglandin E2 (PGE₂) is the most common used agent but it is expensive and usually given vaginally. Misoprostol, however, has the advantage of being cheaper and can be given orally, hence avoiding the need for repeated vaginal examination and possible infection. However, ripening agents often initiate contractions as well which may persist for an unpredictable period of time, resulting in uterine hypertonicity and eventual fetal compromise. The use of computerised interpretation of uterine contractions has revealed different patterns of electrical activity. The evolution of this activity in the labour process and whether this will predict the outcome of induction of labour are still unknown. Studies have been performed to compare PGE2 gel with oral Misoprostol. However, these studies were small and were not confined to the patient subgroup where maximum benefit would be anticipated, namely patients with an unfavourable cervix.

The aims of this study are two folds: Firstly, it is to compare the efficacy of oral Misoprostol with vaginal PGE_2 in cervical ripening and induction of labour in patients with unfavourable cervix; and secondly, it is to assess the uterine activity induced during the cervical ripening using a computerised cardiotocographic interpreter and to determine whether the success of induction can be predicted. (MD97122)

Fraxiparine in Pregnancy

- □ 1 March 1997
- CUHK Departmental Funding

An assay of Anti-Xa activity of patient put on low molecular weight heparin during pregnancy. (MD96213)

Intrauterine Adhesions Following Spontaneous Abortion

- ★ TAM Wing Hung CHEUNG Lai Ping CHUNG Kwok Hung Tony LAU Woon Chung
- □ 1 June 1997
- CUHK Departmental Funding

Intrauterine adhesion is a well-recognized cause of infertility and recurrent abortion. An incidence of 15 % has been reported after conventional surgical treatment for spontaneous abortion. There was a recent changing trend towards medical treatment. The researchers aim to assess the long-term effect of this conservative management. The current study investigates the incidence of intrauterine adhesion after two different modalities of treatment. Outpatient hysteroscopy was performed for patients who underwent either surgical or medical treatments and the incidence of intrauterine adhesion would be reported. (MD96212)

To Determine the Usefulness of 1,5-Anhydroglucitol in the Diagnosis and Monitoring of Gestational Diabetes and Impaired Glucose

- □ 1 May 1998

Tolerance

CUHK Research Committee Funding

Objective: To determine the efficacy of 1, 5-anhydro-D-glucitol for both prediction of gestational diabetes (GDM) and gestational impaired glucose tolerance (GIGT) and monitoring the effect, if any, of dietary treatment on this measure of glycaemic control.

Design: Prospective study.

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

Population: Women with singleton pregnancy being investigated for suspected impairment of glucose tolerance in the third trimester of pregnancy.

Methods: Screening of patients booking for antenatal care before 28 weeks of gestation by both 1,5-anhydro-D-glucitol and 75g oral glucose tolerance test. Monitoring of women with GDM or GIGT by both blood sugar series (BSS) and 1,5-anhydro-D-glucitol.

Main Outcome Measures: Cord insulin and C-peptide concentrations, deviation from idealised birth-weight. Conclusions: If the use of 1,5-anhydro-D-glucitol can be shown to identify those patients with GIGT or GDM, and reflect their glycaemic control then this simple test can be applied to patients with GIGT and GDM for screening and monitoring. (MD97123)

Feasibility of a PCR-Based Technique of Whole Genome Amplification to Screen for Allelic Loss in Cervical Intraepithelial Neoplasia

- WONG Yick Fu ◆ CHUNG Kwok Hung Tony ◆
 CHEUNG Tak Hong
- □ 1 November 1997
- CUHK Research Committee Funding

The objective of this research is to establish a methodology for polymerase chain reaction (PCR)-based amplification of whole genomes and to evaluate the clinical utility of this technique in screening for allelic loss in cervical intraepithelia neoplasia (CIN).

The carcinognesis of cervical cancer remains unclear. The identification of specific chromosome segments that are lost in cervical cancer and its precursor CIN can be used to identify potential tumour suppressor genes. Molecular genetic investigation of CIN is difficult because many of the lesions are very small and sometimes ill defined.

Recently, the researchers have established a collaboration with Professor G. Hampton's research team at the University of California, San Diego, USA and as a result, have established a method of primer extension pre-amplification (PEP) for whole genome amplification of human genomic DNA extracted from frozen tissue. This method may increase the scope for genotypic analysis because potentially, even single cells may provide sufficient template to perform multiple subsequent DNA analyses using PCR. In addition, allelic loss in invasive cervical cancer has been observed predominantly on chromosome 3,4,5, and 11. Therefore, they propose to assess the combined use of PEP and micro-dissection in the investigation of allelic loss on chromosome 3 in CIN. The information obtained from present study can help to identify regions of the chromosome that might harbor tumour suppressor gene(s) related to cervical cancer.

(MD97055)

Randomised Trial Comparing Radially Expanding Trocars with Conventional Cutting Tip Trocars

- **□** 4 September 1997
- Kojima Healthcare Asia Ltd.

Conventional trocars used in laparoscopic surgery can cause bleeding and incisional hernia, especially when the cutting tip trocars are used. A recent report suggested that the use of the new blunt radially expanding access system (REA System) may reduce such complications. The aim of the study is to examine potential benefits of using the REA system by comparing it with the conventional cutting tip trocar in a double blind and randomised manner. (MD97153)

MRI of the Post-Term Cervix and Induction of Labour

- ∠ YIP Shing Kai CHUNG Kwok Hung Tony CHAN Yu Leung (Diagnostic Radiology & Organ Imaging)
- ☐ 1 January 1997
- CUHK Departmental Funding

Analysis of Magnetic Resonance Images of the cervix to assess cervical changes and their association with induction of labour.
(MD96207)

Urodynamic Studies on Patients with Post-Partum Urinary Retention

- □ 1 December 1997
- CUHK Research Committee Funding

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. Pudendal nerve damage are readily assessed by measuring the motor conduction velocities in terms of pudendal terminal motor latency (PTML). This project sets out

to identify patients with post-partum urinary retention and to perform urodynamic studies and PTML measurements on them, and to compare these results with normal controls. As post-partum urinary retention is divided into overt and covert retention, the covert retention group will be identified by ultrasound estimation of the post-void residual bladder volume (PVRBV) of all patients after vaginal delivery. Patients with overt retention are readily identified by post-partum acute urinary retention requiring in-dwelling characterization. (MD97056)

A Collaborative Prospective Randomised Study of Oral Misoprostol and Intramuscular Syntometrine in the Management of the Third Stage of Labour

- ∠ YUEN Pong Mo NG Pui Shan TANG L. C.
 H.* CHEUNG Kai Bun
- ☐ 1 June 1998
- CUHK Departmental Funding

The use of prophylactic administration of parenteral oxytocics in the active management of the third stage of labour reduces the risk of post-partum haemorrhage by 40%. Syntometrine is the most commonly used preparation. It requires intramuscular injection. Misoprostol is an orallyadministered prostaglandin E1 analogue which has recently been found to be effective for induction of abortion, cervical priming and induction of labour. It is quickly absorbed orally and is a potent uterotonic A recent report suggested that oral misoprostol at a dose of 600mg is effective in preventing post-partum haemorrhage. The purpose of the study is to compare the efficacy and safety of oral misoprostol with intramuscular Syntometrine in the management of the third stage of labour. (MD97157)

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

Edition	Title/Investigators
1996-97	Methylation of p16 ^{INK4} Promoter in Gynaecologic Tumours (MD96126)
1995-96	The Effect of the Menopause on Plasma Concentrations of Lipoprotein (a) (MD95179)

Therapeutics)

- 1995-96 A Randomized, Controlled Clinical Trial (RCT) Involving Women Who Have Aborted Spontaneously: The Health, Social and Operational Cost Outcomes of Conservative and Routine Management Protocols (MD95079)
 - ∠
 ∠
 CHUNG Kwok Hung Tony LEE
 Tak Shing Dominic (Psychiatry) •
 HAINES Christopher John WONG
 Chung Kwong (Psychiatry)
- 1996-97 Prevalence and the Significance of DNA Replication Errors in Endometrial Cancer with a Geographic and Racial Comparison (MD96066)
 - ∠ CHUNG Kwok Hung Tony
 ◆
 WONG Yick Fu
- 1996-97 Postnatal Depression in Hong Kong Chinese (MD96014)
 - ∠
 ∠
 CHUNG Kwok Hung Tony LEE
 Tak Shing Dominic (Psychiatry) •
 LEUNG Yip Shing (Psychiatry) •
 NG Kee On* WONG Chung
 Kwong (Psychiatry)
- 1996-97 Measurement of Maternal Plasma Corticotrophin Releasing Hormone (CRH) in the Prediction of Abnormal Pregnancy Outcome (MD96067)
 - ∠ LEUNG Tse Ngong CHUNG Kwok Hung Tony
- 1993-94 Human Fibronectin in Ectopic Pregnancy (MD94002)
 - ∠ LOONG Ping Leung E. YUEN Pong Mo FUNG Yun Mei Hedy[#]
- 1993-94 Effects of Pentoxifylline on Acrosome Reaction in Human Sperm (MD94011)
 - ∠ LOONG Ping Leung E. CHIU Tak Yu Tony • IP Chui Ping (Lee Hysan Clinical Research Laboratories)
- 1996-97 Effects of MTAP Antisense Oligonucleotides on Chemosensitivity of Gynaecologic Cancer Cells *in vitro* (MD96069)
- 1996-97 Intrapartum Monitoring Using the Fetal Electrocardiogram (FECG) (MD96018)
- 1995-96 Alterations of p16^{INK4} Gene and Its Clinical Significance in Vulvar Neoplasia (MD95156)

- WONG Yick Fu CHAN Kwok Mei May (Anatomical & Cellular Pathology) • CHEUNG Tak Hong

1996-97 Comparison of Metabolic and Immunological Response after

Hung Tony

Abdominal and Laparoscopic Hysterectomy (MD96009)

∠ YUEN Pong Mo • ROGERS Michael Scott • SHORT Timothy Gordon (Anaesthesia & Intensive Care)

√ • LAM Wai Kei Christopher (Chemical Pathology)

∠ YUEN Pong Mo • ROGERS ROGERS ROGERS NOTE:

√ ← Company Note:

✓ ← Compa

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<P980202>, <P980466>, <P980830>, <P980847>, <P981011>, <P981651>, <P982475>

RESEARCH PROJECTS

Corneal Stem Cell and Amniotic Membrane

- ∠ LAM Shun Chiu Dennis LAU Tze Kin (Obstetrics & Gynaecology)
- □ 1 July 1997
- CUHK Departmental Funding

To investigate the safety, efficiency and visual outcome of corneal stem cell transplant and amniotic membrane transplant in patients with stem cell decreases of the eye. (MD97162)

Molecular Marker for Familial Adenomatous Polyposis (FAP) and Predictive Value of Congenital Hypertrophy of the Retinal Pigment Epithelium (CHRPE) in FAP

- LAM Shun Chiu Dennis PANG Chi Pui Calvin
 TANG Leung Sang (Chemical Pathology) •
 LAU Wan Yee Joseph (Surgery)
- □ 1 September 1997
- CUHK Research Committee Funding

Familial adenomatous polyposis (FAP) is an autosomal dominant precancerous condition characterised by the appearance of multiple adenomatous polyps throughout the entire colorectum. Almost all (100%) affected individuals will develop colorectal carcinoma from one or more of these polyps. The average age of onset of polyposis is 25year but the affected individual with hundreds of polyps may remain clinically asymptomatic. When clinical symptoms became apparent, about two-thirds of such patients would have already developed carcinoma of colon or rectum. **Prophylactic** colectomy is the preferred and possibly the only effective management for those who have developed

FAP is caused by mutations in a tumour suppresser gene called adenomatous polyposis coli (APC) gene located at chromosome 5q21-22. It comprises 15 exons with a 9kb RNA transcript that gives rise to a 312 kd protein product. Although over 700 somatic and germline mutations in the APC gene have been identified among Caucasian populations, information is available for the Chinese populations. For the mutations already identified, more than 98% of them are frameshift or nonsense mutations leading to the synthesis of a truncated protein. In FAP patients, the number of polyps is correlated with the location of APC mutations. For FAP patients with >5,000 adenomatous polyps, mainly frameshift mutations are found between codon 1255 and 1467. In FAP with number of polyps between 1,000 and 2,000, both frameshift and missense mutations are concentrated in the 5' half of the APC gene where

most germline mutations are located. In Caucasian populations, hot spot mutations have been identified for both germline and somatic APC mutations, codons 1061 and 1309 for the former and codons 1309 and 1450 for the latter. They are all in the 5' half of the gene and leads to production of a truncated APC protein. This APC region contains a dimerization domain and it probably gives rise to a dominant effect of the truncated mutant protein.

A retinal lesion, called congenital hypertrophy of the retinal pigment epithelium (CHRPE) is a benign condition found infrequently in normal individuals. However, multiple and bilateral CHRPE have been documented in 66-97% of patients affected with FAP. The variable prevalence of CHRPE may be attributable to the variation of assessment criteria for CHRPE in different studies. The other factor may be due to the genetic heterogeneity of FAP. It has been reported that the severity of CHRPE is dependent on the position of the mutation. Retinal lesions are almost always absent if the mutation occurs before exon 9, but are systematically present if occurs after this exon. Thus, the range of phenotypic expression observed among affected patients may arise in part from different allelic manifestations of APC mutation. There is, therefore, a need in a comprehensive characterisation of the APC gene in CHRPE and in the assessment of specific mutations in the APC gene to be used for definitive diagnosis of FAP.

Recently, the researchers have reported that in 11 Chinese FAP patients, clinical CHRPE is present in all of them. CHRPE lesions were also found in 9 out of 28 at risk relatives. Since 100% of all the FAP patients in their study have CHRPE, the genetic mutations in the Chinese may be different from that of the Caucasian. It would be worthwhile to investigate whether the genetic mutations in this group of patients are similar to that of the Caucasian counterpart.

CHRPE is the only known phenotypic marker for FAP. It can be easily identified and documented by a simple, cheap and non-invasive bedside ocular eye examination with the binocular indirect ophthalmoscope. Given the fact that it is a congenital condition, it is feasible to detect CHRPE at any time after birth. If they known the status of both the CHRPE and the APC gene in FAP patients, the predictive value of CHRPE in FAP could be estimated. Its value as an accurate phenotypic marker for FAP can then be estimated in the Chinese population. Regular colonoscopic examination for the presence of polyps in CHRPE positive individuals would safeguard prompt advice for prophylactic surgery to at risk individuals, who may otherwise present with late stage symptomatic colorectal carcinoma.

In addition to the practical applications, the identification of CHRPE has defined a subgroup of FAP patients who have an easily demonstrable marker. However, what this marker means in genetic

terms is as yet unknown. It would seem more than coincidence that this is the same marker found in FAP.

So far the researchers have more than 15 CHRPE families under their care, many of those are extended families. It is therefore of great interest and with good potential value for clinical applications to study the APC mutations in this group of patients. (MD97062)

Diagnostic Kits for Early Detection of Genetic Eye Diseases for Blindness Prevention and Genetic Counselling

- ∠ LAM Shun Chiu Dennis PANG Chi Pui Calvin
- ☐ 1 February 1998
- ❖ Industrial Support Fund, Industry & Technology Development Council

Blindness and visual impairment is a serious problem in both developed and developing countries. The human eye is developed from the neural and surface ectoderm through processes which are complex and interactive. These biological processes are governed by genes where abnormalities can lead to common blinding eye diseases like glaucoma and age-related macular degeneration (ARMD). Many gene defects are modulated by external factors for clinical expressions and prevention may be possible if the exact gene defect is known, for instance in glaucoma and ARMD. However, detailed information of these genetic defects in Chinese is lacking.

The researchers propose to establish a data-base for genetic defects of eye disorders in the Chinese population in Hong Kong and to establish laboratory protocols for genetic detection and prediction of eye disorders and subsequent diseases. They will carry out genetic analysis of patients suffering from the targeted eye diseases and their family members. For each study subject, only 10ml of blood is required for the analysis utilising biotechnology such as polymerase chain reaction (PCR) and single strand conformation polymorphism (SSCP). The data will provide information for early diagnosis and prediction of eye disorders, and will benefit patients for disease prevention. Many at-risk individuals may avoid visual deterioration and even blindness by for appropriate precautions eye protection. Prevention is the best cure and results in lesser patients, which means saving for the Health Authorities. The information will also enable them to establish a proper genetic counselling for patients and their family members concerned. (MD97092)

Ultrastructural Studies of Rod and Cone Degeneration in Transgenic Mouse and Pig Models of Retinitis Pigmentosa

- ∠ LAM Tim Tak TSO Mark On Man WONG Fulton*
- □ 1 December 1997
- CUHK Mainline Research Scheme

Retinistic Pigmentosa (RP) is a blinding disease that affects 1 in 4000. The patient experiences night blindness initially, subsequent and gradual loss of peripheral and central vision, and ultimately blindness over a period of decades owing to the loss of rod and cone photoreceptors of the retina. Currently there is no treatment for this blinding disease. In spite of recent advances in molecular genetics, there is limited information on the pathogenesis of RP due to the lack of appropriate animal models of RP that have a large number of cone photoreceptors. The long-term objective of this proposal is to delineate the pathogenetic pathways of rod and cone degeneration in RP for development of a rational approach to therapy. Specifically, the researchers propose to examine and compare the ultrastructural changes at various time points during early, intermediate and late phases of retinal degeneration in transgenic pigs as well as transgenic mice with Pro347Leu or Pro347Ser mutation in the visual signal transduction protein rhodopsin. Animals carrying the Pro347Leu mutation in rhodopsin will show rapid retinal degeneration while the Pro-347Ser mutation will give a slower degeneration corresponding to human RP with similar mutations. In addition, the transgenic pig is the only animal model of RP available with a defined genetic defect and a close to human retinal rod to cone ratio in the retina. This is a part of a multicentered collaborative study to characterize the transgenic pigs and to understand the basic mechanisms of rod and cone degeneration in RP. (MD97025)

Therapeutics for Apoptotic Loss of Retinal Neurons in Glaucoma

- ∠ LAM Tim Tak TSO Mark On Man
- 1 January 1998
- * Research Grants Council

Glaucoma refers to a group of diseases showing cupping and atrophy of the optic nerve head, and loss of retinal nerve fibers and ganglion cells. The mechanism of this neuronal loss is not known while both medical and surgical management targets lowering of intraocular pressure (IOP). There is no established modality in rescuing the neuronal loss the source of visual impairment. The goals of this current proposal are to examine (1) the roles of apoptotic cell death; and (2) the effectiveness of modulators of excitotoxicity or apoptosis in preserving the retinal neurons in a new rat model of chronic glaucoma. Chronic elevated IOP will be

induced in rats by cauterizing the episcleral limbal veins. IOP levels, fundus appearance, histologic changes of the optic nerve head and morphometric changes of retinal ganglion cells and inner retinal thickness will be followed. Apoptosis will be assessed by agarose gel electrophoresis of retinal chromosomal DNA, *in situ* TdT-mediated biotin-dUDP nick end labeling (TUNEL), enzymelinked immuno-sorption assay (ELISA) of cleaved nucleosomes and ultrastructural studies. Modulators of the excitotoxic or apoptotic pathway(s) will be evaluated for their effectiveness in ameliorating the glaucomatous changes. (CU97639)

The Hong Kong Study on Visual Disability in the Aged Population (SAVD Study)

- MICHON John
 LAU Tak Fai Joseph (Centre for Clinical Trials & Epidemiological Research)
- ☐ 1 February 1998
- ❖ World Health Organization

The primary objective of the SAVD study is to calculate the prevalence of visual disability in adults over 60 years of age in Hong Kong. Current life expectancy is 81 years for women and 77 years for men and the proportion of elderly in the population continues to increase. The cohort over age 60 is expected to reach 15.3% of the general population by the year 2000 and that over 75 years to attain 4.4%. Because eye disease and subsequent visual disability increases as a function of age this may constitute a major public health problem. To date there have been no epidemiological studies of eye disease in Hong Kong. This lack of data is an impediment to meet the eye care needs of the population, particularly in the area of preventable visual loss. In order to effectively plan preventive and therapeutic intervention programs for this group there must first be an accurate measurement of the problem. The SAVD study seeks to perform such a measurement. Secondary objectives include examination of individuals who meet visual disability criteria in order to ascertain the cause of the visual disability. The prevalence of cataract surgery and the visual acuity outcomes in this population will also be determined. In addition, the researchers will assess the quality of life and visual function as perceived by the visually disabled. The SAVD study may therefore serve a broader role in health care planning in Hong Kong. The results will have implications for ophthalmologist, other physicians, allied health personnel, health administrators, and the public at (MD97128)

Interactions between Smoking, Diabetes Mellitus and Genes Affecting Lipoprotein Coronary Heart Disease Risk Factors

- ☐ 1 October 1997
- Research Grants Council

It is known that genes have a major effect on cholesterol levels. Lipid levels are strongly related to the risk of developing blood vessel disease, especially coronary disease (CHD). The researchers will assess the contribution of selected genes to differences in cholesterol levels among Hong Kong Chinese, and look for interactions with other factors known to affect lipid levels. This will help to know who should have lifestyle modification and lipid-lowering therapy, both of which reduce risk. They will study blood from subjects in the Hong Kong Risk Factor Prevalence Study, on whom there are extensive data about diabetes mellitus (DM), smoking habit, alcohol consumption, blood pressure, body weight, waist-hip ratio, and lipid biochemical values. The researchers will study a polymorphism -75bp from the start of the transcription site in the apolipoprotein A-I gene and in the lipoprotein lipase gene a HindIII polymorphism in intron 8, the Asp9Asn and the Asp291Ser mutations in the lipoprotein lipase gene. Interactions will be sought with smoking habit, diabetes mellitus and obesity. Smoking and diabetes mellitus are well established and strong risk factors for coronary heart disease; genetic factors may help explain why certain individuals with these risk factors develop clinical disease while others do not. (MD97172)

Study of the Enzymic Properties of Lipoprotein Lipase (LPL) Variants and their Effects on Hyperlipidaemia

- ∠ PANG Chi Pui Calvin TOMLINSON Brian (Medicine & Therapeutics)
- ☐ 1 March 1998
- CUHK Research Committee Funding

Lipoprotein lipase (LPL) is a multifunction enzyme and is rate-determining in lipoprotein hydrolysis. LPL deficiency is a common disorder, incidence about 1:500 in most populations, and is particularly prevalent in diabetes mellitus and coronary artery disease. The human LPL gene spans 30 kb at chromosome 8 p22 comprising 10 exons. About 50 LPL mutations causative for LPL deficiency have been reported, leading to hypertriglyceridaemia, reduced HDL-cholesterol and variable clinical consequences. In this study on the genetic basis of hypertriglyceridaemia in Chinese, the researchers have identified several novel missense and nonsense mutations in the LPL gene. They caused variable decreases in post-heparin LPL activity. Carriers of these mutations have different levels

hyperlipidaemia and clinical features. The enzymic defects and clinical consequences of these LPL mutations which occur only in Chinese are intriguing and complex. The researchers plan to study these LPL mutations by in vitro mutagenesis and expression to explore their enzymic properties. They will prepare LPL protein variants carrying these naturally occurring mutations by recombinant DNA and cell culture techniques. Enzymic properties including catalytic activities, kinetic constants and conformational behaviour will be determined by spectrophotometric, differential electrophoresis and protein truncation techniques. Results of this proposed study will be significant for understanding the genotype-phenotype relationship of LPL variants. Important information of the effects of LPL mutations on its enzymic properties will be obtained. (MD97113)

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

Edition	Title/Investigators			
1995-96	Apoptosis of Photoreceptor Cells (CU95628) ∠ LAM Tim Tak • TSO Mark On Man			
1996-97	Mechanism of Retinal Excitotoxicity (MD96078) ∠ LAM Tim Tak			
1996-97	Neuronal Rescuers for Apoptotic Degeneration of Retinal Ganglion Cells (CU96673) ∠ LAM Tim Tak • TSO Mark On Man			
1995-96	A Pilot Study in the Use of Long-acting Medical Inert Gases in Improving the Success of Glaucoma Surgeries (MD95203) LEE Wing Hong • LAM Simon R.*			
1995-96	The Creation of a Community-oriented Preventive Eye-care Programme, the Hong Kong Eye Care Net (MD95253) ∠ LEE Wing Hong • CHAN Guy Hugh [#]			
1996-97	Occupational Eye Injuries in Hong Kong			

MICHON John

- 1995-96 Genotyping of the Low-Density Receptor
 Defects in Familial
 Hypercholesterolaemia in Hong Kong
 (CU93618)
 - ∠ PANG Chi Pui Calvin MAK Ying Tat* (Chemical Pathology) MAK Wing Lai Tony* (Chemical Pathology) TOMLINSON Brian (Medicine & Therapeutics) SANDERSON John Elsby (Medicine & Therapeutics)
- 1996-97 The Lipoprotein Lipase Gene in Hyperlipidaemia (MD96146)
 - ∠ PANG Chi Pui Calvin
 ▼ TOMLINSON Brian (Medicine & Therapeutics)
- 1996-97 Biochemical and Genetic Markers for Breast Cancer (MD96147)
 - ✓ PANG Chi Pui Calvin KING
 Walter Wing Keung (Surgery)* •
 TANG Leung Sang (Chemical Pathology) LAW Lap Kay
 (Chemical Pathology)
- 1996-97 Molecular Genetics of Alzheimer Disease (MD96148)
 - PANG Chi Pui Calvin NG Ho
 Keung (Anatomical & Cellular
 Pathology) WOO Jean (Medicine
 & Therapeutics)
- 1996-97 Investigation of the *BRCA1* Gene in Breast Cancer (MD96173)
 - ∠ PANG Chi Pui Calvin KING Walter Wing Keung (Surgery)
 ✓ TANG Leung Sang (Chemical Pathology) CHOY Kwong Wai (Chemical Pathology) LAW Lap Kay (Chemical Pathology) YEO W
 ✓ LAM Ping Kuen (Surgery) SUEN Wang Ming Michael (Anatomical & Cellular Pathology) JOHNSON Philip James (Clinical Oncology) HJELM Nils Magnus (Chemical Pathology)

RESEARCH OUTPUTS AND PUBLICATIONS

- A Retrospective Analysis (MD96004)

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RESEARCH PROJECTS

A Cellular and Molecular Study of the Potential Application of Growth Factors in the Enhancement of Tendon Healing Following Sports Injury

- ∠ CHAN Kai Ming LEE Ka Ho Kenneth (Anatomy) CHAN Pui (Hong Kong Centre of Sports Medicine & Sports Science) FU Sai Chuen Bruma QIN Ling CHENG S. H.*
- □ 1 September 1997
- CUHK Research Committee Funding

This study has demonstrated that the selected growth factors, basic fibroblast growth factor (bFGF) and platelet-derived growth factor isoform B (PDGF $_{\rm BB}$), affected the healing patellar tendons in cellular activities, extracellular matrix composition and also the mechanical properties.

An in vitro model of wound closure was established using rat patellar tendon derived fibroblasts. Both bFGF and PDGF_{BB} significantly increased the extent of wound closure as well as the proliferation of the However, PDGF_{BB} only, stimulated fibroblasts. chemotactic movement of the fibroblasts. In vivo, the researchers established a gap wound healing model by creating a window injury in the middle of the rat patellar tendon. The natural healing process of patellar tendon was characterized into three stages; inflammation, proliferation and maturation. morphology of the healing tendons was close to normal at three months post-injury. However, at six months post-injury, the ultimate stress restored to only 70% of the control. The pyridinoline crosslink overshot the control at one month post-injury while hydroxyproline did not restore significantly. Moreover, pyridinoline was better hydroxyproline in associating with the ultimate stress of the healing patellar tendon.

Two delivery system of growth factors were employed, the alginate gel and micro-syringe injection. The effects of bFGF and PDGF_{BB} supplementation in the healing patellar tendon have been examined histologically, biochemically and mechanically. Both growth factors stimulated fibroblast proliferation at the central wound. Besides, bFGF stimulated collagen type III expression at the central wound area while PDGF_{BB} elevated the extracellular expression of collagen type I. Moreover, a simultaneous decrease in pyridinoline and ultimate stress at 1 week post-injury was noted in patellar tendons being supplemented with 1µg of bFGF in alginate, but it was not noted when delivering bFBF by injection. On the other hand, injection of 1µg of $PDGF_{BB}$ on the 7^{th} day post-injury, induced an increase in both pyridinoline and ultimate stress of the healing patellar tendon. In another word, the effects of growth factors in tendon healing were also

affected by the mode of delivery system, the time for delivery and the dosage of the growth factors, which are factors to be considered before applying this knowledge to clinical applications. (MD97057)

Longitudinal Changes in Trunkal Balance after Selective Fusion of King's 2 Curves in Adolescent Idiopathic Scoliosis

- ∠ CHENG Chun Yiu Jack FREZ R* WONG Eric* (Centre for Clinical Trials & Epidemiological Research)
- □ 1 July 1996
- CUHK Departmental Funding

Selective fusion of the thoracic curve in King's 2 curve has been reported to be able to produce good results and arrest of further deterioration of the lumbar curve in selected cases. Detail quantitative analysis of the longitudinal changes and correlation between various clinical and radiological parameters were not readily available in the literature. retrospective study of the longitudinal changes of the trunkal balance in King's 2 curves treated with selective posterior spinal fusion would be conduced. The objectives of this study aimed to determine the effect of selective fusion and the end level of fusion in King's 2 adolescent idiopathic scoliosis on the trunkal balance and the behavior of the unfused lumber curve. Patients with of King's 2 adolescent idiopathic scoliosis treated with Harrington rod and segmental spinous processes wiring in a 10 years period will be analysed clinically and radiologically at preoperative, immediate post-operative period, six months, one year, three years and at final follow up. (MD96201)

Coraline Hydroxyapatite as a Bone Substitute to Enhance Spinal Fusion

- □ 1 September 1996
- CUHK Departmental Funding

Posterior spinal fusion (PSF) is the most common procedure associated with many posterior spinal surgeries with or without instrumentation. Decortication and autografts has been used as the golden standard to achieve bony fusion. Harvesting autologous bone graft for PSF requires an additional operative procedure, which adds considerable Coraline hydroxyapatite (HA) is morbidity. commercially available and has been used successfully as an alternative to autograft in bone defect filling. Aim of the present study was to evaluate the effects on fusion process when coraline HA was used as the graft substitute and to compare the results with autologous bone graft in an experimental PSF procedure in rabbit spine model.

The specimens would be retrieved different intervals and analyzed with microradiography, peripheral quantitative computer tomography, sequential bone labelling and bone histomorphometry. The results of this study would be used to analyse whether HA bone substitute is effective in enhancing spinal fusion and whether the addition of bone marrow can further enhance spinal fusion. (MD96200)

Patterns Clinical of Presentation of Congenital Muscular Torticollis in Infants and Children

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 - TANG S. P.* LEE Sandra*
- □ 1 July 1997
- CUHK Departmental Funding

The reported incidence of congenital muscular torticollis (CMT) varied from 0.45% to 1.9% were mostly based on small numbers of mixed groups of patients over long period of time without proper definition of the type, severity and assessment method. The main objective of the present study was to define the clinical presentation patterns and characteristics of the CMT in infants and children using standard clinical subgrouping and assessment methods.

All patients with CMT seen consecutively over a 12 years period in the researchers' Torticollis Clinic will be analyzed in detail with respect to the many standard parameters recorded. The clinical presentations would be divided into three subgroups of sternomastoid tumor group, muscular torticollis group and postural torticollis group. For each group correlation with the incidence of breech presentation, difficult labor, hip dysplasia, tumor size, degree of head tilt, craniofacial asymmetry and limitation of passive rotation and side flexion would be done. Further correlation of all the parameters with the outcome of treatment would be studied. (MD97138)

Quantitative EMG on Paraspinalis Muscles in **Adolescent Idiopathic Scoliosis**

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- □ 1 July 1997
- CUHK Departmental Funding

There are a number of theories on the etiology and pathogenesis of idiopathic scoliosis. Aim of the present study was to perform quantitative electrophysiological analysis of motor units of paraspinalis muscles of patients with idiopathic scoliosis for evidence of asymmetry.

A group of randomly selected girls aged 11-15 years with adolescent idiopathic scoliosis will be included in the study. Patients would be subdivided into two groups. Group 1 with Cobb's angle of 30 or less and group 2 with Cobb's angle of more than 30 EMG would be performed on the paraspinalis muscles of both sides at level of maximum curvature by using concentric EMG needles and Nicolet Viking IV EMG equipment with standard filter setting. Mean motor unit duration, mean unit amplitude and number of phrases of motor units of paraspinalis muscles would be measured. Difference in all these parameters on the concave side versus convex side would be studied for both groups.

(MD97139)

Abnormal Somatosensory Evoked Potential in Adolescent Idiopathic Scoliosis - Where is the Site of the Abnormality?

- ∠ CHENG Chun Yiu Jack GUO Xia SHER Hing Leung Andy (Lee Hysan Clinical Research Laboratories)
- 1 July 1997
- CUHK Departmental Funding

SEPs is a reliable test that can provide an objective functional assessment of the somatosensory pathway. The researchers previous evaluation of posterior tibial nerve somatosensory evoked potentials (PTN-SEPs) conducted on adolescent idiopathic scoliosis (AIS) patients has demonstrated an overall incidence of 11.6% with abnormal somatosensory cortical evoked potentials. The aim of the present study was to further define the level of the abnormality in the central somatosensory pathway.

A series of AIS patients with abnormal delayed latency of PTN SEPs would be studied again with evoked potentials recorded at the popliteal fossa, the cervical level C4-C6, and the scalp at an interval of 4 to 28 weeks. The level of functional delay in AIS patients with abnormal PTN-SEPs would be determined to see whether they appeared superior or inferior to the cervical level. The MRI at the corticocervical junction would be further studied to correlate with the SEPs to provide a pathoanatomical basis for any abnormal SEPs, which may point to a subclinical hidden group of central neurogenic scoliosis in the heterogenous group of AIS. (MD97140)

Correlation between Curve Severity, Somatosensory Evoked Potential and MRI in **Adolescent Idiopathic Scoliosis**

CHENG Chun Yiu Jack • GUO Xia • SHER Hing Leung Andy (Lee Hysan Clinical Research Laboratories) • CHAN Yu Leung (Diagnostic Radiology & Organ Imaging) • METREWELI Constantine (Diagnostic Radiology & Organ Imaging)

- □ 1 July 1997
- CUHK Departmental Funding

There are increasing reports on the association of idiopathic scoliosis and tonsillar herniation from MRI. The actual link between tonsillar herniation and IS is however not clear. Growing children and adolescents with disorders in somatosensory pathway are known to be more susceptible to the development of scoliosis than healthy individuals. A prospective study on patients with adolescent idiopathic scoliosis (AIS) of different clinical severity using whole spine magnetic resonance imaging (MRI) somatosensory evoked potentials (SEPs) with the main objective to detect and correlate the presence of detected structural disorders including syringomyelia and tonsillar herniation and SEPs detected functional disorders in the hind brain and spinal cord in AIS patients. The results would also be correlated with the clinical severity of the curve measured by Cobb's angle. (MD97141)

Application of Bone Morphogenetic Protein-Hydroxyapatite Composite Implant in Un-Decorticated Posterior Spinal Fusion

- ∠ CHENG Chun Yiu Jack GUO Xia LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) MAK Arthur K.F.* ROSIER Randy N.*
- □ 1 November 1997
- * Research Grants Council

Spinal deformities and degenerative diseases are very common conditions in Orthopaedics many of which would require surgical stabilization with instrumentation and posterior spinal fusion (PSF). Decortication of the vertebral lamina and other posterior structures followed by implantation of autologous bone grafts harvested from the patient's own iliac crest are standard procedures in classic PSF. However there are multiple inherent problems and disadvantages associated with these procedures. Eighty rabbits would be used for this study with the following main objectives:

- (1) To assess the effect of recombinant human bone morphgenetic growth factor 2 (rhBMP2) on decorticated and non-decorticated PSF.
- (2) To assess the effect of hydroxyapatite and (rhBMP-2) composite bone substitute material (HA-TCP/BMP) on decorticated and nondecorticated PSF.
- (3) To evaluate and establish a new nondecorticated surgical approach for PSF

augmented with the proposed composite bone substitute.

The outcome of this project will shed light on the role of decortication as well as the biological efficacy of osteoinductive growth factor in promoting bony fusion of the spine. This new approach would eliminate the additional surgical procedure needed to decorticate and to obtain autologous tissue. It would provide unlimited supply of bone substitutes and reduce significantly the associated complications at the donor site, simplify the operation, shorten the operation time and reduce amply the intra- and post-operative blood loss. (CU97669)

Injectable Hydroxyapatite-Tricalciumphosphate for Orthopaedic Use

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

The aim of the study is to develop an injectable pastelike material with chemical and physical characteristics similar to the mineral phase of bone, by investigating the effect of varying composition of the granules on bone ingrowth. The injectable material is expected for (1) filling of osseous defect; (2) mechanical support of unstable fractures; and (3) augmentation of osteoporotic bone to increase its stiffness.

Fifty-four adult rabbits will be randomly divided into HA-TCP granules in 9 different 9 test groups. combination of composition and size will be injected into segmental bone defect in rabbit's tibial shaft. Postoperatively, weight bearing will be permitted as tolerated. The animals will be observed for 10 weeks before sacrifice. The new bone formation in defect will be observed by plain X ray film, dual-energy Xabsorptiometry (DEXA), quantitative computertomography (QCT), and polychrome sequential labeling. A quantitative estimate of the amount of new bone formation in defect of each group will indicate the best combination of size and composition of the injectable granules. (MD97058)

Scoliosis and Abnormal Postural Balance

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- ☐ 1 April 1998
- CUHK Departmental Funding

Scoliosis is a three dimensional deformity of the spine including lateral curvature and axial rotation. Among the various causes the most common group is adolescent idiopathic scoliosis which typically affection the growing adolescent of the age of 10 to

16. Poor postural balance and equilibrium has been reported. With the advanced gait analyses system it is now possible to study these quantitatively. This study would be done in stages to address the following questions: Stage I: Do the scoliosis patient differs from the normal control group in terms of the measurable gait parameters in the study? Are there differences in the gait study between the Scoliosis patient with or without demonstrable SEP and Or MRI abnormalities? Can researchers predict the underlying neurological imbalance by doing a gait analysis? Stage II: Effect of site of scoliosis, Severity of scoliosis and Stage III: How does the brace treatment and surgical treatment affects these measurable gait parameters? (MD97137)

Quantitative Studies of P-Glycoprotein and Related Biochemical Markers to Monitor Drug Resistance in Malignant Musculoskeletal Tumours

- □ 1 October 1997
- CUHK Research Committee Funding

Musculoskeletal tumours constitute a major histogenetic class of neoplasms with a high malignant potential. Multidrug chemotherapy is the mainstay of treatment for these tumours. However, multidrug (MDR) often limits resistance successful chemotherapy. MDR is mediated by overexpression of the mdr 1 gene product Pglycoprotein which exhibits drug efflux from the tumour cells, as well as by some not yet wellcharacterised mechanisms. It is of clinical importance to correlate the changes in the expression of Pglycoprotein and/or other biochemical markers in the tumour biopsy samples to monitor drug resistance and malignancy. In previous study, the researchers have established the adriamycin binding assay in osteosarcoma tissue as well as serum bone-specific alkaline phosphatase assay to monitor the progress of chemotherapy and relapse in patients with osteosarcoma. In the present project, they aim to use molecular biological techniques to examine the possible changes of mdr 1 gene, antioxidant enzymes and alkaline phosphatase gene, as well as their protein products in tumour tissue samples before and after chemotherapy. Human osteosarcoma cell lines with MDR shall be established and the invasive potential of these MDR tumour cell lines shall be examined. (MD97061)

Study of Relationship between Femoral Neck Bone Density and Failure of Screw Fixation in Femoral Neck Fractures

- ∠ LEUNG Kwok Sui WONG Chin Hong* LI
 Kit Yee*
- □ 23 June 1997
- CUHK Departmental Funding

Purpose: A prospective study of the bone mineral density of patients with fracture neck of femur was carried out at Prince of Wales Hospital from February 1997 to June 1998. The aim was to determine the relationship of bone mineral density and the success rate of simple screw fixation in femoral neck fractures.

Method: A total of 36 patients aged 60 and above with 36 fractures were scanned. The average age was 77.93 years. The scanning were done on the contralateral non-fractured hips. Readings were obtained at 2 weeks, 3 months and 6 months.

Results: The mean BMD for the femoral neck was 0.500g/cm^2 ; the mean BMD of the greater trochanter was 1.647 g/cm^2 and the mean BMD for the Ward's triangle was 0.385 g/cm^2 . The BMD readings for the female group were more than 0.1 g/cm^2 lower than the male group.

There were one non-union and two mechanical failures. The patient with non-union had BMD's lower than the mean. The cases with mechanical failure were both type IV fractures. Both have BMD's lower than the mean values. The fixations failed despite satisfactory reduction.

Conclusion: In displaced fractures, BMD readings might help to sort out patients who are likely to fail with simple screw fixations. (MD96197)

Prospective Study and Review of Intramedullary Nailing in Fractures of Humerus

- ∠ LEUNG Kwok Sui WONG Chin Hong* LI
 Kit Yee*
- □ 23 June 1997
- CUHK Departmental Funding

Background: Humeral fracture is a commonly encountered injury in clinical practice. Various methods of treatment have been used. All of these methods have yielded different results. Complication includes non-union, malunion, unsightly scar and stiffness of shoulder joint. Intramedullary nailing of tibial and femoral fractures is a well-established method of fixation worldwide. Intramedullary nailing allows rigid fixation without excessive soft tissue trauma.

Intramedullary nailing of humeral fractures have been practiced for many years. The method of fixation has not been popular due to frequent complications. These include difficulty with nail insertion, unstable distal locking, nonunion and implant failure. Stiffness

of shoulder joint is by far the most troublesome complication.

The aims of this study are:

- To identify the factors that cause the complications in humeral intramedullary nailing

 rotator cuff response, anatomical factors, antegrade and retrograde insertion.
- (2) To improve the design of the humeral locking nail
- (3) Proposal for better humeral nail insertion technique

Methods:

- (1) Review of outcome of various surgical treatment methods of humeral fractures. Case study in different hospitals.
- (2) Assessment of treatment using various humeral nails design including literature search, clinical review and prospective study with emphasis on Siedel nail and AO flexible nail.
- (3) Anatomical study of Chinese humeri radiological study and dissection to identify the causes of difficult insertion.
- (4) Clinical assessment of the degree of shoulder stiffness.
- (5) Histological correlation in patients with shoulder stiffness.
- (6) Biochemical correlation in patients with shoulder stiffness.
- (7) Animal model -articular response of the marrow content/cartilage injuries.

(MD96198)

Fixation of Radial Neck Fracture Using Forked Plate

- ∠ LEUNG Kwok Sui WONG Chin Hong* LI
 Kit Yee*
- □ 23 June 1997
- CUHK Departmental Funding

Introduction: Treatment of displaced radial neck fractures is difficult, especially for types II and III fractures (O' Brien 1965). The Department of Orthopedics and Traumatology described a method of internal fixation using a modified forked-plate in 1989. From 1986 to 1996, 17 radial neck fractures were fixed using this method. This study aims to assess the functional outcome of this treatment modality.

Methodology: A total of 14 patients were available for assessment. The patients were assessed for range of movement, valgus and varus stability and severity of pain. Elbow and radiocapitullar X-rays were assessed.

Results: Average follow-up period of 4.6 years. The patients' ages ranged from 15 to 49. Flexion loss was 0 to 60 degrees with a mean of 30 degrees. Extension loss was from 0 to 15 degrees with a mean of 6 degrees. Pronation loss was up to 45 degrees.

Supination loss was up to 20 degrees. No avascular necrosis of radial head was noted.

Discussion and Conclusion: The forked-plate was a safe fixation method for difficult radial neck fractures. The fixation method has been particularly useful when here is concomitant radial head fracture necessitation operative reduction. The fixation was stable enough to allow immediate mobilization. An excellent range of movement could be preserved post operatively.

(MD96199)

The Study of Bone Ingrowth and Extraction of the Hamburg Humeral Nail

- LEUNG Kwok Sui CHEUNG Ngai Man •
 CHONG Wai Sing CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)
- □ 1 July 1997
- Howmedica International

Intramedullary nail fixation is the treatment of choice for long bone fractures. In the design of a better nail, flexibility of the nail is one of the most important mechanical properties in promoting fracture healing as well as in the minimising complications during surgery. The researchers have designed a new nail which offers higher degree of flexibility. flexibility of the new nail comes with the special configuration of the troughs on the surface of the nail. In the present study, they are going to study the bone ingrowth into these troughs during fracture healing. The study includes the implantation of the new nail into the femora and tibiae of Chinese mountain goat. Bone ingrowth is studied with histological studies as well as biomechanical study of pull out force. The results will help them to determine the degree of bone ingrowth into these newly designed nail and hence the potential complication in nail removal. (MD97014)

A Study of Physeal Retardation to Osteosarcoma Growth: Its Significance in Clinical and Basic Studies in Tumour Spread

- ∠ 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
- ☐ 1 September 1997
- CUHK Research Committee Funding

Osteosarcoma is the commonest primary malignant tumor of bone and it commonly affects children and young adults. This tumor is usually fatal, only 50% of those affected are likely to survive 5 years or longer. Surgery and chemotherapy are the main treatment. Radical surgery such as amputation does not improve

survival as compared to limb salvage surgery which is the current trend of management. However, limb salvage operation is feasible only if the tumor spread is limited. It has been a common observation that despite aggressive tumor growth, the spread of osteosarcoma in bone is limited by the physeal growth plate cartilage in children. Osteosarcoma cells almost never invade the joint cartilage and transarticular spread is extremely rare in the most aggressive tumors. The researchers postulate that cartilaginous tissue may actively inhibit tumor growth and spread by providing unfavourable conditions for tumor cells and inhibiting the sprouting of new blood vessels required for tumoral spread. This project is designed to investigate the effect of physeal cartilaginous tissue on osteosarcoma cell growth and spread by studying the chondrocyte culture in vitro. The results of this study will help clarify the inhibition mechanism cartilaginous tissue on osteosarcoma cells and could lead to isolation of humoral factors that can be applied clinically to control tumor growth and spread. The purification and the production of such factor(s) will be then future project in the second stage. It will have therapeutical significance in treating the primary as well as the metastatic osteosarcoma clinically. (MD97059)

A Comparative Study of the Mechanical and Histological Properties of Bone to Bone Union and Bone to Tendon Healing

- ∠ LEUNG Kwok Sui QIN Ling CHONG Wai Sing
- □ 1 October 1997
- * ASIF Research Commission

The bone-tendon junction is a complex structure and injuries are not uncommon. Treatment protocols for these injuries are diversified and lack an underlying scientific basis. This study aims to investigate the biological and mechanical aspects of healing in bone (BB), bone to tendon (BT) and tendon to tendon (TT) fixation models using Chinese goat as an animal model. The researchers hypothesize that BB healing is better than the BT or TT healing. Whenever possible, fracture healing should be achieved. In the previous pilot study with rabbit, they have demonstrated that BB healing is superior to other forms of healing both histologically biomechanically. It is hope that from the present study with goat patellar and patellar tendon as the better experimental model, they may able to confirm that the BB biological healing with a sound surgical technique would be histologically and mechanically superior to BT or TT repair. (MD97015)

Identification of Fast Bone Losers Measured with the Most Accurate pQCT (Densiscan 2000) and Specific Bone Turnover Biochemical Markers

- ∠ QIN Ling CHENG Shuk Han CHAN Kai Ming NEFF M.*
- □ 1 October 1997
- CUHK Research Committee Funding

The prevalence of osteoporosis among elderly Hong Kong Chinese, as evidenced by osteoporotic fractures and medical costs, is high. Considering that the proportion of elderly people in Hong Kong is increasing and a highly urbanised population. The researchers propose to use the most accurate peripheral quantitative computed tomograph (pQCT)-Densiscan 2000 to conduct a non-invasive separate measurement of cortical and trabecular bone in a true bone mineral density (BMD) in g/cm³ in women aged of 45-56. The newly available pQCT technique in the CHUK will provide local normative date in women aged of 45-56 for the first time and enable them to identify fast bone loser population with a short period of time, i.e. within 0.5-1 year for effective prevention and treatment of osteoporosis. The BMD values will then be correlated with the most commonly used biochemical markers of bone formation (bone specific alkaline phosphtase) and resorption (urinary pyridinium cross-links) so as to complementary information provide assessment of osteoporosis. It is also hoped to identify the special patterns of biochemical markers in the population of fast bone losers for a costeffective biochemical assessment of osteoporosis. (MD97060)

A Comparative Study of the Mechanical and Histological Properties of Bone to Bone Union and Bone to Tendon Healing - A Goat Model

- WONG Wan Nar Margaret QIN Ling ●
 LEUNG Kwok Sui ZHANG Yuanting (Electronic Engineering)
- ☐ 1 October 1997
- * Research Grants Council

The bone-tendon junction is a complex structure and injuries are not uncommon. Treatment protocols for these injuries are diversified and lack an underlying scientific basis. In the first part of the present project, the researchers propose to investigate the biological and the mechanical aspects of healing three models where the tendon-junction injuries are repaired with bone to bone (BB) fixation, bone to tendon (BT), or tendon to tendon (TT) fixation. The patellar tendon-patella unit of the Chinese goat will be used as the animal model. Serial histological studies will be used to measure the healing phases and outcomes in these three models. Special emphasis will be made on the

regeneration of the normal collagen fibres and the reestablishment of the normal tendon-bone junction structure in the tendon-bone repair model. Mechanical tests will be carried out to compare the difference in the mechanical properties of the three healing models at different stages. In a second phase of the study, several surgical methods of BT repair will be designed including preserving the fibrocartilage zones of the BT junction, reattaching the tendon in a bony slot, and using autogenous cartilage as interpositional material for restoration of physiological BT junction compared with the direct BT data obtained form the first part of the study. The ultimate goal of the study is to find out the best method for the re-establishment of the tendon-bone interface after injury.

The clinical significance of this project is to establish a surgical technique to facilitate the regeneration of the normal bone-tendon junction in post-traumatic repair. The improvement in the surgical treatment of the tendon-bone repair will facilitate postoperative rehabilitation, shorten period of immobilisation of the joints, allowing early mobilisation and weight bearing exercise which lead to early regain of function after injury. The finding will also be important to other reconstructive surgery for non-trauma conditions. (CU97668)

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

Edition <u>Title/Investigators</u>

- 1995-96 Physiotherapeutic Management of Osteoarthritic Knee Pain (MD95231)
 - ∠ CHAN Kai Ming CHAN C. H.* •
 CHEING Gladys* HJELM Nils
 Magnus (Chemical Pathology)
- 1996-97 Chinese Herbal Medicine in the Management of Exercise Injury Muscle Fatigue (MD96129)
 - ∠ CHAN Kai Ming LEE Yuen Lun •
 LI Ming BUT Paul Pui Hay
 (Biology) QIN Ling LI Jing Xian
 (Sports Science & Physical Education)

 ∠ CHAN Kai Ming LEE Yuen Lun •
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- 1996-97 The Effect of Vastus Medialis Strength and Tibial Tuberosity Position on Patellar Tracking and Patellofemoral Joint Pressure (MD96134)
 - ∠ CHAN Kai Ming NG G.* MAK
 A.*
- 1996-97 The Educational Programs of Longitudinal Study on Effects of Regular

- Sports Exercise on Health-Related Physical Fitness in Childhood (ED96030)
- CHAN Kai Ming HONG Youlian (Sports Science & Physical Education)
- 1996-97 An *in vivo* Study of the Change in Type I and Type III Collagen in Healing Rat Patellar Tendon the Effect of Growth Factors (MD96072)
 - ∠ CHAN Kai Ming CHAN Pui
 (Hong Kong Centre of Sports
 Medicine & Sports Science) LEE
 Ka Ho Kenneth (Anatomy)
- 1996-97 Health Benefits of Programmed Physical Exercise on the Prevention of Bone Loss in Postmenopausal Women (MD96021)
 - ∠
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 CHAN Kai Ming QIN Ling LAU
 Edith Ming Chu (Community & Family Medicine) WOO Jean
 (Medicine & Therapeutics) LEE
 Shiu Hung (Community & Family Medicine)
- 1995-96 Correlation of Preoperative and Intraoperative Somatosensory Cortical Evoked Potentials in Scoliosis Surgery (MD95252)
 - CHENG Chun Yiu Jack GUO Xia
 AUN Sui Tee Cindy (Anaesthesia
 & Intensive Care) KAY Li Chi
 Richard (Medicine & Therapeutics)
- 1995-96 An Epidemiological Study on Accident & Injury in Children in Hong Kong (MD95245)
 - ∠ CHENG Chun Yiu Jack WONG
 Tze Wai (Community & Family
 Medicine) CHEUNG W. L.* •
 CHOW C. B.* LUI P. K.*
- 1996-97 Dual Energy X-Ray absorptiometry in Lower Limb Callotasis Lengthening (MD95259)
 - ∠ CHENG Chun Yiu Jack

 MAFFULLI N.* NG B.*
- 1996-97 Osteopenia in Adolescent Idiopathic Scoliosis (MD96174)
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- 1996-97 Transient Synovitis of Hip in Children -A Natural History Review of 235 Cases (MD96175)
 - ∠ CHENG Chun Yiu Jack CHOI K.Y.* NG B.K.W.*

- 1996-97 Osteoinductive Bone Substitute for Posterior Spinal Fusion in a Rabbit Model (MD96071)
 - CHENG Chun Yiu Jack GUO Xia
 YURIANTO Henry# SHER Hing Leung Andy (Lee Hysan Clinical Research Laboratories)
- 1996-97 Analysis of *Tlx* Gene Functions in Oncogenesis and Development Using Gain-of-function and Loss-of-function Mutants in Transgenic Mice (CU96662)

 **CHENG Shuk Han
- 1995-96 Effect of the Muscular Regeneration Regulated Factors on Myoblasts Transfer Therapy in Duchenne Muscular Dystrophy (MD95228)
 - GUO Xia CHENG Chun Yiu Jack• CHAN Kai Ming

Yiu Jack

- 1994-95 Arthroscopy Assisted Management of Distal Radial Fracture (MD95088)
- 1995-96 Biomechanics of Surgical Reconstruction for Shoulder Paralysis (CU95633)
 - ∠
 ∠
 HUNG Leung Kim TANG Chun Yuen[#] MAK F. T. Arthur^{*} KWONG Wing Hang (Anatomy)
- 1996-97 Iontophoresis with Pulsed-short Circuitpulsed Direct Current (PSPDC) Device: Tissue Effects and Drug Permeation (MD96073)
 - × HUNG Leung Kim ◆ ZHANG
 Yuanting (Electronic Engineering) ◆
 ZHAO Li* ◆ WU Hay Tong
- 1996-97 Neurotrophic Factors Derived from Schwann Cells in a "Pre-degenerated" Peripheral Nerve Environment -

- Temporal Changes and Clinical applications (MD96075)
- × HUNG Leung Kim LAO J* ●
 KWONG Wing Hang (Anatomy) ●
 WU Hay Tong
- 1996-97 Interleukin-1 and Interleukin-8 Expression in Burn Wound - *in vivo* and *in vitro* Studies (MD96074)
 - HUNG Leung Kim WU Hay Tong
 CHENG Chi Wa FUNG Ming Chiu (Biology)
- 1994-95 The Use of Adriamycin Binding Assay as a Test to Determine the Chemosensitivity of Patients with Osteogenic Sarcoma (MD94070)
 - KUMTA Shekhar Madhukar YIP Man Hing Kevin • LIN Joanna (Clinical Oncology)#
- 1995-96 Tumour Specific Alkaline Phosphatase in Osteosarcoma (CU95654)
 - KUMTA Shekhar Madhukar •
 LEUNG Kwok Sui FUNG Kwok
 Pui (Biochemistry) LEE Kwong
 Man Simon (Lee Hysan Clinical
 Research Laboratories) CHENG
 Shuk Han
- 1995-96 Use of Pain Drawing Test for Chinese Patients with Low Back Pain (MD95226)
 - ∠ LEE Yuen Lun YUEN Kai Ming[#] •
 LAM Yuk Lan (Accident and Emergency Medicine Academic Unit)
- 1993-94 The Establishment of a Coordinated Research Programme on Cytogenetics and Molecular Biology of Musculoskeletal Tissue (MD93115)
 - LEUNG Kwok Sui LEUNG Ping
 Chung CHAN Kai Ming HUNG
 Leung Kim LEE Yuen Lun YIP
 Man Hing Kevin LEE Kwong Man
 Simon (Lee Hysan Clinical Research
 Laboratories)
- 1995-96 The Biochemical Events of the Regeneration of Osseous Tissue Under Tension and Compression Stress - A Study with Callotasis Model in Goat (CU95655)
 - ∠ LEUNG Kwok Sui LEE Kwong Man Simon (Lee Hysan Clinical

of Proliferative Chondrocytes Cultured

1996-97	Kwok Pui (Biochemistry) The Effect of Reaming Technique on Intramedullary Pressure and Marrow Fat		on a Collagen Matrix (CU95656) LEUNG Ping Chung • LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) • OOI
	Embolisation - A Quantitative Study (CU96631) ∠ LEUNG Kwok Sui • CHEN Zhen		Vincent E. C. (Biology) • FUNG Kwok Pui (Biochemistry)
	Yu (Biochemistry) • WONG Wan Nar Margaret • FUNG Kwok Pui (Biochemistry)	1996-97	Cartilage Reconstruction Using Chondrocytes Transplantation (MD96077) LEUNG Ping Chung
1996-97	Identification of TGF-beta Induced Genes During Chondrogenesis in Rabbit Periosteal-derived Cells Using mRNA Differential Display Analysis (MD96076)	1996-97	Cartilage Elastography (MD96128)
	∠ LEUNG Kwok Sui • CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)	1995-96	Inapparent Hypoxaemia - Its Incidence and Relation to Fat Embolism Syndrome (MD95130)
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	1996-97	Epidemiological Study on Foot and Ankle Disorders (MD96170) WONG Wan Nar Margaret • LEUNG Ping Chung
1995-96	Study on Osteoporosis - The Loss of Calcium Content in Bone with Age (MD94016) ß LEUNG Ping Chung • LAU Edith	1994-95	Histological Localisation of Growth Factors in Post-burn Hypertrophic Scars (MD95080) MUS WU Hay Tong • HUNG Leung Kim
	Ming Chu (Community & Family Medicine) • WOO Jean (Medicine & Therapeutics) • HO Chan Suzanne (Community & Family Medicine) • HAINES Christopher John (Obstetrics & Gynaecology)	1995-96	The Role of Nitric Oxide Synthase Inhibitor in the Prevention of Osteoarthritis in a Rabbit Knee Immobilisation Model (MD95132) ✓ YIP Man Hing Kevin • CHAN Kai Ming • QIN Ling
1005.05			3

RESEARCH OUTPUTS AND PUBLICATIONS

Implantation

1995-96

Biosynthesis

and

Artificial Growth Plate Using Population

Research Laboratories) • FUNG

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RESEARCH PROJECTS

Molecular Analysis of *MLL* and *TEL* Gene Abnormalities in Paediatric Leukaemia

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- ☐ 1 October 1997
- CUHK Research Committee Funding

Leukaemia is the commonest malignancy in childhood. Understanding of the acquired chromosomal aberrations in the leukaemic cells at the time of presentation is important in the risk assessment of the disease. Conventional cytogenetic analysis provided clinician with information of different types of chromosomal translocation. The Philadelphia chromosome is the best known example in human leukaemia. The presence of this marker signifies high risk of treatment failure. Aggressive treatment should be given. However, there are cases of leukaemia with a more favourable outcome. Adequate treatment should be given without undue side effects. The long arm of chromosome 11 and the short arm of chromosome 12 are two sites with frequent chromosomal recombination. The MLL and TEL gene loci are affected resulting in forming fusion products. As a result of these fusion, leukaemic transformation develops. Poor treatment outcome is associated with MLL gene rearrangement while favourable outcome is associated with the TEL gene rearrangement. Hence, the determination of the presence of these markers would delineating the risk group in treatment assignment for leukaemia patients. This project will apply molecular biological technique in delineating the rearrangement. The researchers aim to determine the frequency of these genetic changes in then patients with leukaemia by Southern blotting. Informative cases will be further analysed for the fusion partners. Statistical analysis will be performed to correlate the presence of these rearrangements and the established prognostic markers in the present clinical treatment protocol. (MD97063)

Determination of Local Oxygen Consumption by Healthy and Diseased Lungs in a Rabbit Model

- 1 January 1998
- CUHK Research Committee Funding

Newborns with chronic lung diseases such as bronchopulmonary dysplasia often suffer from growth failure as a result of a significant yet unexplained increase in oxygen (O_2) consumption and energy expenditure. The researchers hypothesize that the phenomenon is the result of an increase in metabolism of the chronically inflamed and

regenerating lung tissues. To evaluate then hypothesis, the researchers have designed a method to estimate the local O₂ utilization by the lungs. Total body O₂ consumption (VO₂) is determined from the O₂ content of the inhaled and exhaled breaths using indirect calorimetry. At the same time O_2 consumption (CalcVO₂) is estimated from the cardiac output (Qt), and O₂ content of arterial and right atrial mixed venous blood using the Fick principle. Since CalcVO₂ measures the amount of O₂ removed from the blood before it passes through the lungs, the difference between VO₂ and CalcVO₂ gives the O₂ consumption of the lungs. In this study, VO2 and CalcVO₂ will first be estimated in 10 healthy adult rabbits mechanically ventilated under general anaesthesia. Indirect calorimetry is measured using a measured using a metabolic analyser. Qt is measured by the thermal dilution method, and arterial and mixed venous blood samples are obtained through an arterial and jugular central venous catheter respectively. The experiment is then repeated in 10 adult rabbits with lung injury induced by subcutaneous injection of N-nitroso-Nmethylurethane. The two groups will be compared for their lung O2 consumption, and the gross (wet weight/dry weight ratio) and histopathological changes of the lungs. (MD97064)

To Provide Gestational Age-Specific Standards of Physical Measurements for Local Chinese Newborns

- ✗ FOK Tai Fai LAU Tak Fai Joseph (Centre for Clinical Trials & Epidemiological Research) •
 NG Pak Cheung CHANG Mang Z. Allan (Obstetrics & Gynaecology) LEE Wai Hong*
 CHOW Chun Bong*
- ☐ 1 June 1998
- Health Services Research Fund, Hospital Authority

Objectives: To provide gestational age-specific standards of physical measurements for local Chinese newborns. These measurements include (1) body weight, head circumference, and body length; and (2) other physical measurements with clinical application including those reflecting the skeletal growth of the face, trunk and limbs, and for males, the penile length. Design: A 2-year cross-sectional study

Setting: 13 regional hospitals in Hong Kong

Subjects: 12,000 newborns of gestations 25 to 43 weeks

Main outcome measures: (1) The birth weight, and crown-heel length, head circumference, and physical measurements reflecting skeletal growth of the face, trunk and limbs, and penile length of male infants, measured 24-48 hours of birth.

Results: The data will be used to construct (1) updated gestational age-specific percentile curves of

body weight, body length and head circumference for Hong Kong Chinese newborns, and (2) a set of normograms on the various physical parameters of Hong Kong Chinese newborns. (MD97086)

A Controlled Study of Obstructive Sleep Apnea Syndrome in Obese Children in Hong Kong

- ★ HUI Hon Lam WING Yun Kwok (Psychiatry)
 LEUNG Suk Fong Sophie[#] FOK Tai Fai CHEN Char Nie (Psychiatry)
 HO Kwok Wah Crover (Psychiatry)
- ☐ 1 August 1997
- Health Services Research Fund, Hospital Authority

Obstructive sleep apnea syndrome (OSAS) is a but grossly under-recognized common undertreated condition in children. Children OSA differ a lot from adult type in terms of pathophysiology, presentation and management. More importantly, OSA in children may lead to various complications including cor pulmonale, neurological sequalae, behavioral disturbance, and possibly sudden death. Obesity is a major risk factor for OSAS and its prevalence is rising rapidly in Hong Kong. In contrary to adult OSA patients who are typically obese, the relationship between obesity and OSA in children is unclear. To our knowledge, there has been few studies of OSA in obese children and none conducted in Asia. Thus we aim to examine the clinical and polysomnographic features of a group of obese children, and compare with that of a group of age and sex matched normal children. These findings, if positive, will help to identify OSAS, its potential complications, and implementation of future management plan for a rapidly increasing condition in our society. (MD97002)

Vincristine Neurotoxicity in Children with Acute Lymphoblastic Leukaemia

- ∠ LEUNG Ting Fan YEUNG Wai Lan CHIK
 Ki Wai
- □ 1 July 1997
- CUHK Departmental Funding

Acute lymphoblastic leukaemia is the commonest childhood malignancy in Hong Kong. Treatment consists mainly of chemotherapy and vincristineis used as one of the main agent. Its main side effect is neurotoxicity which can result in clinically significant neuropathy and hence morbidity. The aim of this study is to investigate on the likelihood of vincristine-related neuropathy in children with acute lymphoblasti leukaemia. This study involves the

clinical assessment and electrophysilogical studies of peripheral neuropathy. (MD97016)

Effects of Platelet Granule Proteins on NF-E2 Expression and Megakaryocytopoiesis

- ∠ LI Karen Kwai Har

 ✓ YANG Mo
- 1 October 1997
- CUHK Research Committee Funding

The commitment of haematopoietic stem cells to the megakaryocyte (MK) lineage is largely regulated by thrombopoietin, a newly identified MK-specific growth factor. A feed-back control on MK maturation by platelet granules also occurs, although the mechanism is not well understood. The researchers' hypothesis is that the platelet/MK granule constituents, platelet factor 4 (PF4) and thrombospondin (TSP) may play a role in the inhibition of MK differentiation and maturation. This feed-back mechanism may involve the MK/erythroid transcription factor NF-E2. The effects of PF4 and TSP in combination with TPO and other cytokines on MK differentiation will be investigated using three models: the human cord blood stem cells, the murine bone marrow stem cells and human and murine cell lines. The link between activators and inhibitors of megakaryocytopoiesis with NF-E2 expression will be investigated at the transcriptional and translational levels using Western blots, Northern blots and reverse-transcriptase polymerase chain reactions (RT-PCR). The differentiation status of the MK lineage will be identified by surface antigens using flow cytometry and the progenitor cells determined by colony assay. Abnormal platelet levels in the circulation may occur due to primary marrow disorders, chemotherapy, transplantation and even viral infections. Understanding the mechanism of MK differentiation may have significant implications in the management of thrombocytopenia and thrombocytosis. (MD97066)

Haematopoietic Stem Cells: Characterization and Retrovirus-Mediated Gene Transfer

- ∠ LI Karen Kwai Har LI Chung Leung*
- ☐ 1 March 1998
- ❖ CUHK Mainline Research Scheme

Pluripotent haematopoietic stem cells (PHSC) are capable of self-renewal and differentiating into all blood cell lineage. As a result, they have become target cells for somatic gene manipulation and therapy of genetic disorders of the blood origin. To date, the reported sources of PHSC are bone marrow, mobilized peripheral blood, cord blood and fetal liver. However, variations occur in the quality and quantity

of PHSC obtained from these cell sources. In addition, the apparent importance of CD34 as a stem cell marker has recently been challenged by the demonstration of the lack of or low level of its expression. For gene therapy, PHSC or targeted progenitors have to be identified, enriched and transfected with the corrective gene. These modified cells should then be assessed in vitro and in animal models such as the severe combined immunodeficient mouse (e.g. NOD/SCID). To our knowledge, the technology of retrovirus-mediated gene transfection into PHSC and the NOD/SCID mouse model is not available in Hong Kong. This project, in collaboration with The Queensland Institute of Medical Research, is targeted to establish such technology in The Chinese University Hong Kong. The specific aims are to (1) characterize PHSC in bone marrow, mobilized peripheral blood and cord blood, paying particular attention to possible CD34 negative progenitors, (2) isolate PHSC using flow cytometry sorting, (3) test various retroviral vectors for efficient gene transfer into PHSC and progenitors (4) study the expression of reporter genes in specific lineage of blood cell development. The researchers would also try to acquire experience with the NOD/SCID model although it is beyond the scope (budget) of this proposal to cover such area. Gene therapies targeting to correct genetic diseases and malignancy have been under clinical trials overseas. This research would have significant contributions to future strategy of gene therapy using haematopoietic stem cells. (MD97096)

Cross Cultural Comparison of Child Care Related Sids Risk Factors

- NELSON Edmund A. S.

 SCHIEFENHOEVEL Wulf*
- ☐ 1 April 1998
- ❖ Germany/Hong Kong Joint Research Scheme

From the mid-1980s certain child care practices (prone sleep position, bed-sharing, soft underbedding, heavy dressing and lack of breast feeding) have been shown to be associated with an increased risk of sudden infant death syndrome. The HRAF (Human Relations Area Files) collections will be used to undertake a cross cultural comparative analysis of these factors. (MD97105)

The Pituitary-Adrenal Response in Preterm Very Low Birth Weight Infants after Treatment with Multiple Courses of Antenatal Corticosteroids

- ✓ NG Pak Cheung LAM Wai Kei Christopher
 (Chemical Pathology) WONG Wing Kin Gary
 FOK Tai Fai LEE Cheuk Hon
- ☐ 1 October 1997

CUHK Research Committee Funding

developmental pathophysiology of lung maturation during the perinatal period has been the subject of fruitful research in the past decades. In many animal species, antenatal corticosteroids have been shown to stimulate cytodifferentiation and induce precocious acceleration of tissue maturation without altering the normal sequence of development. Much evidence has accumulated to show that antenatal corticosteroids do not only reduce the incidence and severity of respiratory distress syndrome (RDS), but could also decrease the incidence bronchopulmonary dysplasia, of intraventricular hemorrhage, necrotizing enterocolitis, and mortality in preterm infants. Although the efficacy of antenatal corticosteriods for prevention of RDS is established and this treatment has become part of routine obstetric management in many institutions, there is relatively little information regarding its effects on the hypothalamic-pituitaryadrenal (HPA) axis in very low birth weight (VLBW) infants. To our knowledge, the pituitary function has not been systematically evaluated in this category of newborns and, in particular, the effect of multiple courses of antenatal dexamethasone on their HPA axis is not known.

The researchers set out in this study to compare the pituitary-adrenal function in preterm, VLBW infants who received multiple courses (>5 courses) and those who did not receive antenatal corticosteroids treatment by prospectively examining their endocrine function with the human CRH (hCRH) stimulation test in a standardized fashion (details described in protocol). The influence of other confounding factors and stressful therapeutic measures on the HPA axis will also be determined. The result will enable them to decide whether corticosteroids replacement therapy is desirable after delivery in preterm, VLBW infants whose mother received multiple courses of dexamethasone. (MD97024)

A Study on Cytokines and Cell Adhesion Molecules Expression in Respiratory Syncytial Virus Bronchiolitis

- SUNG Yn Tz Rita

 HUI Hon Lam

 LAM Wai Kei Christopher (Chemical Pathology)

 CHAN Grace*
- □ 1 September 1997
- CUHK Research Committee Funding

Respiratory syncytial virus is the most common cause of bronchiolitis in infants. It predispose to the development of reactive airways disease. Up to 40% to 50% of children suffer from RSV bronchiolitis have recurrent wheezing up to 5 years after recovery. Viral infection can increase airway reactivity, and may alter immune response to favour overproduction

of IgE antibodies to allergens. RSV infection is thought to be a major predisposing factor in the induction of asthma early of in life. Various immune mediators have been implicated in RSV infection, Increase levels of leukotriene C4 and eosinophil cationic protein has been detected in nasal secretion. High levels of ECP have been associated with clinical evidence of bronchiolitis at the time of RSV infection. A predominance of neutrophil have also been found in airway fluid from intubated children with respiratory failure. Recently increased expression of ICAM-1 and rantes has been found in an vitro airway epithelial cell culture. However, the precise immunological mechanism of RSV bronchiolitis remain unknown. Here the researchers propose a study to examine the levels of cytokines, cell adhesion molecule, eosinophil cationic protein, neutrophil myeloperoxidase, and rantes in RSV infected infants. Tracheal and nasopharyngeal aspirate, and serum will be collected. They hypothesize that levels of certain eosinophil and neutrophils related cytokines and cell adhesion molecules will be elevated. Results of this study will help to further understand the immunological mechanism of RSV bronchiolitis, and its link to the development of asthma in the future. (MD97067)

Bone and Collagen Turnover in Preterm Neonates with Dexamethasone Treatment

- WONG Wing Kin Gary NG Pak Cheung •
 LAM Wai Kei Christopher (Chemical Pathology)
 FOK Tai Fai
- □ 1 November 1997
- CUHK Research Committee Funding

Dexamethasone, a potent glucocorticoid, is widely used for the treatment of bronchopulmonary dysplasia in preterm neonates. Steroid is also known to suppress bone growth. The researchers propose in this study to assess the degree, duration of suppression and recovery of bone turnover by measuring the markers of bone metabolism in neonates receiving dexamethasone treatment. (MD97065)

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

Edition Title/Investigators

1996-97 Evaluation of the Expression of Wilms'
Tumor Gene (WT1) and its Clinical
Relevancy in Estimation of Minimal
Residual Disease in Childhood
Leukemias (MD96113)

∠ CHIK Ki Wai • YUNG Chung Ming Edmund

- 1994-95 Use of Inhaled Beclomethasone in the Treatment of Preterm Newborn Infants Requiring Mechanical Ventilation (MD94104)
 - FOK Tai Fai
 NG Pak Cheung
 WONG Wing Kin Gary
- 1995-96 To Study the Association of Manganese in Parenteral Nutrition Solution with Cholestatic Jaundice, Hepatotoxicity and Neurological Damage in the Newborns (MD95133)
- 1996-97 To Provide Gestation-Specific Standards on Physical Measurements on Chinese Newborns (MD96165)
- 1996-97 Evaluation of the Metered Dose Inhaler, Jet Nebuliser, and Ultrasonic Nebuliser in the Delivery of Salbutamol Aerosol to Newborns with chronic Lung Changes (MD96168)
 - ▼ FOK Tai Fai LAM Kuo[#] CHAN C.K.* NG Pak Cheung
- 1996-97 Development of a Preterm Animal Model for the Study of Oxygen-Induced Lung Damage (MD96164)
- 1996-97 Enterobacter Septicaemia in Newborns: Analysis of Risk Factors (MD96166)
 - FOK Tai Fai LEE Cheuk Hon WONG Ming Chung (Centre for Clinical Trials & Epidemiological Research) LYON Donald James (Microbiology) NG Pak Cheung
- 1996-97 Clinical Prediction of Post-Extubation Radiological Changes of the Chest in Newborns (MD96167)
 - ✓ FOK Tai Fai KEW Jacqueline (Diagnostic Radiology & Organ Imaging) LOFTUS William (Diagnostic Radiology & Organ Imaging) * NG Pak Cheung
- 1996-97 The Role of High Resolution Computed Tomography in Tuberculosis in Children (MD95263)
 - ∠ HUI Hon Lam LOFTUS William (Diagnostic Radiology & Organ)

	Imaging) [#] • ROEBUCK Derek (Diagnostic Radiology & Organ Imaging) • RUSHTON Anthony (Diagnostic Radiology & Organ Imaging) [#] • METREWELI Constantine (Diagnostic Radiology & Organ Imaging) • FOK Tai Fai	1996-97
1996-97	Differentiation and Expansion of Antigen Presenting Dendritic Cells from Hematopoietic Stem Cells (MD96124) LI Karen Kwai Har • LAW Ping*	1996-97
1995-96	International Child Care Practice Study (MD95024)	1995-96

- 1995-96 Effects of Qinghaosu (Artemisinin) on Malarial Growth in Thalassaemic Trait Erythrocytes (MD95205)
 - NELSON Edmund A. S.
 SENOK Abiola[#]
 LI Karen Kwai Har
- 1996-97 Assessment and Monitoring of Poverty Focused Assistance (MD96158)
 - MELSON Edmund A. S. ◆ YU Ly Mee (Centre for Clinical Trials & Epidemiological Research)
- 1995-96 The Diagnostic Value of IL-1β, IL-6, TNF-α, E-selection and CRP in Early Detection of Neonatal Infection (MD95161)
 - MG Pak Cheung CHENG Shuk Han (Orthopaedics & Traumatology)
 FOK Tai Fai • WONG William Lok Chuen • CHEUNG Kam Lau • YUEN Man Pan Patrick
- 1996-97 Pituitary Response in VLBW Infants After Dexamethasone Treatment for Chronic Lung Disease (MD94175)
 - × NG Pak Cheung LAM Wai Kei Christopher (Chemical Pathology) ●
 WONG Wing Kin Gary FOK Tai Fai
- 1996-97 Ambulatory Blood Pressure in Normal Chinese Children and Adolescents (MD96162)

- 996-97 Cytomegalovirus and Chlamydia Pneumonia in Infants: Incidence and New Diagnostic Methods (MD96081)
- 1996-97 Effect of Blood Transfusion on Oxygen Consumption in Premature Babies with Anaemia (MD96161)
 - SUNG Yn Tz Rita YU Chung WahFOK Tai Fai
- 1995-96 The Epidemiology of Childhood Diabetes in Hong Kong (MD90205)
 - WONG Wing Kin Gary LEUNG
 Suk Fong Sophie[#] •
 OPPENHEIMER Stephen James[#]
- 1996-97 Identification of Genetic and Environmental Risk Factors for Childhood Asthma in Hong Kong (CU96609)
 - WONG Wing Kin Gary LEUNG
 Chung Chuen Roland (Medicine &
 Therapeutics) LAI Kei Wai
 Christopher (Medicine &
 Therapeutics) YOUNG Robert P.
 (Medicine & Therapeutics) LAU
 Tak Fai Joseph (Centre for Clinical
 Trials & Epidemiological Research)
- 1996-97 Circulating Haematopoietic Progenitor Cells in Infants (MD96079)
 - YUEN Man Pan Patrick FOK Tai Fai • LI Karen Kwai Har • LI Chi Kong
- 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 Karen Kwai Har PONG Nga Hin Henry

RESEARCH OUTPUTS AND PUBLICATIONS

- <P970561> **Nelson, E.A.S.** "East Meets West: A Research Perspective". Paper presented in the Moving with the Sun 24-Hour Global Telemedicine Conference, organized by The Chinese University of Hong Kong. Hong Kong, 1997.07.01.
- <P970633> 梁淑芳. <愛嬰醫院>. 《親子雜誌》 第44期,頁56.香港,1997.07.

- <P971006> Sakamoto, M.; S. Ishii; H. Kashiwazaki; P.C. Chiu; C.M. Chen; N.S. Chang; S.F. Leung; L.B. Rabuco; E.S. Tee; F.G. Winamo; K. Tontisirin; J. Howden and L.G. Saldanha. "The Relationship Between Nutrition-Related Knowledge and Food Practices in Asian Countries". Abstracts of the 16th International Congress of Nutrition p.178. Canada: The International Union of Nutritional Sciences, 1997.07.27.
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- <P971008> Leung, S.S.F.; Z.Y. Chan and H.Q. Li. "Dietary Pattern in Two Chinese Populations of Lactating Women". Abstracts of the 16th International Congress of Nutrition p.325. Canada: The International Union of Nutritional Sciences, 1997.07.27.
- <P971748> Sung, R.Y.T.; G.Y. Huang; M.K. Shing; S.J. Oppenheimer; C.K. Li; C.K. Li; J. Lau and M.P. Yuen. "Echocardiographic Evaluation of Cardiac Function in Paediatric Oncology Patients Treated with or without Anthracycline". *International Journal of Cardiology* vol.60, pp.239-248. UK, 1997.
- <P971885> Fok, Tai Fai; Kuo Lam; Chak K. Chan; Pak Cheung Ng; Hong Zhuang; William Wong and Kam Lau Cheung. "Aerosol Delivery to Non-Ventilated Infants by Metered Dose Inhaler: Should a Valved Spacer Be Used?". Pediatric Pulmonology vol.24, pp.204-212. UK, 1997.
- <P972101> Senok, A.C.; E.A.S. Nelson; K. Li and S.J. Oppenheimer. "Thalassaemia Trait, Red Blood Cell Age and Oxidant Stress: Effects on *Plasmodium Falciparum* Growth and Sensitivity to Artemisinin". *Transactions of the Royal Society of Tropical Medicine and Hygiene* vol.91, pp.585-589. UK, 1997.
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      < P974822>, < P974900>, < P980066>, < P980350>, < P980372>, < P980375>, < P980380>, < P980405>,

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      < P981139>, < P981653>, < P981670>, < P981831>, < P982038>, < P982230>, < P982362>, < P982381>,
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RESEARCH PROJECTS

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

- ☐ 1 January 1998
- CUHK Research Committee Funding

Prostanoid EP₃-receptors exist as several isoforms due to alternative splicing of the C-terminus: the consequences are different coupling to G-proteins and different modes of agonist desensitization. This project is concerned with the mechanisms whereby EP₃-receptor agonists such as sulprostone induce contraction of vascular smooth muscle. Preliminary experiments indicate the possibility of an exclusive link to a plasma membrane Ca²⁺ channel. The intention is to study the guinea-pig isolated aorta first and then attempt similar studies using human vascular tissue. The experimental protocols involve enzymic digestion of vessels to obtain discrete smooth muscle cells, which will then be "patchclamped" to determine the characteristics of the channel activity induced by the selective EP₃ agonists SC 46275 and ONO-AP-234. The involvement of second messengers (cAMP, IP3, DAG) and direct Gprotein coupling will be determined using appropriate antagonists and inhibitors either in the bathing fluid or the patch-clamp pipette. (MD97068)

Modulatory Effects of Extracellular ATP on Delayed Rectifier \mathbf{K}^+ Channels of Guinea-Pig Single Sino-Atrial Nodal Cells

- KWAN Yiu Wa
- □ 1 October 1997
- CUHK Research Committee Funding

5'-triphosphate Adenosine (ATP) is neurotransmitter which is stored in synaptic vesicles of the autonomic nerves. The sinoatrial node is the pacemaker region of the mammalian heart which is densely innervated with autonomic nerves. addition to L-type Ca²⁺ channels, delayed rectifier K⁺ channels are important in pacemaking activity. This project is concerned with the mechanisms of extracellular ATP ([ATP]₀)on delayed rectifier K⁺ currents of guinea-pig single sinoatrial nodal cells. Guinea-pig single sinoatrial nodal cells will be obtained using standardized collagenase/protease enzymatic dissociation procedures. Delayed rectifier K+ channel currents of sinoatrial nodal cells will be measured using patch-clamp techniques. In this project, the identification of type(s) of purinoceptors involved will be examined. Second messenger pathways involved in [ATP]₀-medoated responses on

sinoatrial nodal cells delayed rectifier K^+ currents will also be investigated using appropriate specific antagonists and inhibitors. (MD97072)

Chloride Influx and Mast Cell Activation

- LAU Hang Yung Alaster
- □ 1 October 1997
- **❖** CUHK Research Committee Funding

Mast cells are widely distributed in body tissues and are important in the initiation of allergic and inflammatory reactions. Although the inhibition of mast cells by disodium cromoglycate contributes to the antiasthmatic activity of the compound, the mechanism of its mast stabilizing action still remains unknown. More recent studies have concentrated on the possibility that DSCG indirectly prevents the influx of calcium by blocking chloride channels. Electro-physiological studies have identified chloride channels in mast cells and the chloride currents through these channels during mast cell activation were speculated to drive the mast cell membrane potential towards E_{cl} and hence a hyperpolarization driven calcium influx would be induced. The influx of extracellular calcium then contributed to the sustained phase of elevated [Ca2+]i observed in mast cell activation. These mast cell chloride channels can be inhibited by chloride channel blockers and intracellularly applied DSCG, suggesting that chloride channel blocking maybe the mechanism of the anti-allergic actions of DSCG. However, a recent pharmacological study has suggested that in addition to chloride channels which are related to the mechanism of histamine secretion, an increase in chloride uptake may also be mediated through a frusemide sensitive, electroneutral Na⁺/K⁺/2Cl⁻ cotransporter. In order to further the understanding of the relationship between chloride channels and mast cell activation, the present proposal will investigate how intracellular calcium and chloride ions will be affected by a selection of chloride channel blockers and mast cells stabilizers. (MD97069)

Chemical and Pharmacological Studies of Beimu, a Commonly Used Antitussive Traditional Chinese Medicine

- ∠ LIN Ge KWAN Yiu Wa HO Yee Ping (Pharmacy) LI Ping*
- ☐ 1 September 1997
- * Research Grants Council

Beimu, the most commonly used traditional Chinese medicine (TCM) for the treatment of cough, has been widely used for centuries in mainland China and Hong Kong. Beimu is derived from several Fritillaria plants and its extensive use is due to it having less side effects and non-addictive properties when compared with commercially available Western morphine-like cough medicines containing codeine. However, the scientific bases for the use of this herbal medicine are not clear cut, and there is a lack of a quality control method for this TCM. Furthermore, the plant origins of Beimus are often confused. Such problems can often lead to reduce therapeutic effect and enhanced toxicity in its medicinal use.

In the proposed project, the researchers will carry out thorough chemical and pharmacological investigation into this TCM. Commercially available Beimus in Hong Kong and China will be purchased, and their quality and identities authenticated. A sensitive and applicable HPLC method will be developed for the qualitative and quantitative analyses of Fritillaria alkaloids. Once developed, this assay can be utilised for the determination of the major bioactive alkaloids present in different Beimus and their main metabolites in biological fluids obtained from dosed rats. Acute toxicity tests of the crude extracts and each isolated compound will be carried out in vivo, which will enable the establishment of the relationship between toxicity and the active principles. The mechanism of antitussive action will be investigated in vitro on isolated tracheal rings. The generated data will provide a sound scientific rationale for the use of Beimu with an aim towards improving the quality, safety and efficacy of these TCMs. (CU97632)

Identification of Brain Areas Involved in Emesis in the Ferret by c-fos Immunocytochemistry

- □ 13 October 1997
- CUHK Research Committee Funding

Understanding the mechanisms controlling the sensation/ production of nausea is clearly important to the rational development of effective anti-emetic drugs. Much is currently known about the brainstem areas involved in the control of vomiting but only limited studies have been performed to identify the brain areas involved in nausea in man. The proposed studies use the ferret to search for the forebrain area(s) that may be activated during treatment with ipecacuanha. The studies will utilize the technique of c-fos immunocytochemistry to map the brain areas that may be activated.

The proposed studies should provide a clearer understanding of the mechanisms resulting in nausea and may lead to the rationale design of anti-nausea drugs. Locating the cortical area(s) that are involved in nausea would have an enormous scientific and therapeutic impact.

(MD97070)

Assessment of Prostanoid Receptor Stimulated Coupling of Gs to Adenylyl Cyclase

- WISE Helen
- □ 1 July 1997
- CUHK Research Committee Funding

Of the superfamily of 7-transmembrane domain receptors coupled to G-proteins, those which couple to Gs have been extensively studied; this is most likely due to the relative ease with which one can assay adenylyl cyclase activity. The prostanoid receptors which are inhibitory for neutrophil activity belong to this family of Gs-coupled receptors. In the course of studying these prostanoid receptors, the researchers have found that the ability to detect very small changes in cyclic AMP production is often hampered by the assay methodology. This problem is of concern given their interest in using partial agonists, for prostacyclin and prostaglandin E₂ receptors, in studies characterising the mechanism of action of prostanoids in various cells and tissue preparations. In order to overcome this problem, they would like to evaluate an alternative method to examine Gs-adenylyl cyclase interactions in cells. It has been reported that agonist stimulation of Gscoupled receptors leads to a marked increase in high affinity binding of [3H]-forskolin to the catalytic subunit of adenylyl cyclase. They anticipate that this [3H]-forskolin binding assay may: (1) show an improved signal to noise ratio; (2) decrease response variability; (3) reduce the use of radioactive materials; (4) reduce costs and (5) provide a more rapid test of adenylyl cyclase activation. More importantly, this new assay will both compliment our existing data and facilitate our continuing study of the role of cyclic AMP in mediating the wide range of activities of prostacyclin and prostaglandin E₂. (MD97001)

The Role of Prostacyclin Receptors in Pain Modulation

- □ 1 September 1997
- * Research Grants Council

Prostacyclin is perhaps best known as a potent antithrombotic agent, however recent studies have described an additional neuronal site of action for prostacyclin with novel IP-receptors present in both the central and enteric nervous systems. Recent evidence from studies using IP-receptor knockout mice clearly identifies a role for prostacyclin in mediating pain associated with inflammatory conditions; results which substantiate suggestions from IP-receptor distribution studies which localised

IP-receptors to primary sensory pathways. purpose of this project is to characterise the IPreceptor/s which mediate the nociceptive action of prostacyclin by studing primary cultures of dorsal root ganglion (DRG) cells as an in vitro model of primary sensory neurons. The researchers will therefore assess the ability of a range of IP-receptor agonists to stimulate the release of substance P from DRG cells (as a model of the direct nociceptive activity of prostacyclin) and measure their effect on bradykinin-induced substance P release (as a model of the hyperalgesic activity of prostacyclin). This characterization data will be supported by measuring changes in the production of second messengers such as cyclic AMP and IP₃. With emerging evidence that COX-2 can act as an early response gene, they also intend to look for regulation of COX-2 activity, and thus prostacyclin production, by substance P. (CU97601)

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

- YEUNG Hok Keung John
- □ 1 November 1997
- CUHK Research Committee Funding

The objective of this study is to investigate the effects of polysaccharide peptide (PSP) on glutathione transferase, glutathione reductase and glutathione peroxidase in order to elucidate the protective mechanism(s) of PSP on drug-induced hepatotoxicity. The study should provide useful information in relation to the use of PSP as an immunomodulator in chemotherapy. (MD97071)

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

Edition	Title/Investigators	
1996-97	Characterisation of Prostacyclin Receptors in Cardiovascular and Neuronal Tissues Using Novel Antagonists (BL96029)	
1996-97	Neuronal Stimulant Actions of Prostacyclin Mimetics on the Rat Vagus Nerve (MD96091)	
1995-96	Characterization of Extracellular ATP- activated Ion Channels in Single Cells Isolated from Guinea-pig Sinoatrial Node (MD93114) KWAN Yiu Wa	

- 1995-96 The Role of Prostaglandins, Nitric Oxide and Neuropeptides in the Regulation of Synovial Blood Flow (CU94608)
 - ∠ LAM Fu Yuen FERRELL William Russell*
- 1996-97 Evaluation of Anti-inflammatory Agents in Animal Models of Arthritis (MD96088)

 LAM Fu Yuen
- 1995-96 Comparative Studies on the Effects of Pharmacological Anti-Allergic Agents on Inflammatory Mediator Release and Intracellular Calcium Mobilization of Purified Rat Peritoneal Mast Cells (MD93002)
 - LAU Hang Yung Alaster
- 1995-96 Neuropeptide Induced Mediator Release from Mast Cells: Effects of Non-peptide Antagonists of Neurokinins (MD95114)
 - ∠ LAU Hang Yung Alaster PEARCE Frederick Lawrence*
- 1996-97 Prostanoid Receptors on Mast Cells (CU96627)
 - ∠ LAU Hang Yung Alaster JONES Robert Leslie
- 1996-97 Effects of Nitric Oxide on Mast Cells: Heterogeneity between Two Strains of Rats (MD96089)
 - LAU Hang Yung Alaster JAMES
 Anthony (Laboratory Animal
 Services Centre)
- 1995-96 Investigation into the Mechanism of Metabolism-induced Hepatotoxicity of the Pyrrolizidine Alkaloid: Clivorine, and the Prevention of Such Hepatotoxicity Using Glycyrrhizin (CU95639)
 - ∠ LIN Ge DAMANI Lyaquatali A.
 (Pharmacy)[#] HAWES Edward
 Miles*
- 1995-96 The Influence of Receptor Subtype Distribution on the Classification of Receptors Using Agonist Potency Ratios: with Particular Reference to the Prostaglandin E₂, Family of Receptors (CU95606)
 - WISE Helen

 WONG Yung Hou*

- 1996-97 Detection of Enzyme Induction During Anti-tuberculosis Therapy by a Novel Monoclonal Anti-6β-hydroxycortisol Antibody-based ELISA Method (MD96090)
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- 1996-97 Pharmacogenetics of Trimethylamine Noxidation in Chinese, and Associated

- Studies on Regulation of the Flavincontaining Monooxygenase in Animals (MD96115)
- ✓ YEUNG Hok Keung John •
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 (Pharmacy)* LIN Ge

RESEARCH OUTPUTS AND PUBLICATIONS

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 $\begin{array}{l} \textbf{see also} < P972559>, < P972814>, < P980324>, < P980454>, < P980845>, < P981004>, < P981196>, < P982329>, < P982445> \\ \end{array}$

RESEARCH PROJECTS

Stability Study of Chlorpheniramine Maleate in Coltalin® Tablets

- ∠ CHIU Chi Keung RAYMOND Kenneth
- □ 7 July 1997
- Fortune Pharmacal Co Ltd

The active ingredient, Chlorpheniramine Maleate in the Coltalin Tablets was suspected to undergo degradation on storage. The aim of this consultancy project was to investigate whether the formulation is unstable, and to develop a validated assay for the quantitation of the active ingredients. (MD97018)

Formulation and Evaluation of Oral Traditional Chinese Medicines (TCMs)

- ∠ CHOW Hee Lum Albert LEE Kwing Chin Kenneth HO Yee Ping HO Suk San Susan LIN Ge (Pharmacology)
- □ 1 September 1997
- ❖ Capsugel of Warner-Lambert (HK) Ltd. ◆ Vita Green Pharmaceuticals (HK) Ltd.

During the last few years, new requirements for the manufacture of Traditional Chinese Medicines and other herbal products have been established. There is a trend towards mono-preparations containing high amounts of extract per unit dose. Recent developments have focused on the extraction, drying of extracts and their formulation into solid dosage forms. In the latter formulation, the extract has to be milled and in most cases converted into a granulate. Due to the high hygroscopicity of most of the extracts, and the high amount which has to be incorporated into a single dosage unit, the formulation of TCMs has presented a real challenge to both the pharmaceutical manufacturers and the formulation scientists.

The objectives of the present study are:

- (1) to gain an understanding of the hygroscopic nature of herbal extracts based on chemical compositions and material properties;
- (2) to evaluate (and improve) the existing formulation options;
- (3) to devise new or alternative formulation approaches; and
- (4) to evaluate the quality and performance of the final products.

(MD97023)

Hygroscopic Growth of Pharmaceutical Aerosols

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

- □ 15 December 1997
- Research Grants Council

The present project is designed to investigate the hygroscopic properties and growth kinetics of pharmaceutical aerosols under well-defined conditions in a specially designed and validated electrodynamic balance (EDB). It has been well documented that the hygroscopic growth of an inhaled aerosolized drug could significantly influence its targeting to and deposition in the respiratory tract. A clear understanding of both equilibrium aerosol growth and aerosol growth kinetics is imperative for the prediction of the extent of deposition and distribution of inhaled medicaments in the lungs. To date, there have been very few studies on these two growth aspects, particularly in the more complicated multicomponent aerosol systems. An EDB will be employed to levitate and hold an aerosol droplet stationary for measurement of water activity, a thermodynamic property closely associated with the hygroscopicity of aerosols. The effects of chemical compositions on the water activities of selected therapeutic drugs in the presence of inert excipients (i.e. additives) will also be studied. The water activity will be analyzed using thermodynamic models to determine whether these applicable multicomponent models to pharmaceutical aerosols for the prediction of water activity. Growth kinetics of the chosen multicomponent aerosols (including coated aerosols) will also be followed in the balance by continuous monitoring of the balancing voltage and light scattering of the particle. Fundamental principles based on mass and heat transfer will be used to interpret the kinetic data. The proposed study could lead to a better design and more optimal delivery of aerosolized drugs administered via the pulmonary route.

(MD97134)

Stability Testing on Repackaged Products

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- ☐ 1 January 1998
- Hospital Authority

This project is designed to provide drug stability testing services to the Hospital Authority in Hong Kong. The services will include qualitative and quantitative drug analysis, accelerated stability testing (at elevated temperatures), and expiry dating of pharmaceutical products in various packages. (MD97089)

Analysis of Pharmaceutical Preparations Chemical Analysis of *Piqjing Sheung Cream*

∠ HO Yee Ping • CHOW Hee Lum Albert

- ☐ 1 February 1998
- United Laboratories Ltd

This project is aimed at providing analytical services to pharmaceutical companies in Hong Kong. The services will include qualitative and quantitative analyses of pharmaceutical preparations using standard analytical techniques. (MD97090)

Study on Antiulcer Effect of Hippophae rhamnoides

- ∠ ZHU Min LI Chi Keung Ronald
- □ 7 May 1998
- National Research Institute of Chinese Medicine (Taiwan)

In order to search for new antiulcer agents, Hippophae rhamnoides (Fam. Elaeagnaceae), a natural drug for burn healing, will be studied for its stomach protective effect. Five ulcer models will be employed in this project including ethanol induced mucosa damage, NSAIDs induced gastric lesions, stress ulcer model, pylorus ligation induced ulcer and acetic acid induced chronic ulcer. Mechanisms of the antiulcer action will be studied by measuring content of gastric acid, pepsin, prostaglandins, and mucus and determining gastric motility and blood flow. Antioxidative effect of the drug will also be investigated. Analgesic and anti-gastric secretion effect of H. rhamnoides will be evaluated by the binding activity of the drug with opiate and histamine receptors. Chemical components of H. rhamnoides will be studied with GC-MS and HPLC-MS. (BL97040)

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

Edition	Title/Investigators
1996-97	Attitudes and Motivations of Pharmacy Students (MD96135) M HO Suk San Susan
1995-96	Effects of Prolonged Bacterial Growth Suppression Demonstrated by Binary Antibiotic Systems: Study of <i>in vitro</i> and <i>in vivo</i> Correlations Using a Pharmacokinetic/Pharmacodynamic Approach (CU95623) LI Chi Keung Ronald • RAYMOND Kenneth • LING Mei Lun Julia

(Microbiology) • CHENG Fun Bun

Augustine (Microbiology)

- 1996-97 Molecular and Biological Characterisation of Resistance Formation in Gram Negative Clinical Isolates and Cost analysis of β-Lactam Antibiotics Commonly Used in Hong Kong (MD96086)
 - ∠ LI Chi Keung Ronald CHAN Wai Chi (Microbiology) • LING Mei Lun Julia (Microbiology) • CHENG Fun Bun Augustine (Microbiology)
- 1996-97 Influence of Metal Chelate Formation on the Efficacy of Oral and Intravenous Administration of Ciprofloxacin (MD96185)
 - LI Chi Keung Ronald CHANG Sophie
- 1995-96 Effects of Drug Input Rates on the Pharmacodynamics of Atenolol in Normal Healthy Chinese Subjects (CU95668)
 - RAYMOND Kenneth LI Chi
 Keung Ronald TOMLINSON
 Brian (Medicine & Therapeutics) •
 CRITCHLEY Julian A.J.H.
 (Medicine & Therapeutics)
- 1995-96 Interactive Computer Programmes to Teach Pharmacokinetics (MD95197)
 - RAYMOND Kenneth LI Chi Keung Ronald
- 1995-96 Prospective Pharmacokinetic Dosage Adjustment of Aminoglycoside Therapy Based on Drug Blood Level Data (MD95196)
 - RAYMOND Kenneth LI Chi Keung Ronald
- 1996-97 Assessing the Pharmacokinetics and Pharmacodynamics of Drugs with Non-linear, Input Rate-dependent Dispositions (MD96087)
 - RAYMOND Kenneth LI Chi Keung Ronald
- 1995-96 The Cytoprotective Effects of *Radix linderae* against Ethanol Induced Gastric
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see also <P972364>, <P972446>, <P972844>, <P973728>, <P973741>, <P974199>, <P980384>, <P980502>, <P980733>, <P980784>, <P980961>, <P981371>

RESEARCH PROJECTS

Identification and Functional Studies of VEGF Receptors in Rat Testicular Macrophages

- ∠ AU Chak Leung LEE Will M.*
- □ 1 December 1997
- * Research Grants Council

Testicular function is under endocrine control of the hypothalamic-pituitary unit. However, there is increasing evidence that this control is modulated by cell-cell interaction within the testis through the production of paracrine factors. Leydig cells and macrophages represent the two major cell types found in the testicular interstitium. morphological evidence as well as functional studies to indicate a close interaction between these two cell types in regulating each others activities and cell numbers. Vascular endothelial growth factor (VEGF) is a potent angiogenic factor which also has the additional effect of inducing monocyte/macrophage activation and migration. The researchers' previous studies have demonstrated the expression of VEGF in Leydig cells and the presence of VEGF receptor immunoreactivities in a population of interstitial cells that resemble testicular macrophages. The overall aim of the present study is to establish whether VEGF receptors are indeed present in testicular macrophages and if so, whether they are involved in mediating the migratory and/or secretory responses of testicular macrophages to VEGF (derived from Leydig cells). Colocalization of VEGF receptors and macrophage markers will be performed on tissue sections. VEGF receptor expression in testicular macrophages will be established using gene cloning, in situ hybridization, Northern and Western blotting. The binding characteristics of VEGF receptors in testicular macrophages will be determined. The developmental changes of VEGF receptor expression in testicular macrophages will be examined. Finally, the migratory and secretory responses of testicular macrophages to VEGF will be studied using a chemotaxis assay and by determinating the changes in cytokine production. (CU97663)

Cellular and Molecular Mechanisms of Brain Natriuretic Peptide (BNP)-Induced Inhibition of Apoptotic Cell Death in PC12 Pheochromocytoma Cells

- □ 1 January 1998
- CUHK Research Committee Funding

Some neurodegenerative diseases, including Alzheimer's disease, involve apoptotic cell death of neurons. Neuronal death in Alzheimer's disease is

now believed to result from: (1) toxic effects of Bamyloid peptide (Aß) and (2) a loss of neurotrophic effect of the secreted form of ß-amyloid precursor protein (ß-APPs). The researchers' laboratory has shown that this neuroprotective effect of B-APPs is mediated by elevation of cyclic GMP (cGMP) and activation of cGMP-kinase (PKG). The researchers have found that brain natriuretic peptide (BNP), a neuropeptide and cardiac hormone, also elevates cGMP levels and protects neural cells. Specifically, BNP inhibits DNA fragmentation (an early step of apoptosis) and delays onset of cell death in serumdeprived PC12 cells, a neuronal cell culture model. The proposed project will determine cellular and molecular mechanisms of the neuroprotective effects of BNP in PC12 cell cultures. The working hypothesis is that BNP, via cGMP/PKG activation, protects neurons during stress by: (1) decreasing entry or release of calcium, (2) increasing expression and activity of antioxidant enzymes (catalase, glutathione peroxidase and superoxide dismutases, [Cu, Zn-SOD and Mn-SOD]), and/or (3) increasing BCL-2, protein product of anti-apoptotic gene bcl-2. Calcium influx and release will be assessed by fura-2 fluorometric technique. Expression and levels of antioxidant enzymes and BCL-2 will be assessed by Northern and Western blot analyses. Results of this project should provide valuable new information about cellular and molecular mechanisms involved in the protection of neurons against developing apoptotic cell death during stress. The results should also provide valuable insight into a potential new physiological role of the neuropeptide/cardiac hormone BNP as a neuroprotective agent. (MD97074)

Study on Mechanisms of Vasodilator Effects of Green Tea Epicatechin Isomers in Spontaneously Hypertensive Rats and Normotensive Rats

- ∠ HUANG Yu CHEN Zhen Yu (Biochemistry)
- □ 1 October 1997
- * Research Grants Council

It is generally believed that green tea contains a large assortment of compounds with a wide range of physiological properties including being antiatherosclerotic, hypocholestrolemic, and antihypertensive. Drinking green tea has been indicated to be an effective preventive measure cardiovascular disease. information about the active components responsible the beneficial effects and biochemical mechanisms involved is very limited. Four biologically active epicatechin isomers have been recently isolated and purified from Chinese green tea in our laboratories and are found to acutely relax rat resistance arteries. The major objectives of the proposed study is to evaluate the effect of green tea

consumption on cardiovascular function, and to investigate the cellular and ionic mechanisms of vasodilator effect of epicatechins in arteries of both normotensive and spontaneously hypertensive rats. These goals will be achieved by using a combination of techniques including in vivo blood pressure measurement, in vitro force and membrane potential measurements, second messenger assay, ionic current recording and arterial smooth muscle cell growth. This study will provide the first detailed examination of pharmacological properties of epicatechins and should elucidate some cellular mechanisms involved in vasodilatation induced by epicatechins and in their long-term beneficial effects in cardiovascular function. (CU97609)

Interaction between G Protein and K+ Channels in Rat Pituitary GH3 Cells

- □ 30 March 1998
- ❖ Germany/Hong Kong Joint Research Scheme

Guanine nucleotide-binding proteins (G proteins) transduce the activation of hormone or transmitter receptors into an intracellular signal. Transducer G proteins are heterotrimeric, membrane-associated molecules that are comprised of α , β and γ . In endocrine cell system G proteins play a central role in coupling the receptors and the effector systems. However, interaction between G proteins and K⁺ channels in GH₃ cells is not well known. objective of the proposed project is therefore to examine the involvement of types of G proteins or their subunits in the alteration of K⁺ channel activity in response to pituitary hormones such as somatostatin and thyrotropin-releasing hormone. This goal will be achieved by microinjection of antisense oligonucleotide into the nuclei of GH₃ cells. Antisense DNA would specifically knock out the G protein under investigation. Changes in the properties of K+ currents affected by drugs will be examined prior to and following injection of antisense DNA. This study should provide useful information on coupling among hormone receptors, G proteins and K⁺ channels. In the wide context, this study would provide new approaches for the pharmacological and physiological investigation of cellular action of endogenous hormonal and transmitter substances. (MD97101)

Electrolyte Transport Mechanisms Underlying the Formation of Seminiferous Tubular Fluid by Rat Sertoli Cells

- □ 1 September 1997

Research Grants Council

Sertoli cells, the "backbone" of the seminiferous tubules inside the testis, play a pivotal role in the process of spermatogenesis, as well as supporting and nourishing the germ cells. The seminiferous tubules are functionally the first portion of the male reproductive tract in which the male gametes are formed. Fully developed spermatozoa are released into the lumen of the seminiferous tubule and are then washed out of the tubules into the rete testis and the epididymis. Although it has been demonstrated that fluid secreted by the Sertoli cells provides the vehicle for sperm transport within the seminiferous tubules, relatively little is known about the mechanisms underlying fluid and electrolytes transport by the Sertoli cells. The aims of the proposed research are (1) to characterize the ionic mechanisms of fluid and electrolyte transport across cultured rat Sertoli cells using electrophysiological and microspectrofluorimetric techniques and (2) to investigate how purinergic agonists act as paracrine/autocrine factors to regulate electrolyte transport activities of the epithelium.

The information obtained from this study will give us a better understanding of how Sertoli cells contribute to the ionic environment inside the seminiferous tubules. In the longer term, this study will shed light on development of new male contraceptive strategies targeting at fluid production by the testis. (CU97640)

Apical P₂ Receptors and the Control of Anion Channel Activity in Epithelial Cells

- ☐ 1 January 1998
- UK/Hong Kong Joint Research Scheme, the British Council

Type 2 purine (P₂) receptors are found in the apical membranes of airway epithelia although their physiological role remains enigmatic. However, agents which activate these receptors may become useful drugs with which to treat the geneticallytransferred disease cystic fibrosis (CF), as they can activate anion channels in the epithelial cells that line the airways of CF patients. This may ameliorate the condition's most morbid symptoms. It is often assumed that this action is mediated via a single population of receptors belonging to the P₂Y2 subclass, which have been described in a large number of epithelial cell types grown under standard conditions. However, our previous work showed that a far more complex population of receptors was present in the apical membranes of cells grown under conditions that favoured the development of the polarised phenotype seen in vivo. The mechanism that allows apical P₂ receptor agonists to activate anion channels in intact epithelia is, therefore not properly understood. The purpose of the experiments is to clarify this mechanism by using a technique that has recently been developed in Hong Kong. This will allow us to measure the effects of P_2 receptor agonists upon transepithelial ion transport and upon intracellular free calcium ($[Ca^{2+}]_i$) simultaneously in polarised epithelial cells. By combining this advanced method with molecular approaches, that will allow us to quantify the rates at which different P_2 receptor subtypes are expressed, we shall be able to determine the pharmacological / physiological properties of the pathways that permit this control. (MD97107)

Testicular Hormone-Regulated Expression of the Renin-Angiotensin II System in the Rat Epididymis

- ∠ LEUNG Po Sing CHAN Hsiao Chang
- □ 1 October 1997
- Research Grants Council

Accumulated evidence has suggested that, in addition to neural and humoral regulation, anion secretion in the epididymis may be subject to local paracrine/autocrine control by a number of vasoactive peptides, including angiotensin II (Ang II). Previous studies have also provided evidence for a local reninangiotensin II system (RAS) which may be important for the maintenance of epididymal function as well as Using specific anti-peptide sperm function. antibodies against Ang II receptors, the researchers have demonstrated differential expression of Ang II receptors in epididymal epithelium at various developmental stages of the rat. This finding may reflect the fine tuning of epididymal functions by Ang II during the course of development. It is possible that the expression of Ang II receptors and other key components of the RAS in the rat epididymis may be regulated by sex hormones during development to maturation. It is the goal of the present study to demonstrate the expression of RAS and its regulation by testicular hormones in the rat epididymis. Expression of the key RAS components in the epididymis will be studied and compared with normal rat epididymis using immunocytochemistry, in situ hybridization, sodium dodecyl sulphateelectrophoresis polyacrylamide gel PAGE)/Western blotting and Northern blotting. The results of the proposed project should shed new light into the expression of epididymal RAS and its The interactions between regulation in the rat. testicular hormones and the epididymal RAS in the regulation of epididymal function may provide new grounds for the development of contraceptive agents. (CU97621)

Expression and Localization of the Pancreatic Renin-Angiotensin System in the Rat

- ∠ LEUNG Po Sing
- ☐ 1 January 1998
- CUHK Research Committee Funding

In this proposal, the localization and expression of the pancreatic renin-angiotensin system components, e.g. angiotensinogen, which is the obligatory component for an intrinsic RAS, is investigated using immunocytochemistry (ICC), western blot analysis, in situ hybridization (ISH), reverse transcription polymerase chain reaction (RT-PCR) and Northern blot techniques. Specific antibodies against the various RAS components are employed for the localization and expression of these protein components using ICC and WB. Specifically designed sense and antisense primers, based on the corresponding gene sequences of RAS components, are utilized for RT-PCR. The total RNA is extracted from the rat pancreas using guanidiniumthiocyanate-phenol-chloroform method. The mRNA is subjected to first strand cDNA synthesis using oligo-dT primers or random hexamers and reverse transcriptase. 1/10 volume of the reaction mixture is directly used for amplification. The amplified mixture is finally analyzed on 2% agarose gel electrophoresis. The localization of mRNAs is achieved by digoxigenin labelled riboprobes. The respective cDNAs are employed as templates for digoxigenin labelled RNA probe preparation and they are used for ISH. Northern blot analysis is also used to study the gene transcripts in the pancreatic tissue. The mRNA is separated by electrophoresis on 1.5% agarose gel containing denaturing mixture of glyoxal / dimethylsulphoxide / sodium sulphate. Gel containing mRNA of angiotensinogen is transblotted by capillary action with 20 xSSC to nylon membrane. The membrane is then hybridized by incubation with random-primer labelled probes with ³²P prepared from template cDNAs. After thorough washings with SSC, the membrane is subjected to autoradiography to detect hybridization bands.

The present proposal is aimed to study the localization and expression of a local RAS in the rat pancreas. The differential expression and its regulation of the pancreatic RAS may be important for its functions, including the pancreatic blood flow and pancreatic ductal secretion.

(MD97073)

Expression & Regulation of Renin and Angiotensin Converting Enzyme in the Rat Pancreas

- ∠ LEUNG Po Sing NOBILING Rainer*
- ☐ 1 March 1998
- Germany/Hong Kong Joint Research Scheme

Angiotensin II and its receptor subtypes, AT₁ And AT₂ have recently been localized

immunohistochemically in the pancreases of rodents. Angiotensinogen and its mRNA, which are the mandatory component for an intrinsic reninangiotensin system (RAS), have also been demonstrated to express in the rat pancreas. It is suggested that a local RAS appears to be present in the rat pancreas which may be primarily involved in exocrine pancreatic functions including fluid and enzyme secretions from ductal and acinar cells as well as blood flow from vascular elements. In this proposal, the expression and possible regulation of two RAS components, namely renin and angiotensin converting enzyme (ACE) are investigated. These components, which constitute the two critical enzymes of the RAS, play a determining role in converting the precursor angiotensinogen into the final physiologically-active product of the RAS, i.e. angiotensin II. Accordingly, study on the expression and regulation of renin and ACE may be important in elucidating the exocrine pancreatic functions. The localization and expression of renin and ACE in the protein and gene levels are investigated using immunocytochemistry and molecular biological Possible regulation of the gene approaches. expression for renin and ACE by factors such as hormones will be studied. In order to achieve this aim, nephrectomized, castrated and control rat groups are used to study how the expression of pancreatic renin and ACE is regulated in the rat.

The results of the proposed study will be the first step in understanding the role of pancreatic RAS in the regulation of pancreatic functions. (MD97104)

Development of Porcine Growth Hormone Immunoassays

- MONG Chun Cheung
- ☐ 15 February 1998
- LeaderGene Limited

In this research and development project, immunoassays for porcine growth hormone would be developed to support the subsequent studies on the biological half-life (t1/2) of recombinant porcine growth hormone in pigs. Polyclonal antibodies are raised in rabbits and these antibodies are available for the generation of affinity chromatography for the purification of recombinant porcine growth hormone produced in LeaderGene Limited. (BL97010)

Studies of the Renin-Angiotensin System in the Rat Epididymis

- MONG Patrick Yee Ding CHAN Hsiao Chang
- □ 1 July 1997
- ❖ Population Council

The aim of the project is to investigate the role of the local renin-angiotensin system in the formation of the epididymal fluid environment. The project involves the use of culture epithelia from the rat epididymis and the measurement of electrolyte secretion using the short-circuit current technique. The project also probes into the biochemical pathways underlying the physiological actions of the angiotensins and the related paracrine hormones. Emphasis is placed on the role of the cyclo-oxygenases and the effects of the non-steroidal anti-inflammatory drugs. It is hoped that this study will increase our understanding of the role of the paracrine factors in the control of epididymal functions under normal physiological conditions and how these homeostatic processes are disturbed under abnormal conditions. (MD97100)

Anion Secretion by the Sertoli Cells from Cystic Fibrosis Transgenic Mice

- ∠ WONG Patrick Yee Ding CUTHBERT Alan W.*
- ☐ 10 February 1998
- ❖ UK/Hong Kong Joint Research Scheme, the British Council

Cystic fibrosis (CF) is a lethal inherited disorder affecting about 1 in 2000 Caucasians. It is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that encodes a cyclic AMP-regulated chloride channel. Epithelial tissues which express the CFTR gene are affected to varying extent. About 90% of men with CF are infertile due to obstruction of the epididymis or agenesis of the vas deferens. These anomalies are caused by abnormal electrolyte/fluid secretion by the epididymal epithelium. The extent to which the testis also contributes to this condition is unknown.

The purpose of the project is to investigate whether secretion by the Sertoli cells of the testis is also affected in a transgenic mouse model of CF. (MD97108)

Tissue Distribution and Characterization of a cGMP-Gated K Channel

- YAO Xiaoqiang
- □ 15 September 1997
- CUHK Research Committee Funding

Potassium channels are essential for a variety of fundamental cell processes. Several types of K channels play a crucial role in the regulation of vascular smooth muscle tone, peripheral vascular resistance and blood pressure. The researchers have cloned a gene from rabbit that encodes a cGMP-gated K channel which can be activated by cGMP. This represents the first molecular description of a

structurally unique K channel which can be activated by cGMP. Since this K channel is expressed in vascular tissues and it is directly activated by cGMP, it is likely that it participates in the regulation of arterial tone and blood pressure. This channel might be also involved in the chemotaxis and fertilization of sperm through a cGMP signalling pathway. The researchers propose to investigate distribution of the channel, especially in male reproductive tissues and resistance arteries which control the blood pressure. Thev also propose to characterize electrophysiological properties of the channel. These studies will help clarify the role of the channel in regulation of blood pressure and sperm fertilization. (MD97075)

The Nigral GABAergic Inhibitory Pathway as an Endogenous Control System of Epileptic Seizures: An Electrophysiological Study

- YUNG Wing Ho
- ☐ 1 September 1997
- * Research Grants Council

Accumulating evidence suggests that there is an endogenous control system within the midbrain substantia nigra which gates the spreading of epileptic seizures. In this context, the role of inhibitory neurotransmission by GABA is ascertained. However, the exact function of substantia nigra neurones in this control system, especially at the level of the functional circuitry and the contribution of different transmitter receptor subtypes, is still largely To advance our knowledge in these aspects, an *in vitro* rat brain slice preparation will be used allowing electrophysiological recordings from substantia nigra neurones. Emphasis will be placed on identifying the subpopulation of neurones involved in this control system, and on understanding how GABA interacts with pre- and postsynaptic receptors on these neurones. In addition, the influence of age in the expression of GABA receptors will be explored and actions of commonly used antiepileptic drugs in the substantia nigra will be elucidated. It is anticipated that the information obtained will provide a foundation for further studies using specific models of epilepsy and for the development of rational approaches to treating epileptic seizures. (CU97626)

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

Edition Title/Investigators

1995-96 Control of Testicular Microvasculature

by Vascular Endothelial Growth Factor (CU95646)

∠ AU Chak Leung • LEE Will M.*

1996-97 Immunolocalization and Functional Studies of VEGF Receptors on Ovarian Macrophages (MD96092)

AU Chak Leung

1995-96 Study of Epithelial Electrolyte Transport (MD95029)

∠ CHAN Hsiao Chang • WONG
Patrick Yee Ding • CHEW Cheng
Siew Boon • KO Wing Hung

1996-97 Local Paracrine/Autocrine Control of Epididymal Anion Secretion by Vasoactive Peptides (CU96612)

∠ CHAN Hsiao Chang • WONG
Patrick Yee Ding • CHEW Cheng
Siew Boon • KO Wing Hung

1996-97 Calcitonin Gene-Related Peptide (CGRP) and Nitric Oxide Interactions in Vascular Smooth Muscle: Cellular Mechanisms and Involvement in Endotoxin Shock (CU96644)

FISCUS Ronald R.

1996-97 Cyclic GMP- and Protein Kinase G (PKG)-Mediated Increases in Gene Expression and Enhanced Survival of Neurons During Glutamate Toxicity (MD96093)

FISCUS Ronald R.

1995-96 Ionic Mechanisms of Action of cGMPand CAMP-elevating Vasodilators (CU95669)

HUANG Yu

1996-97 Effects of Neurotoxins on Signal Transduction in Central Synapses of the Rats (MD96094)

LEUNG Man Sing

1996-97 The Gene Expression and Regulation of the Renin-angiotensin II System in the Rat Epididymis (MD96117)

∠ LEUNG Po Sing

1995-96 Identification and Molecular Cloning of Genes Expressed During the Sexual Differentiation of the Rat Brain (CU95653)

> WONG Chun Cheung • LEUNG Man Sing • LIU Wing Keung Ken (Anatomy)

1996-97 An Electrophysiological Approach To Study Sertoli Cell - Germ Cell Interaction (MD96118) WONG Patrick Yee Ding

1995-96 Mechano-electric Transduction Currents in Merkel Cell Receptors (CU95612)

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RESEARCH PROJECTS

A Study on Factors Affecting Drug Abuse Trend in Hong Kong

- ∠ LEE Tak Shing Dominic LAU Tai Shing (Statistics) SO Man Pui* LEE Albert (Community & Family Medicine) TANG Leung Sang (Chemical Pathology)
- □ 1 March 1998
- ❖ Action Committee Against Narcotics

The objective of this study is to identify cultural, social and economic factors that correlate with drug abuse trend in Hong Kong. Specific factors that contributed to the recent rising trend in female and psychotropic drug abuse will also be elucidated. It is anticipated that through a better understanding of the underlying driving forces of drug abuse in Hong Kong, a model for forecasting future trend can be formulated.

The Central Registry of Drug Abuse (CRDA) and school surveys data will be the predominant data source for this study. The reliability of these data will first be confirmed by corroboration with other longitudinal drug statistics and ad hoc surveys. After then, a detailed descriptive analysis of the CRDA and school surveys data will be conducted. Specifically, absolute numbers will be converted to rates to allow more accurate reflection of drug abuse situation. The CRDA data will also be re-examined for hidden and undiscovered trends. Appropriate statistical adjustment will be made as both CRDA and school surveys data are non-random data.

The potential cultural, social, and economic correlates will be selected, based on various aetiologies of drug abuse. The relationship between these putative factors and drug abuse trend will be examined by inferential statistics. Poisson regression will be used, and the issues of overdispersion will be To cater for non-linear function, nonparametric method will be also be employed. The possibility of omitting "real" important factors will be tackled and regression approach with the hazard rate as dependent variable will also be used. completion of inferential analysis, a predictive model will be constructed to assist forecasting of future drug abuse trend. The power of our model will be studied by computer simulations. The results of this study will help front line workers and policy makers to have better knowledge and insight of the underlying reasons of drug abuse and to decide on strategic policies on supply, demand and harm reduction. (MD97091)

Research on Effectiveness of Voluntary Residential Drug Abuse Treatment Programme in Hong Kong

- ∠ LEE Tak Shing Dominic
- ☐ 1 April 1998
- ❖ Action Committee Against Narcotics

This is a study of effectiveness of voluntary residential drug abuse treatment programme, a major mode of addiction treatment in Hong Kong. Although such treatment has been in operation in Hong Kong for decades, data on treatment effectiveness is very much lacking. The major objective of this study is to assess effectiveness by quantification of outcome and output indicators. This study will provide much awaited information and will advance evidence-based addiction medicine for Chinese populations. (MD97133)

The Effectiveness of Piracetam on ECT-Induced Memory Disturbances

- ✓ UNGVARI Gabor Sandor LEUNG Chi Ming CHUNG Wai Sau Dicky TANG Wai Kwong*
 LEUNG Yip Shing
- ☐ 15 April 1998
- CUHK Research Committee Funding

Electroconvulsive therapy is still the fastest and most effective therapeutic intervention in depression and some other psychiatric disorders. Postictal confusion and transient memory disturbances are the two most frequent adverse effects of ECT that may cause discomfort to patients and prolong hospitalization. Earlier attempts to find pharmacological solution to minimize these adverse effects suggested that piracetam, a nootropic agent, might be useful in alleviating cognitive side effects of ECT. Since there have been no methodologically sound studies in this field, a random-assignment, double-blind, placebo-controlled study was designed to investigate piracetam's effect on ECT-induced disturbances. Consecutively depressed subjects undergoing ECT will be given either placebo or piracetam during the period of ECT sessions and 2 weeks afterwards. The effect of piracetam on ECT-induced confusion and memory disturbances will be evaluated by standardized clinical and psychological tests. In view of the substantial number of ECTs administered in Hong Kong (>100/year), a significant decrease in the of memory disturbances severity administration of an inexpensive medication would make this very important therapeutic modality more acceptable to patients. In addition to diminishing patients' discomfort, faster recovery after treatment and the resulting earlier discharge would reduce the considerable costs associated with depression. Participation in the study would not pose any danger to the subjects; piracetam has no serious adverse effects. No invasive procedures will be employed in the study.

(MD97124)

An Epidemiological Study of Narcolepsy in Hong Kong Chinese

- ✓ WING Yun Kwok CHEN Char Nie HO
 Kwok Wah Crover LEUNG Yip Shing LI
 Kam Tao Philip (Medicine & Therapeutics)
- □ 15 November 1997
- Research Grants Council

Narcolepsy is a lifelong crippling sleep disorder with significant physical and psychosocial impairments. Although its exact etiology and neuropathology is not clear, a strong association with specific Human leucocyte antigen subtype, particularly DR2 and lately DQ1 (particular DQβ1-0602), has been demonstrated across different ethnic groups. However, there is much controversy about the exact prevalence rate of narcolepsy in various ethnic groups. Whereas Japanese researchers reported the prevalence rate to be as common as one in 200, the Israeli group suggested that it could be as rare as one in 500,000. Such 2500 fold differences in the reported prevalence rate may be due to a number of factors including differences in research methodology, studied population and/or possible ethnic differences in predisposition. To date, there is a substantial lack of well-designed epidemiological study of narcolepsy across different ethnic groups. One of the most recent and best estimations of population prevalence rate came from the Finnish twin cohort study at which it was estimated to be 0.026%. However, there has never been any epidemiological study on narcolepsy in Chinese. By using a carefully translated standardized screening questionnaire and international criteria for narcolepsy and followed by a second stage of confirmation by polysomnographic measurements and HLA typing, the researchers aim to determine for the first time the prevalence rate of narcolepsy in Chinese. Not only will the Chinese clinical-polysomnographic-HLA database of information to be obtained allow further cross-ethnic comparison, the study will also lay the foundation for establishing an epidemiological approach to sleep disorders in general. At theoretical level, the finding should help to understand the etiology and ethnic predisposition and its relationship with HLA typing of narcolepsy. At a practical level, the finding should help to determine the size of the sleep problem and assist in better health care planning so as to enable early detection and treatment of the narcoleptic patients and to foster the development and planning of Sleep Medicine. (CU97675)

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

Edition Title/Investigators

- 1996-97 Evaluative Study of the Services of Non-Subvented Voluntary Drug Treatment and Rehabilitation Agencies (MD96190)
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 Dominic LEUNG Yip Shing •
 WING Yun Kwok LEE Sing
- 1996-97 Pharmacokinetics of Tricyclic Antidepressant Treatment: An Integrated Phenotype and Genotype Approach (MD96114)
 - ∠ CHIU Fung Kum Helen WING Yun Kwok CHOW Lok Yee
- 1996-97 Dementia Home Care Project Training for Demented Patient and Carer in a Territory Wide Level (MD96020)
 - ∠ CHIU Fung Kum Helen LI Siu Wah* CHU Dana*
- 1996-97 Schizophrenia and the Microdeletion 22q11 in a Chinese Population (MD96082)
 - ∠ CHOW Lok Yee WAYE Mary Miu Yee (Biochemistry) GARCIA BARCELO Maria
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WING Yun Kwok • LEE Sing • CHEN Char Nie • CHOW Chun Chung Francis (Medicine & Therapeutics)

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RESEARCH PROJECTS

Use of Non-Confluently Cultured Keratinocytes and Fibroblasts in Fibrin and Matrix Gel Suspension as a Permanent Wound Coverage in Athymic Mice Model

- ∠ CHAN Sun Yin Eric LAM Ping Kuen
- ☐ 1 January 1998
- ❖ CUHK Research Committee Funding

Cultured epidermal autograft is widely applied as permanent wound coverage for patients with extensive burns. However the overall take rates of cultured graft are not satisfactory. Moreover, it usually take three weeks or more to develop a stratified confluent cultured sheets. The basement membrane is the key factor for successful take of cultured graft. The purpose of this study is to build up the basement membrane by non-confluently cultured human keratinocytes and fibroblasts in the presence of protein cocktail containing fibrin and matrix gel solution. Consequently, the enhanced formation of the basement membrane can increase the take rate of cultured graft. The use of non-confluent keratinocytes can shorten the preparation time. (MD97078)

Prospective Study on the Relationship of Central Venous Pressure and Blood Loss During Hepatectomy

- ∠ LAI Bo San CHUI Po Tong (Anaesthesia & Intensive Care) LEOW Chon Kar LAU Wan Yee Joseph
- □ 1 November 1996
- CUHK Departmental Funding

Blood loss remains one of the major problems in liver surgery. In this study, the researchers attempt to correlate the level of central venous pressure and the blood loss during liver surgery. If such a correlation can be demonstrated, it is potentially possible to reduce blood loss during liver surgery by manipulating the central venous pressure in patients undergoing hepatectomy. (MD96217)

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

- ∠ LAU Wan Yee Joseph LEOW Chon Kar LIEW Choong Tsek (Anatomical & Cellular Pathology) LAI Bo San
- ☐ 1 December 1997

Research Grants Council

Activated Kupffer cells have increased phagocytic and cytotoxic activity against tumour cells. Binding of tumour cells by noncytotoxic Kupffer cells has been shown to be associated with the development of metastases (Gjoen et al, 1989). Liver metastases in the presence of cirrhosis is rare and unexplained. Detailed information on Kupffer cell population during the development of cirrhosis and in established cirrhosis is lacking. This study has two objectives. Firstly, to determine the precise Kupffer cell kinetics during the evolution of cirrhosis. Subsequently, an attempt will be made to show that Kupffer cells within the cirrhotic liver are activated with increased cytotoxicity against tumour cells arriving at the hepatic sinusoids via the portal venous system and depletion of these activated cells will predispose a cirrhotic liver to the development of liver metastases. If this hypothesis were correct, a search for an agent which would activate the enhance Kupffer cell cytotoxicity towards tumour cells may provide an attractive alternative treatment in preventing patients from developing liver metastases. (CU97648)

Evaluation of the Bioenergetic Basis of Liver Regeneration Following Partial Hepatectomy - An in vivo 31P-MRS Study

- ∠ LAU Wan Yee Joseph MANN Darren HJELM Nils Magnus (Chemical Pathology)
- ☐ 1 December 1997
- CUHK Research Committee Funding

Post-operative hepatic failure is the commonest cause death following resection for primary hepatocellular carcinoma (HCC), and is associated with inadequate liver regeneration. The judgment of operability is currently based on indirect measurements of liver function, and while recovery is expected following removal of up to 65% of a normal liver, the same cannot be said when cirrhosis is The technique of phosphorus magnetic resonance spectroscopy (31P-MRS) allows repeated non-invasive assessment of the metabolic state of tissues. Using this modality, the bioenergetic state of the liver can be assessed preoperatively and correlated with traditional methods of functional The metabolic alterations that evaluation. characterise recovery and liver regeneration can then be measured in the postoperative period by 31P-MRS, which findings can be compared with the clinical course and blood indicators. The outcome of this study should help refine the selection of treatment options for individual patients, and improve scientific knowledge relating to the fundamental bioenergetic processes that underlie liver regeneration. (MD97077)

Adjuvant Intravenous Proton Pump Inhibitor in Bleeding Peptic Ulcers Receiving Endoscopic Therapy: A Double Blind Placebo Controlled Randomized Study

- ∠ LAU Yun Wong James SUNG Joseph Jao Yiu (Medicine & Therapeutics) CHUNG Sheung Chee Sydney LEE Ka Ho Kenneth (Anatomy)
- □ 1 May 1998
- CUHK Departmental Funding

Bleeding peptic ulcer is a common and life threatening condition with a mortality rate of 5-10%. Endoscopic treatment is now the primary intervention in these patients with an initial success rate of 95-98%. Following endoscopic haemostasis, rebleeding occurs in 15-20% of patients and they constitute the majority of death from the condition. The purpose of the study is to evaluate, by a double-blind placebo-controlled randomized study, the potential benefit of high dose intravenous infusion of proton pump inhibitor as an adjunctive therapy to endoscopic treatment in the control of rebleeding and thereby improving outcome in patients with bleeding peptic ulcers. (MD97171)

Immune Modulating Peptides Resemble Microtubule Binding Domains

- ∠ LEUNG Mun Fai
- ☐ 1 June 1998
- CUHK Research Committee Funding

Immunosuppressive drugs are used as adjunct therapy in organ transplant to prevent the rejection of the donor's tissue engraftment by the host immune Since the use of cyclosporin in response. therapy, the number immunosuppressive successful organ transplants performed has greatly increased. Immunophilins have been identified as major intracellular molecules which bind to immunosuppressive drugs such as cyclosporin A, FK506 and rapamycin. Immunophilins have been shown to possess cis-trans peptidyl-prolyl isomerase activity with possible involvement in signal pathway of immune modulation by altering the conformation The laboratory has revealed of target proteins. sequence homology between immunophilins and the microtubule binding domains of the microtubuleassociated proteins. A search of protein databases using these microtubule binding domain sequences of immunophilin resulted in the delineation of a number of proteins that have been previously demonstrated experimentally to be associated with microtubules. Immunophilins may bind to micortubules to form a complex that regulates the immune response signaling proteins through its rotamase activity. Recently, the laboratory has demonstrated that there

is strong association of immunophilins and microtubules. The goal of this proposal is to determine the immune modulating effects of the peptides that resemble the microtubule binding domains. This study will provide new insights on the regulation of immune activity and may lead to the development of immune modulating peptides for therapeutic application. (MD97125)

The Comparative Impact of Videoconsultation on Neurosurgical Health Services

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

This project proposes a randomised controlled trial to evaluate the impact of telemedicine technology on the provision of neurosurgical health services. The study will focus on the differences effected by the use of real-time audio-visual teleconferencing and teleradiology versus conventional consultations in the referral of neurosurgical patients in United Christian Hospital and a tertiary neurosurgical referral centre (Prince of Wales Hospital). Consultations of interest will be restricted to patients with head trauma or cerebrovascular disease. Measures of effectiveness will include those related to clinical and health attributes (e.g. diagnostic accuracy, appropriateness of management, adverse events, health outcome) and those of an economic nature (i.e. cost-effectiveness and value added time). (MD97095)

Development of a New Hyaluronic Acid Membrane Delivery System for Using the Cultured Keratinocytes as a Permanent Wound Cover

- ★ TO Wai Hei KING Walter Wing Keung LAM Ping Kuen CHAN Sun Yin Eric
- ☐ 1 April 1998
- **❖** CUHK Research Committee Funding

Cultured epidermal autograft (CEA) is widely applied as permanent wound cover for patients with extensive burns. However the clinical take rates of CEA are poor on full-thickness wound unless a dermal bed is provided. CEA has two clinical limitations - the time required in growing autografts and the fragility of the grafts. The purpose of this study is to develop a laser-perforated hyaluronic acid membrane delivery system that supports rapid proliferation and differentiation of keratinocytes. The system allows grafting at early confluence without requiring dispase digestion to

release grafts from the petri dish. Consequently this hyaluronic acid delivery system can shorten the preparation time and increase the clinical take rate of CEA.

(MD97126)

An Open Clinical Trial of Dysport in Bilateral Masseteric Hypertrophy

- ★ TO Wai Hei HO Wai Sun*
- □ 1 May 1998
- Beaufour Ipsen International

Bilateral masseteric hypertrophy is a very common condition among the Chinese population. characterized by a "square face" and prominent angles of the lower jaws. Current medical treatment is mainly by surgical reduction of the prominent jaw and muscles. The hypertrophic muscles are, in fact, the primary cause and injection induced atrophy of the muscle will allow remodeling and shrinkage of the prominent bone. Dysport, botulinum toxin A (BtA), is a protein produced by Clostridium botulinum and is the most potent bacterial toxin known. Dysport is an established treatment for blepharospasm and spasmostic torticollis. injection of a small amount into a muscle selectively weakens it. BtA binds specifically to the cholinergic motor end-plate and is actively taken up by motor neurones. Its mechanism of action with the neurone is uncertain, but it blocks release of acetylcholine and causes presynanptic neuromuscular blockage. This study is designed to evaluate the efficacy of Dysport in the treatment of bilateral masseteric hypertrophy. (MD97142)

Neonatal Hearing Screening Using Distortion Product Otoacoustic Emissions (DPOAEs), Steady State Evoked Potentials (SSEPs) and Impedance Audiometry - A Preliminary Study

- ✓ VAN HASSELT Charles Andrew TONG Chi
 Fai Michael WONG Terrence K. C.* •
 LEUNG Eric K. C.* FOK Tai Fai (Paediatrics)
 McPHERSON B.*
- ☐ 1 November 1997
- ❖ CUHK Research Committee Funding

Approximately 1% of normal new born children and up to 5% of neonates in special care units have significant hearing problems. The problems of hearing screening are the availability of accurate screening tests and subsequent confirmation tests. A recently developed technique, steady-state evoked potential is incorporated into an algorithm for hearing screening for newborns in this preliminary study. The results of this study will be invaluable for health care and educational planning for deaf children. (MD97076)

The Effect of Indoor Pollution on the Development of Rhinitis in Office Workers in Hong Kong

- VAN HASSELT Charles Andrew TONG Chi
 Fai Michael TSANG King Yin Raymond* •
 WOO Kong Sang John LAU Tak Fai Joseph
 (Centre for Clinical Trials & Epidemiological
 Research) WONG Ming Chung (Centre for
 Clinical Trials & Epidemiological Research) •
 NG Heung Ling Margaret (Anatomical &
 Cellular Pathology) YU Tak Sun Ignatius
 (Community & Family Medicine)
- ☐ 1 March 1998
- Occupational Safety and Health Council Research Grant

Indoor pollution has developed into a major public health issue in the industrial world. Indoor pollutants have been implicated in the development of rhinitis, asthma and in the aggravation of allergy affecting the upper respiratory tract. Due to the anatomy of the nasal airway, air pollutants are concentrated in the nasal mucosa, which leads to a direct chemical and physical irritation and rhinitis. In addition pollutants have been shown to play an adjuvant role in the development of allergic rhinitis and are cited as a cause for the increasing incidence of both allergic rhinitis and asthma. Phase one of this study aims at identifying the prevalence of rhinitis amongst office workers in office buildings with varying degrees of pollution in Hong Kong. In phase two, cases and controls will be drawn from these office blocks and the effect of the pollutants on the nasal mucosa will be scientifically and objectively assessed. assessment will take the form of nasal endoscopy, acoustic rhinometry, nasal cytology and mucociliary clearance with these outcomes correlated to levels of air pollution, symptoms and quality of life. This study has major implications for the general health of all office workers in Hong Kong and the industrialised world. (MD97019)

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

- YEUNG Chung Kwong
- ☐ 1 October 1997
- CUHK Research Committee Funding

The great advances of minimally invasive surgery in adults has led many to assume that these techniques should apply equally well to paediatric patients with the same degree of efficacy and safety. Over the last few years there has been a rapid expansion of the list

of paediatric surgical operations being performed by laparsocopic approach worldwide, usually conducted with similar equipment and under almost identical operative settings, e.g. intraabdominal pressure for pneumoperitoneum, as in adults. However, scientific data regarding possible differences in physiological response and stress reaction between small children and adults during laparoscopic surgery completely lacking. A prospective, randomized study of laparoscopic versus open appendectomy in children conducted in the researchers unit has revealed no significant benefits of the former approach, and indeed some possible ill effects especially in cases with bacterial contamination of the peritoneal cavity. This highlights the great importance to evaluate comprehensively differences in physiological response between infantile and adult subjects during laparoscopic surgery, both in a clean as well as in a contaminated peritoneal cavity, using a pig model. The results should provide very important clues to the future development of minimally invasive surgery in young children and in particular should shed light on the necessary precautions that may be required for children with compromised cardiopulmonary status. (MD97080)

Investigation of the Efficacy of External Stenting of Saphenous Vein Bypass Grafts in Preventing Deleterious Graft Wall Changes Following Coronary Artery Bypass Surgery

- ✓ YIM Ping Chuen Anthony SANDERSON John Elsby (Medicine & Therapeutics) CHOW Tsun Cheung (Anatomical & Cellular Pathology)
- □ 15 September 1997
- * Research Grants Council

The long term success of coronary artery surgery using the saphenous vein is limited by an average occlusion rate of 50% of all grafts by 10 years. The clinical and economic significance of saphenous vein graft failure should not be underestimated since patients with vein graft stenosis or occlusion are exposed to an increased risk of acute myocardial infarction, sudden death, and heart failure. Furthermore, ten years after a primary coronary artery bypass surgery, at least 20% of patients will require a further revascularisation procedure, which is universally associated with an increased operative mortality and morbidity.

The development of strategies to improve late patency of aphenous vein bypass grafts represent a worthwhile goal. Recent animal experiments by the applicant confirmed that the external support of vein grafts by a Dacron stent have definite favourable effects on vein graft morphology. The aim of the proposed investigation is to study the efficacy of external stenting of saphenous vein bypass grafts in preventing deleterious graft wall changes in patients

undergoing coronary artery bypass surgery. Further animal experiments are also proposed which will help to further elucidate the underlying mechanism behind this effect. (CU97647)

Specific Inactivation of a Growth- and Transformation-Suppressor in Small Cell Lung Cancer

- □ 1 October 1997
- CUHK Research Committee Funding

The promyelocytic leukemia (PML) gene, which encodes a transformation and growth suppressor, was identified first at the non-random chromosomal translocation break point of acute promyelocytic leukemia. To determine if the PML gene may be involved in other neoplasias such as lung cancer, the of PML expression was analvzed immunohistochemical staining of human lung cancer. Low or undetectable expression of PML protein was found in all of the small cell lung cancer (SCLC) examined as compared to normal lung tissues. Increase expression of PML protein in the PML-Oncogenic Domain (POD) structure were found in adenocarcinomas (ADC) and squamous cell carcinomas (SCC). Interestingly, PML was expressed most strongly in the cancer cells at the periphery of ADC and SCC as well as in the surrounding non-tumor cells. Expression was progressively decreased to almost undetectable levels at the center of the tumors. Double staining with the proliferation marker Ki67 indicated that PML was expressed in Ki67-negative non-proliferative cells. Moreover, double staining with the macrophage specific marker KP1 indicated that tumor-associated macrophages were devoid of PML expression, in contrast to the non-tumorigenic tissues. These data indicate that the expression of PML in lung tissues is complex, and that this knows suppressor gene may play an important role in various cell types including the tumor cells. The specific inactivation of PML in SCLC also suggests that this alteration may be an obligatory step in the tumorigenesis of SCLC. (MD97083)

Effect of Short Term Exposure of Saphenous Vein Grafts to Thapsigargin on Medial and Intimal Thickening in a Porcine Arterio-Venous Bypass Graft Model

- 1 November 1997
- CUHK Research Committee Funding

The researchers have recently demonstrated in cell and organ culture models that thapsigargin, an elevator of cytosolic calcium, is a potent inhibitor of *in vitro* vascular smooth muscle cell (VSMC) proliferation and migration and neointima formation in an organ culture model of human saphenous vein. Thapsigargin possesses two properties that set it apart from other mobilisers of intracellular calcium (e.g. ionomycin or calcium ionophore A23187):

- (1) it inhibits VSMC proliferation and migration and neointima formation at extremely low concentrations (<10 nmoles/1) and
- (2) its effect is manifest after only short term exposure and is long lasting.

Pretreatment of vein grafts with thapsigargin prior to implantation may therefore constitute a viable therapeutic approach to long term vein graft failure. In order to explore this possibility, the researchers propose to examine the effect of short term exposure of vein grafts to thapsigargin, prior to implantation, on medial and intimal thickening and related biochemical parameters in an established procine model of saphenous vein — carotid artery interposition grafts.

(MD97079)

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

Edition Title/Investigators

- 1995-96 Evaluation of P-glycoprotein,
 Glutathione S-transferase (GST-π) and
 DNA Ploidy in Predicting
 Chemoresponse in Patients Received
 Neo-adjuvant Chemotherapy for
 Squamous Oesophageal Cancer: A
 Retrospective Study (MD95168)
 - ∠ CHAN Chi Wai Angus CHUNG Sheung Chee Sydney IP Sin Ming[#]
 • METREWELI Constantine (Diagnostic Radiology & Organ Imaging) SUEN Wang Ming Michael (Anatomical & Cellular Pathology)
- 1996-97 Neo-adjuvant Chemotherapy in Squamous Oesophageal Cancer:
 Prediction of Chemoresponse Using Biopsy Sample before Chemotherapy (CU96649)
 - CHAN Chi Wai Angus CHUNG
 Sheung Chee Sydney LAU Yun
 Wong James METREWELI
 Constantine (Diagnostic Radiology
 & Organ Imaging) JOHNSON
 Philip James (Clinical Oncology) •
 NG Enders K. W.*

- 1996-97 A Study of Expression of Prostate Secretory Protein of 94 Amino Acid and its Alternative Transcripts in Normal, Hyperplastic and Neoplastic Human Prostate (MD96095)
 - ∠ CHAN Siu Foon Peter
 ◆ WONG
 Wai Sang
 ◆ CHAN Leung Franky
 (Anatomy)
- 1996-97 Prognostic Factors of Breast Cancer among Women in Hong Kong (MD96101)
 - ∠ CHAN Sun Yin Eric SUEN Wang Ming Michael (Anatomical & Cellular Pathology)
- 1996-97 To Investigate the Clinical Usefulness of Arginase, Amino Acid Profile and Sialic Acid as Tumour Markers for Breast Cancer (MD96096)
 - ∠ CHAN Sun Yin Eric ◆ PANG Chi
 Pui Calvin (Ophthalmology & Visual
 Sciences) ◆ LAM Ping Kuen ◆
 KING Walter Wing Keung

 ∠ CHAN Sun Yin Eric ◆ PANG Chi
 Pui Calvin (Ophthalmology & Visual
 Sciences) ◆ LAM Ping Kuen ◆
 KING Walter Wing Keung

 ∠ CHAN Sun Yin Eric ◆ PANG Chi
 Pui Calvin (Ophthalmology & Visual
 Sciences) ◆ LAM Ping Kuen ◆

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 ∠ CHAN Sun Yin Eric ◆ PANG Chi
 Pui Calvin (Ophthalmology & Visual
 Sciences) ◆ LAM Ping Kuen ◆

 ∠ CHAN Sun Yin Eric ◆ PANG Chi
 Pui Chan Sun Yin Eric
- 1995-96 Can MRCP Replace Diagnostic ERCP in Patients with Suspected Choledocholithiasis? (MD95167)
 - ∠ CHUNG Sheung Chee Sydney CHAN Chi Wai Angus CHAN Yu Leung (Diagnostic Radiology & Organ Imaging) LEE W. H.* NG Enders K. W.* METREWELI Constantine (Diagnostic Radiology & Organ Imaging)
- 1995-96 A Study of p53 Mutations and mdm2 Gene Amplification in Human Gastric Cancer (MD95146)
 - ∠ CHUNG Sheung Chee Sydney LI Arthur K. C.
- 1996-97 Stress Responses and Endotoxaemia in Patients with Generalised Peritonitis: A Randomised Comparison between Laparoscopic and Open Surgery (MD96098)
 - ∠ CHUNG Sheung Chee Sydney
 LAU Yun Wong James
- 1996-97 A Prospective Study on the Prevalence of Helicobacter Pylori Infection in Patients with Perforated Duodenal or Juxtapyloric Ulcers (MD96099)
 - CHUNG Sheung Chee Sydney LAU Yun Wong James
- 1996-97 The Prevalence of Helicobacter Pylori in the Peptic Ulcer Complication of Pyloric

Stenosis: An Implication for Change in Management Strategy (MD96097)

- ∠ CHUNG Sheung Chee Sydney
 LAU Yun Wong James
- 1996-97 A Multicentre Double Blind Study to Assess the Safety and Efficacy of Rantidine Bismuth Citrate 400mg BD Plus Clarithromycin 500mg BD Plus Metronidazole 400mg BD Given for Either 5 or 7 Days in the Eradication of Helicobacter Pylori (MD96184)
 - ∠ CHUNG Sheung Chee Sydney LEUNG Wai Keung* WU Justin*
 CHAN Lek Yuen* WONG Kin Hung* CHING Yuet Ling (Medicine & Therapeutics) YUNG Man Yee SUEN Choi Ying Roamy
- 1996-97 Influence of External Stent Texture on Early Medial and Neointimal Thickening in a Pig Model of Saphenous Vein Bypass Grafting (MD96120)
- 1996-97 The Induction of Apoptosis of Hepatic Cancer Cells by Polyunsaturated Fatty Acids (MD96119)
 - LAU Wan Yee Joseph LAI Bo San• LEOW Chon Kar
- 1996-97 Repeat Endoscopic Treatment or Surgery in the Management of Rebleeding Peptic Ulcers After Initial Endoscopic Haemostasis: A Prospective Randomized Controlled Trial (MD96182)
 - ∠ LAU Yun Wong James SUNG Joseph Jao Yiu (Medicine & Therapeutics) CHUNG Sheung Chee Sydney CHAN Ka Leung Francis (Medicine & Therapeutics)
- 1996-97 Antiemesis Efficacy of Tropisetron: A
 Double-Blind Randomised Trial
 Comparison to a Metoclopramide-Based
 Regimen in Patients with Carcinoma of
 Oesophagus Receiving Cisplatin
 (MD96149)
 - LAU Yun Wong James NG K.W.*• CHUNG Sheung Chee Sydney
- 1996-97 A Multicentre Prospective Randomised Comparison of Laparoscopic Versus Open Cholecystectomy in Acute Cholecystitis (MD96183)
 - ∠ LAU Yun Wong James LEOW Chon Kar • KWONG K.H.* • SIU W.T.* • LI Michael* • KWOK

- Samuel* ◆ CHAN Chi Wai Angus ◆ LAU Wan Yee Joseph ◆ CHUNG Sheung Chee Sydney
- 1996-97 Accelerated Induction of Liver Cirrhosis by Tamoxifen Via the TGF-β - Lipocyte Axis - a Putative Pathway (MD96102)
 - ∠ LEOW Chon Kar LAU Wan Yee
 Joseph LIEW Choong Tsek
 (Anatomical & Cellular Pathology) •
 LAI Bo San
- 1996-97 Innovation Technology to Develop Human Cell Lines for Biomedical Applications and Biopharmaceutical Production (MD96192) ∠ LEUNG Mun Fai • IP Nancy*
- 1995-96 The Detection of Tissue Plasminogen Activator in the Neovasculature of Central Nervous System Tumours - A Molecular Approach (MD95206) ✓ POON Wai Sang • GOH Keith*
- 1996-97 Does Intensive Rehabilitation Improve the Functional Outcome of Traumatic Brain Injury (TBI)? (MD96006)
 - POON Wai Sang ◆ ZHU Xian Lun ◆
 HSIANG John Keung* ◆ CHAN Che
 Hin* ◆ IP Wei Chung* ◆ CHANG
 Wai Ching*
- 1996-97 Neuropsychological Outcome after Mild Head Injury: Any Difference if the Injury is Work-related? (MD96100)
- 1996-97 Molecular Expression of Hypothalamic Atrial Natriuretic Peptide (ANP) and Anti-diuretic Hormone (ADH) in Hyponatraemia Following Experimental Head Injury (MD96103)
 - ∠ POON Wai Sang NG Ho Keung (Anatomical & Cellular Pathology) LOLIN Yvette Ivanka (Chemical Pathology)[#] YEUNG Tok Fai Vincent (Medicine & Therapeutics)
 COCKRAM Clive Stewart (Medicine & Therapeutics)
- 1994-95 Investigations into the Aetiology and Management of Nasopharyngeal Carcinoma (MD94071)
 - ∠ VAN HASSELT Charles Andrew •
 LEE Joseph C. K. (Anatomical & Cellular Pathology)

- 1995-96 A Prospective Randomised Trail on the Effects of Use of Pre-operative Ofloxacin Ototopical Ear Drops on Myringoplasty for Chronic Suppurative Otitis Media (MD95233)
- 1995-96 Epidemiology of Otitis Media with Effusion in Hong Kong Chinese School Children (MD95175)
 - ✓ VAN HASSELT Charles Andrew ●
 TONG Chi Fai Michael WOO
 Kam Sang (Medicine & Therapeutics)
 ● YUE Virgil* FOK Tai Fai
 (Paediatrics) LAU Tak Fai Joseph
 (Centre for Clinical Trials &
 Epidemiological Research)
- 1995-96 A Phase IIB Open Labelled, Single Group Study into the Effect of mTHPCmediated PDT on Recurrent and Advanced NPC after Radiotherapy (MD95235)
 - ✓ VAN HASSELT Charles Andrew WOO Kong Sang John TONG Chi Fai Michael LEUNG Sing Fai (Clinical Oncology) LEE A.* CHANG Mei Kam Amy

 ✓ Kam Am
- 1996-97 Effect of Radiotherapy on the Cochlear and the Central Auditory Conduction Pathway in Patients with Nasopharyngeal Carcinoma (NPC) (MD96012)
 - VAN HASSELT Charles Andrew TONG Chi Fai Michael

- 1996-97 A Double Blind Randomised Placebocontrol Trial on the Efficacy of Perioperative Zithromax as Prophylactic Antibiotic for Functional Endoscopic Sinus Surgery (MD96143)
 - WOO Kong Sang John TONG Chi
 Fai Michael VAN HASSELT
 Charles Andrew KU Peter K. M.*
 CHANG Mei Kam Amy#
- 1996-97 Differences in Prevalence, Phenotype characteristics and Antigenicity of Helicobacter Pylori Infection in Children: A Comparative Study between Hong Kong and Jiangsu (MD96104)
 - YEUNG Chung Kwong CHEN Junshi* WU Yongning* CHUNG Sheung Chee Sydney SUNG Joseph Jao Yiu (Medicine & Therapeutics) PANG Chi Pui Calvin (Ophthalmology & Visual Sciences)
- 1995-96 Video Assisted Thoracic Surgery (MD92192)

 ∠ YIM Ping Chuen Anthony
- 1996-97 A Comparative Study of the Effects of Wedge Lung Resection by Thoracoscopy Versus Thoracotomy on the Metabolic and Immunological Response in a Porcine Model (CU96658)
 - ∠ YIM Ping Chuen Anthony

 → HEWITT Peter[#]

 → HO Jonathan Kei Shing[#]

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see also <P971791>, <P972005>, <P972026>, <P972147>, <P972291>, <P972334>, <P972339>, <P972349>,
<P972353>, <P972376>, <P972426>, <P972427>, <P972433>, <P972434>, <P972452>, <P972452>, <P972581>,
<P972627>, <P972634>, <P972677>, <P972863>, <P972866>, <P972907>, <P973063>, <P973478>,
<P973979>, <P973980>, <P974037>, <P974043>, <P974044>, <P974194>, <P974776>, <P974812>,
<P974901>, <P974903>, <P974904>, <P980094>, <P980129>, <P980134>, <P980176>, <P980216>,
<P980215>, <P980732>, <P98032>, <P980833>, <P980857>, <P980895>, <P980896>, <P980978>,
<P980979>, <P981026>, <P981057>, <P981058>, <P981182>, <P981184>, <P981191>, <P981260>,
<P981325>, <P981327>, <P981435>, <P981848>, <P982368>, <P982379>, <P982473>
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Haemostasis Following Trauma

- ∠ COCKS Robert LAM Yuk Lan RAINER
 Timothy NG Heung Ling Margaret
 (Anatomical & Cellular Pathology) •
 MAYCOCK Paula*
- ☐ 1 April 1998
- CUHK Research Committee Funding

Introduction: Acute coagulopathy, severe enough to require treatment, is present in about 19% of major trauma victims, rising to 61% in those who have received over 4 litres of intravenous fluids. This coagulopathy appears to have two components, the first relating to the effects of the injury itself and the second due to fluid resuscitation. This research project will examine the effects of trauma and resuscitation on the expression of platelet adhesion molecules, and includes laboratory studies to identify factors involved in adhesion molecule control, including the effects of stress hormones.

Methods: 45 trauma patients and 50 normal control subjects will be studied. Platelet adhesion molecules and activation markers will be characterised in both

studies using specific monoclonal antibodies and flow cytometry. Patient groups will include 15 major, 15 moderate and 15 minor trauma patients. Blood from normal controls will be treated with stress hormones, individually and in combination at levels typical of those seen in trauma patients, to determine the role of these factors in adhesion molecule expression. (MD97109)

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

Edition Title/Investigators

1995-96 The Immune Response to Trauma (MD95207)

 ∠ COCKS Robert • CHAN Yau Foon[#]
 • NG Heung Ling Margaret
 (Anatomical & Cellular Pathology) •
 CRITCHLEY Julian A.J.H.
 (Medicine & Therapeutics)

RESEARCH OUTPUTS AND PUBLICATIONS

- <P953656> Barton, R.N.; R.A. Cocks; M.O. Doyle and H. Chambers. "Time Course of the Early Pituitary-Adrenal and Metabolic Responses to Accidental Injury". *The Journal of Trauma: Injury, Infection, and Critical Care* vol.39 no.5, pp.888-894. USA, 1995.12.
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see also <P980311>, <P980382>

Understanding the Adolescent Project - Pilot Implementation and Evaluation Study

- ∠ LAU Tak Fai Joseph CHOI Yuen Wan* LAI Yee Ching Kelly (Psychiatry) • OBORNE David* • HOH Ying*
- □ 1 September 1997
- Social Welfare Department, Hong Kong Government

A new screening instrument called "Student Information Form (SIF)" was developed in a former project by the research team, aiming at the early detection of students with developmental problems. It is suggested that primary developmental programs will be offered to such identified students. The instrument has important implications for large scale applications in Hong Kong. The study represents a pilot exercise which interviews all Secondary One students of 10 schools in Shatin. The students screened positive by SIF are randomly allocated to an intervention group and a control group, the former will be offered a preventive program of four months. The effectiveness of the project will be evaluated by a 18-month follow up longitudinally.

The objectives of the project are:

- (1) To develop a centralized protocol in operating the screening process as well as co-ordinating program for the SIF positive students;
- (2) To validate SIFs in predicting behavioral and psychological needs of the identified youths by using a longitudinal approach;
- (3) To evaluate the effectiveness of a standardized primary developmental programs which will be focused on various aspects of developmental needs for SIF positive students.

(ED97026)

Blood Donor Attitudes towards Blood Safety Counselling and HIV Related Issue in Hong Kong

- ∠ LAU Tak Fai Joseph LIN Chi Kit* JO-THOMAS -
- □ 1 November 1997
- ❖ Council for the AIDS Trust Fund

Some of the recent incidents of transfusion of HIV infected blood to the recipients brings our attention to the importance of taking special efforts to maintain the blood safety. Monitoring the voluntary blood donors' knowledge about the window period for HIV testing, attitude towards HIV testing, risk behaviours and blood safety counselling is an important component of efforts to sustain the blood safety and evaluation of the efficacy of current blood transfusion system in Hong Kong. 1,500 subjects who are donors

from the major Red Cross Donation Centres will be interviewed.

The results of the proposed study will give valuable data necessary for blood donor education and developing proactive donor policy and appropriate legal framework to sustain safe blood supply in Hong Kong.

(MD97127)

The Development of Indicators to Track Awareness, Attitude and Behaviours

- ∠ LAU Tak Fai Joseph LEE Shiu Hung (Community & Family Medicine)
- ☐ 1 March 1998
- Council for the AIDS Trust Fund

The studies proposed will develop a cluster of Program Effectiveness Indicators (PEIs) that will allow researchers/programmers to evaluate the five important dimensions of the AIDS programs in HK, namely, (1) the public awareness and knowledge with regard to AIDS-relevant issues; (2) the trend for discrimination versus support exhibited by the public towards persons living with AIDS; (3) the level of risk behaviours practised by members of the community at large and some particular social groups; (4) the practice of preventive measures taken by the community at large and some particular social groups; (5) the needs, service utilisation patterns and quality of life of the people with AIDS. The data will be obtained from several individual studies.

The development of these PEIs serves four important functions: (1) To evaluate the overall effectiveness of the accumulated impacts from all social programs directed towards the above-mentioned dimensions. (2) To reveal the strategic information about specific aspects of the AIDS campaign from which better policy and programming can be formulated. (3) To form a surveillance system of which both AIDS-relevant awareness and behaviours can be monitored. (4) To address the need of the patients with AIDS in HK.

(MD97129)

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

Edition <u>Title/Investigators</u>

1995-96 A Project to Monitor the Changes in Public Awareness and Attitudes on AIDS in Hong Kong (SS94025)

∠ LAU Tak Fai Joseph • LEE Shui San*

1996-97 Hong Kong Adult Vision Study: A Cross-Sectional Epidemiological Study of Eye Diseases in the 40 Years of Age and Over Population of Hong Kong (MD96016)

John (Ophthalmology & Visual Sciences)

1996-97 Hong Kong AIDS Information Net Project (MD96133)

LAU Tak Fai Joseph

Public Opinion on Child Abuse - A Follow-up Study (SS96042)

∠ LAU Tak Fai Joseph • CHEUNG Chau Kiu (Clinical Pharmacology)

†

RESEARCH OUTPUTS AND PUBLICATIONS

- <P964162> Lo, Peng Iok; Patrick C.P. Ho; Joseph T.F. Lau; Albert Y.K. Cheung; Ernst Goldschmidt and Mark O.M. Tso. "Relationship between Myopia and Optical Components A Study among Chinese Hong Kong Student Population". Eye Science vol.12 no.3, pp.121-125. China, 1996.
- <P972339> **Hsiang, John N.K.; Theresa Yeung; Ashley L.M. Yu and Wai S. Poon.** "High-risk Mild Head Injury". *Journal of Neurosurgery* vol.87, pp.234-238. USA, 1997.08.
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see also <P964124>, <P971748>, <P972005>, <P972448>, <P972449>, <P972623>, <P972691>, <P973521>, <P973706>, <P974539>, <P974564>, <P974878>, <P974884>, <P980026>, <P980046>, <P980164>, <P980243>, <P980540>, <P980706>, <P980712>, <P980766>, <P981352>, <P981592>

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

Edition	Title/Investigators
1995-96	Transgenic Study of Immunoglobulin Gene Hypermutation: Using Selectable, Chimeric <i>E. coli</i> gpt-VJ Gene Constructs to Investigate the Role of Rearranged VJ in Hypermutation (MD94123) ∠ CHUI Yiu Loon • LIM Pak Leona
1996-97	Molecular Mechanism of Immunoglobulin Gene Hypermutation: Does It Resemble the Transcription-DNA Repair System? (CU96664)

∠ CHUI Yiu Loon • LIM Pak Leona

1995-96 To Investigate the Structural Basis for the Carrier Specificity of Antiphosphorylcholine Antibodies (CU94645)

∠ LIM Pak Leone • LEUNG Hei
Wun* • CHUI Yiu Loon • TSANG
Kam Sze Kent* (Anatomical &
Cellular Pathology)

RESEARCH OUTPUTS AND PUBLICATIONS

- <P971879> Lim, P.L.; D.T.M. Leung; L.W.K. Ng; K.C. Wong; S.Y. Song; Y.L. Chui; J.C.K. Leung; K.N. Lai and S.F. Lui. "An Anti-Idiotypic (T14) Antibody Found Commonly in Patients with Systemic Lupus Erythematosus That May Be Pathogenic". Annals of the New York Academy of Sciences vol.815, p.462. USA, 1997.
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see also <P961976>, <P973122>, <P974401>

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

Edition Title/Investigators

1996-97 A Comparison between the Effects of

Percutaneous and Oral 17-Beta Oestradiol on Atheroma Formation and Vascular Reactivity in Cholesterol-Fed Ovariectomised Rabbits (MD96039) ✓ JAMES Anthony • HAINES
Christopher John (Obstetrics &
Gynaecology) • SAHOTA Daljit
(Obstetrics & Gynaecology) •
JONES Robert Leslie
(Pharmacology) • HJELM Nils
Magnus (Chemical Pathology) •
CHOW Tsun Cheung (Anatomical &
Cellular Pathology)

RESEARCH OUTPUTS AND PUBLICATIONS

<P981102> James, A.E.; R. Hamilton; N. Campbell and P. Presidente. "The Pseudoparasite Cyniclomyces guttulatus (Syn. Saccharomycopsis guttulatus) in Rabbit Faeces". Animal Technology vol.49 no.1, pp.35-38. UK, 1998.

see also <P973393>, <P974025>, <P980845>, <P981312>

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

Edition Title/Investigators

1995-96 Cervical Screening in New Territories
East: Prevalence of Unmet Need
(MD95149)

MAZLETT Clarke Blaine

RESEARCH OUTPUTS AND PUBLICATIONS

<P981926> **Hazlett, C.B.** "Teaching Evidence-Based Medicine". *Hong Kong Medical Journal* vol.4 no.2, p.183. Hong Kong, 1998.06.

see also <P972632>, <P980743>, <P982004>, <P982214>, <P982232>