

The background of the page is a grayscale marbled pattern with swirling, organic shapes in various shades of gray, creating a textured and artistic effect.

Faculty of

Medicine

RESEARCH PROJECTS

Effect of Pregnancy on the Concentrations of Propofol Required for Hypnosis and Anaesthesia

- ✉ MORLEY Andrew P.
- ☐ 1 March 1997
- ❖ CUHK Research Committee Funding

This Department was the first to show that pregnancy reduces the concentration of inhalational anaesthetic required for anaesthesia by 30%. The researchers now wish to show that there is also a reduced requirement for the intravenous anaesthetic, propofol. They will look at the response to different concentrations of propofol in two groups of patients; 40 pregnant ladies for elective termination of early pregnancy, and 40 nonpregnant ladies scheduled for elective surgery. The study will take place in the operating theatre suite and will be completed before surgery begins.

A computer controlled infusion pump will give propofol so the blood concentration is constant. During the study they will target eight different concentrations. At each concentration the patients' response will be measured by their degree of hypnosis, and their electroencephalogram, including the bispectral index, which is a processed variable which correlates with degree of sedation.

Blood samples will be taken at each target propofol concentration, when the patient falls asleep, and when she awakens, to confirm the actual concentrations of propofol. Progesterone and endorphin concentrations in blood will be measured. Blood is taken from a radial arterial line.

They will compare various endpoints between the two groups; the propofol concentrations and the bispectral index and sedation scores.

(MD96107)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition	Title/Investigators
1995-96	A Double-Blind Randomised Study of the Addition of Clonidine to Patient-Controlled Epidural Pethidine (MD95076) ✉ CHEN Phoon Ping ● LAM Kwok Key ● CHUI Po Tong ● GIN Tony
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)

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- <P963124> **Buckley, Tom.** "Rafferty-Basics of Transesophageal Echocardiography". *Anaesthesia and Intensive Care* vol.24 no.4, p.519. Australia, 1996.
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- <P963136> **Short T.G.; Buckley T.A.; Rowbottom Y.M. and Oh T.E.** "Long Term Outcome Following Admission to Intensive Care in Hong Kong". Paper presented in the International Hospital Federation Pan Regional Conference. Hong Kong, 1996.
- <P963137> **Buckley, T.A.; Short T.G.; Rowbottom Y.M. and Oh T.E.** "Critical Incident Reporting in the Intensive Care Unit". Paper presented in the International Hospital Federation Pan Regional Conference. Hong Kong, 1996.
- <P963138> **Buckley, T.A.; Gomersall C. and Oh T.E.** "Validation of the Multiple Organ Dysfunction Score in Critically Ill Medical and Surgical Patients". Paper presented in the 21st Australian and New Zealand Scientific Meeting on Intensive Care. Australia, 1996.10.
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- <P963143> **Kee, W.D. Ngan; K.K. Lam; C.J. Twyford and T. Gin.** "Evaluation of a Disposable Device for Patient-Controlled Epidural Analgesia After Caesarean Section". *Anaesthesia and Intensive Care* vol.24 no.1, pp.51-55. Australia, 1996.02.
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see also <P961872>, <P962129>, <P962392>, <P970061>, <P970316>, <P971400>

RESEARCH PROJECTS

Application of Comparative Genomic Hybridization to the Detection of DNA Imbalances in Sinonasal T-cell Lymphoma

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☐ 1 November 1996

❖ The Croucher Foundation

Sinonasal T-Cell Lymphoma (SNTCL) is a common malignant disease seen amongst the Southern Chinese, including those in Hong Kong. The diagnosis of SNTCL is, however, often made difficult largely due to its poor cell morphology and the finding of a sensitive tumour marker shall have an impact on the diagnosis and management of these patients. To date, little information at the molecular level of SNTCL has been published and cell culture of such tumours for conventional chromosomal analysis is made impossible by the poor growth of excised materials. The researchers therefore propose to study the genetic anomalies of SNTCL by a recently developed molecular cytogenetics technique, Comparative Genomic Hybridisation. This is a powerful tool that can rapidly screen the whole tumour genome for excess or diminution of DNA materials. Consistent genomic abnormalities identified by CGH can hence be further evaluated for the possible development of genetic marker by screening, retrospectively, archival materials of SNTCL. (MD96010)

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

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☐ 1 January 1997

❖ CUHK Research Committee Funding

Primary Gastric Lymphoma (PGL) is much more prevalent in Hong Kong than in the West. In contrast to the little data available in the literature, the researchers have previously reported a large percentage of the high-grade PGL's to harbour the EBV genome. While the immunohistochemical detection of bc1-2 and c-myc oncoproteins have been previously studied in PGL, there has been none that correlates with EBV presence and phenotype. As EBV proteins such as the LMP-1 is well known to upregulate bc1-2 and inhibits apoptosis, as c-myc protein overexpression acts synergistically with bc1-2, and as the EBV encoded bc1-2 homologue BHRF1

has functional similarity with bc1-2, it is important to study the expression of these oncoproteins and correlate with EBV status in PGL in the search for pathogenetic mechanisms in view of the common presence of EBV in high grade PGL's. (MD96029)

Molecular Pathology of the Precancerous Lesions in Nasopharyngeal Carcinoma

✉ LEE Joseph C. K. ● HUANG POON Wai Sin Dolly ● TO Ka Fai ● LO Kwok Wai ● LEUNG Sing Fai (Clinical Oncology)

☐ 1 September 1996

❖ Research Grants Council

The objective of this research is to characterize and to identify the histo-morphological and the molecular genetic changes in the precancerous lesions in the nasopharynx and associated nasopharyngeal carcinomas (NPC) and to correlate such changes with the EBV-specific serological data and various other parameters from clinico-pathological findings in the development of NPC.

The long-term significance of such research is to:

- (1) Establish a firm basis on the characteristics and biological behavior of the precancerous changes.
- (2) Provide clues to interrupt the disease process and to initiate early treatment.
- (3) Pave way for screening of the high-risk individuals in Hong Kong and in China.
- (4) Be part of the strategy for experimental gene therapy in the future. (CU96639)

Detection and Clinical Relevance of Genetic Abnormalities (E2A/PBX1 and BCR/ABL) in Pediatric Acute Lymphoblastic Leukemia by Multiplex Polymerase Chain Reaction

✉ LEE Joseph C. K. ● NG Heung Ling Margaret

☐ 1 January 1997

❖ CUHK Research Committee Funding

Acute leukemias account for 20-30% of all pediatric malignancies in Hong Kong. Majority of these leukemias are lymphoblastic and highly curable by standard chemotherapy and radiotherapy with the exception of those harbouring t(1;19) and t(9;22) which show adverse prognosis. Cytogenetic detection of these translocations are limited by sensitivity and specificity. Hence molecular detection of the gene rearrangements (E2A/PBX1 and BCR/ABL) resulted from these translocations by RT-PCR plays an essential role for timely and accurate diagnoses and in planning of an optimal therapy (intensive chemotherapy or BMT). The incidence rates of t(1;19) and t(9;22) vary between 2-6% and 5-6% of the acute lymphoblastic leukemias respectively

in the west. In Hong Kong, the incidence rates have not been documented by any large and systematic study with molecular confirmation. A multiplex RT-PCR technique has recently been developed using five primers in one single reaction so that any of the E2A/PBX1, M-BCR/ABL and mBCR/ABL rearrangements can be diagnosed simultaneously. However, as the PCR is a rather qualitative test, a positive result in a patient in complete remission after treatment may not signify impending relapse. In the current study, a modified protocol with titration technique will be employed to analyse the consecutive newly diagnosed pediatric ALLs so as to (1) document the incidence rates of these genetic rearrangements; (2) correlate the results with routine cytogenetic analysis; (3) detect minimal residual disease and early relapse over the clinical course in target patients.
(MD96030)

Analysis of p16 and p15 Genes in Acute Leukemias

- ✉ NG Heung Ling Margaret ● HUANG POON Wai Sin Dolly
 ☐ 1 January 1997
 ❖ CUHK Research Committee Funding

Both p16 and p15, encoded by the genes located on chromosome 9p21, are inhibitors of cyclin-dependent kinases CDK4/6 and the up-stream regulators of Rb function. Since being characterized, *p16* has emerged as the most commonly involved tumor suppressor gene in human neoplasias of multiple histological types. In hematopoietic malignancies, deletion of *p16/p15* locus was found to be the most common genetic abnormalities in pediatric acute lymphoblastic leukemia (ALL). Recently, *de novo* 5'CpG island hypermethylations have been found associated with transcriptional silencing of *p16/p15*. This alternative mechanism of gene inactivation was also found to be a unique mode in certain diseases. The current study aims to analyse these genes in acute leukemias and evaluate their roles in correlation with FAB, immunophenotype, cytogenetics and prognosis. With PCR technique, the methylation status can serve as a tumor marker for the detection of minimal residual disease and tumor contaminations in autologous bone marrows or peripheral stem cell harvests in autologous bone marrow transplantation.
(MD96028)

Correlation between Apolipoprotein E Genotype and β -Amyloid Deposition in Chinese Brains

- ✉ NG Ho Keung
 ☐ 1 February 1997
 ❖ CUHK Research Committee Funding

There has been little information on Alzheimer's disease (AD) or Alzheimer-type of neurodegenerative changes in Chinese. The definitive diagnosis of AD is histological and international clinicopathological criteria stipulates the diagnosis of definite AD, probable AD, possible AD and normal aging. The pathogenesis of Alzheimer's disease is thought to be closely related to the deposition of a special amyloid protein, β A4P. Recent studies in the west have shown the close association of AD with the E4 allele of the apolipoprotein E gene, the product of which has been suggested to facilitate deposition of amyloid. This study proposes to utilize the well-characterised cases of neurodegenerative and "normal" brains already carefully analyzed under international criteria. DNA will be extracted from these brains and the apoE genotype identified. The total amyloid load as percentage of surface area of positive β A4P staining will be analyzed by an image analyzer. The relationship between apoE4 genotypes and the different categories of AD changes and the total β A4P load will be analyzed. This study will help in contribution to knowledge related to the specificity of apoE4 testing for AD and the role of apoE4 protein in amyloidogenesis in the nervous system. It will also contribute to information concerning possible racial difference in the causative factors of AD.
(MD96031)

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

- ✉ TO Ka Fai ● LO Kwok Wai
 ☐ 1 November 1996
 ❖ CUHK Research Committee Funding

Urinary bladder cancer is significant health care issue in Hong Kong, there are more than 600 new cases and near 200 cancer death per year. It is the sixth commonest cancer in men. Bladder cancer tends to have multiple recurrence and poses a even bigger impact in the health care system and society. However, the nature of the "recurrence" is still unclear. Whether those "recurrence" represent true recurrence of the original cancer or new *de novo* cancer is uncertain. The distinction between these two processes not only enhance our understanding of bladder cancer, but also provide a scientific bases for clinical management of those patient with recurrent cancer.

Microsatellite analysis is a recently developed molecular technique that can study genetic alteration in different parts of different chromosome. Thus, by selecting appropriate markers, one can "mapped up" the patterns of microsatellite alteration in individual cancer, just like fingerprint of individual person. We would be able to distinguish a "true recurrence" and new *de novo* cancer by comparing the patterns of the microsatellite alterations. This would provide a new

insight into the tumor biology of bladder cancer and may have potential clinical implication. (MD96032)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
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
1995-96	A Regional Cervical Screening Programme Evaluation (MD95030) ✉ CHANG Alexander Russell ● HAZLETT Clarke Blaine (Office of Educational Services)
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 <i>in situ</i> Hybridization (FISH) of Sinonasal T-cell Lymphoma (SNTCL) (MD95164) ✉ CHOW John Hei-sing ● WONG Nathalie (Clinical Oncology)
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)
1994-95	Apoptosis in CNS Tumours - Pilot Studies with <i>in situ</i> Labelling and Expression of Oncogenes and Tumour Suppressor Genes (MD95050) ✉ LEE Joseph C. K. ● NG Ho Keung
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	<i>In Situ</i> Hybridization of Estrogen Receptor Gene and Immunohistochemical Studies of Estrogen Receptor Level in Carcinoma of Prostate (MD93087) ✉ Mac-MOUNE LAI Fernand ● LEONG A. S. Y.* ● CHAN Siu Foon Peter (Surgery)
1995-96	To Determine the Incidence of Hereditary Thrombophilia (ATIII, Protein C or Protein S Deficiencies) in Idiopathic Young Stroke Patients Among Hong Kong Chinese (MD95119) ✉ NG Heung Ling Margaret ● WONG Ka Sing Lawrence (Medicine)
1995-96	Brain Disease Laboratory for both Research and Teaching at the University co-ordinated by the Department of Anatomical & Cellular Pathology (MD95057) ✉ 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)
- 1995-96 Molecular Genetics of CNS Diseases in Chinese (MD96001)
✉ NG Ho Keung ● CHEW Eng Ching (Anatomy) ● HUANG POON Wai Sin Dolly ● LEE Joseph C. K. ● LO Kwok Wai ● PANG Chi Pui Calvin (Chemical Pathology) ● POON Wai Sang (Surgery) ● TO Ka Fai
- 1994-95 Molecular Events of Perinatal Asphyxia - Expression of Immediate Early Genes, Basic Fibroblast Growth Factor, N-Methyl-D-Aspartate Receptor and Heat Shock Proteins (MD95049)
✉ TO Ka Fai ● NG Ho Keung
- 1995-96 DNA Ploidy Study and Tumor Proliferation in Renal Cell Carcinoma - Comparison of Flow and Static Image Cytometry with Emphasis in the Intratumoral Heterogeneity of DNA Content (MD95166)
✉ TO Ka Fai ● Mac-MOUNE LAI Fernand ● TSOI Wai Chiu*

RESEARCH OUTPUTS AND PUBLICATIONS

- <P953603> **Leong, A.S-Y.** "Intraoperative Frozen Section Consultation in the Management of Malignant Tumours". Keynote lecture presented in the 1st Scientific Meeting of the Oncology Society of Indonesia. Bandung, Indonesia, 1995.12.
- <P953604> **Leong, A.S-Y.** "Accurate Histological Assessment - the Foundation of Proper Management in Oncology". Paper presented in the 1st Scientific Meeting of the Oncology Society of Indonesia. Bandung, Indonesia, 1995.12.
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- <P962191> **Ng, Ho-Keung; Wai-Sang Poon; Keith Goh and Michael S.Y. Chan.** "Histopathology of Post-Embolized Meningiomas". *The American Journal of Surgical Pathology* vol.20 no.10, pp.1224-1230. USA, 1996.
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RESEARCH PROJECTS

Identification of Up- and Down-regulated cDNAs that are Differentially Expressed between Normal and Dysplastic Prostates of Noble Rat

- ✍ CHAN Leung Franky
- ☐ 1 November 1996
- ❖ CUHK Research Committee Funding

The proposed project is to study the early premalignant stage of prostatic carcinogenesis using Noble rat as the animal model. An abnormal epithelial proliferation, termed "dysplasia", can be induced in the Noble rat by long-term treatment with both androgen and estrogen. The abnormal epithelial lesion resembles closely human prostatic dysplasia or prostatic intraepithelial neoplasia which will turn malignant. Invasive lesions are identified in lateral and ventral prostates which have been treated after 9 months. The proposed study is to identify and isolate the up- and down-regulated mRNAs that are differentially expressed between the normal and dysplastic prostates of the Noble rat using the technique of differential display reverse transcription-polymerase chain reaction (RT-PCR). The main goal of the study is to study the genetic alterations during the early premalignant transformation of the prostate and to identify any activated or inactivated genes as possible markers for the premalignant prostate cancer using the Noble rat as animal model. (MD96033)

Identification of the Molecular Determinants in the Retina that Govern Axon Pathfinding in the Chiasm of Mammals

- ✍ CHAN Sun On ● CHENG Shuk Han (Orthopaedics & Traumatology)
- ☐ 1 January 1997
- ❖ Research Grants Council

Retinal ganglion cells in the temporal retina are different from those in the nasal retina. One major difference is that the temporal retina sends axons to targets on the same side of the brain, while the nasal retina has axons that go to the opposite side of the brain. This projection pattern forms the basis for binocular vision in mammals. The fact that axons from the nasal retina intermingle completely with axons from the temporal retina along their course to the chiasm indicates that the difference that marks the nasal from the temporal axons is determined by location of their cell bodies in the retina. In this study, the researchers investigate the molecular difference between nasal and temporal retina, look for genes that are differentially expressed in the retina, at a stage when this characteristic decussation pattern

is developing in the retinofugal pathway. Functions of these identified genes in relation to the pathfinding of retinal axons at the chiasm will be examined in living preparation of mouse retinofugal pathway. Results of this study will further the understanding on the molecular basis of axon guidance in the development of connections in the central nervous system of mammals. (CU96623)

Embryological Basis of Congenital Heart Defects: A Study Using a Mouse Mutant and a Transgenic Marker

- ✍ CHAN Wood Yee ● COPP A. J.*
- ☐ 1 January 1997
- ❖ CUHK Research Committee Funding

Congenital heart defects are common birth defects (8 in 1,000 live births) and one third of these are severe. The most vulnerable period for teratogens to induce major heart malformations is the first two months of pregnancy during which most of the developmental events are poorly understood, and hence the embryological basis of most of the heart defects are largely speculative. Studies on avian embryos has proposed that a group of embryonic cells known as cardiac neural crest cells participate in heart formation and defective neural crest development leads to heart defects. However, information on the role of mammalian neural crest in normal heart development is scarce and its participation in congenital heart defects in the mammal is still unknown. In the present study, Splotch mutant mouse embryos which have been shown to have major heart defects will be used as an animal model to study heart defects and a transgene (β -globin sequences) will be employed as a marker for the neural crest. The researchers propose to use microsurgical transplantation to study (1) contribution of the neural crest to normal heart formation by transplanting the genetically marked neural crest to normal host embryos; (2) defective neural crest development in the Splotch mutant by a WGA-Au marker; and (3) possibility of restoring the normal heart development by transplanting the normal neural crest into mutant embryos. The present study will provide information on the role of the neural crest in both normal heart development and heart defects and will also evaluate the feasibility of restoring normal heart development by microsurgical transplantation. (MD96034)

Human Papillomavirus 16 E6 and E7 are Associated with the Nuclear Matrix of Cervical Carcinoma Cells

- ✍ CHEW Eng Ching

- 1 January 1996
- ❖ CUHK Research Committee Funding

Carcinoma of uterine cervix is closely associated with human papillomavirus (HPV) infection and HPV 16 DNA has been shown to integrate into the genome of host cancer cells. The subgenomic fragments (E6E7) were found to be present in nuclear matrix (NM) - associated DNA by novel PCR. Further investigation showed the absence of E6 open reading frame (protein encoding sequence) in NM-associated DNA. DNA-protein binding assay (Southwestern blotting) labeled 2 groups of NM proteins that bound commonly to E6E7 DNA and specifically to either E6 or E7 DNA. Complex protein formation that was recognized by E6E7 was suggested. Further investigation into properties of these NM proteins may provide a better understanding of the role of HPV in cervical carcinogenesis. (MD96141)

Nuclear Matrix Proteins of Esophageal Cancer Cell Lines

- ✍ CHEW Eng Ching
- 1 January 1997
- ❖ CUHK Research Committee Funding

Esophageal carcinoma is the commonest malignant tumor in the esophagus. The reported incidences of this disease have increased many fold in the past 20 years and are apparently still rising. Despite the increase of this disease, basic research on the properties of the esophageal carcinoma cells has been limited by the difficulties in the establishment of cancer cell lines from tumor biopsies. Evidence has shown that nuclear matrix is the site of important nuclear processes and it is tissue and cell type specific. Besides, tumor specific nuclear matrix proteins have been demonstrated in prostate, colon, breast, ovary and cervical cancers. The present study will investigate the nuclear matrix proteins in the two human esophageal carcinoma cell lines established in our laboratory. These findings may serve as markers for this tumor and may have some diagnostic value. (MD96035)

Long Term Culture of the Whole Retina of Adult Hamsters as a Model to Study Regeneration of Retinal Ganglion Cells

- ✍ CHO Yu Pang Eric
- 1 January 1997
- ❖ Research Grants Council

Progress in research on the regeneration of the central nervous system (CNS) is increasing but because of the complexity of the nervous system, examining the

responses of CNS neurons maintained in culture is an alternative to elucidate the factors which promote regeneration. However, the situation in culture is quite different from the CNS *in vivo*. For instance, neurons in culture are either being maintained as isolated cells or as very small explants, the time of maintenance is very short, and the regenerating neuronal processes are extending on an artificial substrate which is not the same as that in the CNS. To overcome some of these problems, the researchers have developed a model of culturing the whole retina from adult hamsters as a flat sheet for at least 28 days. This will provide a chance of analysing the responses of neurons over an entire sheet of CNS tissue for a relatively long period of time. They will characterise the cellular organisation of the cultured retina, especially with regard to the survival and morphology of the retinal ganglion cells. With this information, the researchers will examine extrinsic factors which may influence the survival of ganglion cells. Moreover, they will make use of the fact that ganglion cells can undergo sprouting in the retina *in vivo* as a means to assess what extrinsic factors, such as exogenously applied trophic factors, can promote regenerative sprouting in the cultured retina. (CU96632)

The Ampullary Gland, Ventral Prostate and Embryogenesis

- ✍ CHOW Pak Ham Patricia ● O Wai Sum*
- 1 September 1996
- ❖ Research Grants Council

This is a part of the continuing effort of the research team to study the function of the male accessory sex glands. Spermatozoa are bathed in secretions released by these glands at the time of ejaculation. Previously, the researchers reported that in the hamster model, two of these glands i.e. the ampullary gland and ventral prostate, might help to regulate fertility by exerting an affect on embryonic development after fertilization. They postulate that the process of oocyte activation might also be affected even though the rate of fertilization is unchanged. In this project, the researchers propose to investigate the early and late events of fertilization including Ca^{++} oscillation and cortical granule exocytosis in oocytes, sperm decondensation / resumption of oocyte meiosis as well as protein expression / phosphorylation in the zygotes / preimplantation embryos. It is hoped that the results will help to identify a role for these glands in reproduction and eventually, the possible application of this knowledge to improve the outcome of assisted reproductive technology. (BL96033)

Male Accessory Sex Glands and Fertility: The Role of Apoptosis and Angiogenesis During Early Development

- ✉ CHOW Pak Ham Patricia ● YI Xianjin
□ 1 April 1997
❖ CUHK Research Committee Funding

This is a part of the researchers' continuing effort to study the function of the male accessory sex glands. Even though secretions from these glands have been reported to exert such effects on sperms as motility and suppression of immunogenicity of sperms in the female genital tract, the studies have established that they do not affect the rate of fertilization, but are needed for the proper development of embryos after fertilization. Exactly how this is brought about has not been worked out yet. The researchers' previous results suggest that anomalies in embryonic development may take place as early as 48h post coitus (p.c.), and that implantation is jeopardized if secretions of the ASG are ablated from studs. They postulate that this could be caused by a directed death of blastomeres because of failure of early expression of certain genes and problems with angiogenesis during implantation. In this project, the researchers will attempt to detect apoptosis and examine expression of vascular endothelial growth factor and its receptors in the first half of development in hamster embryos. The biological significance of this project are: (1) to elucidate the mechanisms of actions of the male ASG and (2) to provide a scientific basis for using secretions of ASG to enhance the efficiency of assisted reproduction techniques in human and animals.
(BL96031)

Neurotoxicity of Type I Ribosome-inactivating Proteins

- ✉ KWONG Wing Hang ● WONG Jianbin ● SHEN Wei Zai*
□ 1 October 1996
❖ CUHK Departmental Funding

Some ribosome-inactivating proteins are taken up by neurons and cause neuronal death. It is commonly believed that the cell-binding chain of the proteins are required for the entry of the proteins into the neurons. We observed that trichosanthin and ricin A chain, which are ribosome-inactivating proteins without a cell-binding chain, also caused neuronal death when applied to peripheral nerves. Some neurons appeared spared. This project is to investigate how these proteins enter the neurons and why some neurons are resistant to the toxic effect.
(BL96032)

Role of Growth Arrest Specific Gene in Mouse Embryonic Development

- ✉ LEE Ka Ho Kenneth ● BRANCOLINI Claudio*
□ 1 September 1996
❖ CUHK Research Committee Funding

Growth Arrest Specific 1 (GAS1) and 2 (GAS2) genes have been studied extensively in cultured fibroblasts and has been shown to be expressed exclusively in cells that have stopped dividing and enter the G₀ phase of the cell cycle. Although the function of the GAS genes has been investigated extensively *in vitro*, nothing is known of its true function *in vivo*. Therefore, the researchers propose to examine the potential functions of the GAS genes in the developing mouse embryo. The embryo is an excellent model because embryonic cells divide rapidly during morphogenesis and, of course, this process must be checked and tightly regulated otherwise it would produce gross abnormalities. They will first determine where GAS1 and GAS2 genes are expressed in day 9.5 - 13.5 embryos by *in situ* hybridization and *in situ* RT-PCR techniques. As a functional test, they will treat mouse embryos with antisense oligonucleotides targeted against specific sites on the GAS1 and GAS2 mRNAs in order to down-regulate the expression of these genes. The oligonucleotides will be microinjected into the amniotic cavities of day 8.5 and 9.5 intact embryos and will then be cultured on a roller incubator. After 36 hrs of incubation, the experimental embryos will be examined morphologically on a scanning electron microscope and by routine histology to ascertain whether down-regulation of GAS1 and GAS2 expression affects embryonic development.
(MD96036)

The Role of BMP and MSX Genes in the Control of Programme Cell Death in the Limbs of Normal and Hammertoe Mutant Embryos

- ✉ LEE Ka Ho Kenneth ● MUNEOKA Kenneth*
□ 1 May 1997
❖ CUHK Mainline Research Scheme

In this project, the researchers will investigate the role MSX and BMP genes play in the regulation of programmed cell death, or apoptosis, during limb development in the mouse embryo. Specifically, they will focus on the soft connective tissues (interdigital tissues) between the digits of the hand and foot plate. MSX-1, MSX-2, BMP2, BMP-4 and BMP-7 genes are expressed by the interdigital tissues and these tissues normally undergo apoptosis during morphogenesis to establish the spaces that separate the fingers and toes. Clinically, the failure of the interdigital tissues to undergo apoptosis lead to a congenital condition know as syndactyly where the

fingers and toes of the affected are fused together. They have previously reported that when the interdigital tissues were isolated from the hand or foot plates and maintained in culture, they would change their developmental fate and form cartilage instead of dying. They will exploit this phenomenon to determine whether MSX and BMP genes are necessary for initiating and maintaining apoptosis in the developing limb. This will be realized by determining whether the expression of any member of the MSX and BMP gene family is down regulated during interdigital chondrogenesis by RT-PCR and *in situ* hybridization techniques. They will also examine the expression pattern of these genes in the Hammertoe mutant. Apoptosis normally do not occur in the limbs of this mutant so will be a good model for understanding the function of BMP and MSX gene in apoptosis. This pilot study will provide valuable information for application of grants from the National Institute of Health and Research Grant Council. (MD96122)

Mechanisms Underlying the Immunomodulatory and Antitumor Activities of Selected Lectins

- ✍ LIU Wing Keung Ken ● NG Tzi Bun (Biochemistry) ● OOI Vincent E. C. (Biology) ● CHANG Shu Ting (Biology)
- 1 October 1996
- ❖ Research Grants Council

In normal organisms, homeostasis is maintained through a balance between cell proliferation and cell death. Since cell proliferation is a highly regulated process with numerous checks, uncontrolled cell proliferation will result in oncogenesis. Currently, there are two cancer therapeutic methods: one by killing cancer cells directly with cytotoxic or antiproliferative drugs, and another by depleting the vascular and nutritive supply to cancer cells and thus blocking tumor growth. In Asian countries, the enhancement of immunological defense mechanisms against cancer cells by herbal remedies provides an alternative approach to the same end. There is good evidence that lectins from plant or animal origin possess immunomodulatory activities. Recently, some isolated lectins are reported to activate macrophages and lymphocytes and inhibit the proliferation of cancer cells. Even though some of them have already been used as chemotherapeutic agents, their mode of action is still unclear. The objective of the proposed study is to use an animal model and bioassays to investigate the underlying mechanisms of the immunomodulatory and antitumor properties of lectins. Their cytotoxicity on cancer cell lines, stimulatory effects on immune cells and anti-angiogenic effects on endothelial cells will be studied by employing both *in vitro* bioassays and *in vivo* tumor-bearing mouse models. It is anticipated

that this study will allow an insight into the molecular mechanism of the antitumor action of the lectins which would subsequently provide a basis for cancer therapy. (CU96667)

To Study the Relationship of Maternal Diabetes Mellitus, Insulin and Caudal Agenesis in Offspring Using an Animal Model

- ✍ SHUM Sau Wun Alisa
- 1 January 1997
- ❖ CUHK Research Committee Funding

The incidence of congenital malformations among offspring of diabetic women is much higher than that in non-diabetics. The most common anomaly is caudal agenesis, in which the lower portion of the vertebral column is partially or totally missing, and it is found that the majority of diabetic mothers of children with caudal agenesis are insulin users. Caudal agenesis also arises in cases of excess intake of vitamin A. The researchers' previous studies on a mouse model of caudal agenesis induced by retinoic acid, a vitamin A metabolite, have demonstrated that the pathogenetic mechanism underlying the development of caudal agenesis was excessive cell death in the tail bud, which is located at the caudal extremity of the embryo and will differentiate into various tissues at the sacral and coccygeal regions, including the lower vertebrae. Their specific objectives in this project are: (1) to determine whether offspring of diabetic mice show increased susceptibility to retinoic acid-induced caudal agenesis, (2) to determine the effect of insulin on embryo development, and (3) to determine whether insulin induces cell death in the tail bud. (MD96037)

The Effects of Prenatal Heroin Exposure on Postnatal Brain Development and Behavior in Rats

- ✍ STADLIN Alfreda ● ALI Syed F.*
- 1 July 1996
- ❖ Research Grants Council

Heroin addiction is becoming a growing concern in Hong Kong and around the world and has been shown to be the principle narcotics consumed by Asians. In the last decade, substance abuse in pregnancy is also a major concern for public health officials and clinicians.

Opiate withdrawal syndrome (OWS) in neonates is the most common outcome of opiate dependency in pregnant women. This is characterized by infants showing symptoms ranging from irritability, jitteriness to convulsions. There is also impaired psychomotor and cognitive development in the

heroin-exposed infants. Many infants undergo prolonged withdrawal, which is life-threatening if untreated. The mechanism for such prolonged withdrawal and subsequent developmental outcome is not known. It is however known that in the adult, the mesolimbic dopaminergic system in the brain is implicated in the locomotor-activating effects of drug addiction and opiate dependent withdrawal. In order to understand the mechanism(s) underlying OWS and the developmental impairment in the heroin-exposed offspring, the present project aims to use an animal model to study these postnatal changes. Changes in the dopaminergic system in the brain of the rat offspring will be correlated with their behavioral outcome. It is hoped that in elucidating the mechanism of OWS resulting from prenatal heroin exposure, the type of treatment best used for the rehabilitation and postnatal care of these offspring can be devised. (CU96615)

An Animal Model of Proliferative Vitreoretinopathy

- ✉ YEW David Tai Wai
- ☐ 1 December 1996
- ❖ CUHK Research Committee Funding

This study attempts to establish an animal model of proliferative vitreoretinopathy and to investigate the role of astrocytes in the development of retinal detachment. In this work, albino young adult rabbits have been employed and the astrocytes were obtained from the retinae of neonatal albino rabbits after death. These astrocytes isolated from the latter source were cultured and the cultures contained a colony of at least 90% astrocytes as revealed by immunocytochemistry. The astrocytes were injected into the vitreous of the adult albino rabbits under anaesthesia. The subsequent phases of retinal detachment will be noted and the involvement of the astrocytes and the production of the vascular endothelial growth factor (VEGF) will be deciphered using molecular techniques. The study will give us some insight into of the connections between astrocytes, neovascularization and retinal detachment. (MD96038)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition Title/Investigators

1995-96 Glycoconjugates of Ciliary Body Epithelium of the Rat Eye: A Lectin Histochemical and Protein Blotting Study (BL95040)
✉ CHAN Leung Franky

1995-96 Glycoconjugates of Ciliary Epithelium of the Rat Eye: A Lectin Histochemical and Protein Blotting Study (MD95121)
✉ CHAN Leung Franky

1995-96 Developing a Biotinylated Hyaluronan as a Probe for Detection of Hyaluronan-binding proteins in Cells and Tissues (BL95041)
✉ CHAN Leung Franky

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*

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

1995-96 Investigations of the Cellular Mechanisms Underlying the Turning of Uncrossed Retinal Axons at the Midline of the Optic Chiasm (MD95113)
✉ CHAN Sun On ● TAYLOR J. S. H.*

1995-96 Programmed Cell Death and the Expression of p53 and bc1-2 in Borderline and Invasive Epithelial Ovarian Cancers (MD95155)
✉ CHAN Wood Yee ● MOK Samuel C.*

1995-96 The Role of Nuclear Matrix Proteins in Cancer: A Morphological and Molecular Biological Approach (MD95055)
✉ CHEW Eng Ching

1995-96 A Study of the Fluorescent Dye - Induced Sprouting of Retinal Ganglion Cells After Axonal Injury (MD95147)
✉ 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*

- 1995-96 Proteolytic Enzyme Activity in Accessory Sex Gland Secretions of the Male Golden Hamster (*Mesocricetus auratus*) (BL95039)
✍ CHOW Pak Ham Patricia
- 1995-96 Proteolytic Enzyme Activity in Accessory Sex Gland Secretions of the Male Golden Hamster (*Mesocricetus Auratus*) (MD95120)
✍ CHOW Pak Ham Patricia
- 1995-96 Histological, Histochemical and Immunohistochemical Studies of the Uterovesical Junction in Patients with Acute and Chronic Vesicoureteral Reflux (CU95602)
✍ DIXON John Stuart ● GOSLING John Arthur ● GEARHART John Phillip*
- 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
- 1992-93 Neural Influence on Muscle Regeneration (MD92048)
✍ KWONG Wing Hang
- 1994-95 Neuronal Death Caused by Trichosanthin (MD94075)
✍ KWONG Wing Hang ● NG Tzi Bun (Biochemistry)
- 1995-96 Role of Retinoic Acid on Limb Development in Transgenic Mouse Embryos (MD95107)
✍ LEE Ka Ho Kenneth ● EDE Donald* ● PAULIN Denise*
- 1995-96 The Immunomodulatory and Antitumour Properties of Secretory Products from Cultured Mushroom Mycelia (CU93617)
✍ LIU Wing Keung Ken ● OOI Vincent E. C. (Biology) ● NG Tzi Bun (Biochemistry) ● CHANG Shu Ting (Biology)
- 1995-96 The Mechanisms of Transition from Primary to Secondary Neurulation (CU95662)
✍ SHUM Sau Wun Alisa
- 1995-96 To Study the Pathogenesis of Renal Agenesis (MD95111)
✍ SHUM Sau Wun Alisa ● GOSLING John Arthur ● WOOLF Adrian S.*
- 1994-95 Differential Changes in Dopamine Transporter and Tyrosine Hydroxylase in Parkinsonism (MD94069)
✍ STADLIN Alfreda ● CHAN Pui*
- 1995-96 Time Course Expression of Vascular Endothelial Growth Factor as Related to Development of Retinochoroidal Vasculature in Rats (MD95184)
✍ YEW David Tai Wai ● YI Xianjin*
- 1995-96 Aging Changes in the Human Central Nervous System (MD95185)
✍ YEW David Tai Wai

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- <P962030> **Li, Wei Ping; Helen W.L. Lai; Suet Ying Cheng and David T. Yew.** "Somatostatin-Positive Neurons in the Different Parts of the Brain in Normal Aging and Alzheimer's Disease". *Biological Signals* vol.5, pp.343-348. Basel, Switzerland, 1996.
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see also <P961639>, <P962520>, <P962521>, <P962570>, <P962586>, <P970357>, <P970548>

RESEARCH PROJECTS

Biochemical Characterisation of Mas Oncogene: An Antibody Approach

- ✍ CHEUNG Wing Tai
- ☐ 1 September 1996
- ❖ CUHK Research Committee Funding

Mas oncogene was originally isolated from a human tumor, and sequence analysis indicates that it encodes a protein consisting of seven hydrophobic segments. Functional studies have suggested that mas oncogene enhances angiotensin response, but the molecular mechanism and its physiological roles are yet to be determined. It is reasoned that mas is a membrane protein and it mediates its effects through interactions with cytoplasmic proteins of the signal transduction cascade. To isolate the proteins that interact with the mas oncogene, an antiserum against a peptide derived from the predicated C-terminal tail of mas oncogene will be prepared. Affinity purified mono-specific antibodies will be used for immunoprecipitation. In addition, the antibodies will also be used for Western analysis and immunocytochemistry to reveal the spatial and temporal expression patterns of mas oncogene.
(BL96025)

Formulation of Preservation Solution for Transplantation of Heart and Other Organs

- ✍ FUNG Kwok Pui
- ☐ 1 July 1996
- ❖ Industrial Support Fund, Industry & Technology Development Council

Transplantation is now widely applied all over the world in the treatment of patients at end-stage of organ necrosis. The major obstacle of organ transplantation is the lack of an ideal preservation solution which can maintain the organ at a completely viable status at a longer period before operation is taken place. The aim of this research project is to design and develop a better formulation of preservation solution for transplantation of heart and other organs. Since cell swelling and free-radical-mediated cell damage are the major reasons which affect organ viability, the researchers plan to test the protective effect of various new components in the solution including impermeants which may maintain the osmotic pressure across the cell membrane of the organs and antioxidants which may scavenge free-radicals formed in the organs during preservation. The development of new formulations of better preservation solutions for transplantation will generate novel products for Hong Kong

pharmaceutical companies to manufacture and market.
(MD96002)

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

- ✍ FUNG Kwok Pui
- ☐ 1 October 1996
- ❖ Research Grants Council

Many anticancer drugs exhibit their cancer-killing properties partially by a free-radical-mediated reaction. Free radical is a particle with very high energy and it can always cause normal cell damage in the host. The heart contains less self-protective mechanism. It is the reason why the common side effect of free-radical-mediated anticancer drugs is cardiotoxicity. The aim of present project is to search for some strategies to enhance the effectiveness of the cancer-killing abilities of these drugs and at the same time to lower their adverse side effects to the host. Strategies to be investigated involve:

- (1) co-treatment with some new type of antioxidants which possess both anticancer property and protective property on normal cells;
- (2) pretreatment with tumour necrosis factor- α which may protect the heart or other organs;
- (3) lower the intracellular glutathione (which is a molecule in the cancer cell that interferes free-radical-mediated anticancer drugs' abilities) concentration in the cancer cells;
- (4) co-treatment with cis-unsaturated fatty acids which are agents that may increase the drugs' anticancer abilities. The researchers will use both cultured cancer cells and normal cells, and cancer-bearing mice to investigate these treatment modalities. They hope that some strategies to be tested in present proposal might become a useful treatment design of free-radical-mediated anticancer drugs with better efficacies and lower toxic side effects in patients.
(CU96311)

Tumour Necrosis Factor- α : Biological Activities and Action Mechanism in Health and Diseases

- ✍ FUNG Kwok Pui ● CHAN Leung Franky (Anatomy) ● CHENG Hon Ki Christopher ● CHOY Yuen Min ● KONG Siu Kai ● KWOK Tim Tak ● LEUNG Kwok Nam ● WAN David Chi Cheong
- ☐ 1 October 1996
- ❖ CUHK Strategic Research Program

Tumour necrosis factor- α (TNF- α) is a cytokine released primarily from macrophages. It is a major haematopoietic regulatory molecule which plays an

important role in inflammatory and immunological reactions. On the other hand, TNF- α has long been known to be related with various pathological conditions, such as cardiovascular diseases, diabetes mellitus, sepsis and inflammatory diseases. Furthermore, TNF- α , as its name implies, is a potent antitumour agent although its adverse side effects prevent its wide use clinically. The exact mechanism of TNF- α in causing the above-mentioned conditions is not fully understood. How does TNF- α exert its immunomodulatory action and anti-tumour effect is also unclear. This strategic research project aims at linking the experience and expertise of colleagues in Department of Biochemistry and Department of Anatomy to promote the endeavour towards understanding the mechanism and the involvement of TNF- α in health and in various diseased conditions. It is intended that some TNF- α related treatment regimens for cancer, cardiovascular diseases, diabetes mellitus, sepsis and inflammatory diseases can be developed. The aims of the projects are to: (1) study the effect of TNF- α on each system in detail; (2) design and test the intervention(s) *in vitro* or in various animal models of these TNF- α -related diseases. Six projects entitled "Search for novel and efficacious inducers of TNF- α *in vivo*", "TNF- α mediated signalling pathways", "TNF- α as chemo- and radio-sensitizer in cancer therapy", "TNF- α in vascular pathophysiology", "TNF- α and tissue wasting" and "TNF- α in normal and aberrant haematopoiesis" will be carried out. The projects themselves are self-reinforcing and together they constitute an interconnected system. (MD96127)

Mechanistic Studies on the Regulation of Glucose Transporter Expression in Tumour Cells

- ✉ FUNG Kwok Pui
- 15 December 1996
- ❖ CUHK Research Committee Funding

Cellular glucose uptake is mediated by glucose transporters which are proteins in nature. In man, six glucose transporter isoforms have been identified to-date. These glucose transporters exhibit tissue-specific distribution, but overexpression of isoforms type 1 and type 3 have been observed in many types of cancers. Both isoforms, especially type 3 isoform, are characterized by their very high affinity for glucose, and insofar as cancer cells depend mainly on glucose for energy supply and for growth, the overexpression of glucose transporters confer upon them a decided advantage in their competition for glucose supply vis-a-vis their normal counterparts. In the present project, the researchers will study the mechanism by which cancer cells activate their glucose transport system during growth, using both cultured cancer cells and tumour-bearing animals. In

particular, they will examine the factors and circumstances affecting the rate of transcription of the type 1 and 3 glucose transporter genes and the stability and turnover of the messenger RNA molecules, for example, when the tumour-bearing animals are subjected to anti-tumour drugs including *inter alia* methotrexate, tumour necrosis factor or to hyperthermia where it has been shown that glucose transport is inhibited. The consequence of oncogene activation will similarly be examined. In these studies, reverse transcription and polymerase chain reaction will be employed to determine cellular transporter mRNA levels. Since glucose transport is feed-back regulated by glucose and one of its metabolites, phosphoribosyl pyrophosphate (PRPP), the possible mediatory role played by PRPP in the above situations will be scrutinised. It is hoped that from these work a better understanding of the mechanism regulating glucose transport in cancer cells at the molecular level will accrue which might lead to the development of new therapeutic modes in cancer management. (MD96040)

Growth Factor and Drug Sensitivity

- ✉ KWOK Tim Tak
- 1 October 1996
- ❖ CUHK Research Committee Funding

Epidermal growth factor receptor (EGFR) is frequently over-expressed in cancer. The signalling pathway for EGF shares its part with the pathway for anticancer agents and may therefore affect the response of cells to anticancer drugs. The importance of EGF signalling in drug sensitivity is supported by the fact that the drug, doxorubicin, inactivates EGFR in human squamous carcinoma A431 cells and the inactivation is overwhelmed by EGF which in turn increases the drug sensitivity of cells. Experiments are proposed to characterize the sensitization effect in terms of cell lines, growth factors and anticancer drugs. The influence of doxorubicin on the level and the activity of EGFR will be explored. The effect of doxorubicin together with EGF on the expression and the activity of individual member of EGF signalling pathway will be characterized with regards to their possible role in EGF induced chemo-sensitization. These studies will provide insight in basic mechanisms of signalling that causes changes in gene expression in response to anticancer drugs and growth factor. Furthermore, the information obtained can be used in the design of new strategies for cancer therapy targeting specifically the critical molecules in signal transduction pathway. (BL96005)

The Role of Phosphorylation in the Functions of the Exuperantia Protein during Oogenesis in *Drosophila*

- ✉ LUK Ka Shing Sandy
- 1 September 1996
- ❖ Research Grants Council

The proposed project is a continuation of the current project aiming at dissecting the molecular and biochemical structure-function relationship of the *exu* gene product, a phosphoprotein whose only known function is to localize the mRNA of the anterior morphogen bicoid. Recent work from the applicant's laboratory has identified, *in vitro*, that the *exu* protein is phosphorylated by a serine/threonine kinase and that the kinase is mostly likely the cAMP-dependent protein kinase A (PKA). The main focus of the current project therefore is to study the functional significance of phosphorylation of *exu* protein with specific emphasis on the role of phosphorylation in regulating the interaction between the *exu* protein and the cytoskeleton. As protein kinases and protein phosphorylation pervade every areas of cellular regulation, the biochemical characterization of protein kinases and their targets will provide important insight into the research on signal transduction and, in this particular case, on signals that lead to the formation of specific body plan patterns.
(CU96322)

Molecular Dissection of the Transforming Growth Factor Signal Transduction Pathway

- ✉ LUK Ka Shing Sandy ● CHEUNG Wing Tai ● TSANG David Sau Cheuk ● WAN David Chi Cheong
- 1 October 1996
- ❖ CUHK Strategic Research Program

The transforming growth factors (TGFs) are a large family of secreted signalling molecules that mediate a variety of key events in normal growth and development in both invertebrates and vertebrates. These factors were originally identified on the basis of their ability to induce a transformed phenotype of certain cells in culture. Subsequent studies showed that TGFs can in fact inhibit cell proliferation. In *Drosophila*, the TGF- β homolog, *dpp*, is required for the establishment of positional identity in the dorsal region of the embryo. Mutations of *dpp* cause all cells in the dorsal half of the embryo to differentiate into ventral ectoderm. As the body axes in *Drosophila* are determined in the oocyte, signalling events induced by TGF- β during oogenesis will be the primary focus of this study. Specifically, some of these events most likely include activation of the cAMP-dependent protein kinase

(PKA) as it has been demonstrated in the *Drosophila* limb and eye development. Both molecular genetics and protein biochemistry methods will be used to investigate these signalling events.
(BL96027)

An Investigation of the Purification and Biological Activities of Mammalian Carbohydrate-binding Proteins

- ✉ NG Tzi Bun
- 1 December 1996
- ❖ CUHK Research Committee Funding

Lectins are carbohydrate-binding proteins which are neither antibodies nor enzymes. Many lectins have been isolated from plants and their biological activities e.g. antitumor and immunomodulatory activities have been elucidated. By contrast, a considerable number of mammalian lectins have not been extensively studied especially with regard to their physiological roles. Although research on mammalian lectins has a short history of only about two decades, it has attracted the attention and devotion of investigators at prestigious universities and medical research institutes. Lectins have been shown to exist in different tissues of several mammalian species and it is surmised that these carbohydrate-binding proteins elicit different responses in different locations. However, little is known about lectins of the guinea pig other than the demonstration of a mannose binding protein capable of neutralizing the influenza virus and the report that carbohydrate-containing-N-(2-hydroxypropyl) methacrylamide copolymers bind to isolated guinea pig erythrocytes indicating the presence of lectins in the guinea pig gastrointestinal tract. Furthermore, the guinea pig is an interesting animal with unique features in its insulin, vitamin C-collagen biochemistry, and growth hormone which is more important as a metabolic than as a growth-promoting hormone. Hence a study on guinea pig lectins may lead to interesting observations. The pig is another mammal about which there are very few, if any, reports on its endogenous lectins. Its tissues are readily available. Thus it is selected, in addition to the guinea pig, as an object of study in this investigation. Different tissues including the spleens, gastrointestinal tracts, livers and kidneys and gonads of these two mammals will be extracted and subjected to chromatographic fractionation for purification of lectins. The chemical properties and biological activities of these purified lectins will be examined and compared. It is hoped that a study of mammalian lectins would lead to a better understanding of their physiological roles and in the long run, a development of these proteins, their recombinant forms or their inhibitors as drugs for the treatment of certain human diseases.
(BL96024)

Transcriptional Regulation of Human Glycogen Synthase Kinase-3 α and -3 β -cloning and Analysis of Their Promoters

✉ SHAW Pang Chui ● ANDERTON Brian H.* ● MILLER C. C. J.*

□ 1 January 1997

❖ Research Grants Council

There is evidence implying that tau hyperphosphorylation in Alzheimer's disease may be due to aberrant levels of either or both GSK-3 α and GSK-3 β enzymes in nerve cells and results in the development of neurofibrillary tangles. In order to understand how GSK-3 α and -3 β are regulated in the nerve cells, the promoters of these two genes will be cloned and sequenced. The regions which interact with their transcriptional factors and the transcription factors involved will be elucidated by DNase I footprinting, gel mobility shift assay and methylation interference assay. (CU96305)

Characterization of Isoforms of Endothelin Converting Enzyme in Cultured Endothelial Cells

✉ WAN David Chi Cheong

□ 1 November 1996

❖ CUHK Research Committee Funding

Endothelin (ETs) are potent vasoconstrictive 21 amino-acid peptides originally isolated from the supernatant of porcine aortic endothelial cells. ETs are generated from a 38- to 39- residues intermediate peptide big endothelins (big ETs) by a unique proteolytic cleavage at the Trp²¹-Val²² or Trp²¹-Ile²² catalyzed by an endothelin converting enzyme (ECE). ECE has been proposed as the potential site of regulation of ET biosynthesis and regarded as a major target for therapeutic intervention in diseases associated with pathological increases in ET production. Recent advances in the cloning and characterization of ECE have demonstrated that ECE is a unique, highly glycosylated neutral pH optimum endopeptidase with a single transmembrane domain near the N-terminal. Isoforms for this ECE (termed ECE-1) had been discovered. Another novel metalloprotease ECE (termed ECE-2) with an acidic pH optimum has recently been cloned which has an overall identity of 59% to the previously cloned ECE (termed ECE-1). The cloning of two different ECEs raises the question of their relative importance in the *de novo* synthesis of ETs. To better understand their role in ET synthesis, the researchers propose to study the regulation of their genes using human umbilical cord endothelial cells (HUVC) as a model system. ECE-1 has been cloned in this laboratory and ECE-2 will be cloned in order to obtain specific probe for gene expression analysis. Hormonal and humoral

factors (such as thrombin, lipopolysaccharide, transforming growth factor) that are known to increase ET synthesis will be examined to determine whether ECE-1 or ECE-2 are coordinately regulated. (BL96008)

Molecular Cloning and Characterization of Human Heart cDNAs Coding for LIM Domain Containing Proteins

✉ WAYE Mary Miu Yee ● LEE Cheuk Yu ● FUNG Kwok Pui

□ 1 October 1996

❖ Research Grants Council

Using random cDNA sequencing as an approach, the researchers have sequenced over 5,000 human heart cDNA clones. Of these cDNAs, approximately 2,000 clones are novel or previously unidentified sequences. Since LIM domain-containing proteins were suggested to regulate various aspects of cell differentiation, they plan to clone and characterize five cDNAs encoding LIM containing proteins from human heart cDNA library: hCRHP (human cysteine rich heart protein), hRIL, hCRP2 (human cysteine rich protein), FHL-1 and FHL-2 (four and a half LIM proteins). hCRHP, a protein homologous to rat cysteine-rich intestinal protein (CRIP), has been tentatively demonstrated to be involved in development of the heart. hRIL is a human homologue or *ril*, the expression of which has been reported to be decreased or down-regulated in cells undergoing transformation to the cancerous state. hCRP2 is a human homologue of CRP2 which is expressed most abundantly in heart and lung. FHL-1 and FHL-2 code for two novel LIM containing proteins whose functions are not known. The objective of this research is to clone and sequence the full length cDNAs of these LIM-motif containing clones, to understand the functional role of these genes by studying their tissue distribution by northern blot analyses and *in situ* hybridization techniques. The researchers will further identify if there are any protein partners for these proteins by using a yeast two-hybrid system. (CU96313)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition	Title/Investigators
1995-96	Purification and Enzymatic Characterization of Fish Alcohol Dehydrogenases (BL95031) ✉ FONG Wing Ping

- 1994-95 Search for Effective Natural Antioxidants for the Treatment of Myocardial Ischemia-reperfusion (MD95039)
✍ FUNG Kwok Pui
- 1995-96 Mechanism of Combination Treatment of Tumour Necrosis Factor- α and Hyperthermia on Tumour Cells (CU95316)
✍ FUNG Kwok Pui
- 1995-96 Examination of a New Strategy for Attachment of Antibodies Against Tumour Antigens to Sterically Stabilized Liposomes Containing Entrapped Antitumour Drugs (MD95198)
✍ FUNG Kwok Pui
- 1995-96 Mutant p53 and Drug Resistance (MD95199)
✍ KWOK Tim Tak
- 1995-96 Gene Mapping of Heart cDNA Using Fluorescent *in situ* Hybridization Technique (MD95058)
✍ LEE Cheuk Yu ● WAYE Mary Miu Yee ● FUNG Kwok Pui
- 1995-96 Sequence Analysis of Human Heart cDNA Clones (CU95642)
✍ LEE Cheuk Yu ● WAYE Mary Miu Yee ● FUNG Kwok Pui
- 1993-94 Biochemical Characterization of the *Drosophila exuperantia* Protein (BP93010)
✍ LUK Ka Shing Sandy
- 1995-96 Molecular and Biochemical Characterization of the *Drosophila Exuperantia* Protein: Identification of Structural/Functional Domains (CU94322)
✍ LUK Ka Shing Sandy
- 1995-96 Investigation of the Relationship Among the Diverse Enzymic and Pharmacological Activities of Antiviral Proteins (CU95325)
✍ NG Tzi Bun ● FONG Wing Ping ● YEUNG Hin Wing ● WONG Ngok Shun Ricky* ● MAK Nai Ki*
- 1995-96 Trypsin Inhibitors from Plants (BL95026)
✍ NG Tzi Bun
- 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 ● WAN David Chi Cheong
- 1995-96 Identification of Chinese Medicinal Herbs by Combined Molecular and Chemical Approaches (CU93306)
✍ SHAW Pang Chui ● BUT Paul Pui Hay (Biology)
- 1995-96 Trichosanthin Derivatives with Reduced Immunogenicity and Nephrotoxicity and Long Plasma Half-life (CU95324)
✍ SHAW Pang Chui ● TAM Michael S. C. (Physiology)
- 1993-94 Dopamine D4 Receptor Gene Polymorphism and Its Relevance to Psychiatric Disorder (BP93013)
✍ WAN David Chi Cheong
- 1994-95 Isolation and Characterization of Endothelin Converting Enzyme (BL94012)
✍ WAN David Chi Cheong
- 1995-96 Characterization of Brain Specific Endothelin Converting Enzyme(s) and Its Role in Cerebral Ischemia (BL95027)
✍ WAN David Chi Cheong
- 1995-96 Molecular Characterisation of Natural Heterozygosity and Mutation Process in *Candida Albicans* (CU95313)
✍ WANG Jun ● SAMARANAYAKE Lakshman Perera*
- 1995-96 Sequence Analysis of Human Heart cDNA Clones (CU93303)
✍ WAYE Mary Miu Yee ● LEE Cheuk Yu

RESEARCH OUTPUTS AND PUBLICATIONS

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RESEARCH PROJECTS

Clinical Usefulness of a Novel Serum Marker, 1,5-anhydroglucitol in Monitoring Glycaemic Control

- ✉ ARUMANAYAGAM Manoharan ●
COCKRAM Clive Stewart (Medicine)
- ☐ 1 April 1997
- ❖ CUHK Research Committee Funding

Glycated haemoglobin (Hb A_{1c}) although used as a gold standard in monitoring long term glycaemic control, still has certain disadvantages: (1) methodological differences in the measured value (2) narrow range of Hb A_{1c} values, corresponding to changes in glycaemic control and (3) includes a component of information on glycaemic control that occurred 2-3 months earlier. Fructosamine has been used to give information on glycaemic control over 2-3 weeks, but has been discontinued for a variety of reasons. In addition, there are several conditions in which Hb A_{1c} is less useful viz. gestational diabetes mellitus (GDM), subjects with certain haematological disorders including increased turnover of erythrocytes.

The polyol, 1,5 anhydro-D-glucitol (1,5 AG) is a 1-deoxy form of glucopyranose and several studies, mainly from Japan (Yamanouchi *et al.* Lancet 1996;347:1514) have demonstrated that this compound shows a sensitive and specific change in patients with DM. Furthermore, 1,5 AG has been shown to be superior to HbA_{1c} and fructosamine in a multicentre study (Yamanouchi *et al.* Diabetes 1991;40:52-57).

The aim of the project is (1) to establish an enzymatic method for the determination of 1,5 AG (Fukumura *et al.* Clin Chem 1994;40:2013) using Cobas-Mira analytical instrument; and (2) determine its effectiveness in the assessment of glycaemic control in NIDDM and GDM without severe complications such as nephropathy (plasma creatinine > 200 µmol/L), anaemia (haemoglobin < 10.0 g/dL) or hypoalbuminaemia (serum albumin < 30 g/L). Fasting glucose and HbA_{1c} will also be determined to assess the merits of 1,5 AG. (MD96111)

Development and Application of an *in situ* PCR Method for the Detection of Mutations and DNA Polymorphisms in Single Intact Cells

- ✉ HJELM Nils Magnus ● LO Yuk Ming
- ☐ 1 December 1996
- ❖ CUHK Research Committee Funding

The purpose is to develop novel applications of *in situ* polymerase chain reaction (PCR) technology. *In situ* PCR allows the amplification of nucleic acid

sequences inside single intact cells, thus allowing a correlation between cellular morphology and nucleic acid sequence. Thus far, single base discrimination by *in situ* PCR has not been reported. The project is based on preliminary work which has been accomplished by Dr YMD Lo at Oxford University, soon to transfer to the Department of Chemical Pathology, Prince of Wales Hospital. This outcome of this work clearly establishes a working protocol for this powerful technique and has demonstrated for the first time that *in situ PCR inside intact cell can be carried out to distinguish single base pair changes*. The first phase of the study involves the transfer of this technology to the Department of Chemical Pathology at The Chinese University of Hong Kong. Further refinement of the technique will be carried out on parameters such as cell fixation, permeabilisation and amplification conditions. Potential clinical applications such as noninvasive prenatal diagnosis and the detection of post bone marrow transplantation chimaerism will then be explored. This technique will ultimately allow the correlation between cellular morphology and sequence polymorphisms or mutations and will be a powerful addition to the currently available repertoire of molecular diagnostic tools. (MD96052)

Molecular Epidemiology of Diabetes Mellitus: Detection and Prevalence of a Mutation in Mitochondrial DNA

- ✉ LAM Ching Wan ● PANG Chi Pui Calvin ●
TSANG M. W.* ● HJELM Nils Magnus
- ☐ 1 April 1997
- ❖ CUHK Research Committee Funding

Diabetes mellitus is a common and severe disease in most populations, and it affects 5% of the Chinese population in Hong Kong. Despite a general belief that diabetes mellitus is a polygenic disease, a significant proportion of diabetic mellitus patients have the tRNA^{Leu}(^{UR})3243 A → G mutation detected in their mitochondrial DNA. This study aims to establish if the prevalence of mitochondrial diabetes mellitus is large in the local population. A positive outcome will provide basis for considering other biochemical mechanisms than those in the classical polygenic models, resulting in diabetes mellitus. (MD96109)

The Lipoprotein Lipase Gene in Hyperlipidaemia

- ✉ PANG Chi Pui Calvin ● TOMLINSON Brian
(Clinical Pharmacology)
- ☐ 1 July 1995
- ❖ CUHK Departmental Funding

Hyperlipidaemia is found in many genetically determined disorders including familial hypercholesterolaemia, hypertriglyceridaemia and combined hyperlipidaemia. Affected individuals of these disorders are susceptible to the development of premature coronary atherosclerosis. One of the candidate genes for these familial lipid disorders is lipoprotein lipase. More than 30 missense and nonsense point mutations, deletions, insertions and duplications have been reported in the LPL gene causing LPL deficiency. Clinical manifestations of LPL mutations are diversified and there are important gene-gene and gene-environment effects. The researchers have identified several novel mutations in the LPL gene in hypertriglyceridaemic subjects. Clinical features of these subjects are diversified, some have hypercholesterolaemia, hypertension and/or diabetes, but some are still non-symptomatic. The researchers are investigating these LPL mutations further by detecting for their presence in hyperlipidaemic patients and their associations with related genes including the low density lipoprotein receptor gene, apolipoprotein B gene and the apolipoprotein CII gene. The researchers are also to carry out *in vitro* mutagenesis and expression studies to detect the de facto effects of these mutations on LPL activities. Results of these proposed studies will enable them to draw conclusions on the significance of LPL gene mutations on hyperlipidaemia. (MD96146)

Biochemical and Genetic Markers for Breast Cancer

- ✉ PANG Chi Pui Calvin ● KING Walter Wing Keung (Surgery) ● TANG Leung Sang ● LAW Lap Kay
- ☐ 1 July 1996
- ❖ CUHK Departmental Funding

Breast cancer is the second most common cause of cancer mortality in women in Hong Kong and its incidence is rising every year. It occurs both in hereditary and sporadic forms. Early detection is extremely important for appropriate treatment and improvement of prognosis but conventional clinical and radiographic detection are not always adequate. Some cancer markers including CA15-3 and p53 mutations have been extensively studied but the sensitivity and specificity are not sufficiently satisfactory. The researchers are studying novel genetic markers, including BRCA1 and BRCA2 mutations, and new biochemical markers, such as a new TPS assay, together with established markers for early diagnosis and accurate prognostic indication of breast cancer. The researchers' results over the last several months have strongly indicated that some potentially useful marker systems should be obtained from their assays. (MD96147)

Molecular Genetics of Alzheimer Disease

- ✉ PANG Chi Pui Calvin ● NG Ho Keung (Anatomical & Cellular Pathology) ● WOO Jean (Medicine)
- ☐ 1 July 1996
- ❖ CUHK Departmental Funding

Alzheimer's disease (AD) is a severe and progressive neurodegenerative disorder. It is the most common cause of dementia in the elderly in Western populations. In Chinese the incidence of dementia among the elderly is high. AD is associated with a number of genes: β -amyloid protein, presenilin I, presenilin II and apolipoprotein E, although not one of them is the candidate gene causative of AD. The researchers have found the involvement of apolipoprotein E polymorphic alleles in the development of AD. They therefore are proceeding to study in detail, related genes, such as the very-low-density and low-density lipoprotein receptors in AD. The researchers are attempting to detect gene mutations in AD and their effects on the histopathology. While the researchers are investigating the molecular genetics of AD, they also aim to establish genetic markers for AD detection. (MD96148)

Investigation of the BRCA1 Gene in Breast Cancer

- ✉ PANG Chi Pui Calvin ● KING Walter Wing Keung (Surgery) ● TANG Leung Sang ● CHOY Kwong Wai ● LAW Lap Kay ● YEO W* ● LAM Ping Kuen (Surgery) ● SUEN Wang Ming Michael (Anatomical & Cellular Pathology) ● JOHNSON Philip James (Clinical Oncology) ● HJELM Nils Magnus
- ☐ 1 July 1996
- ❖ CUHK Departmental Funding

Breast cancer occurs in both hereditary and sporadic forms. Susceptibility to hereditary breast cancer is conferred by a mutated BRCA1 or BRCA2 gene, located on chromosomes 17q12-21 and 13q12-13 respectively, which can be inherited from either the father or the mother. More than 100 germline BRCA1/BRCA2 mutations have been identified but no somatic mutation is known. The researchers are in a process to study BRCA1 mutations in Chinese women with breast cancer. They have extracted DNA from archived tumour tissues of 148 breast cancer cases and blood specimens from over 100 breast cancer patients, about 30 of them with family history. All the clinical and histological data has been documented. They are screening all 22 coding exons of BRCA1 for base changes by polymerase chain reaction (PCR), single strand conformation polymorphism (SSCP) and direct DNA sequencing. Microsatellite markers flanking the BRCA1/BRCA2

genes and related loci will also be analysed to investigate the loss of heterozygosity for determination of the linkage of BRCA1 with sporadic breast cancer. Their preliminary investigations on exons 2, 11, 12, 20 and 22 of BRCA1 have revealed 3 base changes one of which is a missense mutation. (MD96173)

Detection of Tumor Cells and Tumor DNA in Peripheral Circulation in Patients with Breast Carcinoma

✉ TANG Leung Sang ● PANG Chi Pui Calvin ● KING Walter Wing Keung (Surgery) ● HJELM Nils Magnus

□ 1 March 1997

❖ CUHK Research Committee Funding

The reverse transcription-polymerase chain reaction can provide sensitive identification of circulating tumor cells. Another promising technique for detection of occult disease in malignancy is the detection of mutant tumor DNA microsatellite repeats in plasma. The propose to apply these two techniques as alternative approaches for the detection of breast cancer. The study will include (1) selection of specific mRNA transcripts for circulating breast cancer cells; (2) the development of methodology for detecting mutant DNA microsatellite repeats in plasma from breast cancer; and (3) a comparison of these two diagnostic approaches with respects to pathological staging and clinical outcome in breast cancer patients. (MD96110)

Please refer to previous issues of *Research Projects Summary* 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)

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)

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) ● WOO Kong Sang John (Surgery) ● HJELM Nils Magnus ● LAI Kar Neng (Medicine) ● 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)

1994-95 A Study of the Genetic Basis of Hypertriglyceridaemia in Hong Kong (MD95027)

✉ PANG Chi Pui Calvin ● LAM Wai Kei Christopher

1995-96 Genotyping of the Low-Density Receptor Defects in Familial Hypercholesterolaemia in Hong Kong (CU93618)

✉ PANG Chi Pui Calvin ● MAK Ying Tat* ● MAK Wing Lai Tony* ● TOMLINSON Brian (Clinical Pharmacology) ● SANDERSON John Elsbj (Medicine)

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- <P962532> **Panesar, N.S. and C.W. Poon.** "Human Chorionic Gonadotropin Binding Protein in the Pancreas of Rats". *Proceedings of 16th ICC* pp.422-423. London: The Association of Clinical Biochemists, 1996.07.
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- <P963255> **Hjelm, N.M.** "Inherited Metabolic Disease in Hong Kong". *Hong Kong Medical Journal* vol.2 no.3, pp.236-237. Hong Kong, 1996.09.
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- <P963261> **Zhong, Nan; Weina Ju; Dennis Curley; Daowen Wang; James Pietrofesa; Guanyan Wu; Yan Shen; Calvin Pang; Priscilla Poon; Xixian Liu; Shen Gou; Eliisa Kajanoja; Markku Rynanen; Carl Dobkin and W. Ted Brown.** "A Survey of *FRAXE* Allele Sizes in Three Populations". *American Journal of Medical Genetics* vol.64, pp.415-419. USA, 1996.08.
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- <P963265> **Poon, Priscilla M.K.; Z. Zhao; X.Q. Wu; Y.X. Ni and C.P. Pang.** "FMR-I Alleles in the Normal Chinese Population". *Proceedings of the 16th International Congress of Clinical Chemistry* p.322. London: The Association of Clinical Biochemists, 1996.07.
- <P963266> **Poon, Priscilla M.K.; Zhen Zhao; Chang H. Yin; Xiang-Qian Wu; Yu-Xing Ni and Calvin C.P. Pang.** "Normal FMR-1 Alleles in the Chinese Population". *Neonatal and Perinatal Screening: The Asian Pacific Perspectives* ed. by Stephen T.S. Lam and Calvin C.P. Pang. pp.99-105. Hong Kong: The Chinese University Press, 1996.
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- <P963271> **Mak, Ying Tat; Lisa S.Y. Chan; Jun Zhang; T.M.L. Mak; B. Tomlinson; J.R.L. Masarei and C.P. Pang.** "Mutations of the Low Density Lipoprotein Receptor Gene in Chinese". *Proceedings of the 16th International Congress of Clinical Chemistry* p.305. London: The Association of Clinical Biochemists, 1996.07.
- <P963274> **Pang, C.P.; Chang H. Yin; Priscilla M.K. Poon; Geetha Bharathi and C.W.K. Lam.** "A Rapid Screening Procedure for the Z and S Mutations in the α -1-Antitrypsin Gene". *Proceedings of the 16th International Congress of Clinical Chemistry* p.322. London: The Association of Clinical Biochemists, 1996.07.
- <P963443> **Lam, Stephen T.S. and Calvin C.P. Pang. ed.** *Neonatal and Perinatal Screening: The Asian Pacific Perspectives*. 199 pgs. Hong Kong: The Chinese University Press, 1996.
- <P970130> **Hjelm, N.M.** "Treating Inherited Metabolic Disease". *Journal of Paediatrics and Child Health* vol.33, p.S15. Australia, 1997.03.
- <P970254> **Lam, C.W.; B. But; S.F. Tong; C.C. Shek; K.H. Poon; C.P. Pang and N.M. Hjelm.** "A Novel DNA Polymorphism Found in a Local Chinese Patient with Glycogen Storage Disease Type 1A". *Proceedings of the 1st Hong Kong Medical Genetics Conference* p.25. Hong Kong: Hong Kong Society of Medical Genetics, 1997.01.25.
- <P971353> **Lam, C.W.; A.M. Lawson and N.M. Hjelm.** "Electrospray Mass Spectrometry of Proteins in Biomedicine". *Journal of International Federation of Clinical Chemistry* vol.9 no.2, pp.72-75. USA, 1997.06.
- <P971355> **Pang, C.P.; Priscilla M.K. Poon; Qian L. Chen; Kelly Y.C. Lai; C.H. Lau and C.K. Wong.** "CCG Repeat Pattern in the *FMR-1* Gene in Mentally Retarded Patients". *Proceedings of the 1st Hong Kong Medical Genetics Conference* p.4. Hong Kong: Hong Kong Society of Medical Genetics, 1997.01.
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- <P971357> **Poon, Priscilla M.K.; C.P. Pang; Qian L. Chen; Kelly Y.C. Lai; C.H. Lau and C.K. Wong.** "Distribution of *FMR-1* Alleles in Chinese Children with Mild Mental Retardation". *Journal of Paediatrics Child Health* (Presented at the 9th Asian Congress of Paediatrics). vol.33, p.S53. Australia, 1997.03.
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RESEARCH PROJECTS

A Phase II Study of Temozolamide (Temodal SCH 52365) in the Treatment of Patients with Advanced Nasopharyngeal Carcinoma

✉ CHAN Anthony Tak Cheung ● LEUNG Wai Tong Thomas ● JOHNSON Philip James

☐ 1 July 1996

❖ Schering-Plough

This is a single center, phase II study designed to determine the efficacy and safety of Temozolamide (Temodal SCH 52365) in the treatment of patients with advanced nasopharyngeal carcinoma. (MD96153)

Cell Kinetic Studies in Undifferentiated Nasopharyngeal Carcinoma and the Implications for Clinical Management

✉ CHAN Anthony Tak Cheung ● TEO Man Lung Peter ● LEUNG Wai Tong Thomas ● CHANG Alexander Russell (Anatomical & Cellular Pathology) ● JOHNSON Philip James

☐ 1 September 1996

❖ Research Grants Council

Nasopharyngeal Carcinoma (NPC) is endemic in Hong Kong and Southern China. The 5 year survival rate with conventional radiotherapy (RT) is only 52%. At the Prince of Wales Hospital 2 prospective randomized clinical trials (RCTS) comparing conventional RT with either hyperfractionated RT or concomitant chemotherapy-RT have been started. The aim of this proposal is to determine the cell kinetic parameters in NPC patients treated in these 2 RCTS using two different techniques, flow cytometric analysis and immunohistochemical analysis of bromodeoxyuridine incorporation in tumour after *in vivo* administration. The prognostic significance of the cell kinetic parameters will be defined by correlating with the clinical outcomes of the 2 RCTS. If these parameters can predict before treatment which patients are likely to do worse with conventional RT and which patients are likely to benefit from hyperfractionated RT or concomitant chemotherapy-RT, this will have major implications on the treatment protocol for patients with NPC in future.

(CU96636)

Functional Analysis of a New Gene that Response to DNA Damage and Retinoic Acid, and Interact with the TNF-Receptor

✉ CHAN Yeuk Hon John

☐ 1 December 1996

❖ CUHK Research Committee Funding

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 p53 TNF receptor. They propose to: (1) determine the interaction between the p53-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. (MD96043)

Isolation, Purification and Structural Elucidation of Disease-specific Isoforms of Glycoproteins and Glycopeptide Hormones

✉ JOHNSON Philip James ● HJELM Nils Magnus (Chemical Pathology) ● LAWSON Alexander M.*

☐ 2 October 1996

❖ Research Grants Council

Alphafetoprotein (AFP) is a useful serological marker for the diagnosis of hepatocellular carcinoma (HCC) and for the monitoring of response to treatment in both HCC and non-seminomatous germ cell tumours (NSGCT). However, at low concentrations, the specificity of the test for HCC is poor and serum AFP cannot reliably be used to distinguish between benign liver conditions such as cirrhosis, and HCC. The researchers have recently described the use of isoelectric focusing (IEF) to detect isoforms of this protein which appear to be much more specific for different pathological conditions. In particular this technique permits serological distinction between benign and malignant liver disease and between HCC and NSGCT. In this proposal, the researchers will investigate the underlying biochemical basis of these isoforms using standard methods of protein separation and preparative IEF followed by Mass Spectroscopy and ^1H NMR and ^{13}C NMR Spectroscopy. They will then apply a similar approach to a glycopeptide tumour marker, beta human chorionic gonadotrophin (β -HCG). Having

identified and isolated the specific isoforms of AFP and, possibly other proteins, it may be possible to use these antigens to develop monoclonal antibodies with the ultimate aim of developing immunological assays which are highly specific for individual tumours. (CU96633)

The Pathophysiology of Hepatitis B Reactivation in Lymphoma Patients

✉ JOHNSON Philip James ● WICKHAM Nicholas ● STEINBERG Joyce ● LEUNG Wai Yee Nancy (Medicine) ● TAM Siu Lun John (Microbiology) ● CHAN Kay Sheung Paul (Microbiology)

□ 1 January 1997

❖ CUHK Research Committee Funding

The purpose of this study is to examine prospectively the factors involved in hepatitis B reactivation in patients receiving chemotherapy. The patients studied will be participants in a clinical trial using the new anti-viral agent lamivudine which will be given when there is evidence of hepatitis B reactivation. Approximately 20% of Hong Kong Chinese patients with lymphomas are chronic carriers of hepatitis B and, of these, 25% will reactivate their hepatitis during treatment which, in 5% of cases, progresses to fulminant hepatic failure and death. This phenomenon has been well documented, but is poorly understood. Immune mechanisms have been implicated as immunosuppression allows viral replication during chemotherapy which, when discontinued, leads to restoration of the immune response which then targets the virally-involved liver. The researchers intend to prospectively collect serological samples on high-risk lymphoma patients at regular intervals throughout their chemotherapy, with retrospective analysis of those who reactivate plus appropriate control samples from non-reactivators, to determine the time course of viral replication and associated immune responses, particularly T-cell subsets, which will be analysed prospectively on selected cases. It is hoped that they will be able to (1) identify a subgroup of lymphoma patients who are chronic hepatitis B carriers at high risk for reactivation; (2) confirm the effectiveness of lamivudine in this situation; and (3) elucidate the process, timing and nature of the viral and immunological events involved in hepatitis B reactivation.

(MD96046)

Novel Mutations in HBV PreS2/S Gene in Hepatocellular Carcinomas: Potential Induction of the Transactivator Function During Oncogenesis

✉ JOHNSON Philip James ● CHAN Yeuk Hon John

□ 1 February 1997

❖ CUHK Research Committee Funding

The hepatitis B virus (HBV) is known to play essential roles in the pathogenesis of hepatocellular carcinomas (HCC), but the precise molecular mechanism is still unclear. The researchers have recently found that in a majority of HBV-associated HCCs, novel mutations were present in the *PreS2/S* gene, which could induce the transactivator function. These molecular lesions may be causally related to the oncogenic process by activating critical cellular genes. They propose: (1) to determine *in vivo* if the novel mutations in *PreS2/S* gene of the tumors are associated with the expression of the S antigens, and with target genes of the transactivator function including *c-myc*, *c-fos* and *Il-6*; (2) to clone the mutated *PreS2/S* gene into expression vectors, and to determine the transactivator function by co-transfecting cells with reporter constructs for the promoters of target genes.

(MD96044)

The Application of Comparative Genomic Hybridisation for the Detection of Genomic Imbalances in Nasopharyngeal Carcinoma

✉ LEUNG Sing Fai ● WONG Nathalie ● HUANG POON Wai Sin Dolly (Anatomical & Cellular Pathology) ● TSAO George* ● JOHNSON Philip James

□ 1 August 1996

❖ Research Grants Council

Nasopharyngeal carcinoma (NPC) is a common tumour in the Southern Chinese, where it is characterised by a strong association with the Epstein-Barr virus and a young peak incidence. Recent genetic studies have revealed a non-random deletion of chromosome 3p together with mutations and homozygous deletions on chromosome 9. However, conventional cytogenetic analysis by karyotyping is, as with all solid tumours, difficult because of the scarcity of dividing cells. CGH is a recently developed molecular cytogenetic method that can rapidly screen the whole tumour genome for any excess or diminution of chromosomal materials. The application of CGH to the investigation of NPC has particular advantages in that it does not require cell culture and allows a complete survey of the tumour genome for DNA imbalances. It provides many more opportunities to detect new abnormal sites which will be further analysed to identify possible new oncogenes or tumour suppressor genes. The combined CGH and molecular findings are expected to contribute to our understanding of the development and progression of NPC, with the prospect of the development of genetic markers for screening, prognostication and detection of subclinical NPC.

(CU96637)

Randomised Trial of Radiotherapy Alone Versus Concomitant Radiotherapy and Chemotherapy in Locoregional Advanced Nasopharyngeal Carcinoma

- ✉ LEUNG Wai Tong Thomas ● CHAN Anthony Tak Cheung ● TEO Man Lung Peter ● LEUNG Sing Fai
- 1 January 1996
- ❖ CUHK Departmental Funding

The use of concomitant chemoradiotherapy in the treatment of head and neck cancers has been shown to be effective in locoregionally advanced tumours. This prospective randomized study aims to compare the use of concomitant cisplatin-radiotherapy versus radiotherapy alone in locoregionally advanced nasopharyngeal carcinoma in terms of tumour response, locoregional control, overall and disease free survival.
(MD96152)

A Phase II/III Randomized Controlled Study of Thymitaq (AG337) Versus Doxorubicin in Patients Having Hepatocellular Carcinoma

- ✉ LEUNG Wai Tong Thomas ● JOHNSON Philip James ● LAU Wan Yee Joseph (Surgery) ● CHAN Anthony Tak Cheung ● YEO Winnie ● MOK Shu Kam
- 24 June 1996
- ❖ Agouron Pharmaceuticals Inc.

Thymitaq is a new novel thymidylate synthetase inhibitor which has shown activity in head and neck cancer and other incurable cancer failed standard therapy. In this phase II/III trial, the researchers try to look into activity of the new drug on hepatocellular carcinoma and compare its activity with systemic chemotherapy.
(MD96155)

A Molecular Approach to Delineate Anti-estrogenic Drug Effects on Breast Cancer Cell Lines

- ✉ LEUNG Wai Tong Thomas ● CHUI Chung Hin
- 1 March 1997
- ❖ CUHK Research Committee Funding

Breast cancer is very common in Europe and America. In Hong Kong, its occurrence is gradually increasing because of the shifting of living style from Eastern to Western. Studies have shown that some premenopausal and postmenopausal breast cancer tumours were estrogen receptor (ER) positive, indicating that estrogen may play some roles in the development of breast cancer. However, there is still

little understanding about the intracellular signalling after estrogen binding.

Cancer is usually associated with the gain of function of proto-oncogene and loss of function of tumour suppressor gene. Many proto-oncogenes code for tyrosine kinase (e.g. *c-kit*) and they are important in signal transduction after ligand binding (*Kit* ligand or stem cell factor, SCF). Abnormality of proto-oncogene in breast cancer had been reported which included the amplification of *HER2* tyrosine kinase. Previously, it was also reported that breast cancer is associated with loss of *c-kit* product.

The researchers aim to study the relationship between some anti-estrogenic drugs and proto-oncogene/tumour suppressor gene expression. They would use some commercially available drugs (Example: Tamoxifen) and other anti-estrogenic compounds and different breast cancer cell lines in our study. Moreover, they would also look for any genomic DNA rearrangement after the application of the drugs. In addition, they also want to study any apoptosis effects of the drugs. The study can potentially find a better marker for breast cancer and model for testing drug effects on breast cancer cells.
(MD96108)

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

- ✉ 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)
- 10 April 1997
- ❖ GlaxoWellcome Pharmaceutical Inc.

FUMB2008 (776C85) is a new novel compound which was found to potentiate 5FU cytotoxicity *in vitro*. In this phase II study, a combination of 5FU and FUMB2008 is used to detect for clinical activity in inoperable hepatocellular carcinoma.
(MD96156)

Phase III Randomised Trial of ⁹⁰Yttrium-Microspheres Selective Internal Radiation Versus Systemic Doxorubicin in the Treatment of Inoperable Hepatocellular Carcinoma

- ✉ 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*
- 28 May 1997
- ❖ CUHK Departmental Funding

Selective internal radiation with Yttrium-90 microspheres has been found to be feasible and effective for patients with inoperable cancer. The current study is going to study the effect of treatment in a randomised phase III setting to compare with systemic chemotherapy.
(MD96157)

Investigation of Possible Subtypes of Prostatic Specific Antigen Related to Prostatic Cancer and Benign Prostatic Hypertrophy by Isoelectric Focusing Technique

- ✉ MOK Shu Kam ● LEUNG Wai Tong Thomas ● HO Stephen K. W.* ● CHAN Siu Foon Peter (Surgery) ● JOHNSON Philip James
- 15 September 1996
- ❖ CUHK Research Committee Funding

The purpose of this study is to develop a more specific serologic marker for prostate cancer. Prostatic specific antigen (PSA) is a sensitive serological marker for monitoring the response of prostate cancer to treatment (Chodak et al., 1990; Dupont et al., 1991). Despite the fact that PSA is the only tumour marker with FDA approval, its role as a screening test remains controversial. The major limitation is the lack of specificity (Bernstein et al., 1990). Elevation is observed in benign prostate hypertrophy (BPH), prostatitis and prostate trauma, up to 28% of men with BPH have increase of PSA over 4.0 ng/ml (Hudson et al., 1989). PSA level over 10 ng/ml carries a predictive value of 65%, and level between 4.0 ng/ml and 10.0 ng/ml has limited value (Catalona et al. 1991). Thus FDA stressed that PSA is specific for prostatic tissue but not for prostatic cancer.

Burditt et al. (1994) successfully applied the method of Isoelectric Focusing (IEF) to identify two alpha-fetoprotein variants specific for hepatocellular carcinoma (HCC). Subsequently Ho et al. (1996) confirmed the finding by testing sera from 110 HCC patients and 10 cirrhotic patients with non-diagnostic alpha-fetoprotein (AFP) level (50-500 ng/ml). They reported the presence of the characteristic bands is 96% of HCC patients and none in the non-malignant group, which implied significant improvement in the specificity.

Similar to AFP, PSA is a glycoprotein, thus IEF may be effective in defining isoproteins specific to malignancy. The researchers plan to analyse initially the sera of 10 prostatic cancer patients with PSA level between 4.0 and 10.0 ng/ml together with 10 BPH patients with similar PSA level. By identifying any specific variant band in the prostate cancer group, they may then proceed further to improve the specificity of PSA as a tumour marker for prostatic cancer.
(MD96045)

Phase II Study of Gemcitabine and Oral Etoposide in Treatment of Advanced Non-small Cell Lung Cancer

- ✉ MOK Shu Kam ● CHAN Anthony Tak Cheung ● YEO Winnie ● YIM Ping Chuen Anthony (Surgery) ● HUI P.* ● JOHNSON Philip James
- 15 May 1997
- ❖ Eli Eilly

Gemcitabine is a novel chemotherapeutic drug with proven clinical efficacy as single agent in treatment of non-small cell lung cancer. The side effect of the drug is less than the standard chemotherapy. The combination of this drug with oral etoposide have never been studied clinically. The purpose of the project is to study the clinical efficacy of this new combination chemotherapy.
(MD96154)

Detection of Genetic Imbalance in Multiple Myeloma by Comparative Genomic Hybridization

- ✉ WONG Nathalie ● NG Heung Ling Margaret (Anatomical & Cellular Pathology)
- 1 December 1996
- ❖ CUHK Research Committee Funding

Comparative genomic hybridization (CGH) is a newly described molecular cytogenetic technique that allows the global analysis of tumour genome for genetic imbalances. The technique has the advantages of requiring no cell culture and prior knowledge of genetic aberrations involved in the tumour to be investigated. CGH has therefore a major application in investigating malignancies that has little known genetic abnormalities, such as Multiple Myeloma (MM). Cytogenetic information on MM has long been hampered by the low proliferative index of the neoplastic plasma cells. Alternative study on MM by flow cytometry demonstrated aneuploidy but provided little information on individual chromosomal changes. Recent literature on MM reported on the finding of non-random numerical aberrations by employing the technique of fluorescence *in situ* hybridization (FISH) on interphase nuclei. In these studies, selected centromeric probes were applied on interphase nuclei and scored by FISH analysis. Such an approach is both time consuming and has provided information only on numerical changes. The researchers propose to apply the technique of CGH to the study of MM. This should allow a thorough investigation into the net gains and losses of DNA sequences in the whole tumour genome. The finding of any non-random regions of amplification and deletion might also shed some insight into the possible involvement of oncogenes and tumour suppressor genes in this malignancy.

(MD96047)

Application of Reverse Transcriptase Polymerase Chain Reaction in the Detection of Circulating Tumour Cells in Peripheral Blood

✍ YEO Winnie ● WONG Hing Nam (Anatomical & Cellular Pathology) ● JOHNSON Philip James

□ 1 January 1997

❖ CUHK Research Committee Funding

Breast cancer and colorectal cancer are two of the most common malignancies that occur in Hong Kong. The prognosis of patients with such malignant diseases correlates directly with the presence of metastatic spread. Despite advances in the treatment of these cancers, the development of recurrences and metastasis continue to present major problems in clinical management. Detection of occult carcinoma in patients with these cancers may aid the establishment of prognosis and development of new therapeutic approaches. There is a need for establishing sensitive assays to detect early subclinical metastases to enable early intervention and improve the patients' clinical outcomes. While morphology, flow cytometry, conventional cytogenetics and immunocytochemistry enable tumour cell detection at a level between one tumour cell per 100 to 10⁵ normal cells, one of the most sensitive method for tumour detection to-date is the application of reverse transcriptase polymerase chain reaction (RT-PCR) which has a level of sensitivity of detecting one malignant cell in 10⁷ normal cells. RT-PCR may be useful in monitoring treatment used in present practice, it also provide information in the identification of high risk patients, allowing a more rational allocation of present adjuvant chemotherapy and new therapies (such as intensive high dose chemotherapy or alternative approaches such as immunological therapy and biological response modifiers). RT-PCR is useful in detecting subclinical metastases at the time of disease recurrences in solid tumours, and may redefine the timing of commencing salvage chemotherapy for metastatic diseases. It may also be proved to be useful in determining surrogate end-points, and give a new definition to complete response to cancer therapy.

(MD96048)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition Title/Investigators

1994-95 Detection of Cytogenetic Abnormalities in Non-Hogkin's Lymphoma Using a Fish Assay (MD94092)

✍ CHAN Anthony Tak Cheung ● WONG Nathalie ● WICKHAM Nicholas ● YEO Winnie

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)

1995-96 Alterations in the Growth Suppressor PML during Cellular Response to DNA Damage and in Oncogenesis (MD95201)

✍ CHAN Yeuk Hon John

1993-94 Susceptibility to Viral Carcinogenesis in Relation to Hepatocellular Carcinoma in Southern China: Influence of HLA Antigens (MD93080)

✍ JOHNSON Philip James ● LIN Joanna

1995-96 Detection of Tumour Specific Variants of Alphafetoprotein by Isoelectric Focusing; Sensitivity and Specificity as a Diagnostic Marker (CU95644)

✍ JOHNSON Philip James ● HO Stephen K. W.* ● WONG Nathalie

1995-96 The Application of Comparative Genomic Hybridization to the Study of Leukaemia (MD95150)

✍ LEUNG Wai Tong Thomas ● JOHNSON Philip James ● WONG Nathalie ● WICKHAM Nicholas

1995-96 Intercellular Communication and Gap Junction Formation Between Human Endothelial Cells and Inflammatory or Malignant Cells (CU95645)

✍ WICKHAM Nicholas ● WONG Nathalie

1995-96 The Prospective Measurement of Suspected Thrombotic Mediators in Breast Cancer Patients Receiving either High Dose or Conventional Dose

- Adjuvant Cytotoxic Chemotherapy (MD95165)
✉ WICKHAM Nicholas ● YEO Winnie
- 1995-96 Detection of Chromosome Deletions in Paraffin Sections of Hepatocellular Carcinomas by Fluorescence *In-situ* Hybridisation (MD95208)
✉ WONG Nathalie ● JOHNSON Philip James
- 1995-96 The Incidence of BRCA1 and BRCA2 Gene Mutations in Hong Kong Chinese (MD95163)
✉ YEO Winnie ● WONG Hing Nam (Anatomical & Cellular Pathology) ● JOHNSON Philip James ● KING Walter Wing Keung (Surgery) ● KWAN Wing Hong

RESEARCH OUTPUTS AND PUBLICATIONS

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- <P953236> **Johnson, P.J. and Eddleston, A.L.W.F.** "Autoimmune Hepatitis". *Oxford Textbook of Medicine* ed. by D.J. Weatherall, J.G.G. Ledingham and D.A. Warrell. 3rd ed. pp.2069-2073. New York: Oxford University Press, 1995.
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- <P961703> **Kwan, W.H.; P.H.K. Choi; C.K. Li; M.K. Shing; K.W. Chik; P. Yuen and L.T.C. Chow.** "Breast Metastasis in Adolescents with Alveolar Rhabdomyosarcoma of the Extremities: Report of Two Cases". *Pediatric Hematology and Oncology* vol.13, pp.277-285. USA, 1996.
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- <P961840> **Chan, A.T.C.; Yeo W.; Leung W.T. and Johnson P.J.** "Thromboembolic Events with Paclitaxel". *Clinical Oncology* vol.8, p.133. UK, 1996.
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RESEARCH PROJECTS

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

✉ CHAN Yan Keung Thomas ● CHAN Chung Ngor Juliana (Medicine) ● YOUNG Robert P. ● TOMLINSON Brian ● CRITCHLEY Julian A.J.H.

□ 1 August 1996

❖ Research Grants Council

The researchers have been studying the relative importance of various natriuretic systems (renal dopamine, atrial natriuretic peptide, the natriuretic hormone) and antinatriuretic systems (sympathetic activity, renin-angiotensin-natriuretic peptide, the natriuretic hormone) and antinatriuretic systems (sympathetic activity, renin-angiotensin-aldosterone system) in the regulation of sodium balance and blood pressure during changes in salt intake in Chinese subjects. The activation of these natriuretic systems and suppression of antinatriuretic systems in healthy Chinese subjects can account for some but not all of the natriuretic response to salt loading. In particular, the increase in urine dopamine was small and unsustainable compared with Caucasian subjects. It has become apparent that the renal kallikrein-kinin system also participates in the regulation of extracellular volume, renal sodium excretion and blood pressure. The renal excretion of kallikrein is strongly influenced by genetic factors. Subjects having decreased renal kallikrein excretion (e.g. those with a family history of hypertension or low-renin hypertension) tend to be salt-sensitive. The researchers are going to study the role of the renal kallikrein-kinin system and its interactions with other natriuretic and antinatriuretic systems in the regulation of sodium balance and blood pressure in healthy Chinese subjects with or without a genetic risk of hypertension. They will also study normotensive NIDDM patients and hypertensive patients with and without NIDDM. They consider the latter to be particularly interesting as the group has found significant differences in the responses to angiotensin converting enzyme inhibitors between these two types of Chinese hypertensives which may be related to differences in the activation of the kallikrein-kinin system.
(CU96675)

Investigation of the Genetic Region of the Lipoprotein Lipase Gene in Families of Dyslipidaemic Patients and Relation to Blood Pressure and Insulin Resistance

✉ TOMLINSON Brian ● CHENG Shuk Han (Orthopaedics & Traumatology) ● CRITCHLEY Julian A.J.H. ● YOUNG Robert P.

□ 1 January 1997

❖ CUHK Research Committee Funding

Dyslipidaemia with raised triglycerides and low HDL-cholesterol is strongly associated with non-insulin dependent diabetes mellitus (NIDDM) and hypertension. These appear to be manifestations of an underlying condition called the metabolic syndrome which is characterised by hyperinsulinaemia and insulin resistance. Dyslipidaemia, hypertension and NIDDM may occur separately but they are often found together in the same individual and run together in families. A survey of patients attending the lipid clinic with mild-moderate hypertriglyceridaemia showed that over two thirds had hypertension and many had NIDDM. The researchers have studied different aspects of the metabolic syndrome in a large group of patients with dyslipidaemia and they have established that most of them are insulin resistant and many have abdominal obesity on MRI scans. They have examined the lipoprotein lipase gene and found mutations in only 5 out of 100 patients with hypertriglyceridaemia. The activity of lipoprotein lipase appears to be a central abnormality in the development of dyslipidaemia in the metabolic syndrome and a recent study from investigators in Taiwan and the United States has shown that an area on chromosome 8p22 at or near the lipoprotein lipase gene may be important in determining blood pressure in patients with NIDDM. This is an important finding which may provide some explanation of the link between these conditions. They now plan to study this genetic region in patients with dyslipidaemia to see whether changes here are related to the presence of hypertension or diabetes. In a pilot study they will examine this genetic 'trait' in 50 patients with hypertriglyceridaemia who have already been characterised as insulin resistant and they now propose to study this in these patients' siblings and identify whether they also have similar phenotypes.
(MD96050)

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

✉ TOMLINSON Brian ● CHAN Chung Ngor Juliana (Medicine) ● CRITCHLEY Julian A.J.H. ● YOUNG Robert P. ● PANG Chi Pui Calvin (Chemical Pathology) ● ARUMANAYAGAM Manoharan (Chemical Pathology) ● CHAN Yu Leung (Diagnostic Radiology & Organ Imaging) ● CHAN Yan Keung Thomas ● SANDERSON John Elsby (Medicine) ● COCKRAM Clive Stewart (Medicine) ● YEUNG Tok Fai Vincent (Medicine) ● CHOW C. C.* (Medicine)

□ 1 May 1997

❖ CUHK Strategic Research Program

The Metabolic Syndrome is a multi-faceted condition which may manifest as hypertension, non-insulin dependent diabetes mellitus, dyslipidaemia or obesity (particularly central or visceral obesity) or any combination of these. It is a major cause for increased cardiovascular risk, especially in some Asian populations and these features represent the main modifiable risk factors for major diseases such as stroke, coronary artery disease, heart failure and renal failure. Insulin resistance and hyperinsulinaemia appear to be central linking features of this syndrome. Other associated disorders include abnormalities of blood coagulation factors, salt sensitivity of blood pressure, abnormalities of membrane sodium transport, microalbuminuria, left ventricular hypertrophy and endothelial dysfunction. This project will facilitate the rapid characterisation of the underlying pathophysiology by examining these phenotypes with currently available methodologies and relating these to different genotypes in patients with these problems and their family members using a multi-disciplinary research team approach. This will provide an understanding of the inheritance of these disorders and their interaction with environmental factors allowing a more rational approach to the choice and assessments of therapies.

The studies involved include:

- (1) Investigation of the relationships between phenotypic expression of conditions associated with insulin resistance and genotypes of candidate loci in families with the Metabolic Syndrome identified by dyslipidaemia or atherosclerosis.
- (2) The heritability of diabetes mellitus and the interactions between genetic and environmental factors in its pathogenesis.
- (3) Investigation of the Metabolic Syndrome in hypertensive patients - inter-relationships between

salt sensitivity, insulin resistance, glucose intolerance and dyslipidaemia and genotypes of candidate loci. (MD96027)

Genetic Polymorphisms of the CYP and GST Isoenzymes: A Role in Hepatocellular Carcinoma and Nasopharyngeal Carcinoma

✉ YOUNG Robert P. ● CRITCHLEY Julian A.J.H.

□ 1 December 1996

❖ CUHK Research Committee Funding

Hepatocellular carcinoma (HCC) and Nasopharyngeal carcinoma (NPC) are two of the most common occurring cancers in Hong Kong Chinese. In addition to environmental factors such as viral infection, exposure to ingested procarcinogens (aflatoxin in HCC and nitrosamines in NPC) has also been implicated in their pathogenesis. These procarcinogens are metabolised into carcinogens by cytochrome P450 (CYP) isoenzymes and detoxified by glutathione S-transferase (GST) isoenzymes, both found predominantly in the liver and under genetic control. Variation in the activities of these enzymes, determined either through genotyping studies or by quantifying enzyme-derived metabolites, is believed to render some individuals at greater risk of cancer than others following exposure to these procarcinogens. Studies have shown that genetic polymorphisms of the genes encoding the CYP 2D6 and 2E1 isoenzymes are more frequent in patients with liver cancer compared to controls. The researchers have recently shown that urinary recoveries of metabolites derived from CYP 1A2 and 2E1 isoenzymes (Leung et al. *Cancer Lett*; 1991) and from the CYP 3A isoenzymes (CUHK Direct grant SP-45, 93/94 - Ng et al. *Cancer*; 1996). are higher in patients with HCC compared to those with other chronic liver diseases. They have also shown that urinary recoveries of metabolites derived from CYP 1A2 and 2E1 isoenzymes are significantly reduced in patients with NPC compared to controls (pending publication). Using molecular methods, well established in the laboratory, the researchers propose to investigate the role of the CYP 2D6, CYP 2E1 and GSTM1 genetic polymorphisms in their study groups consisting of HCC patients (n=95), NPC patients (n=147) and controls (n=150). Identification of "cancer susceptibility genes" may help to advance current understanding of the complex factors leading to the development of these cancers.

(MD96049)

Oestrogen Receptor Gene Polymorphism and Bone Mineral Density in Chinese Men and Women

✉ YOUNG Robert P. ● LAU Edith Ming Chu (Community & Family Medicine) ● HO Chan Suzanne (Community & Family Medicine) ● CRITCHLEY Julian A.J.H. ● WOO Jean (Medicine)

□ 1 December 1996

❖ CUHK Research Committee Funding

Osteoporosis is a degenerative disease of the bone and is complicated by hip fractures, vertebral fractures and distal forearm fractures. In addition to genetic factors, which account for 70% of the variance in bone mineral density (BMD), other factors contributing to the development of osteoporotic fractures include age, oestrogen status, calcium intake, smoking, exercise and ethnicity. Current treatment strategies include oestrogen replacement therapy (HRT) and calcium supplementation, but they are not without their complications. Recently, a polymorphism (mutations) in the vitamin D receptor (VDR) gene has been associated with the development of osteoporosis in Caucasian and Black populations and, in the former, shown to determine the response to calcium treatment. The researchers have examined the importance of the VDR gene polymorphism in a sample of 500 HK Chinese (The Chinese University of Hong Kong Direct grant 95.026) and found the VDR gene also relates to differences in BMD in perimenopausal and postmenopausal Chinese women (results pending publication). They also made the observation that interethnic differences in the frequency of this polymorphism may account for up to 70% of the interethnic differences in age-adjusted hip fracture rates (The Chinese University of Hong Kong Direct Grant 95.026 - Lancet; 1996: letter in press). Recently, a Japanese group reported that a polymorphism in the oestrogen receptor gene was associated with BMD in Japanese postmenopausal women. They now propose to examine this new polymorphism in our population of 500 women, recently expanded to include 300 men. An understanding of the relative importance of these genetic polymorphisms to BMD in Chinese will have important clinical implications with regard to both primary and secondary prevention strategies in osteoporosis in Hong Kong. (MD96051)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition	Title/Investigators
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 (Medicine) ● CRITCHLEY Julian A.J.H. ● YOUNG Robert P. ● COCKRAM Clive Stewart (Medicine)
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 (Medicine) ● WOO Kam Sang (Medicine) ● WOO Jean (Medicine) ● CHAN Yan Keung Thomas ● CRITCHLEY Julian A.J.H.
1995-96	Molecular Biology of Hypertension: A Study of the Genetic Markers of Essential Hypertension in the Chinese Population of Hong Kong (CU94641) ✉ YOUNG Robert P. ● CHAN Yan Keung Thomas ● CHAN Chung Ngor Juliana (Medicine) ● TOMLINSON Brian ● SANDERSON John Elsby (Medicine) ● WOO Kam Sang (Medicine) ● CRITCHLEY Julian A.J.H.
1995-96	Vitamin D Receptor Polymorphism and Osteoporosis in Chinese (MD95123) ✉ YOUNG Robert P. ● LAU Edith Ming Chu (Community & Family Medicine) ● HO Chan Suzanne (Community & Family Medicine) ● CRITCHLEY Julian A.J.H. ● WOO Jean (Medicine)

RESEARCH OUTPUTS AND PUBLICATIONS

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- <P961771> **Chan, Thomas Y.K.; Bonnie S.Y. Lam; Nicole K.L. Ng and A.J.H. Critchley.** "Drug Interactions in General Medical Patients". *Pharmacoepidemiology and Drug Safety* vol.5 Supplement 1, p.108. West Sussex, 1996.
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- <P961867> **Chan, Thomas Y.K.** "Potential Dangers from Topical Preparations Containing Methyl Salicylate". *Human & Experimental Toxicology* vol.15, pp.747-750. UK, 1996.
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- <P962215> **Chan, T.Y.K.** "Symptomatic Hypercalcaemia is Rare in Tuberculous Patients in Hong Kong". *Annals of Tropical Medicine and Parasitology* vol.90 no.6, pp.663-664. London, 1996.
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- <P962612> **Chan, Paul; Brian Tomlinson; Ching Bing Lee; Wen-Harn Pan and Ying Shiung Lee.** "Beneficial Effects of Pravastatin on Fasting Hyperinsulinemia in Elderly Hypertensive Hypercholesterolemic Subjects". *Hypertension* vol.28, pp.647-651. Dallas, USA, 1996.10.
- <P970050> **Tomlinson, Brian; Robert P. Young; Juliana C.N. Chan; Thomas Y.K. Chan and Julian A.J.H. Critchley.** "Pharmacoepidemiology of ACE Inhibitor - Induced Cough". *Drug Safety* vol.16 no.2, pp.150-151. New Zealand, 1997.02.01.
- <P970263> **Chan, T.Y.K.** "Rational Prescribing in General Practice". *The Hong Kong Practitioner* vol.19 no.1, pp.26-27. Hong Kong, 1997.01.
- <P970278> **Benzie, Iris F.F.; Brian Tomlinson and Irene Wu.** "A Comparison of *in vitro* Antioxidant Power of Tea, Wine, and the Chinese Herbal Medicine, Lingzhi". *Oxidants and Antioxidants in Biology* (Annual Meeting of Oxygen Club of California). p.102. California, USA, 1997.03.01.
- <P970348> **Tomlinson, Brian and Paul Chan.** "Treating Hypercholesterolaemia: Novel Methods". *Medical Progress* pp.5-8. Hong Kong, 1997.04.
- <P970349> **Chan, P. and Tomlinson B.** "Double-blind Comparison of Losartan, Lisinopril, and Metolazone in Elderly Hypertensive Patients with a Previous Angiotensin Converting Enzyme Inhibitor-associated Cough". *Abstracts of the 5th International Symposium on ACE Inhibitors & Other Inhibitors of the Renin-Angiotensin System* p.53. Hong Kong, 1997.04.03.
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RESEARCH PROJECTS

A Population Based Case-control Study of Risk Factors for Low Back Pain in Hong Kong Perimenopausal Women

- ✉ HO Chan Suzanne ● LAU Yip Yin Bing* ● CHAN Sieu Gaen
- 1 August 1996
- ❖ Health Services Research Fund, Hospital Authority

The problems of low back pain are exceptionally widespread and have tremendous cost both in humans and economics. Given the high prevalence and enormous impact of LBP among perimenopausal women, strategies for reducing the occurrence of this common cause of morbidity are urgently needed. A rational approach to low back pain prevention requires the determination of the risk factors which are common to the middle age women. A population-based case-control study will be conducted in Hong Kong Chinese women aged 45-55 years to determine the risk factors associated with the occurrence of low-back pain. The effects of menopausal status, parity, central obesity, physical activities and psychological stress on low back pain will be explored. Moreover, the health outcomes and uses of health services related to this health problem will be studied. With the very limited population based data available at present, the information collected will throw light on the extent and burden of the problem and possible preventive measures to be employed for the reduction of this disability in women in mid-life and in older ages. (MD96008)

Habitual Physical Activity, Health Fitness and Behaviour among Adult Population in Hong Kong

- ✉ HO Chan Suzanne ● LEE Shiu Hung ● CHAN Sieu Gaen
- 20 August 1996
- ❖ Health Care & Promotion Fund, Hospital Authority

Studies have shown that the risks of developing chronic illnesses and disability in old age may be prevented and alleviated by adopting a more physically active lifestyle. While it is recognized that activity levels tend to decline with increasing age, the reasons for this decline are inadequately understood. Besides intentional physical activities in sports and exercises, levels of customary physical activity also seem to decline from mid-life onwards. As successful health promotion effort and strategies should be based on knowledge of health behaviour and evaluation of potential barriers for individuals,

the objectives of this study are firstly to assess the pattern of habitual physical activity, health fitness and behavior among the adult population aged 40-59; and secondly to assess their knowledge on the relation between exercise and health, their attitudes towards exercise and perceived barriers for increasing physical activity. The modification of behavior during this stage of life would be essential in the promotion and maintenance of physical activity, and in the preservation of health and reduction of health risks in later life. (MD96011)

The Relationship between Sex Hormones and Bone Mass in Chinese Perimenopausal Women

- ✉ HO Chan Suzanne ● LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) ● WOO Jean (Medicine) ● CHAN Shiu Yee Cynthia ● CHAN Sieu Gaen
- 1 January 1997
- ❖ CUHK Research Committee Funding

Among the major factors, the female sex hormones (estrogens) play an important role in influencing women's bone mass and bone loss around menopausal period. The decline in estrogens is the major cause of menopausal symptoms and bone loss. There are incomplete understanding of the hormonal profiles and changes occurring during menopause and most studies have been carried out in Caucasian women, cross-sectional in design, and many have not measured the confounding or potential interactive effect of other influencing factors on bone loss. Caucasian women have higher premenopausal estrogen levels and a greater decline in estrogen levels during menopause. Studies have reported more frequent and severe experiences of menopausal symptoms and higher incidences of hip fracture in Caucasian than in Asian women. Interesting questions arise as to the role of hormonal changes on bone loss during menopause, and how these phenomena might vary among different populations. This study aims to investigate the effects of changes in sex hormones on bone loss through the months/years just before the cessation of menses, and during peri-, and early menopausal periods in Chinese women while taking into account the other pertinent lifestyle and physiological predicting factors on bone loss. This study will give useful insights into alternative managements of menopausal symptoms and preventive strategies in bone loss and osteoporosis in later life. (MD96041)

Osteoporosis - The Burden of Illness in Hong Kong

- ✉ LAU Edith Ming Chu ● HO L. S.*
- 1 August 1996

❖ Merck Sharp & Dohme (Asia) Ltd

The objectives of this project are to measure the burden of illness due to osteoporosis in Hong Kong. Data on incidence of fractures will be obtained. The cost associated with fracture will be estimated and the total burden of illness compiled.
(MD96191)

The Vitamin D Receptor Gene, Lifestyle Factors and the Aetiology of Osteoporosis in Chinese

✉ LAU Edith Ming Chu ● YOUNG Robert P. (Clinical Pharmacology) ● HO Chan Suzanne ● CRITCHLEY Julian A.J.H. (Clinical Pharmacology) ● WOO Jean (Medicine)

☐ 1 October 1996

❖ Research Grants Council

Osteoporosis is an increasingly important health problem in the aging population of Hong Kong. It has been estimated that one per thousand elderly women fracture their hip in a year and one third have vertebral fracture from osteoporosis. The life-style factors predisposing for osteoporosis have been studied in Hong Kong Chinese by the research group, but genetic factors have remained unexplored.

Two recent studies in Australian Caucasians have shown an association between allelic variants of the vitamin D receptor gene (VDR) and bone mineral density and, more importantly, rate of change of bone mineral density. Small-scale surveys conducted in Japanese indicated that the osteoporosis related gene may be rarer but its effects may be the same as in Caucasians. This project is the first population-based study to investigate the role of the vitamin D receptor gene and its interaction with lifestyle factors in the aetiology of osteoporosis in Chinese. The researchers aim to study the prevalence of the allelic variations in the vitamin D receptor gene, to describe how such allelic variations affect bone density and bone loss, to analyse how genetic effects interact with environmental factors, and to outline the mechanisms by which such genes regulate bone density. Five hundred early postmenopausal and elderly women will be studied, for the effects of the vitamin D receptor gene are believed to be different in these groups. The vitamin D receptor pattern will be described by testing for frequent restriction fragment length polymorphism using established techniques. Bone density and bone loss will be measured by the accurate method of dual X-Ray densitometry, and life-style factors by a validated questionnaire. The researchers have considerable expertise with all the aforementioned experimental techniques.

The study results may enable them to identify those at high and low risk of osteoporosis, to formulate preventive strategies and to predict those who will respond to current prevention/treatment strategies.
(CU96626)

Asian Osteoporosis Study (AOS)

✉ LAU Edith Ming Chu

☐ 1 March 1997

❖ Merck Sharp & Dohme (Asia) Ltd

This is the first collaborative study on osteoporosis and hip fracture conducted in the region of Asia. The participating countries will include Hong Kong, Malaysia, Philippines, Singapore, Taiwan and Thailand. Hong Kong will be the coordinating centre. The objectives of the project are to study incidence rates and risk factors for hip fracture in the countries concerned. Population surveys, hospital surveys and case control studies will be conducted according to standardized protocols. The result of the project will have a major impact on the prevention of osteoporosis in this region.
(MD96193)

A Randomized Controlled Trial of the Effect of Milk Supplementation on the Rate of Bone Loss in the Post Menopausal Women in Hong Kong

✉ LAU Edith Ming Chu

☐ 7 April 1997

❖ New Zealand Dairy Board

The objectives are to study the effects of milk supplementation on the rate of bone loss in post menopausal women in Hong Kong. Two hundred subjects will be randomized to receive daily milk supplement (equivalent to 800mg calcium) or no supplement. Bone mineral density will be measured by dual-X-Ray densitometry (Hologic) at baseline and then at 6 months' interval. The rate of change of bone mineral density in the treatment and control group will be studied.
(MD96136)

Sero-epidemiology of Hepatitis A and B amongst Hong Kong Chinese Adolescents

✉ LEE Albert ● CHENG Fung Khing ● LEUNG Choi Har L. ● FABB Wesley Earl ● CHAN Shiu Yee Cynthia ● CHAO Vai Kiong

☐ 1 October 1996

❖ Smithkline Beecham Pharmaceuticals

Hepatitis A is endemic in Hong Kong. Out of those cases, approximately 80% were in the 11 to 30 year age group. The figures may have grossly underestimated the true incidence. Whether symptomatic or not, they may spread the infection at home or in their working environment. A cost benefit study has been carried out locally and revealed that every dollar spent on the vaccine could save \$9.48 on average on treatment and lost of

productivity. The age at which hepatitis A occurs has shifted from early childhood to adolescence and early adult life over the last two decades in Hong Kong. The low or moderate prevalence of anti-HAV in adulthood can lead to significant increase in the disease with the introduction of HAV among certain population groups such as contact with individual transmitters from foreign countries. A hepatitis A vaccination strategy will depend on the epidemiological circumstances of the country concerned. Because the disease is under-reported and the infection often goes unnoticed, the epidemiology of hepatitis A is best defined by measuring humoral antibodies. Thus this study aims to identify the high risk groups amongst adolescents.

Hong Kong is a high prevalence of hepatitis B infection. Liver cancer ranked the second highest for cancer mortality. The infection in adolescents is probably acquired through intimate contact with infected playmates, classmates and other contacts in the household; horizontal transmission plays a large part in hepatitis B dissemination.

A hepatitis B vaccination programme was started in 1984 in Hong Kong. The adolescent group is not yet included. In countries of high endemicity, the most effective means of controlling infection is probably mass vaccination of neonates, susceptible children and adolescents, all of whom have a relatively greater chance of becoming chronic carriers after infection. A health economic study in USA in 1981 showed an expenditure of at least US\$197 million for direct medical costs and US\$126 million for the associated cost of work loss as consequences of acute and chronic hepatitis B virus related liver disease. There is evidence to recommend all adolescents receiving hepatitis B immunization. Therefore it is important to have more information on the sero-epidemiology of hepatitis B in this age group.
(MD96145)

Level of and Reasons for Utilising Accident and Emergency Services by Non Urgent Patients

- ✉ LEE Albert ● LAU Fei Lung* ● HAZLETT Clarke Blaine (Office of Educational Services)
□ 7 April 1997
❖ Health Services Research Fund, Hospital Authority

This study proposes to establish the diagnostic accuracy of patient classifications undertaken by nurses at the time of admission to selected A & E departments. This level of validity will be compared to that of the patients' attending physicians (utilizing the same A & E developed classification criteria) and the patient (using criteria related to patient's perceived level of morbidity, the length of time of being aware of the problem and need for treatment). The gold standard used to establish these levels of validity in the above A & E patient classifications

will be consensus classifications based on a retrospective record review conducted independently by panel of emergency physicians some 3 to 10 days following the patient visit to A & E. A random subsample of those classified as nonurgent will be interviewed and compared to a matched (via morbidity status) sample of primary care patients who have attended a hospital's Out Patient Department (OPD) or a Family Medicine Outpatient Clinic - in order to determine which, if any, demographic, biographic or perceived morbidity factors distinguish these two patient groups.

The results of the study have direct implications for estimating the potential extent of inappropriate use of A & E, the organisation of admitting procedures within such services, and the education of patients in the purpose and appropriate use of A & E facilities.
(MD96022)

Systematic Review of Effectiveness of Traditional Chinese Medicine: A Preliminary Study

- ✉ TANG Jinling
□ 1 December 1996
❖ CUHK Research Committee Funding

Traditional Chinese medicine (TCM) has a history of several thousand years and is one of the two official forms of medical practice in China today. Traditional medicine has also gained increasing popularity in patients, governments and research institutions in European and North American countries. Randomized clinical trials have exposed the widespread use of ineffective or even harmful therapies in medicine. It is therefore an urgent need that TCM be systematically evaluated. As urged by the World Cochrane Collaboration and evidence-based medicine, the evidence from evaluation studies should be regularly reviewed and disseminated, and doctors practising TCM should recognize the importance of evaluation and learn how to integrate their personal clinical experience with the best available external evidence from organized research. Although TCM has started to be subjected to evaluation, the progress has been slow and unsystematic and the quality of studies are generally poor. Some methodological and technical issues have yet to be resolved. This study is therefore proposed to investigate accomplishments, problems and difficulties in the evaluation of TCM. It will provide the necessary information for the larger second phase of the study: preparing, maintaining and disseminating systematic reviews of the evidence from randomized controlled trials. It will also provide information useful for improving the quality of the evaluation studies and stimulate interest in the issue.
(MD96042)

Occupational Noise Exposure and Hearing Impairment among Employees in the Transport Industries in Hong Kong

✉ WONG Tze Wai ● YU Tak Sun Ignatius ● WONG Toi Ling Louisa* ● AU Kin Kwok Dennis*

☐ 1 July 1996

❖ Occupational Safety and Health Research Grant

A sample of workers in the transport industries (about 3,000 in number) will be audiometrically screened and followed up by diagnostic audiometric test. Their hearing thresholds will be determined and the prevalence of noise induced hearing loss will be estimated. Occupational and personal risk factors will be studied in respect of hearing impairment. The noise profile for selected worksites and the personal dosimetry will be obtained to characterize the pattern of noise exposure. Current preventive measures against noise-induced hearing loss will be evaluated and strategies for its prevention will be developed. (MD96005)

Standardised Proportional Mortality Ratio Study among Food-service Workers in Hong Kong

✉ YU Tak Sun Ignatius ● WONG Siu Lan

☐ 1 August 1996

❖ Health Services Research Fund, Hospital Authority

This study attempts to find out whether workers working in kitchens (especially cooks) of Chinese restaurants in Hong Kong have a higher risk of developing lung cancer when compared to the general population. Chinese cooks are occupationally exposed to oil fumes/mist generated from over-heated cooking oils during stir-frying, the usual method of cooking Chinese dishes. These fumes have been shown to contain carcinogenic substances in animal studies and may be responsible for the unusually high lung cancer mortality rates among Chinese women in Hong Kong and other parts of the world. The Standardized Proportional Mortality Ratio method is used in this study as it is less time consuming and requires information from dead members of the cohort only. Personal and occupational data for dead members of the cohort will be abstracted from union records and copies of death certificates will be obtained to determine the underlying causes of death. The proportions of death due to various causes (including lung cancer) among a cohort of kitchen workers will be compared to those of the general population in Hong Kong using the indirect standardization method adjusting for age and calendar time at death. A more comprehensive historical cohort study, which can give a more definitive conclusion about the relationship between

cooking oil fume/mist exposure and lung cancer, will be conducted later if the results from the current study suggest an increased risk for lung cancer among Chinese kitchen workers.

(MD96003)

Occupational Noise Exposure and Hearing Impairment Among Employees in the Service Industry in Hong Kong

✉ YU Tak Sun Ignatius ● WONG Tze Wai

☐ 1 April 1997

❖ Health Services Research Fund, Hospital Authority

This is a study looking into the characteristics (levels, frequency patterns, duration) of noise exposure and hearing thresholds for workers in selected noisy processes/jobs in the non-industrial service employment sectors, including workers working in restaurants and motion pictures and other entertainment services. About 2,000 workers will be surveyed at the work place using screening audiometry; those with abnormality in the screening test will go through subsequent diagnostic audiometric tests to confirm the diagnosis. The prevalence of noise-induced hearing impairment in the various service sectors will be determined. The association with various occupational and personal risk factors will be explored to define priorities for intervention. This study will provide important data for the needs assessment of related health services, the evaluation of future intervention programmes, as well as scientific evidence for future amendments of the compensation legislation. (MD96025)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition	Title/Investigators
1995-96	A Three-year Followup Study of Health Risks, Health Changes and Quality of Life Among the Hong Kong Old-old (MD94117) ✉ HO Chan Suzanne ● WOO Jean (Medicine) ● LAU Tak Fai Joseph (Centre for Clinical Trials & Epidemiological Research)
1995-96	A Study of Bone Mass and Bone Loss in Chinese Perimenopausal Women (MD95065) ✉ HO Chan Suzanne ● WOO Jean (Medicine) ● CHAN Shiu Yee Cynthia ● LEUNG Ping Chung (Orthopaedics & Traumatology) ● CHAN Siu Gaen

- 1995-96 Incidence of and Risk Factors for Falls Among the Community-dwelling Chinese Elderly: A Prospective Study (CU95610)
✍ HO Chan Suzanne ● WOO Jean (Medicine) ● LEUNG Ping Chung (Orthopaedics & Traumatology)
- 1995-96 The Diagnosis, Prevalence of and Risk Factors for Vertebral Osteoporotic Fracture in Elderly Hong Kong Chinese (CU94601)
✍ LAU Edith Ming Chu ● WOO Jean (Medicine) ● LEUNG Ping Chung (Orthopaedics & Traumatology) ● CHAN Henry Hin Lee* (Medicine) ● LIN Michael (Diagnostic Radiology & Organ Imaging) ● YIP Man Hing Kevin (Orthopaedics & Traumatology)
- 1995-96 The Incidence of and Risk Factors for Avoidable Hospital Readmissions in Elderly Chinese - A Cohort Study (MD95033)
✍ LAU Edith Ming Chu ● WOO Jean (Medicine) ● KWOK Chi Yui Timothy (Medicine) ● LEE Shiu Hung
- 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.*
- 1995-96 Standardised Proportional Mortality Ratio Study among Food-service Workers in Hong Kong (MD95200)
✍ YU Tak Sun Ignatius ● WONG Siu Lan

RESEARCH OUTPUTS AND PUBLICATIONS

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- <P953615> **Lee, Professor S.H.** "Three Decades of Achievement in the Prevention and Control of Communicable Diseases in Hong Kong". *30th Anniversary Jubilee Publication (1965-1995)* ed. by Chang Kan. pp.102-104. Hong Kong: Federation of Medical Societies of Hong Kong, 1995.10.
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- <P961764> **Wong, T.W.; Lloyd O.L.; Wong S.L.; Yu T.S. and Sham L.K.** "Cancer Mapping in Hong Kong". *Epidemiology* (Abstracts of the 8th Annual Conference of the International Society for Environmental Epidemiology). vol.7 no.4, p.S94. Baltimore, USA, 1996.07.01.
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RESEARCH PROJECTS

Magnetic Resonance as a Single Examination to Replace Ultrasound, Radioisotope Scintigraphy, and Intra-arterial Digital Subtraction Antigiography in the Evaluation of Suspected Transplant Renal Artery Stenosis

✉ CHAN Yu Leung

☐ 28 October 1996

❖ Lee Hysan Endowment Research Grant

Stenosis of the renal-transplant artery is an important complication of renal transplantation as it may result in renovascular hypertension and poor renal function. Intra-arterial angiography has been the gold standard of diagnosis but it has the drawbacks of invasiveness and nephrotoxicity of iodinated contrast. Parenchymal abnormality is also not detected with angiography. Ultrasound with flow Doppler is a non-invasive technique capable of diagnosing stenosis from evaluation of the flow haemodynamics. The transplanted kidney can also be evaluated. It is however operator dependent, with a variable result of sensitivity and specificity, and direct anatomical demonstration of the stenosed artery is not possible. Radio-isotope scintigraphy with DTPA gives functional information. Coupled with captopril, it has a moderate accuracy in diagnosing renal-transplant artery stenosis. Use of captopril introduces the risk of renal shutdown. Inherently, radioisotope scintigraphic examination cannot provide morphological information and it carries radiation hazards. It is obvious that each of these modalities can provide different types of useful information with different accuracy. Magnetic resonance imaging is a non-invasive procedure with established use in the abdomen and pelvis. The objective of this study is to assess the role of MRI in the investigation of suspected renal-transplant artery stenosis compared to intra-arterial angiography. Doppler ultrasound and radio-isotope study.
(MD96140)

Magnetic Resonance Signal Changes in Processed and Fresh Frozen Bone Allografts: An *in vitro* Study

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

☐ 1 July 1996

❖ CUHK Research Committee Funding

Bone Allografts are increasingly being used in the reconstruction of massive defects following tumor excision. These bone allografts are pre-processed using deep freezing techniques as well as lyophilization. This affects their appearance on the MR Imaging, and may prevent the radiologists from interpreting the MRI correctly, as little is known about the normal signal characteristics of these grafts. In this proposed study the researchers aim to study the signal characteristics of these allografts with and without the presence of metal implants so that their appearance is well recognised. They will also aim to develop software systems that will enable them to recognize and eliminate such artefacts and allow them to restore the MRI as a sensitive and useful imaging modality for the monitoring of patients with musculoskeletal tumors.
(MD96053)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
1995-96	The Feasibility and Role of Magnetic Resonance Cholangiography in Paediatric Biliary Disorders (MD95148) ✉ CHAN Yu Leung ● METREWELI Constantine ● YEUNG Chung Kwong (Surgery)
1995-96	To Use MRI (Magnetic Resonance Imaging) to Assess Intra-abdominal and Subcutaneous Fat in Normal and Obese Children of Hong Kong (MD95178) ✉ CHAN Yu Leung ● LEUNG Suk Fong Sophie (Paediatrics)
1995-96	The Role of Technetium-99m Methoxyisobutylisonitrile (Tc-99m MIBI) Breast Scintigraphy in Breast Carcinoma (MD95043) ✉ LAM Wai Man Wynn ● YANG Wei Tse ● STEWART Ian Edward Tam ● METREWELI Constantine ● KING Walter Wing Keung (Surgery)

RESEARCH OUTPUTS AND PUBLICATIONS

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- <P961680> **Kew, J.; Hughes P.J.; Scott P.M.J.; Leung S.F.; Ahuja A.; Cheung D.M.C.; Hasselt C.A. and Metreweli C.** "Swallowing Abnormalities in Patients with Nasopharyngeal Carcinoma Treated with Radiation". Paper presented in the 4th International Conference on Head and Neck Cancer, organized by the Society of Head and Neck Surgeons and the American Society for Head and Neck Surgery. p735. Canada, 1996.07.28.
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RESEARCH PROJECTS

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

✉ COCKRAM Clive Stewart ● YEUNG Tok Fai Vincent ● KO Tin Choi ● SUNG Joseph Jao Yiu

☐ 1 January 1997

❖ CUHK Research Committee Funding

Gastrointestinal (GI) symptoms have been reported in up to 76% of patients with diabetes mellitus (DM). Most of them are related to abnormal GI motility. Data on the prevalence of GI motility disorders (GMD) in Chinese patients with non-insulin-dependent diabetes mellitus (NIDDM) are scanty. In view of the large patient population of NIDDM in our locality many of whom are young, the morbidity due to GMD in these patients is under-estimated. Cisapride is a GI prokinetic agent. It is the first prokinetic agent which has demonstrated efficacy in improving solid-phase emptying and GI symptoms for up to 1 year in patients with idiopathic, diabetic and other gastropathic conditions. Information in the use of cisapride in Chinese NIDDM patients with GMD is lacking. Data generated from this study will be useful for assessing the prevalence of GMD in Chinese NIDDM patients and hence understanding the severity of the problem, as well as evaluating the effect of cisapride as treatment on this debilitating disorder.

(MD96054)

Pilot Study of Clomethiazole in the Treatment of Intracerebral Haemorrhage

✉ KAY Li Chi Richard ● WONG Ka Sing Lawrence ● AHUJA Anil Tejbhan (Diagnostic Radiology & Organ Imaging)

☐ 1 December 1996

❖ CUHK Research Committee Funding

Approximately 25% of patients admitted to hospitals in Hong Kong with a stroke will have an intracerebral haemorrhage (ICH). Of 121 patients admitted to the Medical Service of the Prince of Wales Hospital during the first six months of 1996, 32(26%) died during hospitalisation. Only nine (7%) patients were considered suitable for surgical intervention. For the remainder of the patients, no specific medical treatment which has been shown to improve survival or recovery is currently available.

Clomethiazole (Heminevrin) is a sedative and anticonvulsant drug which has been used worldwide for more than 30 years. Recent studies have

identified the GABA_A receptor as a site of action for clomethiazole. In animal studies, clomethiazole has been found to have a neuroprotective effect. In open studies involving ischaemic stroke patients, clomethiazole was found to be safe in doses up to 75 mg/kg/d.

The aim of this pilot study is to assess the feasibility of treating ICH patients with clomethiazole. Forty patients will be randomised to receive open clomethiazole or no clomethiazole. The primary measure of outcome will be death or severe disability after three months.

(MD96055)

Interaction of Mesangial Cells with Polymeric IgA: Exploration of the Mechanism and the New Treatment of Glomerular Injury in IgA Nephropathy (IgAN)

✉ LAI Kar Neng ● LEUNG Chi Kam Joseph (Clinical Immunology Unit)

☐ 1 January 1997

❖ Research Grants Council

IgA nephropathy (IgAN), recognized to be the most common glomerulonephritis worldwide, is one of the leading causes of kidney failure. The disease is characterized by proliferation of mesangial cell/matrix with deposition of "pathogenetic" immunoglobulin A (IgA) in the mesangial area of the glomerulus. Recently, transforming growth factor- β (TGF- β) has been shown to exert widespread effects on extracellular matrix by enhancing its accumulation and altering the glomerular filtration, thus leading to glomerulosclerosis and progressive renal failure. Apparently, angiotensin II induces synthesis of TGF- β in mesangial cells. Preliminary data from our pilot study show a selective binding of polymeric -IgA from patients with IgAN to cultured mesangial cells. Furthermore, mRNA encoding for the components of the renin-angiotensin system (including angiotensin II) are present in mesangial cells. Our proposed project will provide further insight of the mechanisms by which mesangial sclerosis and kidney failure are developed in IgAN. Experimental inhibition of these pathways by blocking the renin-angiotensin system in mesangial cells would provide a scientific basis for newer therapeutic strategy in IgAN.

(CU96607)

Identification of Genetic and Environmental Risk Factors for Childhood Asthma in Hong Kong

✉ LAI Kei Wai Christopher ● LEUNG Chung Chuen Roland ● WONG Wing Kin Gary (Paediatrics) ● YOUNG Robert P. (Clinical Pharmacology) ● LAU Tak Fai Joseph (Centre for Clinical Trials & Epidemiological Research)

☐ 1 October 1996

❖ Research Grants Council

The prevalence of childhood asthma is increasing in Hong Kong. The parallel increase in other allergic disease including allergic rhinitis and eczema suggests a more broadly based change in reactivity possibly due to increased exposure to allergens and other environmental factors. Although the exact role of the environment in childhood asthma is unknown, there is data to suggest the indoor exposure to house dust mite, tobacco smoke and nitrogen dioxide generated from cooking stoves may be important. The proposed study aims to determine the association of exposure to these factors and childhood asthma in Hong Kong. The researchers have identified a group of asthmatic children in their previous survey and in the proposed study, home visits to these children's home will be conducted to collect dust samples from the bedrooms to measure dust mite exposure. A urine sample will be collected to measure exposure to cigarette smoke, and each child will wear a sampler on the clothing to measure nitrogen dioxide exposure at home. Allergic status and airway reactivity will also be determined by standard methods. The researchers believe the results of their study will facilitate the implementation of strategies to prevent and better control the disease by reducing exposure to important environmental factors.
(CU96609)

Relationship between Air Quality and Hospital Admissions for Respiratory Disease in Hong Kong

✉ LAI Kei Wai Christopher ● LAU Tai Shing (Statistics) ● LEUNG Chung Chuen Roland ● WONG Wing Kin Gary (Paediatrics) ● YAM Loretta*

□ 1 January 1997

❖ CUHK Research Committee Funding

Concern has been expressed on the health effects of outdoor air pollution in Hong Kong. While some studies in Europe and North America have indicated that rises in the ambient levels of particulate matters, NO₂, SO₂ and O₃ may lead to increased morbidity and/or mortality in susceptible subjects such as those with asthma or chronic obstructive airway disease (COAD), others have not been able to confirm these findings. Similar data in Hong Kong is lacking. This application seeks to establish the temporal relationships between ambient levels of each of the above-mentioned air pollutants and hospital admissions due to respiratory illness, particularly for asthma and COAD, in our territory. Computerised admission data from Prince of Wales Hospital and Pamela Youde Nethersole Hospital will be analysed together with air quality data obtained from the Royal Observatory. Results from this study will be useful in assessing the public health costs and formulating

appropriate measures to reduce the health risks of air pollution.
(MD96056)

Prevalence of Sleep Disorder Breathing in Young Adults in Hong Kong

✉ LEUNG Chung Chuen Roland ● LAI Kei Wai Christopher

□ 1 March 1997

❖ CUHK Research Committee Funding

Sleep related breathing disorder (SBD) is a common medical problem and has only become recognised as an important clinical entity in the last fifteen years. The prevalence of SBD is estimated to be 4% in men and 2% in women of middle-age. Its prevalence in young adults has not been previously defined. As SBD has profound effects on work performance, neuropsychological functions and cardiovascular morbidity, it is important to identify at risk groups early so that curative and preventive treatments can be promptly initiated. The proposed study aims to determine the prevalence of symptoms related to SBD in a university student population in Hong Kong. The subjects will consist of all first year students enrolling at The Chinese University of Hong Kong in the academic year of 1996. Each student will be sent a questionnaire on sleep symptoms and a subsample will be selected to undergo overnight sleep monitoring in their homes. It is envisaged that the proposed study will provide for the first time data on the frequency distribution of sleep related symptoms and the prevalence of SBD in young adults. This will form the basis of future studies in identifying important risk factors for SBD which in turn will facilitate the implementation of preventive measures for this common condition.
(MD96057)

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

✉ SANDERSON John Elsby ● CHOW Tsun Cheung (Anatomical & Cellular Pathology) ● WOO Kam Sang

□ 1 October 1996

❖ Research Grants Council

The purpose of this investigation is to determine the role of cytokines in the development of myocardial fibrosis and left ventricular diastolic dysfunction in patients with heart failure. Studies have shown that a restrictive filing pattern, which is a marker of myocardial stiffness, is an important predictor of outcome and mortality. Thus to discover the aetiology of the increased myocardial fibrosis and

collagen in patients with heart failure is of considerable importance especially as there is the potential for reversal of the collagen accumulation.

Objectives:

(1) Determine whether there is increased production of cytokines by macrophages by assessing gene expression (mRNA levels) using rt-PCR and measuring plasma levels of the relevant cytokines (transforming growth factor- β and platelet derived growth factor- β) in at least 100 patients with typical end-stage congestive heart failure due to idiopathic dilated cardiomyopathy or ischaemic heart disease compared to age and sex matched controls.

(2) Correlate the levels of cytokines (both gene expression and plasma levels) with a non-invasive Doppler-echocardiographic assessment of diastolic function, in particular whether the restrictive filling is associated with higher levels of cytokines or gene expression.

(3) In a subset of patients in whom endomyocardial biopsy is justifiable on clinical grounds (to exclude myocarditis), to correlate the presence of macrophages or lymphocytes with cytokine levels within the myocardium and the collagen volume fraction.

(CU96670)

Does Progesterone Attenuate the Estrogen Induced Increase in Coronary Blood Flow?

✉ SANDERSON John Elsby ● HAINES Christopher John (Obstetrics & Gynaecology) ● CHAN Wai Man Wilson ● WOO Kam Sang ● WOO Jean

□ 1 January 1997

❖ Heart and Hypertension Fund ● Novo Nordisk

Estrogen has been shown to have a protective cardiovascular effect in postmenopausal women and to induce coronary and peripheral artery dilatation. However, the majority of post-menopausal women will still have a uterus and estrogen replacement therapy alone will not be suitable because of the adverse effects of unopposed estrogen on the endometrium and combined therapy with progesterone would be preferable. However, it is possible that progestones will counteract the beneficial effects of estrogen. In this study the researchers will assess directly the effect of combined therapy on endothelium mediated and direct coronary artery dilation using intracoronary Doppler flow-probes.

(MD96139)

Does Eradication of *Helicobacter pylori* Prevents NSAID-related Ulcers and Complications

✉ SUNG Joseph Jao Yiu ● CHAN Ka Leung Francis ● CHUNG Sheung Chee Sydney (Surgery) ● LING Kin Wah Thomas

(Microbiology) ● CHENG Fun Bun Augustine (Microbiology)

□ 1 September 1996

❖ Research Grants Council

Both non-steroidal anti-inflammatory drugs (NSAIDs) and *helicobacter pylori* infection are the most important risk factors for peptic ulcer disease. Previously the researchers have shown that eradication of *H. pylori* without acid suppression therapy effectively heals non-NSAID ulcers and markedly reduces ulcer recurrence. The relationship between NSAID and *H. pylori* infection in the pathogenesis of ulcer is largely unknown. The researchers resolve to study this question in three aspects:

(1) to follow the changes of mucosal prostaglandins and gastric mucosal blood flow in *H. pylori* infected patients before and after receiving NSAID therapy,

(2) to study whether eradication of *H. pylori* infection prior to NSAID therapy would reduce the occurrence of gastroduodenal ulcers, and

(3) to study whether eradication of *H. pylori* would reduce recurrent ulcer complications in high risk patients who need to continue taking NSAID.

The pilot study has shown that eradication of *H. pylori* infection markedly reduces the risk of subsequent NSAID-induced gastroduodenal damage. Better understanding of the relationship between *H. pylori* infection and NSAID usage may ultimately reduce the risk of ulcers, their complications, and the need for expensive prophylactic therapy in the future. (CU96604)

Effects of Pretreatment with Vasodilating β -Blockers on Experimental Cardiac Failure-Induced Changes in mRNA Levels for Types I and III Collagen and TGF β 1

✉ WEI Shan ● SANDERSON John Elsby ● SHUM Oi Ling Irene ● CHOW Tsun Cheung (Anatomical & Cellular Pathology)

□ 1 August 1996

❖ CUHK Research Committee Funding

The pathologic basis of heart failure and in particular the restrictive filling pattern is largely due to increased stiffness of the ventricles due to accumulation of collagen and fibrosis. In previous studies, the researchers have shown in their patients with heart failure that significantly higher mRNA levels for transforming growth factor- β 1 (TGF β 1) and platelet derived growth factor B in peripheral macrophages compared to controls, and TGF β 1 is present in the myocardium associated with fibrillar collagen and fibrosis. Several studies have confirmed the beneficial effects of metoprolol and recently vasodilating β -blockers such as carvedilol have been shown to reduce mortality. They hypothesize that

TGF β 1 may play a key role in regulating collagen synthesis during the development of heart failure. The beneficial effects of β -blockers may in part be related to lower TGF β 1 mRNA expression, secondarily reducing the appearance of myocardial fibrosis in heart failure and thus favourably affect remodeling of the left ventricle. The researchers wish now to use an animal model of myocardial infarction, to investigate (1) whether there are alterations in expression of TGF β 1, type I and III procollagen genes involved in the development of heart failure post myocardial infarction; (2) Whether pretreatment with carvedilol reduces left ventricular fibrosis and collagen, alters the gene expression of TGF β 1, type I and III procollagen. This research will be important in understanding of the pathogenesis of the failing heart syndrome, and will lead to more effective treatment regimens. (MD96058)

A Prospective Study of Patients with Middle Cerebral Artery Stenosis Diagnosed After First Ever Ischemic Stroke

✉ WONG Ka Sing Lawrence ● KAY Li Chi Richard ● AHUJA Anil Tejbhan (Diagnostic Radiology & Organ Imaging)

□ 1 January 1997

❖ Research Grants Council

Stroke is one of the top three killer diseases in Hong Kong and 70% of stroke is due to cerebral infarction. In Western countries, carotid stenosis is the most important cause of cerebral infarction. Intracranial stenosis is shown to be more common than carotid stenosis in Chinese patients in a few autopsy and angiographic studies on selected patient groups. However, there has been no prospective study of the importance of intracranial stenosis in the Chinese stroke patients. With the advances in the non-invasive investigations of the cerebral vasculature, it is now possible to study consecutive stroke in a systematic manner. As surgery is not feasible in treating intracranial stenosis, risk factors modification is the only option available. Nevertheless, there is little data on the risk factors of intracranial stenosis. The researchers plan to investigate non-invasively the cerebral vasculature of consecutive surviving ischaemic stroke patients who are admitted to a regional hospital. By identifying and following up the group of patient with severe middle artery stenosis, they can obtain data on the risk factors and the prognosis of this cohort of patients. These data will be invaluable in formulating the future stroke prevention strategy in patients with middle cerebral artery stenosis. (CU96605)

Regress of Cerebral Artery Stenosis Study

✉ WONG Ka Sing Lawrence ● LAM Wai Man Wynn (Diagnostic Radiology & Organ Imaging) ● CHAN Yu Leung (Diagnostic Radiology & Organ Imaging) ● KAY Li Chi Richard

□ 1 January 1997

❖ CUHK Research Committee Funding

Stroke is the third commonest cause of mortality in Hong Kong. In Chinese, Japanese and the Blacks, intracranial stenosis is the commonest vascular lesion found in patient with acute ischaemic stroke. Intracranial arterial atheroma is technically more difficult to remove surgically than extracranial carotid atheroma. Therefore, anti-atheroma medication is one of the most promising approach for stroke prevention in the Orientals. Lipid lowering agents have been shown to regress coronary artery stenosis. The ACAPS study showed that lovastatin is effective in preventing the progression of early carotid atherosclerosis. In the ACAPS and the 4S study, the incidence of stroke were significantly lower in the treatment group. Thus, the use of statins is expected to prevent the progression of intracranial large artery stenosis. Regression of Cerebral Artery Stenosis (ROCAS) is a randomized double-blind placebo controlled study. The aim is to investigate the effect of simvastatin on the regression/progression of asymptomatic intracranial atherosclerotic stenosis. Outcome measures include (1) global change score as determined by the change in the lumen of the middle cerebral artery as shown by the magnetic resonance angiography two years after treatment with simvastatin or placebo; (2) the change in the minimal diameter of the middle cerebral artery; (3) the change in the peak velocity of the middle cerebral artery by transcranial Doppler ultrasonography; and (4) the occurrence of stroke or transient ischemic attack. (MD96059)

Domiciliary Pulmonary Rehabilitation Program: A Randomised Controlled Clinical Trial

✉ WOO Jean ● LUM Christopher* ● HUI E.* ● LEUNG Chung Chuen Roland

□ 18 November 1996

❖ Health Services Research Fund, Hospital Authority

More than 6% of Chinese elderly have chronic obstructive pulmonary disease, resulting in repeated hospital admission, reduced functional level and unsatisfactory perceived quality of life. The researchers propose to perform a randomised controlled clinical trial to develop a comprehensive domiciliary pulmonary rehabilitation program to

improve the functional status and quality of life of this group of elderly living in Nursing Homes. (MD96017)

Transgenic Expression of C-type Natriuretic Peptide in Mouse Astrocytes to Study its Roles in Central Haemodynamic and Endocrine Control

✉ YEUNG Tok Fai Vincent ● CHUI Yiu Loon (Clinical Immunology Unit) ● COCKRAM Clive Stewart

☐ 1 December 1996

❖ CUHK Research Committee Funding

C-type natriuretic peptide (CNP) is the third member of the natriuretic peptide family. There is recent evidence that CNP could play important roles in the central control of blood pressure and fluid balance and pituitary hormone secretion. The research group has established that astrocytes, an important and most abundant cell type in the central nervous system (CNS), constitute a useful cellular model for studying centrally-acting peptide hormones. These cells produce a characteristic protein, glial fibrillary acidic protein (GFAP), which is unique to astrocytes and which can be utilized as a marker of their presence.

The researchers propose to generate transgenic mice bearing a GFAP/CNP fusion gene so that CNP can be produced in abundance by astrocytes. The effects of increased expression of CNP in the CNS upon the blood pressure, water and electrolyte balance, and secretion of pituitary hormones will then be examined. The *in-vivo* studies should complement information obtained from their *in-vitro* studies on cultured astrocytes by allowing elucidation of the central effects of CNP on blood pressure, electrolytes, body fluid homeostasis and neuroendocrine regulation in the living animal. The results may have clinical relevance to the management of hypertension and fluid balance disorders.

(MD96060)

Biocompatibility of 1-Lactate/Pyruvate Buffered PDS: Its Effects on the Host Defense Mechanism and Viability of the Peritoneal Mesothelial Cells

✉ YU Wai Yin Alex ● LAI Kar Neng

☐ 1 November 1996

❖ Research Grants Council

CAPD (continuous ambulatory peritoneal dialysis) is the commonest mode of dialysis therapy for patients with end stage renal failure in Hong Kong. However, the peritoneal dialysis solution (PDS) that has been on the market for more than 20 years is bioincompatible. It has low pH and contains high concentrations of dl-lactate and glucose. PDS favors bacterial growth as functions of peritoneal macrophage and leukocytes are compromised. This

may account for the high incidence of peritonitis in patients on CAPD. Repeated peritonitis leads to peritoneal sclerosis, resulting in ultrafiltration failure and need for more expensive hemodialysis. High concentration of dl-lactate has been identified as one of the culprits. Lactate and H⁺ are co-transported into the cells causing intracellular acidosis, inhibiting oxidative metabolism, superoxide and cytokine formation. Bactericidal activities of the neutrophils are thus affected.

The ratio of l-lactate to pyruvate is controlled tightly in the blood of healthy individuals. It is postulated that the absence of pyruvate alters the redox potential of the cells exposed to the PDS, decreasing the extent of most of the cell's energy-linked reactions. In this project, the researchers will investigate the effects of a lower concentration of l-lactate in combination with pyruvate-buffered PDS on leukocytic intracellular pH, superoxide and cytokine formation. The viability of the mesothelial cells on exposure to l-lactate/pyruvate buffered PDS will also be tested in comparison to the dl-lactate-buffered conventional PDS. The method used in this project can serve as a model for testing other preparation of PDS in future for biocompatibility.

(CU96621)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
1995-96	The Role of Insulin Resistance, Its Relationship with Hypertension and the Significance of Autoantibodies to Glutamic Acid Decarboxylase (Anti-GAD) in the Pathogenesis of Diabetes Mellitus among Hong Kong Chinese (CU94610) ✉ CHAN Chung Ngor Juliana ● COCKRAM Clive Stewart ● CRITCHLEY Julian A.J.H. (Clinical Pharmacology) ● YEUNG Tok Fai Vincent ● CHOW Chun Chung Francis ● TOMLINSON Brian (Clinical Pharmacology) ● CHAN Yan Keung Thomas (Clinical Pharmacology) ● YOUNG Robert P. (Clinical Pharmacology)
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

- 1995-96 Expression of Cytokine Genes in CD4+ T Helper Cells that Control IgA Synthesis: A Molecular Exploration of the Pathogenesis of IgA Nephropathy (CU93603)
 ✍ LAI Kar Neng ● CHUI Yiu Loon (Clinical Immunology Unit)
- 1995-96 The Role of "Sclerogenic Cytokines" in the Development of Ultrafiltration Failure of Peritoneal Membrane in Patients with Renal Failure Undergoing Continuous Ambulatory Peritoneal Dialysis (CU95603)
 ✍ LAI Kar Neng ● LI Kam Tao Philip
- 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
- 1995-96 A Double-Blind, Placebo - Controlled Study to Determine the Efficacy and Safety of Two Dosage Regimens of Lamivudine in Patients with Chronic Hepatitis B Infection (MD94157)
 ✍ LEUNG Wai Yee Nancy
- 1995-96 A Study of the Prevalence of Pre-core Mutant Among Chronic Hepatitis B Patients in Hong Kong and an Evaluation of its Clinical Significance (MD95172)
 ✍ LEUNG Wai Yee Nancy ● TAM Siu Lun John (Microbiology) ● IP Margaret (Microbiology) ● LIEW Choong Tsek (Anatomical & Cellular Pathology)
- 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 Beta-blockers in Heart Failure: Do Vasodilating Beta-blockers Have Long-term Advantages Over Metoprolol? A Randomized Placebo Controlled Trial of Celiprolol Versus Metoprolol (MD94174)
 ✍ SANDERSON John Elsby ● YU Cheuk Man* ● CHAN Wai Man Wilson ● RAYMOND Kenneth (Pharmacy) ● CHAN Kam Wing (Diagnostic Radiology & Organ Imaging) ● WOO Kam Sang
- 1995-96 Congestive Cardiac Failure: The Role of Angiotensin-converting Enzyme Genes in the Development of Myocardial Fibrosis and Left Ventricular Diastolic Dysfunction (CU95651)
 ✍ SANDERSON John Elsby ● YOUNG Robert P. (Clinical Pharmacology) ● WOO Kam Sang ● CRITCHLEY Julian A.J.H. (Clinical Pharmacology) ● ARUMANAYAGAM Manoharan (Chemical Pathology)
- 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
- 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*
- 1995-96 A Nutritional Survey of the Hong Kong Population in Relation to Cardiovascular Health (MD95034)
 ✍ WOO Jean ● LEUNG Suk Fong Sophie (Paediatrics) ● HO Chan Suzanne (Community & Family Medicine)
- 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 (Chemical Pathology) ● HO Chan Suzanne (Community & Family Medicine) ● CHAN Kam Yin Daniel*
- 1995-96 Clinical Audit and Registry of Acute Myocardial Infarction in Hong Kong (MD94065)
 ✉ WOO Kam Sang ● WONG S. P.* ● CHAN W. K.* ● CHUNG Hau Kwong ● LAU Tak Fai Joseph (Centre for Clinical Trials & Epidemiological Research)
- 1995-96 An Investigation of the Efficacy and Tolerability of Combination Therapy Using Acipimox and Lovastatin in Chinese Patients with Non-insulin-dependent Diabetes Mellitus (NIDDM) and Mixed Hyperlipidemia (MD95157)
 ✉ YEUNG Tok Fai Vincent ● KO Tin Choi ● MAK Wing Lai Tony* (Chemical Pathology) ● LAM Wai Kei Christopher (Chemical Pathology) ● COCKRAM Clive Stewart
- 1994-95 Systemic Effect of Sodium Hydroxide in Experimental Hypoxic Lactic Acidosis (MD95044)
 ✉ YU Wai Yin Alex
- 1995-96 Biocompatibility of Alternative Peritoneal Dialysis Solutions; Comparison of 1-Lactate/Pyruvate-Buffered and d1-Lactate-Buffered Solutions (MD95126)
 ✉ YU Wai Yin Alex
- 1995-96 Effect of Calcium Channel Blockers on Diurnal Blood Pressure Variations in Hypertensive Renal Transplant Patients (MD95243)
 ✉ YU Wai Yin Alex ● HO Kelvin*
- 1995-96 Comparative Effect of Amlodipine and Nefidipine Retard on Renal Function and Blood Pressure Control in Renal Transplant Patients (MD95244)
 ✉ YU Wai Yin Alex ● LAI Kar Neng ● HO Kelvin*

RESEARCH OUTPUTS AND PUBLICATIONS

- <P952090> **Chan, K.L.; J.Y. Sung; R. Hsu and C.T. Liew.** "The Association of Amoebic Colitis and Chronic Ulcerative Colitis". *Singapore Medical Journal* vol.36, pp.303-305. Singapore, 1995.
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RESEARCH PROJECTS

Molecular Mechanism of Immunoglobulin Gene Hypermutation: Does It Resemble the Transcription-DNA Repair System?

- ✉ CHUI Yiu Loon ● LIM Pak Leong
- ☐ 1 September 1996
- ❖ Research Grants Council

During an immune response, the antibody genes in B cells can somatically mutate at a rate which is 10^5 times faster than that normally observed for spontaneous mutation. Molecular basis of this powerful hypermutation mechanism is entirely unknown. DNA sequence analysis has revealed that hypermutation occurs exclusively within the antigen-binding site. Such specific targeting of hypermutation must require the presence of some landmark sequences. Transgenic studies using antibody light chain gene have failed to identify positively any such sequences within the targeted region and its flanking sequences. An important clue is provided by the observations that the hypermutation is biased to one DNA strand. This suggests a link between transcription and hypermutation, and the further possibility that the promoter itself could be the sought-after landmark sequence. Transcription is known to be related to DNA repair, and hypermutation has also long been postulated to be caused by some error-prone DNA repair system. To test the idea of whether or not the hypermutation system is indeed derived from or linked to the globally common transcription-DNA repair machinery, the researchers propose to generate antibody transgenes with modified transcriptional features to observe how that would affect their hypermutation. In addition, a modified polymerase chain reaction methodology which is sensitive enough to detect DNA strand break in genome will be adopted for the first time in hypermutation study

to investigate the possible involvement of DNA repair. They envisage that their result will be able to provide clear insights into the nature of the molecular mechanism of hypermutation.
(CU96664)

Please refer to previous issues of *Research Projects Summary* 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 Leong
1995-96	Production of Autoantigens by Genetic Engineering and Peptide Synthesis for Use in the Immunodiagnosis of Autoimmune Disease (CU93615) ✉ LIM Pak Leong ● CHUI Yiu Loon
1995-96	To Investigate the Structural Basis for the Carrier Specificity of Anti-phosphorylcholine Antibodies (CU94645) ✉ LIM Pak Leong ● LEUNG Hei Wun* ● CHUI Yiu Loon ● TSANG Kam Sze Kent* (Anatomical & Cellular Pathology)
1995-96	Cloning and Expression in Bacteriophage of Immunoglobulin Genes from Lupus (SLE) Patients Which Encode and Anti-idiotypic Antibody (CU95638) ✉ LIM Pak Leong ● CHUI Yiu Loon ● WONG Kong Chiu (Medicine)

RESEARCH OUTPUTS AND PUBLICATIONS

- <P963754> **Lim, Pak-Leong; Lawrence W.K. Ng; Danny T.M. Leung; Kong-Chiu Wong; Si-Yang Song; Yiu-Loon Chui; Joseph C.K. Leung; Kar-Neng Lai and Siu-Fai Lui.** "Common Occurrence of an Antiidiotypic Antibody That Recognizes T14+ Anti-DNA Antibodies in Patients with Systemic Lupus Erythematosus". *Arthritis and Rheumatism* vol.39 no.12, p.1980. USA, 1996.12.12.
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<P972017> **Lim, Pak Leong; Frankie C.H. Tam; Yiu Loon Chui and Lawrence W.K. Ng.** "Identification of a Surrogate TSL-1 Antigen of *Trichinella Spiralis* from a Phage Library of Random Peptides". *Parasite Immunology* vol.19, pp.281-286. England, 1997.02.21.

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RESEARCH PROJECTS

A Survey of the Presence of Human Herpesviruses 6 and 7 in Normal and Neoplastic Brain Tissues

- ✉ CHAN Kay Sheung Paul ● NG Ho Keung (Anatomical & Cellular Pathology) ● TAM Siu Lun John ● CHENG Fun Bun Augustine ● FUNG Sau Chun Kitty
- 1 November 1996
- ❖ CUHK Research Committee Funding

Human herpesviruses 6 and 7 (HHV-6 and HHV-7) are the two recently identified herpesviruses which cause persistent infection in a majority of the general population. Although both HHV-6 and HHV-7 are mainly lymphotropic, *in vitro* data suggested HHV-6 may be neurotropic as well. HHV-6 genome has been demonstrated in normal and neoplastic human brain tissues and a putative transforming gene have been identified. Although, little information is available regarding the neurotropism and transforming potential of HHV-7, the fact that HHV-6 and HHV-7 belong to the same sub-family, betaherpesvirinae, in which the prototype, human cytomegalovirus, is a well-characterized neurotropic pathogen in immunocompromised individuals, it is felt worthwhile to study the neurotropic and oncogenic potential of these two novel human herpesviruses. The objectives of this study are: (1) to define the presence of HHV-6 and HHV-7 genome in human brain tissue; (2) to compare their prevalence in normal and neoplastic brain tissues; (3) to investigate the anatomical distribution of the two viruses; and (4) to observe the effect of one virus on the persistence of the other. These data will be valuable for further studies on their pathogenic role in neurological diseases.

Total DNA will be extracted from 200 normal and neoplastic brain tissues and subjected to HHV-6 and HHV-7 DNA detection by nested PCR. Results will be confirmed by dot blot hybridization and HHV-6 detected will be typed into variants A and B. Molecular analyses to compare the normal tissue-associated and the tumour-associated viral DNA sequences will be attempted. (MD96061)

An *in-vitro* Antimicrobial Susceptibility of Trovafloxacin

- ✉ CHENG Fun Bun Augustine ● LING Kin Wah Thomas
- 1 September 1996
- ❖ Pfizer Corporation

Fluoroquinolones possess high activity against many bacterial strains and are widely been used for the

treatment of infections. Currently used fluoroquinolones including ciprofloxacin and ofloxacin have good activities against Gram-negative bacteria but have only marginally activities against *Streptococcus pneumoniae* and are less active against anaerobes. Trovafloxacin is a new fluoroquinolone which demonstrates potent antimicrobial activity against Gram-negative bacteria. Its *in-vitro* activity profile is extended towards both Gram-positive and anaerobic organisms.

The Prince of Wales Hospital, Hong Kong has a large and well documented collection of bacterial strains which reflect the clinical isolates of various resistance patterns and representing this geographic area. This study demonstrates the antimicrobial activity of trovafloxacin in comparison with other antimicrobial agents. (MD96137)

An *in-vitro* Antimicrobial Susceptibility of Meropenem

- ✉ CHENG Fun Bun Augustine ● LING Kin Wah Thomas
- 1 March 1997
- ❖ Zeneca (China) Ltd

Meropenem is a parenteral carbapenem antibiotic which has excellent bactericidal activity *in-vitro* against almost all common clinical isolates including both aerobes and anaerobes. It is the first dehydropeptidase-stable carbapenem which can be given as a single agent. Bacterial isolates were collected from the Prince of Wales Hospital during 1989 to 1996: These strains will be chosen to represent the various resistance patterns commonly encountered in this geographic area. This study will ascertain the efficacy of meropenem in Hong Kong. (MD96138)

The Development of a GLC Procedure for the Analysis of Ethambutol in Clinical Specimens

- ✉ CHENG Fun Bun Augustine
- 1 April 1997
- ❖ CUHK Research Committee Funding

Tuberculosis has been a serious worldwide problem. Treatment of this disease usually makes use of peroral administration of first-line drugs including rifampicin, isoniazid and ethambutol. Since the researchers' department has been providing routine therapeutic monitoring service of various antimicrobials to clinicians and patients at the Prince of Wales Hospital, and pharmacokinetics, mycobacteriology as well as clinical trials on antimicrobials have been projects of their mainline research, they have been developing different assay methods for the quantitation of different

antimicrobials. Although a lot of the antimicrobials that would not normally produce toxic side effects need not be assayed, quantitative analyses for their bioavailabilities are sometimes necessary when the patients do not respond to therapy. Most of the antimicrobials, including the anti-tuberculous drugs of rifampicin, isoniazid and pyrazinamide, can be analysed by HPLC in our laboratory. However, the analysis of ethambutol by HPLC cannot be performed owing to the chemical nature of the compound, and gas-liquid chromatography (GLC) remained the only choice for quantitative analysis of this drug. Several GLC assay procedures for ethambutol have been investigated during the early 1980s, but these methods would require modification before further evaluation can be made for clinical application. The development of a sensitive and accurate assay procedure would allow our laboratory to extend our mycobacteriology research in addition to provide clinical service of therapeutic drug monitoring.
(MD96112)

A Comparison of *Acinetobacter spp* Distribution in Humans and in Raw Vegetables in Hong Kong and London

- ✉ HOUANG Ting Sou Elizabeth ● CHU Yiu Wai ● CHENG Fun Bun Augustine
- 1 September 1996
- ❖ CUHK Research Committee Funding

The taxonomy of *Acinetobacter spp* has caused much confusion. The organism is now responsible for an increasing incidence of outbreaks and endemic infections world-wide. There is a recognised higher prevalence of these infections in Hong Kong, including an unusually high incidence of community-acquired infection. Important factors may include the hot, humid climate, racial differences (e.g. patterns of skin fatty acids), diets or different genotypes. In collaboration with the Laboratory of Hospital Infection, Central Public Health Laboratory, UK, using new molecular techniques, the researchers intend to carry out a cross-sectional comparative study on the skin carriage of *Acinetobacter spp* in healthy students at a UK university and The Chinese University of Hong Kong, once in summer and once in winter. The genus will be sought by examining swab cultures of various skin sites and a rectal swab when possible from each volunteer, as well as from locally grown raw vegetables. In addition, they will also examine groups of patients on admission and after 7 days in the Prince of Wales Hospital. Thus, the carriage and skin fatty acid tolerance of different genospecies of *Acinetobacter* in Caucasians in London and Chinese in Hong Kong may be compared, together with the contribution of vegetables and climate to colonization of subjects.
(MD96062)

Nosocomial (Hospital-acquired) Colonization of Hospital Employees

- ✉ HOUANG Ting Sou Elizabeth ● LYON Donald James
- 1 November 1996
- ❖ Occupational Safety and Health Research Grant

There is little evidence that colonization of multiply resistant *Staphylococcus aureus* (MRSA) and multiply resistant Gram-negative rods (MRGNR) in healthy subjects is a health hazard. Nevertheless, it is desirable to avoid acquisition of these organisms whenever possible. The researchers would like to determine, in the first instance, whether exposure to hospital environment increases the rates of colonization of staff. They propose two related studies on 3 intakes of new student nurses over a period of 14 months. A nose, throat, groin and rectal swab will be taken from the student at the time of entry (community samples) and again after each clinical period over the study period. At the same time, samples will also be taken from the corresponding 3rd year student nurses, representing a group with exposure of high intensity. Exposure history will be obtained by questionnaires at each sampling time, including demographic features, previous illness/treatment, types of ward, level of patient contact, meal habits and recent travel. The first study is a cross-sectional survey to compare the carriage rates of MRSA and MRGNR between the 3 intakes of new entrants and their corresponding 3 intakes of 3rd year students. The frequencies of demographic features and exposures for each group will be calculated and compared between the two groups. The second study is prospective cohort in design to compare colonization rates of these organisms in the new students at the entry time with those obtained after their first and second clinical period respectively. Measures of association, the relative risk and the attributable risk will be calculated. If their hypothesis is proven, studies of risk factors of staff colonization should follow. Such information would be valuable not only in preventing staff colonization, but also allow the researchers to adopt a more rational approach in deciding the appropriate extent and manner of barrier procedures when nosocomial pathogens are involved, resulting in a more cost-effective allocation of resources.
(MD96013)

Ulcerative Keratitis and Contact Lens Related Infection in Hong Kong

- ✉ HOUANG Ting Sou Elizabeth ● LAM Shun Chiu Dennis (Ophthalmology & Visual Sciences) ● TSO Mark On Man (Ophthalmology & Visual Sciences) ● CHENG Fun Bun Augustine ● LYON Donald James
- 1 January 1997

- ❖ Health Services Research Fund, Hospital Authority

Ulcerative keratitis is a potentially blinding condition and contact lens (CL) wear is a major predisposing factor. Infection is the major cause and a wide range of organisms may be implicated. There is no information on the incidence and types of ulcerative keratitis and risk factors in CL related infection in Asia, although the number of CL wearers is increasing rapidly, especially among the young. The researchers propose to carry out a prospective cohort study in Kowloon and New Territories East Region by examining all cases of ulcerative keratitis clinically and microbiologically and using questionnaires to determine patient demographic and exposure features over a period of 18 months. For CL patients, controls will be matched from healthy CL users randomly selected from optometrists' lists, so that risk factors for CL related infection may be determined. The results should enable them to modify their clinical practice and institute appropriate and timely therapies, achieving financial savings and a better visual outcome for patients with ulcerative keratitis. The researchers will also be able to make relevant recommendations for the dispensing and care of contact lenses and their storage cases to prevent CL-related keratitis in Hong Kong. (MD96015)

A Comparison of *Acinetobacter spp* Distribution in Humans and in Raw Vegetables in Hong Kong and London

- ✉ HOUANG Ting Sou Elizabeth ● PITT Tyrone Leslie*
- 1 March 1997
- ❖ UK/Hong Kong Joint Research Scheme, the British Council

Acinetobacter spp are now responsible for an increasing number of infections world-wide. Hong Kong appears to have a higher prevalence of these infections. Using new molecular techniques, the researchers intend to carry out a cross-sectional comparative study on the skin carriage and skin fatty acid tolerance of different genospecies of acinetobacters in Caucasian university students in London and Chinese students in The Chinese University of Hong Kong, once in summer and once in winter. Genospecies distribution of *Acinetobacter* in raw vegetables will also be examined. The lectures and workshop given by United Kingdom partners will ensure the rapid transfer of technology which can be sustained. The data obtained from Hong Kong will contribute towards research activities of the United Kingdom centre. The manpower and consumables will be fully funded locally. The findings will be published in peer-

reviewed international journals and likely to generate future collaborative projects. (MD96019)

Molecular and Seroepidemiology of Acute Hepatitis E Infection in Hong Kong

- ✉ IP Margaret ● TAM Siu Lun John ● CHAN Tak Shing (Accident and Emergency Academic Unit) ● CHENG Fun Bun Augustine
- 1 January 1997
- ❖ CUHK Research Committee Funding

Acute viral hepatitis remains highly prevalent in Hong Kong and China and is a common clinical presentation to the Accident & Emergency Department. These patients are routinely screened for markers of acute hepatitis A and B infection. Preliminary data from Prince of Wales Hospital, Shatin revealed that >25% of these patients were positive to IgM for hepatitis E virus (HEV) [1]. A study from Taiwan showed that >20% of the non-A, non-B, non-C acute hepatitis were due to hepatitis E virus [2]. Hence, with the large numbers of cases involved, HEV may be an important cause of morbidity and even mortality.

The objectives of this study are to establish the incidence of acute HEV infection in patients presented to the Accident and Emergency with acute viral hepatitis and to identify the characteristics, seasonality and other clinical parameters associated with HEV infection. In addition, the significance of HEV in the exacerbation of hepatitis in chronic carriers of hepatitis B or/and C infections will be investigated.

>300 sera will be collected from patients with a clinical picture of acute viral hepatitis over a period of one year. Diagnosis of acute HEV infection will be made by a combination of IgM antibody detection using commercial enzyme immunoassays (EIA) and by RT-PCR of the HEV RNA from the patients' sera. Primer sets for the conserved non-structural region of the viral genome will be used. Factors related to the transmission of the disease will also be determined. The analysis of these data will facilitate further understanding of the epidemiology of HEV in Hong Kong. (MD96063)

Detection of Virulence Genes in *Salmonella typhimurium* by an Amplification Technique

- ✉ LING Mei Lun Julia
- 1 November 1996
- ❖ CUHK Research Committee Funding

Salmonellosis remains an important public health problem in Hong Kong. It commonly affects children especially those younger than two years,

resulting in gastroenteritis often requiring hospitalization and serious complications such as septicaemia or meningitis may also occur. *Salmonella typhimurium* was the most prevalent *Salmonella* serotype isolated in Hong Kong until 1995 when it became second to *S. enteritidis* in prevalence. The ability of *S. typhimurium* in causing disease has been attributed to its ability to adhere and invade intestinal mucosal cells. Such ability is the result of expression of virulence genes present on plasmids and chromosome of the organism. Previously, the presence of virulence genes was detected by animal studies, rabbit ileal-loop test or cell cultures. However, such experiments were time consuming and specialized techniques were involved. This study aims to utilize a rapid molecular technique, namely, amplification of a specific sequence of the virulence gene to detect its presence in *S. typhimurium*. The detection of such gene would help to explain why *S. typhimurium* was the most prevalent *Salmonella* serotype causing infection in Hong Kong. The technique can also be developed for the study of the epidemiology of *Salmonella*.
(MD96064)

Extended-spectrum β -lactamases in Clinical Resistance in Hong Kong

- ✉ LING Mei Lun Julia ● LIVERMORE D M*
 ☐ 1 November 1996
 ❖ CUHK Mainline Research Scheme

β -Lactamases are the most important cause of resistance to β -lactam antibiotics, which are the antimicrobials most often used in clinical practice. Plasmids encoding 'TEM-1' and 'SHV-1' β -lactamases spread amongst gram-negative bacteria from the 1960s onwards, and have hugely compromised previously-effective penicillins, such as ampicillin and ticarcillin. Cephalosporins stable to these enzymes were developed during the 1980s, and represented a major breakthrough, but have since succumbed to attack by new β -lactamase types, resulting in renewed therapeutic problems. 'Extended-spectrum' TEM-or SHV-enzymes are amongst the potent new β -lactamases responsible for resistance to ' β -lactamase-stable' cephalosporins. They are mutants of the classical TEM-1 and SHV-1 enzymes and are increasingly prevalent in the US and Europe. Data on potent β -lactamases types from Hong Kong and other SE Asia centres are scanty. Nevertheless the prevalence of enterobacteria resistant to the broad-spectrum cephalosporins at Prince of Wales Hospital, Hong Kong, rose from 0% in 1987 to about 13% in 1995, suggesting that such enzymes are present. Treatment is more difficult and expensive in consequence. Accordingly, the proposed project aims to identify the β -lactamases responsible for cephalosporin resistance amongst

isolates from Prince of Wales Hospital and, in particular, to identify whether novel types are involved. Besides from its fundamental academic interest, such data has great potential to assist in the design of rational local antibiotic-usage policies.
(MD96125)

A Multicentre Study to Determine the Efficacy of High-Dose Interferon Alpha-2b in the Treatment of Chronic Hepatitis B Virus Infection in Asia

- ✉ TAM Siu Lun John ● CHENG Fun Bun Augustine ● LEUNG Nancy*
 ☐ 1 October 1996
 ❖ Schering-Plough

Hepatitis B virus (HBV) infection remains a major community health problem estimated to last at least another three decades. This is particularly true in developing nations where the peak incidence is found during the early adult years and the young, i.e. the present and near-future labor force crucial to the development of these countries.

The main objective of the study is to re-examine the efficacy of interferon in the treatment of chronic hepatitis B virus (HBV) infection. Institutions from 4 different countries in Asia are involved. The study was designed as a double-blind, randomized and multicentre trial in 250 adult patients with chronic HBV infection. Only patients with active disease (presence of HBeAg; elevated HBV DNA level and liver enzyme activity) will be included. All patients will be followed up for 12 months after the treatment period (either 16 or 24 weeks) for HBeAg, HBV DNA and ALT. Treatment is considered successful if the patient seroconverted from HBeAg positive to anti-HBe positive and the disappearance of HBV DNA or the disappearance of HBsAg.
(MD96180)

Molecular Epidemiology and Genomic Diversity of Small Round Structured viruses (SRSVs) Associated with Acute Infectious Gastroenteritis

- ✉ TAM Siu Lun John ● CHAN Kay Sheung Paul ● CHENG Fun Bun Augustine
 ☐ 1 January 1997
 ❖ CUHK Research Committee Funding

The purpose of the project is to investigate the importance of small round structured viruses (SRSVs) in gastroenteritis in Hong Kong by developing a reverse transcriptase-polymerase chain reactions (RT-PCR) for the amplification of different regions of the viral genome and to study the sequence variability of the targeted regions of the viral genome. SRSVs are important aetiological agents for sporadic cases and outbreaks of viral gastroenteritis. Epidemiological studies of this virus is hampered by the difficulties

associated with the detection of the virus. The SRSVs are RNA viruses belonging to the *Caliciviridae* with extensive serological and genomic variability. The researchers intended to study the molecular epidemiology of SRSVs isolated in Hong Kong and to examine its relative importance in diarrhoeal diseases. RT-PCR procedures will be developed and detailed genomic analysis based on the PCR products of the polymerase gene will be carried out.
(MD96065)

Please refer to previous issues of *Research Projects Summary* 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*
1995-96	<i>In Vitro</i> and <i>In Vivo</i> Post-antibiotic Effects of Anti-tuberculous Drugs Alone and in Combination Against Mycobacterium Tuberculosis (CU95613) ✉ CHAN Chiu Yeung Raphael
1995-96	The Development of an HPLC Procedure for the Analysis of Different Macrolide Antibiotics in Clinical Specimens (MD95127) ✉ CHENG Fun Bun Augustine
1995-96	An <i>In Vitro</i> Antimicrobial Susceptibility of Cefitibuten (MD95240) ✉ CHENG Fun Bun Augustine ● LING Kin Wah Thomas

1995-96	The <i>In Vitro</i> Antimicrobial Susceptibilities of Penicillin-resistant <i>Streptococcus pneumoniae</i> in Hong Kong (MD95247) ✉ CHENG Fun Bun Augustine ● LYON Donald James ● LING Kin Wah Thomas ● SCHEEL Olaf ● FUNG Kitty S. C.*
1995-96	<i>In Vitro</i> Antimicrobial Susceptibility and Post-antibiotic Effects (PAE) of RP59500 (MD95248) ✉ CHENG Fun Bun Augustine ● LING Kin Wah Thomas ● FUNG Kitty S. C.*
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
1995-96	The Resistance and Plasmid Profiles of <i>Shigella</i> Isolates During the Period 1987 to 1995 in Hong Kong (BL95042) ✉ HOUANG Ting Sou Elizabeth
1995-96	Molecular Genotyping of <i>Salmonella</i> Typhimurium and S Derby in Hong Kong (CU95605) ✉ LING Mei Lun Julia
1995-96	A Study of The Epidemiology of <i>Enterobacter</i> Infection in Hospital and Characterisation of Extended-Spectrum β -Lactamases (MD95099) ✉ LYON Donald James ● CHENG Fun Bun Augustine ● NORRBY Sven Ragnar

RESEARCH OUTPUTS AND PUBLICATIONS

- <P961986> **Tain, L.P.; E.A.S. Nelson; A.C. Senok; L.M. Yu; S.J. Oppenheimer and K. Li.** "Red Cell Age and Susceptibility to Malaria During Pregnancy". *Abstracts of the 7th International Congress for Infectious Diseases* p.189. Hong Kong: International Society for Infectious Diseases, 1996.06.01.
- <P962271> **Tam, John S.; N. Leung; G. Lau; L.Y. Lam; I.O.L. Shum and A.F.B. Cheng.** "Hepatitis B Virus DNA in Peripheral Blood Leukocytes of Patients with HBV-Associated Liver Diseases". Paper presented in the 64th Conjoint Meeting on Infectious Diseases. Canada, 1996.11.

- <P962272> **Ling, T.K.W.; Tsui C.P.; Sung J.J.Y.; Li E.K.M.; Ng E.K.W.; Chung S.S.C.; Woo J. and Cheng A.F.B.** "Comparison of Commercially Available Enzyme Immunoassay Tests for the Detection of Serum IgG Antibodies to *Helicobacter pylori*". Paper presented in the International Workshop on *Helicobacter pylori*. Hong Kong, 1996.12.
- <P962274> **Chan, T.H.; K.C. Ng; A. Ho; O. Scheel; C.K.W. Lai and R. Leung.** "Urinary Tract Infection Caused by *Mycobacterium Terrae* Complex". *Tubercle and Lung Disease* vol.77, pp.555-557. UK, 1996.
- <P962591> **Adeyemi-Doro, F.A.B.; Lyon, D.J.; Ling, T.K.W. and Cheng, A.F.B.** "Comparison of E-Test and Agar Dilution Methods for Antimicrobial Susceptibility Testing of *Neisseria gonorrhoeae*". Paper presented in the 5th Western Pacific Congress of Chemotherapy and Infectious Diseases, organized by the Society of Infectious Disease. Singapore, 1996.12.01.
- <P962604> **Scheel, O.; Lyon D.J.; Ling T.K.W.; Fung K.S.C.; Yung R.W.H.; Cheng A.F.B. and Henrichsen J.** "Antimicrobial Susceptibility and Capsular Types of *Streptococcus pneumoniae* in Hong Kong". Paper presented in the 5th Western Pacific Congress of Chemotherapy and Infectious Diseases, organized by the Society of Infectious Disease. Singapore, 1996.12.01.
- <P962656> **Ling, Thomas K.W.; Augustine F.B. Cheng; Joseph J.Y. Sung; Phyllis Y.L. Yiu and Sydney S.C. Chung.** "An Increase in *Helicobacter pylori* Strains Resistant to Metronidazole: A Five-Year Study". *Helicobacter* vol.1 no.1, pp.57-61. USA, 1996.
- <P962702> **Tam, John S.; G.N. Thomas; R.C.K. Chan and A.F.B. Cheng.** "Molecular Epidemiology of Rotavirus VP7 Genotypes in Hong Kong from 1985 to 1994". Paper presented in the 64th Conjoint Meeting on Infectious Diseases. Canada, 1996.11.
- <P962714> **Chan, C.H.S.; J. Woo; C.B. Hazlett; S.C. Ho; R. Chan and A. Cheng.** "Tuberculosis in Resident Homes for the Elderly in Hong Kong". *Hong Kong Journal of Gerontology* vol.10 Supplement, p.111. Hong Kong, 1996.11.
- <P963036> **Ling, J.M.; N.W.S. Lo; Y.M. Ho; K.M. Kam; C.H. Ma; S.C. Wong and A.F. Cheng.** "Emerging Resistance in *Salmonella Enterica* Serotype Typhi in Hong Kong". *International Journal of Antimicrobial Agents* vol.7, pp.161-166. The Netherlands, 1996.
- <P963037> **Lyon, Donald J.; Olaf Scheel; Kitty S.C. Fung; Augustine F.B. Cheng and Jorgen Henrichsen.** "Rapid Emergence of Penicillin-Resistant Pneumococci in Hong Kong". *Scandinavian Journal of Infectious Disease* vol.28, pp.375-376. Sweden, 1996.
- <P963038> **Ng, Tony K.C.; Julia M. Ling; Augustine F.B. Cheng and S. Ragnar Norrby.** "A Retrospective Study of Clinical Characteristics of *Acinetobacter* Bacteremia". *Scandinavian Journal of Infectious Disease* vol.101, pp.26-32. Sweden, 1996.
- <P963039> **Ling, Julia M.; Tony K.C. Ng; Augustine F. Cheng and S. Ragnar Norrby.** "Susceptibilities to 23 Antimicrobial Agents and α -Lactamase Production of Blood Culture Isolates of *Acinetobacter* Sp in Hong Kong". *Scandinavian Journal of Infectious Disease* vol.101, pp.21-25. Sweden, 1996.
- <P963041> **Lyon, Donald J.; Olaf Scheel; Folorunso A.B. Adeyemi-Doro; Thomas K.W. Ling; Augustine F.B. Cheng and S. Ragnar Norrby.** "Antimicrobial Susceptibility and Extended-Spectrum α -Lactamases of Hong Kong Isolates of Enterobacteriaceae". *Scandinavian Journal of Infectious Disease* vol.101, pp.17-20. Sweden, 1996.
- <P970638> **Ling, T.K.W.; E.Y.M. Liu and A.F.B. Cheng.** "Comparative *in vitro* Activities of Ceftibuten and Other β -Lactam Antibiotics Against Hospital Pathogens". Paper presented in the 8th European Congress of Clinical Microbiology and Infectious Diseases. Switzerland, 1997.05.25.
- <P970639> **Ling, J.M.; I.C. Koo and A.F. Cheng.** "Epidemiological Investigation of *Salmonella Enterica* Ser. Enteritidis in Hong Kong by Molecular Methods". Paper presented in the 8th European Congress of Clinical Microbiology and Infectious Diseases. Switzerland, 1997.05.25.

- <P970640> **Chu, Y.W.; E. Houang; J.M. Ling; D.J. Lyon; T.K. Ng and A.F.B. Cheng.** "Antimicrobial Resistance of Shigella Flexneri and Shigella Sonnei in Hong Kong 1986-1995". Paper presented in the 8th European Congress of Clinical Microbiology and Infectious Diseases. Switzerland, 1997.05.25.
- <P970886> **Ho, Y.I.I.; C.Y. Chan and A.F.B. Cheng.** "In-vitro Activities of Aminoglycoside-Aminocyclitols Against Mycobacteria". *Journal of Antimicrobial Chemotherapy* vol.40, pp.27-32. UK, 1997.
- <P970918> **Houang, E.T.S.; K.C. Chu; A.P. Koehler and A.F.B. Cheng.** "Use of Chromagar Candida for Genital Specimens in the Diagnostic Laboratory". *Journal of Clinical Pathology* vol.50, pp.563-565. UK, 1997.
- <P971132> **Thomas, G. Neil; Olaf Scheel; Ann P. Koehler; David C.J. Bassett and Augustine F.B. Cheng.** "Respiratory Chlamydial Infections in a Hong Kong Teaching Hospital and Association with Coronary Heart Disease". *Scandinavian Journal of Infectious Disease* vol.104 Supplement, pp.30-33. Sweden, 1997.
- <P971215> **Nuttall, Nichalas; Donald J. Lyon; Joan L. Faoagali; Narelle M. George and Augustine F.B. Cheng.** "Penicillin Resistant *Streptococcus Pneumoniae*: A 1996 Comparison of Two Western Pacific Hospitals". Paper presented in the 20th International Congress of Chemotherapy. Australia, 1997.06.29.

see also <P962077>, <P962273>, <P962430>, <P962503>, <P962735>, <P962752>, <P963040>, <P963359>, <P970139>, <P970637>, <P970771>, <P970804>, <P970939>

RESEARCH PROJECTS

Being a Mature Age Nursing Student on Campus

✍ CHAN Wai Chi Sally ● YUEN Felix*

☐ 1 April 1996

❖ CUHK Research Committee Funding

Over the past decade, there has been an increasing number of research studies addressing student stress in tertiary education. The increasing interest in the distinct educational problems of students reflects the rise of the students' movement and with it, the empowerment of students to control their educational process and personal welfare.

The aims of the study were to examine the psychosocial needs of mature age nursing students and to identify the concerns of the students in relation to the learning environment. Data were collected by questionnaire and focused-group interview. All mature age nursing students who were studying a part-time bachelor degree programme in a university in Hong Kong were invited to participate in this study. Preliminary results indicated that majority of the respondents felt inadequate in their study skills and they found it hard to meet the multiple demands in their life. This study is significant in providing an opportunity to examine the problems and needs of mature age students in higher education setting, and to communicate these perceptions to the policy makers and organisations who organise, fund and provide the educational services.

(ED96061)

A Pilot Study on the Use of Critical Pathway in Caring for Clients in the Community Psychiatric Nursing Service in Hong Kong

✍ CHAN Wai Chi Sally

☐ 1 October 1996

❖ CUHK Departmental Funding

Critical pathway is a tool to manage care. It is a standardized plan of care that developed with focus on target symptoms and critical interventions determined to be necessary for a specific diagnosis. It defines multidisciplinary staff members' responsibilities, time lines, patient outcomes and serves as guideposts to map usual interventions and outcomes. The purpose of this study is to develop a critical pathway for the care of schizophrenic clients and evaluate its use in community psychiatric nursing services. The process of developing a critical pathway will be described. The impact of the use of critical pathway on clients' clinical status and satisfaction will be measured. Nurses' attitude on the use of critical pathway will also be examined. It is expected that through the use of the pathway,

consensus on schizophrenic client care can be achieved among the health care team members, improvement can be made on the outcome of client care.

(MD96144)

How Chinese Elders Adjust to Residential Home Life

✍ LEE Tze Fan Diana

☐ 1 December 1996

❖ CUHK Departmental Funding

Although the population of elderly people moving into residential care facilities is on the rise in Hong Kong, little is understood about how Chinese elderly people adjust to residential home life and how this process can be facilitated. The aim of this study is to identify how Chinese elders adjust to living in residential homes. Twenty elders newly admitted to a residential home will be invited to participate in this study. To identify the adjustment experiences of these elders, audio-taped informal interviews will be conducted at the time of admission and then every monthly until saturation of data. Non-participant observation will also be carried out to explore the adjustment behaviour of these elders. The elders' medical and nursing records will be reviewed to obtain comprehensive data about the elderly's adjustment process. Findings of this study will contribute to development of nursing interventions to facilitate the new residents' adjustment to residential home life.

(MD96179)

Hospital Readmission Among Elderly Patients: A Preliminary Study

✍ LEE Tze Fan Diana ● MacKENZIE Ann ● LEE Fung Kam ● CHAN YIP Carmen Wing Han

☐ 1 March 1997

❖ CUHK Departmental Funding

Repetitive hospitalizations are a major problem for elderly people especially those with chronic diseases. Yet there is a lack of available data about the risk factors associated with readmission. The aim of this preliminary study is to identify factors contributing to early readmission among elderly people in 2 geriatric units in Hong Kong. All patients who are readmitted within 28 days after previous discharge and able to communicate are invited to participate in this study. Data will be collected for a period of 12 weeks by a researcher-developed checklist drawn from the literature and experience of specialist gerontological nurses. Previous admission information from the patients' medical and nursing notes will also be noted using the checklist. Frequency and ranking of reasons for admission will be calculated and correlated with

demographic and biographical data to identify risk factors contributing to early readmission among elderly people.
(MD96178)

Facilitating and Making Informed Choices During Pregnancy: A Study of Midwives and Pregnant Women

- ✍ LEVY Valerie
☐ 1 September 1993
❖ Smith, Nephew Foundation, London

Over the past several years various authors and Government reports have urged that women be enabled to make informed choices regarding their care during pregnancy and childbirth. The facilitation and making of these choices involves complex processes, however, which apparently have not yet been studied in depth; this is the purpose of this study. A grounded theory approach to data collection and analysis has been used within an interpretive framework, influenced by symbolic interaction, to develop middle range, substantive theory. Midwives and pregnant women were accessed from four maternity units. Data were collected by means of focused interviews and observation. Convenience sampling was supplemented later in the study by theoretical sampling. Data were analysed and theoretical frameworks constructed according to grounded theory method. Core and substantive categories were identified which accounted for the processes involved when facilitating and making informed choices. Two main over-arching issues, power and trust, were apparent. Issues of power related to the study are considered mainly in terms of Foucault's and Lukes' interpretations of power. Trust is discussed in relation to existing theories and their application to this study. Recommendations for midwifery practice are made, together with hypotheses for further exploration.
(MD93160)

Assessing the Needs of Family Carers Who Are Looking After Stroke Patients: The Practices of Community Nurses in Hong Kong

- ✍ MacKENZIE Ann ● HOLROYD Eleanor
☐ 1 December 1995
❖ CUHK Departmental Funding

The aims of the research were to identify the current practice of community nurses in Hong Kong in assessing stroke patients and their families and to pilot an assessment scale for inclusion in the routine assessment of Chinese carers & families. Interviews, examination of nursing records and observations of nurses determined the assessment strategies used by

nurses. Comparison of a carers' assessment scale found differences between nurses perceived needs of carers and carers' own needs.
(MD95261)

Hong Kong High School Students' Attitudes Towards Nursing Profession

- ✍ ROSSITER Joh Chin ● FOONG Lai Sun ● CHAN Po Tai
☐ 16 January 1997
❖ CUHK Departmental Funding

With the new development of hospital services over the last decade, the demand for nurses and nursing services has increased. Despite the improvements in education and remuneration implemented by the Hong Kong Government, the problems of shortage and wastage in the nursing profession remains critical. In general, literature suggests that the public image of nursing tends to be negative. This study aimed to examine the high school students' attitudes towards the nursing profession within the context of Hong Kong, and to determine its contributing factors affecting shortage and wastage of nurses in Hong Kong.

A convenience sample of 375 high school students was recruited from the area of Hong Kong island, Kowloon and the New Territories. Data were collected by a questionnaire to measure their knowledge about, attitudes towards nursing and intention to select nursing as their future career; and their demographic details. Descriptive and inferential statistics were used to describe their career preference and to compare knowledge, attitudes and intention scales between gender and nursing exposure groups. Results indicate that the students were generally knowledgeable about nursing but were reluctant to pursue nursing as a career. However, students who were socially acquainted with a nurse demonstrated a slightly more positive attitude towards nursing and slightly higher intention to pursue nursing as a career compared with those having no social acquaintance with a nurse. Implications for promotion of nursing profession and limitation of study were discussed. Recommendations were suggested for future research.
(MD96172)

An Evaluation of Nursing to Patient Care in a Multidisciplinary Community Based Rehabilitation Service

- ✍ TWINN Sheila Frances ● HOLROYD Eleanor ● SHIU Tak Ying ● LAM Ann*
☐ 15 January 1997
❖ CUHK Departmental Funding

The importance of high quality community care in determining the quality of life of people with chronic health problems and their families is well demonstrated in research. The lack of formal care available to the community in Hong Kong has been identified. In response to this need the Community Rehabilitation Network (CRN) was established (funded by the Hong Kong Jockey Club). The CRN provides health promotion, the fostering of self help and a networking of client care using a multidisciplinary approach including registered nurses. The aim of this study was to identify the nursing interventions provided in the CRN and to evaluate the contribution of nursing interventions to patients with cardiac disease. To meet these aims a multiple case study design was used employing both qualitative and qualitative methods of data collection. The sample for the study involved a total population of nurses in one CRN centre (2) and a total population of cardiac patients (95) meeting the selection criteria. Quantitative methods involved structured interviews with patients to assess levels of satisfaction with care, quality of life and demographic and health data. Non-participant observations of nursing activities were undertaken. Qualitative methods involved the nurses keeping journals and a semi-structured interview with the nurses and a purposive sample of patients and carers. The analysis of these data demonstrates high levels of satisfaction with nursing care, particularly patient education and support. The interpersonal skills and caring attitudes of the nurse were valued by both patients and carers. Although attending the CRN was attributed to improved quality of life, patients found it more difficult to distinguish the contribution of nursing from other members of the multidisciplinary team. (MD96181)

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

- ✉ TWINN Sheila Frances ● MAK Mui Hing June
- ☐ 1 June 1997
- ❖ Health Care & Promotion Fund, Hospital Authority

The aim of this two year project is to develop a community outreach programme to increase women's knowledge about the prevention of cervical cancer and the uptake of Pap smear screening employing multiple preventive strategies. These strategies involve a survey of women's knowledge and information needs, the development of public education programmes using both formal and informal methods of health education and direct mailing to women living in the targeted location. Evaluation of the programme is integral to the project and involves both impact and process strategies.

Impact strategies will involve the analysis of service providers records and pre and post intervention structured telephone interviews. Focus group interviews and the use of journaling to record nursing activities and experiences will be used for process evaluation. Data analysis will be undertaken using parametric statistical analysis and content analysis. It is anticipated that the project will make a major contribution to current health promotion programmes targeting women's health. (MD96026)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
1994-95	Exploring Perception of Health Care and Service Provision for Hong Kong's Elderly: Implication for Families and Community Nurses (MD94170) ✉ HOLROYD Eleanor
1995-96	Exploring Perceptions of Health Care and Service Provision for Hong Kong's Elderly, Implications for Families and Community Nurses (MD95115) ✉ HOLROYD Eleanor
1995-96	A Pilot Project to Explore Chinese Elders' Adjustment to Residential Homes (MD95238) ✉ LEE Tze Fan Diana
1995-96	The Effectiveness of Nursing Care: Use of a protocol to Promote Stroke Rehabilitation (MD95032) ✉ MacKENZIE Ann ● CHANG Anne Marie
1995-96	Quality Assurance in Public Health Nursing: The Development of a Core Set of Standards for Practice (MD95209) ✉ TWINN Sheila Frances ● WU Catherine*
1995-96	The Efficacy of Screening Programmes for Cervical Cancer Amongst Hong Kong Chinese Women: A Case Study of the Contribution of the Nurse Practitioner (MD95062) ✉ TWINN Sheila Frances ● CHENG Fung Khing (Community & Family Medicine)
1995-96	The Ethical Dilemmas of Acute Care Nursing Practice in Hong Kong (MD95222) ✉ YUNG Ha Ping Hilary

RESEARCH OUTPUTS AND PUBLICATIONS

- <P953425> **Mak, Mui Hing June.** "Book Review: *Health Assessment in Nursing*". *Asian Journal of Nursing Studies* vol.2 no.4, p.68. Hong Kong, 1995.
- <P953480> **Au, V.M.K.; G.C.L. Chui; C.H. Lee; Y.M. Leung and E. Holroyd.** "Exploring Nutritional Knowledge Levels in Paediatric and Obstetric Nurses in Hong Kong". *Hong Kong Journal of Paediatrics* vol.12, pp.31-39. Hong Kong, 1995.
- <P953527> **Molassiotis, Alexander; Brian J. Boughton; Tracey Burgoyne and Olga B.A. Van Den Akker.** "Comparison of the Overall Quality of Life in 50 Long-Term Survivors of Autologous and Allogeneic Bone Marrow Transplantation". *Journal of Advanced Nursing* vol.22, pp.509-516. Oxford, UK, 1995.
- <P953528> **Molassiotis, A. and O.B.A. Van Den Akker.** "Psychological Stress in Nursing and Medical Staff on Bone Marrow Transplant Units". *Bone Marrow Transplantation* vol.15, pp.449-454. Basingstoke, UK, 1995.
- <P953529> **Molassiotis, A.; O.B.A. van den Akker; D.W. Milligan and B.J. Boughton.** "Gonadal Function and Psychosexual Adjustment in Male Long-Term Survivors of Bone Marrow Transplantation". *Bone Marrow Transplantation* vol.16, pp.253-259. Basingstoke, UK, 1995.
- <P953530> **Molassiotis, Alexander.** "Use of Physical Restraints 2: Alternatives". *British Journal of Nursing* vol.4 no.4, pp.201-202. London, UK, 1995.
- <P953531> **Molassiotis, Alexander.** "Use of Physical Restraints 1: Consequences". *British Journal of Nursing* vol.4 no.3, pp.155-157. London, UK, 1995.
- <P953534> **Molassiotis, A.** "Data Reduction as a Method of Identifying Psychosocial Transitions". Paper presented in the International Nursing Congress, organized by International Council of Nursing. Athene, Greece, 1995.06.
- <P953535> **Molassiotis, A.** "Evaluation of Burnout and Job Satisfaction in Marrow Transplant Nurses". Paper presented in the 5th International Bone Marrow Transplant Nursing Symposium, organized by the FRED Hutchinson Cancer Research Center. Seattle, USA, 1995.10.
- <P953536> **Molassiotis, A.** "Assessment of Mood Changes, Symptom Distress and Coping Mechanisms During Isolation for Bone". Paper presented in the 21st Annual Meeting of the European Blood and Marrow Transplant Group. Davos, Switzerland, 1995.03.
- <P953551> **Callaghan, Patrick; S.S. Cheung; S.Y. Lau; W.C. Lo and L.K. Tsui.** "Attitude Towards Mental Illness: Does a Psychiatric Secondment Make a Difference to General Student Nurses in Hong Kong?". *Hong Kong Nursing Journal* Issue no.71, pp.12-16. Hong Kong, 1995.
- <P953600> **Wong, Frances; Sally Chan; Alice Loke and Aggie Tiwari.** "An Action Research Study into the Development of Teacher-Student Partnership in Educating Experienced Nurses". *Proceedings of the New Zealand Nurse Educators Conference* p.11. Hamilton, New Zealand: Department of Nursing and Health Studies, Waikato Polytechnic, 1995.10.17.
- <P953606> **Hui, Flora; Sally Chan; Miranda Wong Cheng; Lau King-Kwan; Jacqueline Leung and Teresa Lee.** "Stress Perceived by Psychiatric Student Nurses". *The Hong Kong Nursing Journal* vol.71, pp.3-11. Hong Kong, 1995.
- <P961548> **Gibb, Heather and Eleanor Holroyd.** "Images of Old Age in the Hong Kong Print Media". *Aging and Society* vol.16, pp.151-175. UK, 1996.

- <P962033> **Simsen, Barbara J.; Holroyd E. and Sellick K.** "Postgraduate Education Expectations: A Survey of Hong Kong Graduate Nurses". *Journal of Advanced Nursing* vol.24, pp.827-835. UK, 1996.
- <P962157> **Lau, Victor Ming Ho and Ann Mackenzie.** "Attributes of Nurses that Determine the Quality of Care for Mentally Handicapped People in an Institution". *Journal of Advanced Nursing* vol.24, pp.1109-1115. UK, 1996.
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- <P962448> **Jo, Alexander; Valerie Levy and Sarah Roch. ed.** *Midwifery Practice: Core Topics 1.* 164 pgs. Basingstoke, England: Macmillan Education, 1996.
- <P962504> **Chan, Carmen Wing Han.** *Perceived Stress and Its Impact Among Family Caregivers of Terminal Cancer Patients.* (A Thesis submitted to the Department of Nursing, The Chinese University of Hong Kong, in partial fulfilment of the requirements for the Degree of Master of Philosophy in Nursing) 121 pgs. Hong Kong, 1996.12.
- <P962743> **Ip, Wan-Yim; Janita Chau; Mei-Ching Leung; Yau-Sheung Leung; Yui-Man Foo and Anne M. Chang.** "Relationship Between Self Concept and Perception of Self Care Ability of Elderly in a Hong Kong Hostel". *The Hong Kong Nursing Journal* vol.72, pp.6-12. Hong Kong, 1996.
- <P962896> **Molassiotis, A.; O.B.A. van den Akker; D.W. Milligan; J.M. Goldman; B.J. Boughton; J.A. Holmes and S. Thomas.** "Quality of Life in Long-Term Survivors of Marrow Transplantation: Comparison with a Matched Group Receiving Maintenance Chemotherapy". *Bone Marrow Transplantation* vol.17, pp.249-258. Basingstoke, UK, 1996.
- <P962897> **Molassiotis, Alexander and Robert Newell.** "Nurses' Awareness of Restraint Use with Elderly People in Greece and the UK: A Cross-Cultural Pilot Study". *International Journal of Nursing Studies* vol.33 no.2, pp.201-211. UK, 1996.
- <P962898> **Molassiotis, A.; O.B.A. Van Den Akker; D.W. Milligan; J.M. Goldman and B.J. Boughton.** "Psychological Adaptation and Symptom Distress in Bone Marrow Transplant Recipients". *Psycho-Oncology* vol.5, pp.9-22. Chichester, UK, 1996.
- <P962899> **Molassiotis, Alexander.** "Late Psychosocial Effects of Conditioning for BMT". *British Journal of Nursing* vol.5 no.21, pp.1296-1302. London, UK, 1996.
- <P962900> **Molassiotis, Alexander and Mel Haberman.** "Evaluation of Burnout and Job Satisfaction in Marrow Transplant Nurses". *Cancer Nursing* vol.19, pp.360-362. USA, 1996.
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see also <P971653>

RESEARCH PROJECTS

Methylation of p16^{INK4} Promoter in Gynaecologic Tumours

- ✉ CHANG Mang Z. Allan ● WONG Yick Fu
- 1 November 1996
- ❖ CUHK Mainline Research Scheme

The p16^{INK4}, a gene located at chromosome 9p21, has been featured as a candidate tumour suppressor gene. It is frequently inactivated in many human tumours through homozygous deletion. It is recently shown that *de novo* hypermethylation of gene promoter regions called CpG island may be as an alternate mechanism of the gene inactivation. The researchers previously found a low rate of homozygous deletion and no mutation of p16^{INK4} in cervical, endometrial and ovarian cancers. In order to further understand the role of p16^{INK4} in the tumorigenesis of these gynaecologic malignancies the researchers will develop a simple PCR-based assay to investigate the methylation of p16^{INK4} promoter. The methylation detected in these cancers will be correlated with their clinico-pathologic features. If the methylation status of p16^{INK4} promoter contributes to the development and/or progression of a subgroup of gynaecologic tumours, it would also open new strategies for diagnosis, predicting the prognosis and treatment of these tumours. This study will be a collaborative project with the Prof. T Nobori's team that pioneered the p16^{INK4} gene at the University of California San Diego, USA.
(MD96126)

Prevalence and the Significance of DNA Replication Errors in Endometrial Cancer with a Geographic and Racial Comparison

- ✉ CHUNG Kwok Hung Tony ● WONG Yick Fu
- 1 October 1996
- ❖ CUHK Research Committee Funding

The recognition of defects in DNA repair pathways as a route for human carcinogenesis and the use of the replication error (RER) assay to recognise tumours with such defects are new advances in cancer research. One of the most exciting findings in cancer research is that instability of DNA sequences is a pathophysiologic lesion predisposing the emergence of wide variety of inherited and sporadic cancers. This phenotype has been referred as either "microsatellite instability" or the RER phenotype. Endometrial cancer is a common gynaecologic cancer. However, little is known about the molecular pathogenesis of endometrial cancer. This study will establish a genomic strategy to screen for RER and investigate the roles of 4 mismatch DNA repair genes

in tumorigenesis of endometrial carcinoma. If the RER does contribute to the development and/progression of a large subgroup of sporadic and familial endometrial cancers, it will advance the application of this new knowledge to better identify persons at risk for cancer, and to open new strategies for treating this cancer. The study will be a part of collaborative project involved in four centres in USA and the researchers under the direction of Prof. Frederick Li, Harvard University. Prof. Li is describer on Li-Fraumeni syndrome.
(MD96066)

Postnatal Depression in Hong Kong Chinese

- ✉ CHUNG Kwok Hung Tony ● LEE Tak Shing Dominic (Psychiatry) ● LEUNG Yip Shing (Psychiatry) ● NG Kee On* ● WONG Chung Kwong (Psychiatry)
- 1 November 1996
- ❖ Health Services Research Fund, Hospital Authority

Postnatal depression affects 10-20% of all parturients according to International studies. Significant psychological, social and medical morbidity and even mortality (from suicide and infanticide) have been documented. However, this area has been largely ignored in Hong Kong, so much so that there is no reliable data on which planning for health care needs for these women can be based. This is surprising given the potential of this condition to affect so many in this community. The researchers propose to determine the incidence, risk factors and consequences of postnatal depression in 1200 Hong Kong Chinese parturients.
(MD96014)

Measurement of Maternal Plasma Corticotrophin Releasing Hormone (CRH) in the Prediction of Abnormal Pregnancy Outcome

- ✉ LEUNG Tse Ngong ● CHUNG Kwok Hung Tony
- 1 May 1996
- ❖ CUHK Research Committee Funding

Corticotrophin releasing hormone (CRH) is a 41 amino acid peptide released from the hypothalamus in response to stress. The plasma levels of CRH are low or undetectable in normal non-pregnant women. However, CRH levels are measurable in normal pregnant women from the late second trimester, rising dramatically in the third trimester and peaking at delivery before falling rapidly after delivery. The higher CRH levels in pregnancy are placental in origin. Serial measurement of CRH in pregnancy has suggested a relationship between elevated levels and

various abnormal pregnancy outcomes, including preterm labour, pre-eclampsia and intrauterine growth retardation. Therefore, with the establishment of normal range at different gestational ages, the measurement of the hormone may be used to predict abnormal pregnancy outcomes by detecting elevated levels. Furthermore, if the assay is sensitive enough to detect abnormal levels in the mid-trimester, it is expected that this information can serve to alter the subsequent management.
(MD96067)

Pathophysiology of Ischaemic Heart Disease in Women - A Comparison between Pre & Post-Menopausal Levels of Endothelin-1 and the Influence of Phytoestrogens

✉ ROACH Vijay ● HAINES Christopher John ● WONG Yick Fu ● HJELM Nils Magnus (Chemical Pathology) ● CHEUNG T.F.* ● MA Waring*

- 1 October 1996
- ❖ CUHK Research Committee Funding

Phytoestrogens are biologically active steroids found in plant materials. Racial groups with a high dietary intake of phytoestrogens have differing disease patterns when compared to those with a low intake. Phytoestrogen levels in Chinese women are not known. Levels of several important phytoestrogens will be performed by high-performance liquid chromatographic assay of urine from menopausal women. The researchers will determine phytoestrogen levels in Chinese women and increase the understanding of their role in oestrogen-related disease. Endothelin-1 (ET-1) is a vaso-active peptide that is thought to play a significant role in the pathophysiology of ischaemic heart disease (IHD). The incidence of IHD is low in pre-menopausal women, but increases following the menopause. They will determine ET-1 levels in pre and post-menopausal women and correlate the results with plasma oestrogen and urinary phytoestrogen levels. The hypothesis is that ET-1 levels may play role in the aetiology of increased risk of IHD in post-menopausal women.
(MD96068)

Effects of MTAP Antisense Oligonucleotides on Chemosensitivity of Gynaecologic Cancer Cells *in vitro*

✉ ROGERS Michael Scott ● WONG Yick Fu

- 1 January 1997
- ❖ CUHK Research Committee Funding

The physiological role of enzyme 5'-deoxy-5' methylthioadenosine phosphorylase is to convert 5'-deoxy-5' methylthioadenosine (MTA) to salvageable

intermediates including adenine and 5'-methylthioribose 1-phosphate. Normal cells reconvert MTA to adenine nucleotides and methionine, whereas MTAP deficient tumour cells have lost these salvage pathways. Therefore, cancers with deletions of MTAP gene may be especially susceptible to chemotherapeutic regimes that interfere with purine or methionine utilisation. Recently, MTAP gene which locates at chromosome 9 short arm was cloned. In this study, observations are made to determine whether the phosphothioate antisense oligonucleotides complementary to overlapping region of MTAP start codon can easily access the gynaecologic cancer cells containing intact MTAP gene and can increase the sensitivity to anti-metabolism drug methotrexate (MTX) that interferes with purine utilisation. The information from this study can broaden our understanding of MTAP function in gynaecologic cancer and may guide us to make more suitable treatment.
(MD96069)

Intrapartum Monitoring Using the Fetal Electrocardiogram (FECG)

✉ SAHOTA Daljit ● SYMONDS Edwin Malcolm*

- 1 November 1996
- ❖ UK/Hong Kong Joint Research Scheme, the British Council

The objective of this one year collaborative venture is to produce a comprehensive reference book for medics, bio-engineers and researchers who are studying and analysing the FECG during labour.
(MD96018)

Refinement of a Region of Loss of Heterozygosity at Chromosome 1 Short Arm in Cervical Cancer

✉ WONG Yick Fu ● CHUNG Kwok Hung Tony

- 1 January 1997
- ❖ CUHK Research Committee Funding

Cervical carcinoma remains one of the leading causes of death among women. An increasing number of studies have indicated that tumorigenesis is probably related to abnormal cell growth promoted by proto-oncogenes and/or tumour suppressor genes [1,2]. Detection of loss of heterozygosity (LOH) is an essential step towards the cloning of tumour suppressor genes. The objective of this study is to further refine a region of LOH at chromosome 1 short arm in cervical cancer based on the researchers' findings from a previous study. Twelve polymorphic microsatellite repeat loci located at chromosome 1p36 and closed region will be analysed by PCR in 100 cervical squamous cell carcinomas. This analysis may provide a starting point for positional cloning of

candidate tumour suppressor gene(s) related to cervical cancer. In addition, the LOH status in these cancers will be correlated with their clinicopathologic features. If the LOH within the region detected by the microsatellite markers contributes to the development and/or progression of a subgroup of cervical cancer, it would also open new strategies for predicting the prognosis of this subgroup.

This study will be a collaborative project with Prof. G.M. Hampton' team that is well-known in research on allelic imbalance in gynaecologic cancer at the Ludwig Institute For Cancer Research, San Diego, United States.
(MD96070)

Comparison of Metabolic and Immunological Response after Abdominal and Laparoscopic Hysterectomy

✉ YUEN Pong Mo ● ROGERS Michael Scott ● SHORT Timothy Gordon (Anaesthesia & Intensive Care) ● LAM Wai Kei Christopher (Chemical Pathology)

☐ 1 December 1996

❖ CUHK Research Committee Funding

Since the first report in 1989 laparoscopic hysterectomy is rapidly gaining popularity. Its advantage over conventional laparotomy are the avoidance of large abdominal incision, reduction of post-operative pain and morbidity, shortening of hospital stay and earlier recovery. Surgical trauma is also believed to be reduced but there is no objective assessment to support this.

Acute trauma, whether surgical or accidental, result in a series of metabolic and immunological changes. Metabolic and immunological responses after laparoscopic cholecystectomy have been studied and there are some evidence to support that the laparoscopic approach is associated with a reduction in the acute phase metabolic response and immunological suppression compared with the laparotomy. There is no similar study performed on hysterectomy.

The purpose of this study is to evaluate the metabolic response and the post-operative immunological changes in laparoscopic and abdominal hysterectomy, with an aim to quantify and compare the effects of surgical trauma resulting from these two approaches.
(MD96009)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition Title/Investigators

1995-96 The Effect of the Menopause on Plasma Concentrations of Lipoprotein (a)
(MD95179)

✉ CHEUNG L. P. ● HAINES Christopher John ● LAM Wai Kei Christopher (Chemical Pathology) ● TOMLINSON Brian (Clinical Pharmacology)

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)

1995-96 The Effect of Misoprostol on Uterine Blood Flow in Pregnant and Non Pregnant Women: A Comparison (MD95193)

✉ CHUNG Kwok Hung Tony ● TSE Angel*

1995-96 An Examination of the Relationship between Lipoprotein (a) and Pregnancy Complicated by Either Hypertension or Intrauterine Growth Retardation (MD95162)

✉ HAINES Christopher John ● LEUNG Tse Ngong ● LAM Wai Kei Christopher (Chemical Pathology) ● TO Ka Fai (Anatomical & Cellular Pathology)

1995-96 A Study of the Effect of Hormonal Replacement Therapy in Postmenopausal Women on Peripheral Vascular Blood Flow (MD94161)

✉ LAU Tze Kin ● HAINES Christopher John ● SANDERSON John Elsby (Medicine)

1995-96 Detection of Alpha-Thalassaemia by Coelocentesis in Early Pregnancy: A New Approach to Prenatal Diagnosis (MD95151)

✉ LAU Tze Kin ● FUNG Yun Mei Hedy

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)

- 1994-95 Rapid Screening for the Mutations of C-myc Gene in Cervical Cancer with a Sensitive Heteroduplex Detection Technique (MD94099)
 ✎ ROGERS Michael Scott ● WONG Yick Fu ● CHEUNG Tak Hong ● CHUNG Kwok Hung Tony
- 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
- 1994-95 Randomized Comparative Study of Operative Laparoscopy Versus Laparotomy in the Management of Ectopic Pregnancy (MD94166)
- ✎ YUEN Pong Mo ● YU K. M.* ● LAU Woon Chung* ● ROGERS Michael Scott
- 1995-96 Comparison of Metabolic and Immunological Response After Abdominal and Laparoscopic Hysterectomy (MD95158)
 ✎ YUEN Pong Mo ● ROGERS Michael Scott ● MAK Wing Lai Tony* (Chemical Pathology) ● SHORT Timothy Gordon (Anaesthesia & Intensive Care) ● LAM Wai Kei Christopher (Chemical Pathology)

RESEARCH OUTPUTS AND PUBLICATIONS

- <P933133> **Lo, Wing Kit and Rogers, M.S.** "A Controlled Trial of Amnioinfusion in Labour". *Abstracts of the 2nd International Scientific Meeting of the Royal College of Obstetricians and Gynaecologists* p.150. Hong Kong, 1993.09.07.
- <P953496> 王煒、王益夫, 譯. <妊娠伴發腕管綜合徵>. 《中國實用婦科與產科雜誌》第 11 卷 第 1 期, 頁 57. 中國, 1995.
- <P953497> 王益夫, <生長調節基因在卵巢癌發病機理中的變化>. 《全國第六次婦產科學術會議論文選編》頁 A1017. 中國上海: 中華醫學會, 1995.09.25.
- <P961637> **Fung, Hedy Yun Mei; Shu Pong Wong and Michael Rogers.** "The Influence of Glucose Tolerance Tests on Subsequent Carbohydrate Metabolism in Pregnancy". *Acta Obstetrica et Gynecologica Scandinavica* vol.75, pp.347-351. Denmark, 1996.
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- <P961843> **Yuen, Pong Mo; Hilda Y.Y. Pang; T. Chung and A. Chang.** "Cervical Ripening Before Induction of Labour in Patients with an Unfavourable Cervix: A Comparative Randomized Study of the Atad Ripener Device, Prostaglandin E₂ Vaginal Pessary, and Prostaglandin E₂ Intracervical Gel". *Australian & New Zealand Journal of Obstetrics and Gynaecology* vol.36 no.3, pp.291-295. Australia, 1996.
- <P961853> **Wong, Y.F.; T.K.H. Chung; T.H. Cheung; S.K. Lam; T. Nobori and A.M.Z. Chang.** "Deletions of P16^{INK4} and P15^{INK4B} in Gynaecologic Malignancies". *Abstracts of the 3rd International Scientific Meeting of the Royal College of Obstetricians and Gynaecologists on Women in a Changing World* p.286. New Delhi, 1996.03.12.
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- <P962116> 王益夫. <滋養細胞疾病診治進展>. 《中國實用婦科與產科雜誌》第11卷第2期,頁117-118. 中國, 1996.
- <P962117> 林兆強、王益夫. <第二十七屆英國婦產科學大會紀要>. 《中國實用婦科與產科雜誌》第12卷第2期,頁121-122. 中國, 1996.
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RESEARCH PROJECTS

Mechanism of Retinal Excitotoxicity

- ✉ LAM Tim Tak
- ☐ 1 November 1996
- ❖ CUHK Research Committee Funding

Loss of inner retinal neurons is a common cause of visual impairment in a wide variety of ocular diseases such as glaucoma, diabetic retinopathy, retinal arterial and venous occlusion, hypertensive retinopathy, radiation retinopathy and others. Recently, an important role of excitotoxicity by exposure to excitatory neurotransmitters, such as glutamate, in the loss of retinal neurons is implicated in glaucoma and ischemic diseases of the retina. In addition, the researchers noted apoptotic death of retinal neurons in excitotoxicity and ischemia of the retina. Hence, understanding the mechanism of neuronal loss in excitotoxicity induced apoptosis becomes pivotal to a rational development of therapeutic strategies. The primary purpose of this proposal is to identify if interleukin 1 β converting enzyme (ICE)-like activities, nitric oxide synthase (NOS) or poly-ADP-ribose polymerase (PARP) is involved in apoptotic death of retinal neurons after exposure to the excitatory amino acid, N-methyl-D-aspartate (NMDA), to form a base for further detail study of the pathway(s) of apoptosis in retinal excitotoxicity.

Specifically, they plan to employ a pharmacological approach by examining the dose depend effects of the tetrapeptide YVAD chloromethyl ketone (YVAD.CMK), a specific inhibitor for ICE, N-nitro-arginine, an inhibitor of NOS, or 3-amino-benzamide (3-ABA), an inhibitor of PARP, on several markers of apoptosis in retinal excitotoxicity: (1) DNA fragmentation study by agarose gel electrophoresis (2) *in situ* TdT-mediated biotin-dUTP nick-end labeling (TUNEL) technique; (3) enzyme-linked immunosorption assay (ELISA) of cleaved nucleosomes; and (4) morphologic study. (MD96078)

Neuronal Rescuers for Apoptotic Degeneration of Retinal Ganglion Cells

- ✉ LAM Tim Tak ● TSO Mark On Man
- ☐ 1 January 1997
- ❖ Research Grants Council

Visual impairment in retinal ischemia, as noted in diabetic retinopathy, retinal and venous occlusion, hypertensive retinopathy, and glaucoma, is associated with the loss of retinal ganglion cells and inner neuronal elements. Currently there is no therapy for preserving these neurons. The long term objective of

this proposal is to develop strategies for rescuing the inner retinal neurons by examining the mechanism(s) of neuronal loss. Specifically the researchers propose to examine the contribution of and the pathway(s) of apoptosis, an energy dependent and highly regulated process of cell death, in inner retinal loss. They have established a rat model of inner retinal neuronal loss by transiently elevating the intraocular pressure and noted apoptotic death of inner retinal neurons. In this grant period, the researchers will examine some of the steps of the apoptotic pathways using pharmacological agents such as calcium blockers and inhibitors of interleukin-1 β -converting enzyme (ICE) as well as transglutaminase. The effects of these agents on the apoptotic death of inner retinal neurons will be examined morphologically, morphometrically and biochemically. This study will provide insight into the mechanism(s) of neuronal death of the inner retina and new therapeutic strategies for rescuing inner retinal neurons in retinal ischemic diseases and acute glaucoma. (CU96673)

Occupational Eye Injuries in Hong Kong - A Retrospective Analysis

- ✉ MICHON John
- ☐ 1 October 1996
- ❖ Occupational Safety and Health Research Grant

Eye injuries in the workplace are a common cause of occupational disability in Hong Kong. The delicacy, exposure and limited healing powers of the eye make it a prime target of injury. A wide variety of mechanical, chemical, and electromagnetic workplace hazards exist may cause visual loss or even total blindness. There is currently little information available on the incidence and severity of these injuries in Hong Kong despite the disfigurement and visual disability they cause and their impact on employers, employees, family members and society. The researchers propose to measure this problem and describe the spectrum of occupational eye injuries in Hong Kong. (MD96004)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition	Title/Investigators
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
- 1995-96 Apoptosis of Photoreceptor Cells (CU95628)
✉ TSO Mark On Man ● LAM Tim Tak

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- <P953577> **Lam, T.T.; J. Fu; S.H. Li; A.S. Abler and M.O.M. Tso.** "N-Methyl-D-Aspartate (NMDA) Induced Apoptosis in Rat Retina". *Investigative Ophthalmology & Visual Science* vol.36 no.4, p.S934. USA, 1995.03.15.
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- <P953579> **Tso, M.O.M.** "Academic Ophthalmology at a Crossroads in Hong Kong". *Hong Kong Medical Journal* vol.1 no.4, pp.299-301. Hong Kong, 1995.12.
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RESEARCH PROJECTS

Chinese Herbal Medicine in the Management of Exercise Injury Muscle Fatigue

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● BUT Paul Pui Hay (Biology) ● QIN Ling ●
LI Jing Xian
- ☐ 1 September 1996
- ❖ Postdoctoral Grant

Exercise fatigue has long been a concern in the field of sports medicine and sports science and a research area of much activities in recent years. Exercise fatigue is often closely associated with muscle fiber injury. The major symptoms include muscle soreness, loss of contractility, increase activities of plasma enzymes such as lactate dehydrogenase (LDH), and creatine kinase (CK), elevation of free radicals and lipid peroxidation (malondialdehyde : MDA), and micro-structural damage of the cell (including mitochondria swelling), damage of cell membrane system). Fatigue directly reduces and individuals. Physiological functioning at work in sports, and it may even lead to illness and injuries. Hence, it is of paramount important to study the representative index of muscle fatigue on a biochemical, histomorphological and biophysical basis. There is increasing anecdotal evidence that some Chinese herbal medicine may have positive impact on muscle fatigue (and by implication), this may have been cross validated by China's recent and rapid rise to world status in international swimming and distance running competitions). Accordingly, the researchers also propose to determine if and why some of the Chinese herbal medicine have apparent "fatigue-relief" effect in term of these noted biochemical, histomorphological, and biophysical indices. (MD96129)

The Effect of Vastus Medialis Strength and Tibial Tuberosity Position on Patellar Tracking and Patellofemoral Joint Pressure

- ✍ CHAN Kai Ming ● NG G.* ● MAK A.*
- ☐ 1 September 1996
- ❖ Hong Kong Polytechnic University Central Research Grant

Patellofemoral (P/F) joint pain is a common condition, and the incidence of this has been estimated to be as high as 25% in the general population (Levine 1979). Many patients with severe P/F joint pain may not have an identified pathology (Andrish 1985), and their symptom is often exacerbated by sporting activities, stair climbing and prolonged sitting with flexed knees (Levine 1979, Micheli and Stanitski 1981).

Various factors have been suggested to cause P/F joint pain, which include iliotibial band tightness (McNicol 1981), hamstring tightness (Winter 1983), abnormal Q-angle (Huberti & Hayes 1984), weakness of vastus medialis obliquus (VMO) (LeVeau & Rogers 1980), and over pronation of foot (Buchbinder et al 1979). Among these, VMO insufficiency may be the single most important factor that researchers and clinicians have focused (Reynolds et al 1983, Brownstein et al 1985, McConnell 1986, Hanten & Schulthies 1990, Sczepanski et al 1991, Karst & Jewett 1993). Clinically, VMO training has become a major part of the rehabilitation programme for patients with P/F joint pain.

However, most of the above studies that examined the role of VMO *in-vitro* were performed in an open kinetic chain condition (Lieb & Perry 1968, Ahmed et al 1983, Goh et al 1995), in which the femur was fixed and the tibia was free to move. Findings of these studies may not be applicable in predicting the role of VMO during normal functional closed kinetic chain action, because the normal tibiofemoral joint loading during weight bearing is not replicated in open chain actions. Also, the centre of rotation of the knee joint is different between open and closed kinetic chain movements (O'Connor et al 1990). Therefore, in order to accurately-quantify the role of VMO in a closed kinetic chain situation, the test needs to be conducted in a simulated weight bearing position. In light of this, there are three aims in the present study: (1) To assess the role of VMO in controlling patellar alignment during a simulated weight bearing testing position. (2) To assess the change in P/F joint pressure with VMO weakness. (3) To assess the change in patellar alignment and P/F joint pressure with tibial tuberosity transposition. (MD96134)

The Educational Programs of Longitudinal Study on Effects of Regular Sports Exercise on Health-Related Physical Fitness in Childhood

- ✍ CHAN Kai Ming ● HONG Youlian (Sports Science & Physical Education)
- ☐ 1 October 1996
- ❖ World Health Organization Collaborating Centre for Sports Medicine and Health Promotion

The purpose of this study is to examine the effectiveness of regular sports exercises on health-related physical fitness in childhood. A total of 50 5- to 7-year-old school children who voluntarily participate in two exercise programs (table tennis and swimming) will form the exercising groups, with each group/program containing 25 children. Another 40 children randomly selected from the same schools will be assigned to control group. Every exercising subject will practice three times per week, one hour each time, for total of 12 months. They will begin

from studying basic knowledge and skill of the mode of exercise. The intensity of exercise is set at the level of below 70% VO₂max. The results of test among groups will be compared on the measures of health-related physical fitness at the beginning, the middle and the end of the exercising period. (ED96030)

An *in vivo* Study of the Change in Type I and Type III Collagen in Healing Rat Patellar Tendon - the Effect of Growth Factors

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□ 1 December 1996

❖ CUHK Research Committee Funding

Tendon and ligament injuries are becoming common in sporting activities. To date, there is still no single optimal method for managing soft tissue injuries and there is now intense effort to develop a method for soft tissue healing.

Normal tendons are composed almost exclusively of type-I collagen, but the presence of a considerable amount of collagen type-III can be demonstrated in injured tissue. Collagen type III is important for rapid cross-linking and stabilization of newly synthesized fibers. Therefore, the change in collagen typing during healing may be of great significance in the restoration of tissue integrity.

Growth factors such as TGF-β & IGF-2 have been reported as inducers of collagen I and III synthesis in cultured fibroblasts. However, connective tissue cells behave different in culture and *in vivo*. In this study, the researchers will determine spatial changes of collagen type I and III during tendon healing *in vivo*. They will also quantify the changes in collagen type I and III by SDS-PAGE and collagen gene expression by competitive RT-PCR. Since it is a common belief that collagen type I is responsible to provide mechanical strength while collagen type III is inversely proportional to mechanical strength of healing tissue, the change in collagen typing *in vivo* will yield important information about the restoration of mechanical properties of the injured tissue. This study will also generate an *in vivo* model delivering growth factors in impaired soft tissue healing such as anterior cruciate ligament (ACL) deficiency as this tissue lacks intrinsic healing properties. (MD96072)

Health Benefits of Programmed Physical Exercise on the Prevention of Bone Loss in Postmenopausal Women

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□ 1 January 1997

❖ Health Services Research Fund, Hospital Authority

The prevalence of osteoporosis among elderly Hong Kong Chinese, as evidenced by the incidence of osteoporotic fractures and medical costs, is high. The researchers propose to conduct a randomised controlled trial to investigate the effects of brisk walking and tai-chi on muscle strength and bone mineral density in 450 postmenopausal women. Supervised exercise will be performed 45 minutes for 5 days a week, and bone mineral density (BMD) will be measured by bone densitometer (DEXA). Muscle strength at the upper and lower limb will be measured, and the percentage changes in muscle strength and BMD between the two exercise one control group will be compared at 4, 8 and 12 months. (MD96021)

Use of a Composite "Visco-Elasticity-Thickness Chart" - A New Way to Record the Progress of Post-Burn Hypertrophic Scar

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□ 1 January 1995

❖ Oriental Charity Foundation

During the maturation of hypertrophic scar, the properties will be changed until a dynamic balance of degradation and generation of collagen tissues reached. In clinical situation, the progress of hypertrophic scar is recorded and reported descriptively. However, the author would like to suggest a graphical presentation of the longitudinal change of visco-elasticity, thickness clinical grading of hypertrophic scar with a composite "Visco-elasticity-Thickness Chart".

The objective of this paper is to introduce a new way to present the progress of post-burn hypertrophic scar graphically, by the use of a composite "Visco-elasticity-Thickness Chart" (VT chart). Several typical cases were adopted to illustrate the use and interpretation of the progress. (MD95260)

Change of Foot Size with Weightbearing: A Study of 2829 Children 3 to 18 Years of Ages

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□ 1 July 1995

❖ CUHK Departmental Funding

In pediatric practice, arm span, segmental lengths of tibia, forearm, and humerus have been used to predict height with very high correlations. The predicted

height can be used to estimate the body surface area, drug dosage, basic energy requirements, nutritional assessments, and pulmonary function normalization. Differences in body stature and proportion are known to be caused by numerous factors including gender, age, socioeconomic status, nutritional status, and racial differences. Among these, racial and ethnic differences provide the most significant contribution. Foot length measurements have also been reported to give reliable correlation with the other anthropometric parameters in an individual. However, most of the studies were either confined to the newborn or small child up to the age of 5 years or derived from adult feet measurements. Comprehensive studies are few and limited. The relationship between the length and width of the foot and the changes in dimension with weightbearing have rarely been studied in the growing child. It is the aim of this study to address many of the queries discussed above. This includes correlating the pattern of changes of foot length and width with age and gender, and correlating these changes with weightbearing versus nonweightbearing. The significance of side dominance and the correlation with body height were also analyzed. (MD95258)

Dual Energy X-Ray absorptiometry in Lower Limb Callotaxis Lengthening

- ✍ CHENG Chun Yiu Jack ● MAFFULLI N.* ● NG B.*
□ 1 August 1995
❖ CUHK Departmental Funding

Significant limb length inequality can constitute a major orthopaedic and psychological problem. Gradual callus distraction has become a reliable and predictable means of correction. The process of lengthening is carefully monitored on an in- and out-patient basis to ensure that pin sites are kept clean, that correct alignment is maintained, and that bone formation takes place. Alignment is generally evaluated using sequential antero-posterior and lateral radiographs, possibly with additional views centred over the distraction site. Radiographs are taken initially at one- to two-week intervals, and distraction rate is varied according to the radiographic appearance of the regenerate bone at and around the distraction site. The decision on when to discontinue the distraction, and on when to remove the frame, is a clinical judgment, based on the length achieved and the appearance of cortico-medullary differentiation. The assessment of the quality of the regenerate bone will be done with the more accurate and objective dual energy X-ray absorptiometry (DEXA) scanning in this study longitudinally on a series of patients undergoing limb distraction callotaxis. The absolute BMD and the rate of changes throughout the distraction period till the end of

rehabilitation would be monitored and charted. The predictive value of the BMD in the early phase on the progress of callotaxis and time of removal of the frame would be studied. (MD95259)

Osteopenia in Adolescent Idiopathic Scoliosis

- ✍ CHENG Chun Yiu Jack ● GUO Xia
□ 1 January 1996
❖ CUHK Departmental Funding

A cross sectional study to assess the lumbar spinal and proximal femoral bone mineral density (BMD) in girls aged 12, 13 or 14 years with adolescent idiopathic scoliosis (AIS) and to compare with an age-matched control group. Objectives are to determine whether there is an association of osteopenia with idiopathic scoliosis (IS). To test the differences of BMD in scoliosis patients in different age groups Vs normal controls and to correlate the BMD with the scoliotic parameters including the curve pattern and magnitude. Routine radiographs allows very limited assessment of osteopenia. Therefore only a few studies were found to have documented a state of osteopenia in scoliosis patients compared with the normal. New techniques allowed a more reliable quantification of the bone mineral state in adolescent idiopathic scoliosis. Available series in the literature were either small in number, with inadequate controls or with a large spread of age range. Using dual energy X-ray absorptiometer (DEXA) BMD was measured in the predominant trabecular bone area, i.e. the lumbar spine(L2-4) and bilateral proximal femur on 81 girls with idiopathic scoliosis of various degree of severity, aged 12 to 14 years old. Results were compared with 220 age-matched healthy control girls. (MD96174)

Transient Synovitis of Hip in Children - A Natural History Review of 235 Cases

- ✍ CHENG Chun Yiu Jack ● CHOI K.Y.* ● NG B.K.W.*
□ 1 July 1996
❖ CUHK Departmental Funding

Aim: A retrospective study of the natural history and outcome of paediatric patients with transient synovitis of the hips.
Method: Three hundred and six children under 12 years old with the provisional diagnosis of transient synovitis of hip were admitted to the Prince of Wales Hospital from 1985 to 1995. A standard protocol of management was followed including radiographs, blood checking and in some cases ultrasound and hip aspiration. The presentation, physical findings,

investigation results, time course to complete resolution and the final outcome and diagnosis were reviewed and studied in 235 patients with available records and follow-ups.
(MD96175)

Changing Trend of Management - A 10 Year Review of 6600 Paediatric Fractures

✍ CHENG Chun Yiu Jack ● YING S.Y.* ● LAM T.P.* ● KONG C.C.*

☐ 1 July 1996

❖ CUHK Departmental Funding

Objective: Over the past decades, Hong Kong has experienced considerable changes in the pattern of diseases among all age groups. Among all the different diseases presented to our Emergency Department, trauma is still the commonest surgical problem and pediatric fractures remain one of the most important group; not only because of its number, but also due to its short term and long term morbidity problems associated with it. Most studies give an overall injury pattern without analyzing the temporal change, the current study was conducted with the aim to analyze the changes in the epidemiological, demographic data, clinical pattern and trend of clinical management of paediatric fractures in the past 10 years in Prince of Wales Hospital.

Medical records of all children admitted with fractures to Orthopaedic Department of Prince of Wales Hospital during the period of 1984 to 1996 will be retrieved and analyzed retrospectively. Apart from studying the overall pattern of injury, children were further categorized into the 0-3 year, 4-7 year, 8-11 year and 12-15 year age groups. The side, site, sex, management, technique of reduction and immobilization will be further analyzed.
(MD96176)

Osteoinductive Bone Substitute for Posterior Spinal Fusion in a Rabbit Model

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☐ 1 December 1996

❖ CUHK Research Committee Funding

Most bone grafts used today in posterior spinal fusion during scoliosis corrective surgery are autografts removed from the patient's iliac crest. The primary goal of autograft is inducing arthrodesis through its osteogenic and osteoinductive properties. However it is not always possible to get sufficient autograft bone, such as in long spinal fusion for scoliosis or kyphosis, or scoliosis patients with neuromuscular scoliosis. In addition the harvesting of autograft needs separated surgical procedure and can result in unnecessary

blood loss. The results of using pure banked allograft bone to substitute autograft are up to date not optimal, since the banked allograft bone can only provide osteoconduction, but lack of osteogenic and osteoinductive properties. Animal experiments indicate that, impregnating allograft bone with autograft marrow can introduce osteogenic and osteoinductive properties into allograft bone. Results of clinical applications of such composites for treatment of nonunion or bone cysts in limb bone, or treatment for mandibular defect are successful. It is expected with this study to investigate whether composite of banked allograft bone and autograft marrow is equal or superior to autograft in posterior spinal fusion. Aim of the experiment is to search for a suitable substitute of the autologous bonegraft for posterior spinal fusion (PSF). We will realize this goal by (1) testing the hypothesis that the addition of recombinant human bone morphogenetic protein 2 (rhBMP-2) to a biodegradable osteoconductive material would result in a material with bone fusion efficacy greater than that of the osteoconductive material alone; and (2) testing the hypothesis that combination of the osteoinductive rhBMP-2 and osteoconductive material would function with efficacy equivalent to that of autogenous bone.
(MD96071)

Early Operative Fixation of Femoral Neck Fractures in Children - A Study of the Medium Term Outcome

✍ CHENG Chun Yiu Jack ● TANG N.* ● GRIFFITH James (Diagnostic Radiology & Organ Imaging)

☐ 1 January 1997

❖ CUHK Departmental Funding

Introduction: Pediatric femoral neck fractures are rare and are associated with a high rate of early and late complication rate in previous studies (mixed groups of treatment with hip spica and operation). The effect of early operative fixation is not frequently reported in the literature. This is a retrospective study to review our experience of pediatric femoral neck fractures to see how fracture type and early management affected short and medium term outcome.
(MD96177)

Analysis of *Tlx* Gene Functions in Oncogenesis and Development Using Gain-of-function and Loss-of-function Mutants in Transgenic Mice

✍ CHENG Shuk Han

☐ 1 September 1996

❖ Research Grants Council

In this project, the researchers will investigate the roles of *HOX-11* in oncogenesis. *HOX-11* was first isolated from chromosomal translocations in the childhood T-cell acute lymphoblastic leukemia. They will try to mimic the deregulated expression of this gene, using transgenic models, in the lymphoid compartment and investigate whether this event itself is sufficient to initiate oncogenesis. The researchers will also investigate the cooperative effects of the tumour suppressor gene p53. Loss of function of the p53 gene is frequently detected in solid tumours and haematopoietic malignancy. They aim to set up a scenario, using a bi-transgenic model, where the ectopic expression of the *HOX-11* gene is compounded with a deficiency in the p53 gene. It would be interesting to determine whether these two events will display synergism and accelerate the pathway of oncogenesis. In order to understand the roles of *HOX-11* in oncogenesis, the researchers will need to know how it functions in its endogenous roles. Gene Targeting of the murine homolog of *HOX-11*, *Tlx-1* gene has led to the development of an asplenic mouse. Knocking out its related member, the *Tlx-2* gene, resulted in death *in utero*. In this project, the researchers propose the disruption of the third member of the *Tlx* family by homologous recombination using embryonic stem cells. The phenotypic analyses of this mutant mice will complement previous work in this direction and would be essential in the elucidation of the functional roles of this family of genes.
(CU96662)

Iontophoresis with Pulsed-short Circuit-pulsed Direct Current (PSPDC) Device: Tissue Effects and Drug Permeation

- ✉ HUNG Leung Kim ● ZHANG Yuanting (Electronic Engineering) ● ZHAO Li* ● WU Hay Tong
- 1 October 1996
- ❖ CUHK Research Committee Funding

Iontophoresis is an established method of drug delivery through the skin in a controlled manner. It avoids the use of a needle and enables the delivery of medication directly to a local pathology: a hypertrophic scar or an inflamed tendon. In a previous grant: The researchers modified the electronic circuit by adding a short-circuit to the field (the PSPDC) so that polarisation of the skin is reduced to the minimum. This was shown to be effective in increasing the efficiency of permeation of salicylate and lignocaine across the skin (thesis of Dr. Zhao). This theoretically will also reduce the likelihood of skin damage. Before the method could be put into clinical use for treating hypertrophic scars, it is proposed to further establish the tissue safety of PSPDC and the tissue effects of PSPDC will be investigated with histochemistry, electric impedance

and electron microscopy. It is also proposed to study in animal models the relationship between tissue nature, electric impedance, and the permeation of drugs. The angiotensin 2* model will be used as well as a direct assay of corticosteroid permeated by the PSPDC. Corticosteroid is effective in the control of hypertrophic scars.
(MD96073)

Neurotrophic Factors Derived from Schwann Cells in a "Pre-degenerated" Peripheral Nerve Environment - Temporal Changes and Clinical applications

- ✉ HUNG Leung Kim ● LAO J* ● KWONG Wing Hang (Anatomy) ● WU Hay Tong
- 1 October 1996
- ❖ CUHK Research Committee Funding

Neurotrophic factors are essential for regeneration of axons after nerve injury and Schwann cells play a critical role. Schwann cells in the injured nerve produce these neurotrophic factors as well as binding and storing these (secreted by non-neuronal cells) to prepare for the regeneration of the axons. The researchers observed a time-dependent enhancement of nerve regeneration in nerve grafts which were 'pre-degenerated' for 1-2 weeks in an adult rat forelimb median nerve defect model. They postulate that the Schwann cells inside these grafts were activated and secrete growth factors in a time-dependent fashion. Brain-derived neurotrophic factor (BDNF) and Ciliary neurotrophic factor (CNTF) are two currently intensively studied factors. Utilising the same rat model, Schwann cells will be released from these 'pre-degenerated' grafts and cultured and BDNF and CNTF will be assayed with rt-mRNA technique. The time course of variation of these factors will provide useful information for the design of autologous or homologous cultured Schwann cell implants for nerve repair. These implants will provide a more biological, more specific and sustained enhancement of nerve regeneration in comparison to the recent attempts of using implantable reservoirs or osmotic pumps.
(MD96075)

Interleukin-1 and Interleukin-8 Expression in Burn Wound - *in vivo* and *in vitro* Studies

- ✉ HUNG Leung Kim ● WU Hay Tong ● CHENG Chi Wa ● FUNG Ming Chiu (Biology)
- 1 January 1997
- ❖ CUHK Research Committee Funding

Wound healing of thermal injury is always problematic. The lesion remains inflamed for a prolonged period of time, and most likely develops into a hypertrophic scar which causes severe

functional impairment. Evidences suggested that this healing process was regulated by cytokines. Interleukin-1 (IL-1), a pro-inflammatory cytokine, is known to appear early in normal wound healing. It can induce network of cytokine reactions, and the regulation of IL-1 agonists and antagonists is complex. Another important proinflammatory cytokine is interleukin-8 which has neutrophils chemotatic and angiogenesis properties. Recent reports suggested that the expression of IL-8 in burn patients was extremely high and it should play an important role in burn wound healing. However, there is no complete picture of the regulation of the agonists and antagonists of these 2 factors in thermal injury. The present study is aimed to determine the regulation of these 2 factors in different stages of the burn wound healing. Semi-quantitative RT-PCR and immunostaining will be applied to detect the expression of these factors. In addition, the keratinocytes and fibroblasts of the burn wounds will also be cultured and any phenotypic changes in the cultured cells can be determined.
(MD96074)

The Use of Electrophysiological Monitoring in Cervical and Lumbar Myelopathy

- ✉ LEE Yuen Lun
- ☐ 1 May 1996
- ❖ CUHK Departmental Funding

Cervical & lumbar myelopathy is traditionally diagnosed by clinical symptom and signs. Radiological assessment tools like the MRI can then describe the morphological change involved. Unfortunately, the correlation between the two is not high. Short-latency somatosensory evoked potential (ssep), a sophisticated technique that have been developed and proved to be reliable, provides an objective and quantitative measurement of the function of the sensory system. In this study, the clinical efficacy: reliability and the practical difficulty for its use in Prince of Wales Hospital will be reported.
(MD96171)

The Effect of Reaming Technique on Intramedullary Pressure and Marrow Fat Embolisation - A Quantitative Study

- ✉ LEUNG Kwok Sui ● CHEN Zhen Yu (Biochemistry) ● WONG Wan Nar Margaret ● FUNG Kwok Pui (Biochemistry)
- ☐ 1 October 1996
- ❖ Research Grants Council

Intramedullary fixation of long bone fractures is one of the commonest operations performed for musculoskeletal trauma. Reaming the medullary

cavity is an essential part of the operative procedure in which the medullary canal is enlarged by mechanically removing the cortical bone. Reaming facilitates nail insertion and also allows the implantation of nail with larger diameter to provide better mechanical stability. The recent recognition of the side effects from reaming has led to numerous studies. Of the many side effects, the increase in the intramedullary pressure is the most detrimental one by causing extrusion of the marrow content. The extrusion of the marrow content causes intravasation into systemic circulation which is thought to be related to the clinical manifestation of fat embolic phenomenon. Although there are many studies in the documentation of this complication, there is a lack of the quantitative data on the relationship between the pressure rise and the severity of marrow embolisation. Furthermore, the exact role of marrow fat in the development of the potentially fatal complication is still unknown. This study is designed to quantify the pressure rise and the severity of marrow fat embolisation. The biochemical event of the marrow fat in leading to the full blown picture of fat embolic syndrome will also be studied. It is hoped that the results from this study will improve the surgical technique and surgical instrument design which will lead to decrease of the magnitude of intramedullary pressure rise during reaming. By clarifying the role of the marrow fat in the development of pulmonary complications, specific treatment can be established.
(CU96631)

Identification of TGF-beta Induced Genes During Chondrogenesis in Rabbit Periosteal-derived Cells Using mRNA Differential Display Analysis

- ✉ LEUNG Kwok Sui ● CHAN Chun Wai (Lee Hysan Clinical Research Laboratories)
- ☐ 1 October 1996
- ❖ CUHK Research Committee Funding

Periosteum is a tissue that covers the surface of bone. Periosteal cells were shown osteogenic that differentiate into osteoblast (bone-forming cells) in normal bone growth. However it shows chondrogenic in fracture healing and callus distraction in which mesenchymal periosteal cells will differentiated into proliferative chondrocyte transiently and become hypertrophic eventually and then bone matrix deposits into the degenerating cartilage matrix by osteoblast. Transforming growth factor- β are abundantly in bone matrix and blood platelets and also in articular cartilage. It was found to be responsible for the chondrogenesis of periosteum in explants and fracture healing. In this project, cell culture model of rabbit periosteal cells is developed for TGF- β stimulation. The TGF- β induced genes during chondrogenesis of periosteal cells are screened and identified by mRNA differential display analysis. The sequence of the

newly synthesised cDNAs is also characterised. The study of this project will help to realise not only the mechanism of chondrogenesis but also the molecular mechanism of regulation in fracture healing and callus distraction and chondrogenic potential to repair of full-thickness articular defects as well as enhancement of recovery rate of bone and cartilage injury.
(MD96076)

A Study to Correlate the Hand Function with the Physical and Physiological Structure of the Cervical Spine in Cervical Myelopathy

✍ LEUNG Kwok Sui ● LEE Yuen Lun
□ 1 October 1996
❖ CUHK Departmental Funding

Cervical myelopathy is very common in old people. It has many causes and the most commonest are ossification of posterior longitudinal ligament (OPLL) and cervical spondylotic myelopathy (CSM). The diagnosis is mainly depending on the radiological findings as well as the functional findings. Some research review that the most accurate radiological measurement is the magnetic resonance imaging (MRI) and computerized tomographic myelogram (CTMM). Clinically, patient always present with pain, numbness, spasticity and neurological deficits which lead to problems to gait, hand function, co-ordination and the self protective system. The location and degree of spinal stenosis are crucial factors of the neurological deficits. Therefore, this study is aimed at finding out the relationship between the physical and physiological structure as well as the hand function. Through this study, a reference point will be obtained to aid in predicting the rehabilitation potential and longitudinal ligament or cervical spondylotic myelopathy.
(MD96169)

Cartilage Reconstruction Using Chondrocytes Transplantation

✍ LEUNG Ping Chung
□ 1 December 1996
❖ CUHK Research Committee Funding

Cartilage damage is the cause of a lot of orthopaedic problems, ranging from congenital deformities to degenerative arthritis. Up to today, no technique is available for the restoration of damaged cartilage. Transplantation of cartilage, either in gross form, or in cell culture form, is a popular experiment. The researcher's PhD student has worked out a practical way of isolating specific crops of chondrocytes which have more proliferative ability. Transplantation of this group of cells to animals with artificially

produced cartilage defects may give exceptional results of cartilage reconstruction.
(MD96077)

Cartilage Elastography

✍ QIN Ling ● MAK F. T. Arthur* ● MOW Van C.*
□ 1 October 1996
❖ Research Grants Council

Articular Cartilage is a biological weight-bearing material covering the bony ends of articulating joints. Degeneration of cartilage under pathological situations such as osteoarthritis could lead to significant compromises in joint functions and thus disabilities of the patient. Currently, there is a lack of reliable diagnostic techniques for early signs of osteoarthritis.

The overall objective of this research programme is to develop an ultrasound elastography system for articular cartilage evaluation. It is proposed that an ultrasound force-deformation sensing probe together with the proposed segmental cross-correlation technique for ultrasound echo time-shift analysis could be used to map the cartilage strain field during compression. This strain mapping of the material properties of the tissue through its thickness.

The sensitivity of this elastography system to changes in the biomechanical properties of cartilage will be studied by examining the elastographies of bovine cartilage discs that have been treated biochemically with trypsin or other enzymes for different periods of time. The elastography of each specimen will be compared to its own quantitative histological profile obtained after the biomechanical testings and elastography imaging.

This cartilage elastography system would be a significant contribution to the professional community not only as an important research equipment for cartilage analysis but also as a potential clinical diagnostic methodology for early cartilage degeneration.
(MD96128)

Epidemiological Study on Foot and Ankle Disorders

✍ WONG Wan Nar Margaret ● LEUNG Ping Chung
□ 1 January 1997
❖ CUHK Departmental Funding

The foot and ankle region has long been a neglected part in Orthopaedics. However, the prevalence of the disorders, with a significant impact on cost and subsequent functional deficit, should not be an oversight. In this study, the incidence of the foot and ankle will be evaluated. At the same time, the

disease pattern, the distribution among different age and sex groups, relationships between habits and activities of the patients, outcome of treatment as well as long term disabilities will be studied. This is a prospective longitudinal study by reviewing medical records and interviewing all patients who come to Prince of Wales Hospital seeking orthopaedic consultations and treatments the first time, within period of January 1997 to December 1997. Data collected will be entered into database for statistical analysis. The ultimate objective of this project is to raise the awareness on foot and ankle care of both clinicians and the public. (MD96170)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
1994-95	Healing of Patellar Tendon Donor Site after the Removal of the Central One-third - A Comparison between "Close" and "Open" Procedure (MD95021) ✉ CHAN Kai Ming
1994-95	A Co-ordinated Sports Medicine and Sports Science Research Programme - the Way Forward in the 21st Century (MD95035) ✉ CHAN Kai Ming ● HUNG Leung Kim ● CHENG Chun Yiu Jack ● LEUNG Suk Fong Sophie (Paediatrics) ● LAM Wai Kei Christopher (Chemical Pathology) ● WOO Kam Sang (Medicine) ● LEE Ka Ho Kenneth (Anatomy) ● BRUTON Joseph D. (Physiology) ● SUEN Wang Ming Michael (Anatomical & Cellular Pathology) ● HONG Youlian (Sports Science & Physical Education)
1995-96	Physiotherapeutic Management of Osteoarthritic Knee Pain (MD95231) ✉ CHAN Kai Ming ● CHAN C. H.* ● CHEING Gladys* ● HJELM Nils Magnus (Chemical Pathology)
1995-96	Effect of Different Electrical Stimulation Protocols for Rehabilitation of Anterior Cruciate Ligament Injuries (MD95232) ✉ CHAN Kai Ming ● NG G.* ● CHAN C. H.*
1994-95	Anthropometric Measurements in Chinese Children (MD95105) ✉ CHENG Chun Yiu Jack

1995-96	The Cutometer and Ultrasonography in the Assessment of Post-Burn Hypertrophic Scar (MD95101) ✉ CHENG Chun Yiu Jack ● HUNG Leung Kim
1995-96	Modular Seating System for Children with Neuromuscular Diseases (MD95104) ✉ CHENG Chun Yiu Jack
1995-96	Treatment of Displaced Forearm Shaft Fractures in Children with Percutaneous Intramedullary Kirschner Wires (MD95251) ✉ CHENG Chun Yiu Jack ● LAM Chor Yin* ● LAM Tsz Ping ● HO Pak Cheong ● CHOI Kai-yiu*
1995-96	Posterior Spinal Fusion with Different Type of Bone Graft in a Rabbit Model (MD95131) ✉ CHENG Chun Yiu Jack ● GUO Xia
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)
1995-96	Bony Fusion Between Hydroxyapatite and Cortical Bone - Feasibility of Posterior Spinal Fusion Without Decortication (MD95236) ✉ CHENG Chun Yiu Jack ● GUO Xia
1995-96	Isokinetic Trunk Muscle Strength in Structurally Normal Girls and Girls with Idiopathic Scoliosis (MD95237) ✉ CHENG Chun Yiu Jack ● LI Che Tin Raymond ● GUO Xia
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.*
1995-96	Expression Studies of the Murine <i>Tlx</i> Genes during Development and Disruption of these Genes in the Embryonic Stem Cells (CU94644) ✉ CHENG Shuk Han

- 1995-96 Frequency Distribution of Variable Number of Tandem Repeats Loci in Hong Kong Chinese (MD95204)
✍ CHENG Shuk Han ● NG Heung Ling Margaret (Anatomical & Cellular Pathology)
- 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
- 1994-95 Endoscopic Release of Carpal Tunnel Compression (MD94150)
✍ HO Pak Cheong ● HUNG Leung Kim
- 1994-95 A Survey of Circular Saw Hand Injuries (MD95102)
✍ HO Pak Cheong ● HUNG Leung Kim
- 1993-94 Distraction Lengthening of Upper Limb Anomalies in Children (MD94145)
✍ HUNG Leung Kim ● CHENG Chun Yiu Jack
- 1994-95 Arthroscopy Assisted Management of Distal Radial Fracture (MD95088)
✍ HUNG Leung Kim ● HO Pak Cheong* ● CHOI Kai Yiu*
- 1994-95 Outcome Study of Nerve Injuries and the Role of Sensory Re-education (MD95094)
✍ HUNG Leung Kim ● CHENG Shu Kei Andy*
- 1994-95 Hydroxyapatite Implant for Spinal Fusion (MD95081)
✍ HUNG Leung Kim ● CHENG Chi Wa ● CHENG Chun Yiu Jack
- 1995-96 Biomechanics of Surgical Reconstruction for Shoulder Paralysis (CU95633)
✍ HUNG Leung Kim ● TANG Chun Yuen ● MAK F. T. Arthur* ● KWONG Wing Hang (Anatomy)
- 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) ● CHOW Louis Tsun Cheung* (Anatomical & Cellular Pathology)
- 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 Investigating the Mechanical and Biochemical Barrier Effect of the Physcal Growth Plate Towards Osteosarcoma Extension (MD95129)
✍ KUMTA Shekhar Madhukar ● LEUNG Kwok Sui ● LEUNG Ping Chung ● FUNG Kwok Pui (Biochemistry)
- 1995-96 Correlation of Decompression Technique and Results in Cervical Spondylotic Myelopathy (MD95223)
✍ LEE Yuen Lun ● POON Kai Ming ● WONG K. C.*
- 1995-96 Evaluation of Radiologically Guided Biopsy in Spinal Disorder (MD95224)
✍ LEE Yuen Lun ● LAW S. W.* ● YU S.*
- 1995-96 Use of Computerized Seating Pressure Mapping Device in Patients with Spinal Cord Injury (MD95225)
✍ LEE Yuen Lun ● LAU Miranda W. Y.*
- 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 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

- Research Laboratories) ● FUNG Kwok Pui (Biochemistry)
- 1995-96 Study on Osteoporosis - The Loss of Calcium Content in Bone with Age (MD94016)
 ✎ LEUNG Ping Chung ● LAU Edith Ming Chu (Community & Family Medicine) ● WOO Jean (Medicine) ● HO Chan Suzanne (Community & Family Medicine) ● HAINES Christopher John (Obstetrics & Gynaecology)
- 1995-96 Biosynthesis and Implantation of Artificial Growth Plate Using Population of Proliferative Chondrocytes Cultured on a Collagen Matrix (CU95656)
 ✎ LEUNG Ping Chung ● LEE Kwong Man Simon (Lee Hysan Clinical Research Laboratories) ● OOI Vincent E. C. (Biology) ● FUNG Kwok Pui (Biochemistry)
- 1994-95 The Use of a New Animal Model of Osteoarthritis to Assess the Efficacy of New Chemical (Hyaluronate) and Physical (Laser) Treatments on Articular Cartilage (MD95002)
 ✎ QIN Ling ● CHAN Kai Ming
- 1995-96 Inapparent Hypoxaemia - Its Incidence and Relation to Fat Embolism Syndrome (MD95130)
 ✎ WONG Wan Nar Margaret
- 1995-96 Optimisation of Humeral Nail Locking Mechanism (MD95246)
 ✎ WONG Wan Nar Margaret ● CHOW Daniel* ● LEUNG Kwok Sui
- 1994-95 Histological Localisation of Growth Factors in Post-burn Hypertrophic Scars (MD95080)
 ✎ WU Hay Tong ● HUNG Leung Kim
- 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
- 1995-96 The Role of Nitrous Oxide Synthase Inhibitor in the Prevention of Osteoarthritis in an Animal Immobilization Model (MD95229)
 ✎ YIP Man Hing Kevin ● CHAN Kai Ming ● QIN Ling

RESEARCH OUTPUTS AND PUBLICATIONS

- <P952503> **Yip, K.M.H.; J. Lin and K.W. Ng.** "Long Survival with Metastatic Tenosynovial Clear Cell Sarcoma". *Proceedings of the 1st Asia-Pacific Musculoskeletal Tumour Society* p.96. Tokyo, Japan: Japanese Orthopaedic Association, 1996.07.
- <P953503> **Leung, K.S.; L.L.K. Fu; L. Qin and F.C.W. Chan.** "Comparative Study of Bone to Bone Healing and Bone to Tendon Healing". *Abstract of WPOA 1995 Congress Incorporating HKOA 15th Annual Congress* ed. by Leung K.S., Fu L.L.K., Qin L. and Chan F.C.W. p.51. Hong Kong, 1995.11.12.
- <P961691> **Wong, M.W.N.; K.S. Leung; S.S.W. Chan; K.M. Lee and C.H. Wong.** "A Study of Bone Mineral Density in the Appendicular Skeleton in Chinese". *Abstracts of 7th World Congress of Societe Internationale de Recherche Orthopedique et de Traumatologis* p.51. Amsterdam, 1996.08.16.
- <P961692> **Leung, K.S.; K.M. Lee; K.P. Fung; M.W.N. Wong; F.C.W. Chan and A.F.T. Mak.** "Mechanical Characterisation of Regenerated Osseous Tissue During Callotaxis and its Related Biological Phenomenon". *Abstracts of 7th World Congress of Societe Internationale de Recherche Orthopedique et de Traumatologis* p.8. Amsterdam, 1996.08.16.
- <P961693> **Leung, K.S.; L.K. Fu; L. Qin and C.W. Chan.** "Comparative Study of Bone to Bone Healing and Bone to Tendon Healing". *Abstracts of the 7th World Congress of Societe Internationale de Recherche Orthopedique et de Traumatologis* p.491. Amsterdam, 1996.08.16.

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- <P961817> **Cheng, J.C.Y.; Guo X. and Sher H.L.** "Bone Mineral Density in Adolescent Idiopathic Scoliosis Versus Normal Controls". Paper presented in the 16th Annual Congress of the Hong Kong Orthopaedics Association. p.91. Hong Kong, 1996.11.
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- <P961820> **Tam, Eric; Jack Cheng and John Evans.** "Seating Children with Duchenne Muscular Dystrophy". Paper presented in the 16th Annual Congress of the Hong Kong Orthopaedics Association. p.89. Hong Kong, 1996.11.01.
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- <P961823> **Ying, S.Y.; J.C.Y. Cheng; T.P. Lam and C.C. Kong.** "Changing Trend of Management-A 10 Year Review of 6600 Paediatric Fractures". Paper presented in the 16th Annual Congress of the Hong Kong Orthopaedics Association. p.84. Hong Kong, 1996.11.01.
- <P961824> **Cheng, Jack C.Y. and Guo Xia.** "Bone Mineral Density in Adolescent Idiopathic Scoliosis". *Abstracts of the 3rd Combined Meeting of Spinal & Paediatric Sections of WPOA* Abstracts no.P74, p.200. Japan, 1996.11.
- <P961825> **Cheng, J.C.Y.; C.Y. Lam; P.C. Ho and K.Y. Choi.** "Treatment of Displaced Forearm Shaft Fractures in Children with Percutaneous Intramedullary Kirschner Wires". *Abstracts of the 3rd Combined Meeting of Spinal & Paediatric Sections of WPOA* Abstracts no.P67, p.196. Japan, 1996.11.01.
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RESEARCH PROJECTS

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

- ✉ CHIK Ki Wai ● YUNG Chung Ming Edmund
- ☐ 1 March 1997
- ❖ CUHK Research Committee Funding

Expression of the Wilms' tumor gene (WT1) has been reported in various types of human leukemia. Semiquantitative estimation of the expression level of the WT1 gene has also been noted useful in assessing the leukemic burden in the body. Present standard clinical laboratory in Hong Kong does not have the capacity to determine the level of the residual disease beyond remission. At present, one of the major problems in the treatment of leukemia is eradication of the minimal residual disease in the body. The availability of autologous haemopoietic stem cell transplant also poses the question of the leukemic contamination within the infused graft. Methodology involving polymerase chain reaction has developed over the past few years to detect minimal residual disease. This is a highly sensitive and specific test in detecting a very low level of residual leukemia (one leukemic cell among 10^5 normal cells). This proposal aims at establishing the WT1 gene expression in childhood leukemic patients and evaluating the level of expression in semiquantitative terms during various phases of treatment. The latter will provide information on the level of minimal residual disease in the individual patient. This project will provide local data on the relationship of WT1 and childhood leukemias. The ability of estimation of minimal residual disease in various types of leukemias will give us important information on leukemic contamination in autologous transplant setting. (MD96113)

To Provide Gestation-Specific Standards on Physical Measurements on Chinese Newborns

- ✉ FOK Tai Fai ● LAU Tak Fai Joseph (Centre for Clinical Trials & Epidemiological Research) ● SO Hung Kwan
- ☐ 1 January 1996
- ❖ CUHK Departmental Funding

By obtaining a variety of physical measurements from ethnic Chinese newborns who are products of normal pregnancy, this project is designed to provide gestation-specific standard reference for (1) birth weight, head circumference, and body length; and (2) other physical measurements, including those reflecting head growth, facial configuration, trunk

and limb growth, and penile length (male infants). The measurements would be used to construct normal percentile charts for the local Chinese population. These charts would provide important references required for identifying infants who are at risk of developing complications because of distorted prenatal growth, and also for the evaluation of those with possible dysmorphic features, syndromes, and/or structural anomalies. The data obtained will also enable us to identify maternal and environmental risk factors that are associated with abnormal fetal growth in the local population. So far about 2000 infants have been measured, and more need to be studied to increase the precision of the centiles. (MD96165)

Evaluation of the Metered Dose Inhaler, Jet Nebuliser, and Ultrasonic Nebuliser in the Delivery of Salbutamol Aerosol to Newborns with chronic Lung Changes

- ✉ FOK Tai Fai ● LAM Kuo ● CHAN C.K.* ● NG Pak Cheung
- ☐ 1 January 1996
- ❖ CUHK Departmental Funding

Bronchodilator aerosols are used commonly for the relief of bronchiolar obstruction in newborns with bronchopulmonary dysplasia. The major limitation of this therapeutic modality in small infants is the small amount of drug that can be delivered to the lower respiratory tract. Furthermore, it is not known which delivery device has the greatest therapeutic efficacy. The researchers compared the currently available devices, the metered dose inhaler, the jet nebuliser, and the ultrasonic nebuliser in a group of ventilated and non-ventilated infants with chronic lung changes. The infants were given a uniform dose of salbutamol aerosol from each device at 4h intervals, and at random sequence. By using the improvement in airway resistance and functional residual capacity as the outcome measure, they were able to show that the ultrasonic nebuliser could bring about the greatest improvement in both ventilated and non-ventilated infants, and jet nebuliser had poorest performance in both groups. The study, now completed, will provide guidance for clinicians in their choice of delivery devices for the treatment of newborns and small infants. (MD96168)

Development of a Preterm Animal Model for the Study of Oxygen-Induced Lung Damage

- ✉ FOK Tai Fai ● XU Feng ● YIN Ai Tsang Jane
- ☐ 1 September 1996
- ❖ CUHK Departmental Funding

Oxygen-induced lung damage plays an important role in the causation of acute and chronic lung disease in preterm neonates. In order to study the pathogenesis and effects of drugs on the prevention and treatment of this condition, we developed a lung model of preterm rats who were delivered at 21 days gestation by hysterotomy. Vigorous resuscitation at birth resulted in a significant higher survival rate reported in literature. When compared to litters delivered spontaneously at term (gestation 22 days), these preterm rats had immature pulmonary surfactant composition with low total phospholipid and phosphatidylcholine level. The concentration of the antioxidant enzymes, superoxide dismutase and catalase were also significantly lower. The model was tested in an experiment on hyperoxia induce lung injury in which preterm rats were randomised to breathe either >95% oxygen or room air for 7-14 days. Animals exposed to hyperoxia had a significantly higher mortality rate than those exposed to room air. Pulmonary edema and histological features of lung damage was observed in the hyperoxia but not the room air group. Compared to larger animals, the preterm rat model is relatively cheap and readily available, and should be suitable for the study of acute and chronic lung damage related to prematurity.
(MD96164)

Enterobacter Septicaemia in Newborns: Analysis of Risk Factors

- ✉ FOK Tai Fai ● LEE Cheuk Hon ● WONG Ming Chung (Centre for Clinical Trials & Epidemiological Research) ● LYON Donald James (Microbiology) ● NG Pak Cheung
- 1 September 1996
- ❖ CUHK Departmental Funding

Enterobacter spp. are common intestinal commensals in newborns and have in recent years emerged as an important nosocomially acquired infection in neonatal units. There are however very few studies on the risk factors of this important infection. The researchers conducted a case control study on 30 cases of septicaemia caused by Enterobacter cloacae and Enterobacter aerogenes and 60 controls to evaluate the association of the infection with 32 perinatal factors. Risk factors that were identified to be important determinates of the infection included ongoing parenteral nutrition, bladder catheterisation, and prolonged use of antibiotics. The study, now completed, highlights the importance of strict aseptic precaution in preparing parenteral nutrition, avoidance of bladder catheterisation, and judicious use of antibiotics in neonates.
(MD96166)

Clinical Prediction of Post-Extubation Radiological Changes of the Chest in Newborns

- ✉ FOK Tai Fai ● KEW Jacqueline (Diagnostic Radiology & Organ Imaging) ● LOFTUS William (Diagnostic Radiology & Organ Imaging) ● NG Pak Cheung
- 1 October 1996
- ❖ CUHK Departmental Funding

Partial atelectasis of the lung is a known complication following extubation in ventilated newborns, but the need for routine post-extubation chest radiograph is a controversy in clinical neonatal practice. By following the clinical progress of a cohort of ventilated infants after extubation, this prospective study was designed to determine the usefulness of a number of clinical parameters in predicting post-extubation radiological deterioration. The study has been completed, and shows that most infants with significant radiological changes could be identified clinically. The findings provide an evaluation on whether a selective policy can safely be adopted, and information on the discriminatory abilities of the various clinical parameters in predicting radiological changes.
(MD96167)

Improvement in Physician Consultation Time and Patient Knowledge with a Paediatric Asthma Management Program in Hong Kong

- ✉ HUI Hon Lam ● HA G.* ● LAW W. Y.* ● FOK Tai Fai
- 1 August 1995
- ❖ CUHK Departmental Funding

Asthma is a prevalent condition amongst children in Hong Kong and its incidence is on the rise. Current management plans for asthma is complex requiring adequate knowledge from the patients and parents. This involves understanding of the disease, avoidance of risk factors such as house dust mite and smoking, and improve technique of drug delivery. The researchers have instituted an asthma management program in the Paediatric clinic at Prince of Wales Hospital since August 1995. They would like to report an assessment on the program in respect to patient's knowledge and reduction in physician consulting time. The education program consists of a talk on asthma pathophysiology, trigger factors, environmental control, and treatment. Individual patients were supervised for technique of drug inhalation device. Patient's knowledge as assessed before and after the program using a standardised questionnaire with score 0 to 13. Consultation time was assessed for asthma patients before and 3 months after institution of the program. During the study period, up to 40% of 1000 patients per month

attending the paediatric outpatient suffer from asthma. A total of 60 patients complete the program from 28/11/95 to 30/1/96. The mean score after the program 12.2 (12-12.5) was significantly higher than that before 8.3 (7.6-9.0) with a p value of <0.05. Mean consultation time for new cases reduced from 16.5 to 14.6 minute, and that for old cases from 8.2 to 6,8 minutes. Their results support asthma management program in improving patient knowledge of the disease and its management, and reduction in physician consultation time hence better cost effectiveness in outpatient clinic. Further study is planned to evaluate the effectiveness of asthma management program on asthma severity and hospitalisation. (MD95262)

The Role of High Resolution Computed Tomography in Tuberculosis in Children

✍ 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

□ 1 June 1996

❖ CUHK Departmental Funding

Tuberculosis is a prevalent disease affecting up to one third of the world's population. It is also prevalent in children with 1.3 million new cases and 450,000 death per year in developing countries. The diagnosis of tuberculosis in children pose many problems. Emphasis has been placed on chest radiographic features along with clinical presentation, contact screening, and tuberculosis skin test. However, chest radiography can be normal in positive cases and minor changes such as lymphadenopathy can be missed. High resolution computed tomography (HRCT) scan of the lungs in adult showed typical parenchymal changes in up to 95% of cases. No study has yet assessed the HRCT features of childhood tuberculosis. A prospective case control study has been conducted from June 96 of which 25 children with tuberculosis have been recruited. 20 patients manifested changes consistent with tuberculosis on HRCT scan in compare to 12 patients on CXR ($p < 0.012$). The most common abnormality is lymphadenopathy and is commonly seen in the hilar and paratracheal regions. Parenchymal changes were detected in 15 patients on HRCT scan. The typical adult parenchymal changes were only seen in 5 cases. Follow up scans at 6 months showed an improvement in both lymphadenopathy and parenchymal changes. The researchers conclude that HRCT scan has a better diagnostic yield than CXR in childhood tuberculosis.

Further study is planned to compare HRCT scan with conventional CT. (MD95263)

Nutritional Status of Chinese Vegetarians

✍ LEUNG Suk Fong Sophie ● LEE Shiu Hung (Community & Family Medicine) ● HJELM Nils Magnus (Chemical Pathology) ● CHENG Chun Yiu Jack (Orthopaedics & Traumatology)

□ 1 December 1995

❖ CUHK Research Committee Funding

Dietary practices varies between the East and the West. Even vegetarian foods are different in different cultures. Although studies have shown that the Western vegetarians are prone to have nutritional deficiencies the issue was unclear in the local Chinese. A study was performed in families who have been practicing vegetarian for more than a year. 52 children, 4-13 years and 69 adults 25-60 years were examined for dietary intake over a week, body fatness, iron status, serum lipids and bone mineral content (BMC).

Main results are as follows:

- (1) Only four individuals (adults) were diagnosed to have iron deficiency anaemia.
- (2) Nine individuals (2 children and 7 adults) were diagnosed to have iron deficiency but not anaemia.
- (3) Obesity is diagnosed in 12 children and 17 adults.
- (4) BMC of all individuals were similar to the omnivores.
- (5) Mean serum total cholesterol was 4.78 ± 0.78 mmol/L for men and 4.42 ± 0.71 mmol/L for women, slightly lower than the omnivores
6. Serum linoleic acid level was $38.13 \pm 2.87\%$ in male and $38.22 \pm 4.51\%$ in women, significantly higher than those of omnivores: $29.71 \pm 5.89\%$ in male and $29.36 \pm 8.59\%$ in female.

In conclusion, local Chinese vegetarians were generally healthy. Special attention should be addressed to the awareness of iron deficiency. Control of obesity is also important to reduce coronary risk. (MD96080)

Serum Fatty Acids in Chinese Adults

✍ LEUNG Suk Fong Sophie ● CHEN Zhen Yu (Biochemistry) ● HO Chan Suzanne (Community & Family Medicine) ● WOO Jean (Medicine) ● JANUS E.D.*

□ 1 January 1996

❖ CUHK Departmental Funding

Purpose: It is now recognized that different fatty acids have different effects on serum cholesterol level.

To measure serum fatty acids is much more accurate than to check the dietary fatty acids. This is the first study in Chinese to examine the fatty acid profile of adults in relation to serum lipids.

Methods: 163 normal subjects, aged 20-60, were studied. Blood was taken after an overnight fast for the measurement of serum individual fatty acids and total cholesterol (TC), triglycerides (TG) and high density lipoprotein cholesterol (HDL-C). Dietary intake over 7 days was assessed using a food frequency questionnaire and nutrients were calculated according to values obtained from food tables.

Results: The mean serum total cholesterol level of this population was 5.00 ± 0.97 mmol/L. Dietary fat contributed $29.56 \pm 5.57\%$ of total daily energy intake with a P/S ratio of 0.90 ± 0.29 . Serum saturated fatty acids (C14 & C16), and serum monounsaturated fatty acids demonstrated significant positive correlations with TG and negative correlation with HDL-C, while serum polyunsaturated fatty acid, particularly n-6 showed a reverse correlations, i.e. negatively with TG and positively with HDL-C, with values in the range of 0.2-0.4 and $p < 0.05$. Compared to the Americans, Chinese adults of above 50 years still has significantly lower total cholesterol level: 5.59 mmol/L versus 6.77 mmol/L and also significantly lower serum C14:0, and C16:0. Myristic acid (C14:0) is found mainly in milk fat and coconut oil, while palmitic acid (C16:0) is found mainly in palm oil and meat fat.

Conclusion: To combat the rising prevalence of coronary heart disease in Hong Kong, health education in modifying dietary fat is essential and should aim to prevent further increase in myristic and palmitic acid intake.

(MD96163)

Differentiation and Expansion of Antigen Presenting Dendritic Cells from Hematopoietic Stem Cells

✉ LI Karen Kwai Har ● LAW Ping*

☐ 1 November 1996

❖ CUHK Mainline Research Scheme

Dendritic cells (DC) are the most potent antigen presenting cells involved in primary immune responses, including those against malignancy. In both animal and human studies, DC have been prepulsed with tumour antigens and then used as a vehicle for the induction of cytotoxic T cell activities against these antigens. DC are bone marrow-derived leukocytes and are present in the peripheral blood at low concentrations (1-2%). The application of this 'nature's adjuvant' for vaccination against cancer cells is made possible by the recent identification of cytokines which expand DC *ex vivo*.

The long term goal of this collaboration is to establish immunotherapy programs targeting on some common malignancies of the Chinese population.

The immediate objectives are to establish the *ex vivo* expansion of DC from cord blood, peripheral blood and bone marrow using cytokine combinations. DC are a heterogeneous population consisting of cells at various stages of the differentiation pathway. It is important to obtain pure populations of DC effective for antigen processing and presentation. To avoid the production of cells of multiple lineages, the researchers would test the feasibility of starting the expansion from a committed progenitor rather than the pluripotent stem cells. The efficiency of T cell activation by subsets of immature DC from the expansion procedure will also be studied. It is anticipated that the technique of stem cell sorting and characterization of DC can be acquired in the Stem Cell Laboratories of The University of California, San Diego. Once established, the study would be run parallel in the two collaborative laboratories. (MD96124)

Assessment and Monitoring of Poverty Focused Assistance

✉ NELSON Edmund A. S. ● YU Ly Mee (Centre for Clinical Trials & Epidemiological Research)

☐ 1 January 1996

❖ CUHK Departmental Funding

Official Development Assistance (ODA), is defined as concessional aid (more than 25% grant element) provided by the official sector (i.e. governments) to promote economic development and welfare in developing countries. Although it might be assumed that the neediest people in the poorest countries are the main recipients of ODA, this is not the case. The United Nation's target of 0.7% of GNP to be allocated for ODA is seldom reached, with most rich countries giving less than 0.3%. The researchers have previously analysed British Development Aid for the 5 year period 88/89-92/93 and shown that the median percentage of bilateral aid allocated to the social development sectors of education and health was 8% and 5% respectively. Only 38% of bilateral British ODA was directed to the world's Least Developed Countries. The researchers defined a sub-category of ODA called Poverty focused assistance (PFA) which is concessional aid (100% grant element) that is provided by the official sector and spent within the world's Least Developed Countries to promote social development. They have estimated that in terms of bilateral ODA, approximately 0.008% of British GNP would be defined as PFA. The researchers now plan to repeat the analysis for the 3 year period 93/94-95/96 with data provided by the British Department of International Development. (MD96158)

Pituitary Response in VLBW Infants After Dexamethasone Treatment for Chronic Lung Disease

✉ NG Pak Cheung ● LAM Wai Kei Christopher (Chemical Pathology) ● WONG Wing Kin Gary ● FOK Tai Fai

☐ 1 October 1994

❖ CUHK Research Committee Funding

High dose dexamethasone is increasingly used for the treatment of bronchopulmonary dysplasia (BPD) in preterm very low birthweight (VLBW) infants to facilitate weaning from mechanical ventilation. In recent years, its use has become more liberal and there is now a tendency to prescribe the drug even earlier and for lessening the severity of respiratory distress syndrome. The researchers have previously investigated the adrenal response in preterm infants using the short tetracosactrin (synacthen) stimulation test before and after a 3 week course of dexamethasone, and showed that the adrenal glands were suppressed at the end of steroid treatment. Although moderate recovery was noted 4 weeks after stopping therapy, a proportion of infants continued to have low basal cortisol concentrations indicating possibly prolonged suppression of the hypothalamic-pituitary centers. In a recent study, the researchers have also shown that the human corticotropin releasing hormone stimulation test is safe, reproducible, and capable of producing a consistent pituitary-adrenal response in preterm VLBW infants similar to those seen in older children and adults. As no systematic evaluation of pituitary-adrenal reserve has been performed with the hCRH stimulation test in this group of preterm infants before and after corticosteroid treatment for assessing the magnitude of dexamethasone-induced pituitary-adrenal suppression and recovery, this study was undertaken to prospectively evaluate a cohort of VLBW infants at risk of hypothalamic-pituitary-adrenal axis suppression after receiving high dose dexamethasone for BPD. (MD94175)

Effect of Blood Transfusion on Left Ventricular Output in Premature Babies with Anaemia

✉ SUNG Yn Tz Rita ● YU Chung Wah ● FOK Tai Fai

☐ 15 April 1996

❖ CUHK Departmental Funding

Anaemia is common in premature babies in the neonatal intensive care unit. It may lead to cellular hypoxia and activate compensatory mechanisms such as an increase in cardiac output to maintain an adequate oxygen gradient. However, the adverse effect of anaemia on circulation in premature babies

has not been thoroughly evaluated and there is no universally accepted definition of anaemia or criteria for transfusion in these infants.

The aim of this study was to investigate the acute effects of red blood cell transfusion on the haemodynamics of anaemic preterm infants in the neonatal ICU. Cardiac output and left ventricular systolic function were measured by echocardiogram before and after transfusion. The researchers hope this may help to address the issue of whether and when a red blood cell transfusion is necessary in a premature baby with anaemia.

(MD96160)

Ambulatory Blood Pressure in Normal Chinese Children and Adolescents

✉ SUNG Yn Tz Rita ● YU Chung Wah

☐ 1 June 1996

❖ CUHK Departmental Funding

In this study children's blood pressure will be measured repetitively during a 24 hour period using a portable, non-invasive blood pressure recorder. It is known that ambulatory blood pressure monitoring (ABPM) is superior to casual BP measurements in predicting target organ involvement in patients with hypertension (White) and ABPM has been used more and more often in the diagnosis and management of hypertension in adults. This method of continuous monitoring of blood pressure however has not been adopted and evaluated in Chinese children. The researchers hope to establish normal reference values of ambulatory blood pressure in Chinese adolescents through this study.

(MD96162)

Cytomegalovirus and Chlamydia Pneumonia in Infants: Incidence and New Diagnostic Methods

✉ SUNG Yn Tz Rita ● IP Margaret (Microbiology) ● CHAN Kay Sheung Paul (Microbiology)

☐ 1 December 1996

❖ CUHK Research Committee Funding

About 13% of the seven to eight thousand patients admitted annually to the paediatric wards of the Prince of Wales Hospital are suffering from pneumonia. 23% of the patients are infants under one year old. Bacterial pathogens are isolated from less than 20% of these patients, the remainder are presumed to be caused by non-bacterial agents such as viruses, mycoplasma, and chlamydia. With the improvement of antibiotics and some antiviral agents, definitive aetiological diagnosis is a prerequisite for the proper management of severe pneumonia.

The researchers have already confirmed that respiratory syncytial virus (RSV) is the most common non-bacterial cause of pneumonia in infants in Hong

Kong, adenovirus, influenza and parainfluenza are other common causes. Pneumonia caused by Chlamydia trachomatis, cytomegalovirus (CMV) and coxsackie B virus however has not been extensively studied and their incidence is uncertain in Hong Kong. The objective of this study is to pursue in greater depth on the detection of Chlamydia and CMV in infants with pneumonia. They plan to use standard viral culture, serological test, immunofluorescence test and PCR/DNA method to detect these organisms in blood, nasopharyngeal aspirate/swab, urine and stool of 100 infants under one year of age admitted because of pneumonia and 100 age matched controls admitted for non-respiratory causes over a period of 1 year. The goal of this prospective study is to gain more insight into the aetiology of pneumonia, in particular, the incidence of pneumonia due to CMV and Chlamydia trachomatis. To set up reliable and practical diagnostic methods of CMV and chlamydia. (MD96081)

Effect of Blood Transfusion on Oxygen Consumption in Premature Babies with Anaemia

✍ SUNG Yn Tz Rita ● YU Chung Wah ● FOK Tai Fai

☐ 1 February 1997

❖ CUHK Departmental Funding

Anaemia is common in premature babies and may cause signs and symptoms attributable to tissue hypoxia. Transfusion may be required to improve the oxygen supply in these babies.

Data are scanty in demonstrating the transfusion effect on oxygen consumption in anaemic infants. In the present study, the researchers compare the oxygen consumption in anaemic premature babies before and after blood transfusion, by using a Deltatic II metabolic monitor.

(MD96161)

Circulating Haematopoietic Progenitor Cells in Infants

✍ YUEN Man Pan Patrick ● FOK Tai Fai ● LI Karen Kwai Har ● LI Chi Kong

☐ 1 October 1996

❖ CUHK Research Committee Funding

Cord blood has recently been identified as an alternative source of stem cells for transplantation. It contains high levels of primitive, pluripotent stem cells and has been reported to tolerate multiple HLA mismatches during transplantation. However, there are intrinsic disadvantages associated with cord blood collection. These include the small and variable volume which has limited the suitability only to recipients with low body weight. Microbial contamination also occurs more frequently in cord

blood collections when compared to those of bone marrow or peripheral blood stem cells.

This project aims to tackle the problem by investigating into the possibility of a supplementary collection of neonatal blood through exchange transfusion from donors whose siblings are awaiting transplantation. Neonatal blood stem cells decline drastically within hours after birth. The suitability of neonatal blood for transplantation will be studied using engraftment markers in terms of the levels of pluripotent stem cells, early progenitors and the clonogenicity. To investigate the mechanism of the rapid decline of stem cells in the neonate, the kinetics of 'homing molecules' expressed on the surface of stem cells will be assessed. If proved to be suitable, neonatal blood collection may increase the chance of engraftment in situations where the cord blood volume is small or contaminated. It would also benefit the recipient who is of a large body weight and cannot wait for the normal collection of bone marrow or peripheral stem cells from the baby sibling. Neonatal blood may be an additional source of stem cells which has never been suggested before.

(MD96079)

The Correlation between Graft-versus-Host Disease and Cytokine Profiles in Bone Marrow and Peripheral Blood Stem Cell Transplantation

✍ YUEN Man Pan Patrick ● CHENG Shuk Han (Orthopaedics & Traumatology) ● PONG Nga Hin Henry

☐ 1 January 1997

❖ Research Grants Council

In this project, the researchers intend to study the cytokine profiles of patients following BMT or peripheral blood stem cell transplantation (PBST) and correlate their observations with the clinical outcome. They will trace cytokine secretions at three different angles in order to put together a picture of how the activation of Th1 and Th2 cells respectively can result in different forms of GvHD. They will measure secreted cytokines in the serum by enzyme linked immunoassay (ELISA). The researchers will also study cytokine gene expression in peripheral blood mononuclear cells (PBMC) by reverse transcribing the mRNA and amplifying them by polymerase chain reaction. They will study cytokine levels in the cytoplasm of different subsets of PBMC by dual fluorescence cytometry. The activation of Th1 cells can be indicated by an increase in the levels of IFN- γ , IL-2 and IL-12, while the involvement of Th2 cells result in elevated levels of IL-3, IL-5 and IL-10. Findings of this project will explain the roles of Th1 and Th2 cells in the initiation and propagation of GvHD. They are also interested in establishing an assay system with which they can predict whether GvHD will occur or not. They will set up an *in vitro* model, using mixed lymphocyte cultures (MLC), to

study the production of cytokines when mature donor PBMC are presented with the host alloantigens. Preliminary data from other investigators suggests that his model can be used to predict the occurrence and the severity of GvHD (4,5). With the database collected from this project, they will find out whether they can anticipate GvHD by looking at cytokine secretions from the patient following bone marrow or stem cells transplant.

The project objectives and long-term significance:

(1) The correlation between the cytokine profiles and graft-versus-host-disease (GvHD) development in Paediatric patients undergoing bone marrow or peripheral blood stem cell transplants.

(2) The roles of different subsets of T helper cells, Th1 and Th2, in the initiation and development of GvHD in transplant patients.

(3) The predictive value of measuring cytokine induction in mixed lymphocyte cultures (MLC) in the occurrence and severity GvHD.

(CU96663)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition	Title/Investigators
1995-96	Study of Minimal Residual Disease in Childhood Acute Lymphoblastic Leukaemia by Polymerase Chain Reaction Detection of Rearranged T Cell Receptors δ and γ (MD95250) ✉ CHIK Ki Wai
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) ✉ FOK Tai Fai ● HJELM Nils Magnus (Chemical Pathology)
1995-96	<i>Ex Vivo</i> Expansion of Cord Blood Stem Cells (MD95160) ✉ LI Karen Kwai Har ● TSANG Kam Sze Kent* (Anatomical & Cellular

	Pathology) ● WONG Yuen Kwan Annie ● YUEN Man Pan Patrick
1995-96	International Child Care Practice Study (MD95024) ✉ NELSON Edmund A. S.
1995-96	Effects of Qinghaosu (Artemisinin) on Malarial Growth in Thalassaemic Trait Erythrocytes (MD95205) ✉ NELSON Edmund A. S. ● SENOK Abiola ● LI Karen Kwai Har
1995-96	The Diagnostic Value of IL-1 β , IL-6, TNF- α , E-selection and CRP in Early Detection of Neonatal Infection (MD95161) ✉ NG Pak Cheung ● CHENG Shuk Han (Orthopaedics & Traumatology) ● FOK Tai Fai ● WONG William Lok Chuen ● CHEUNG Kam Lau ● YUEN Man Pan Patrick
1994-95	The Molecular Abnormalities and Their Relationship to the Expression of Organ-Specific Autoimmunity in Chinese Children with Diabetes Mellitus (MD95004) ✉ WONG Wing Kin Gary ● CHENG Shuk Han (Orthopaedics & Traumatology)
1995-96	The Epidemiology of Childhood Diabetes in Hong Kong (MD90205) ✉ WONG Wing Kin Gary ● LEUNG Suk Fong Sophie ● OPPENHEIMER Stephen James
1995-96	Detection of Genetic Mutation(s) in a Family with Hereditary Blood Coagulation Factor XII Deficiency (MD95153) ✉ YUEN Man Pan Patrick ● CHENG Shuk Han (Orthopaedics & Traumatology)
1995-96	Iron Supplementation in Transfused Preterm Infants (MD95134) ✉ YUEN Man Pan Patrick ● FOK Tai Fai ● NG Heung Ling Margaret (Anatomical & Cellular Pathology) ● LAM Wai Kei Christopher (Chemical Pathology)

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RESEARCH PROJECTS

Characterisation of Prostacyclin Receptors in Cardiovascular and Neuronal Tissues Using Novel Antagonists

- ✉ JONES Robert Leslie ● WISE Helen
- ☐ 1 January 1997
- ❖ Roche Bioscience, CA, USA

The project involves the characterisation of prostacyclin receptors (IP-receptors) using novel receptor antagonists synthesized by Roche Bioscience, U.S.A. The potencies of the antagonists will be estimated against both stable prostacyclin agonists (cicaprost, carbacyclin) and non-prostanoid prostacyclin receptor mimetics (BMY 45778) on platelet and vascular smooth muscle preparations from man and rat.

The ability of the antagonists to block the neuronal stimulant actions of cicaprost will also be investigated. These experiments may allow the identification of IP-receptor subtypes and point to further studies to elucidate the physiological and pathophysiological roles of prostacyclin. (BL96029)

Neuronal Stimulant Actions of Prostacyclin Mimetics on the Rat Vagus Nerve

- ✉ JONES Robert Leslie ● RUDD John A.
- ☐ 1 January 1997
- ❖ CUHK Research Committee Funding

Currently there is much interest in the neuronal stimulant actions of prostacyclin and the possibility that neuronal prostacyclin (IP-) receptors are different from the classical IP-receptors present in platelets and blood vessels. The aim of the project is to characterise the IP-receptor(s) mediating the neuronal stimulant action of prostacyclin on the rat isolated vagus nerve preparation; this is a robust electrophysiological preparation suitable for the lengthy experiments envisaged. A range of prostacyclin analogues (iloprost, taprostene) will be investigated and cicaprost will be used as the standard agonist. Several non-prostanoid prostacyclin mimetics will also be used, since on other prostacyclin-sensitive neuronal preparations they either show little agonist activity (octimibate, CU 23) or induce a slowly developing block of cicaprost action (BMY 45778). The nature of the depolarising action of cicaprost will be investigated using agents that specifically block K^+ -channels in the axonal membrane. In addition the interaction of cicaprost with 5-HT, which depolarises the vagus nerve preparation via activation of 5-HT₃-receptors, will be investigated. The results obtained will

hopefully throw light on the functions of IP-receptors in the peripheral and central nervous systems. (MD96091)

Evaluation of Anti-inflammatory Agents in Animal Models of Arthritis

- ✉ LAM Fu Yuen
- ☐ 10 January 1997
- ❖ CUHK Research Committee Funding

The number of possible mediators in inflammatory joint diseases is vast. Conventional drug therapy for inflammatory diseases normally employs either glucocorticoids or non-steroidal anti-inflammatory drugs (NSAIDs) for their modulatory effects on cells and mediators involved in the inflammatory processes. These treatments can only provide partial relief for patients as the drugs are effective in inhibiting only some of the inflammatory mediators involved.

An important group of inflammatory mediators that have been neglected in current anti-arthritis therapy are the neuropeptides that originate from nerves innervating the joint. In this proposed study, the mechanisms of neuropeptide-induced inflammation in normal and chronically-inflamed rat knee joints are to be elucidated. Furthermore, the effectiveness of a variety of some novel and some standard anti-inflammatory agents in arresting neuropeptide-induced inflammation will be tested separately and also in combinations with neuropeptide antagonists to assess for their therapeutic potentials in the treatment of inflammatory joint diseases. (MD96088)

Prostanoid Receptors on Mast Cells

- ✉ LAU Hang Yung Alaster ● JONES Robert Leslie
- ☐ 16 September 1996
- ❖ Research Grants Council

The prostanoids are important modulators of inflammation whereas the mast cells are pivotal in the initiation of the inflammatory process. However, the interaction of these two important elements in the pathogenesis of inflammation has never been carefully and systematically investigated. The main objective of the present proposal is to systematically characterise the prostanoid receptors present on rat peritoneal mast cells. This project will provide important information for defining the roles of the various prostanoids in the initiation of inflammation in terms of their actions on the activation of mast cells. This information is useful for the future design of more specific prophylactic drugs for the treatment of allergy.

The key areas of investigation include:

- (1) The effects of prostanoids and their synthetic agonists on the spontaneous release of histamine from mast cells.
 - (2) The effects of the prostanoids and their synthetic agonists on immunologically and non-immunologically activated mast cells.
 - (3) Comparative studies on the effects of prostanoids on rat peritoneal mast cells.
 - (4) The characterization of the prostanoid receptor subtypes by (a) comparing the rank order of potency of the various prostanoids and (b) studying the effects of specific prostanoid antagonists on the activities of the prostanoids.
 - (5) The identification of the underlying biochemical mechanisms of actions following mast cell prostanoid receptor activation by measuring the intracellular second messengers: calcium, cyclic 3',5'-adenosine monophosphate (cAMP) and inositol trisphosphate (IP₃).
- (CU96627)

Effects of Nitric Oxide on Mast Cells: Heterogeneity between Two Strains of Rats

- ✉ LAU Hang Yung Alaster ● JAMES Anthony (Animal House)
- ☐ 1 January 1997
- ❖ CUHK Research Committee Funding

Mast cells are pivotal in the pathogenesis of allergic diseases. Myriads of mediators are released from activated mast cells to modulate the inflammatory reactions associated with allergic responses. It is hence essential to control the activation of mast cells in the clinical management of allergic reactions. Recent studies on rat peritoneal mast cells have suggested that both exogenous and endogenous nitric oxide may regulate mast cell mediator release. However, contradictory results have been observed by the researchers and other investigators. When further investigating into the discrepancy, the researchers have noticed that it may be due to the use of different strains of rats for investigations. Mast cell heterogeneity in terms of anatomical locations and species have been widely studied but information on inter-strain heterogeneity is extremely scarce. Hence the primary aims of this project to investigate if the current discrepancy among the literatures on nitric oxide and mast cells is due to inter-strain mast cell heterogeneity. The results obtained will also be important for identifying the proper rat mast cell model for the further studies on the interaction of mast cells and nitric oxide.

(MD96089)

Investigation of the Anti-emetic Potential of ZK200.775 in a Ferret Model of Emesis

- ✉ RUDD John A.
- ☐ 10 February 1997

❖ Schering AG

Chemotherapy-induced emesis in man can be divided into 'acute' and 'delayed' phases based on the temporal distribution of the events and the pharmacological characteristics of the responses. Good control of acute emesis can be made by the use of 5-HT₃ receptor antagonists in combination with corticosteroids. Unfortunately, however, the treatment of the emesis that occurs on subsequent days is not satisfactorily controlled. The present studies use a ferret model of chemotherapy-induced emesis to investigate the mechanisms that may be activated during the delayed phase. The studies should hopefully lead to the introduction of new anti-emetic drugs that could be used to improve the care of the cancer patient.

(MD96132)

Detection of Enzyme Induction During Anti-tuberculosis Therapy by a Novel Monoclonal Anti-6β-hydroxycortisol Antibody-based ELISA Method

- ✉ YEUNG Hok Keung John ● LAI Kei Wai Christopher (Medicine) ● TAI Kwok Ping*
- ☐ 1 October 1996
- ❖ CUHK Research Committee Funding

The objectives of this study are to validate the application of a novel monoclonal antibody-based ELISA in measuring enzyme induction in patients undergoing anti-tuberculosis treatment and to follow the activity of CYP3A4 prior to, during and after drug treatment. Urinary 6β-hydroxycortisol is measured by the monoclonal antibody-based ELISA developed in our laboratory. The study should provide information on the inducibility of CYP3A4 in Chinese patients given multiple drug treatment.

(MD96090)

Pharmacogenetics of Trimethylamine N-oxidation in Chinese, and Associated Studies on Regulation of the Flavin-containing Monooxygenase in Animals

- ✉ YEUNG Hok Keung John ● DAMANI Lyaquatali A. (Pharmacy) ● LIN Ge
- ☐ 1 January 1997
- ❖ CUHK Research Committee Funding

Trimethylamine (TMA) is a strongly basic simple tertiary aliphatic amine. TMA is a normal constituent of human urine and is derived mainly from common dietary components such as choline and carnitine. TMA undergoes extensive *N*-oxidation *in vivo* to form the polar metabolite trimethylamine *N*-oxide (TMAO) and this reaction is mediated by the flavin-containing monooxygenase (FMO). The ratio of

trimethylamine / trimethylamine *N*-oxide (TMA / TMAO) in human urine has been used successfully to probe into the genetic condition trimethylaminurea or fish odour syndrome. *N*-Oxidation of TMA is genetically determined, and exhibits polymorphism in a white Caucasian population. The ability to *N*-oxidise TMA derived from normal dietary sources was found to be skewed in terms of its population distribution when investigated in 169 British white individuals. The major aim of the present proposal is to determine whether this genetic defect (trimethylaminurea) occurs in Chinese, and to estimate its frequency. This study *does not* involve dosing volunteers or patients with any drug - it merely involves collection of 24 hr urine samples for TMA/TMAO analysis, and completion of questionnaire by volunteer/patient. The effect of certain diseases or drug treatment regimens on the urinary excretion of TMA/TMAO will also be examined.
(MD96115)

1995-96 Neuropeptide Induced Mediator Release from Mast Cells: Effects of Non-Peptide Antagonists of Neurokinins (MD95170)
✍ LAU Hang Yung Alaster ● LAM Fu Yuen ● PEARCE Frederick Lawrence*

1995-96 Neuropeptide Induced Mediator Release from Mast Cells: Effects of Non-peptide Antagonists of Neurokinins (MD95114)
✍ LAU Hang Yung Alaster ● PEARCE Frederick Lawrence*

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*

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition Title/Investigators

1995-96 Synthesis and Testing of Potential Prostacyclin Receptor Antagonists (CU92311)
✍ JONES Robert Leslie ● WONG Nai Ching Henry (Chemistry) ● WISE Helen

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*

1995-96 Characterisation of Neuropeptide Actions in Coronary Blood Vessels of the Guinea-Pig (MD95137)
✍ 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 Study on the Structure-Activity Relationship of the Potent α_1 -adrenoceptor Antagonist, Diccitrine and Its Structurally Related Analogues on Rat Isolated Aorta (MD95139)
✍ LIN Ge ● KWAN Yiu Wa

1994-95 Development of Models of Acute and Delayed Emesis to Cisplatin in the Ferret (MD95040)
✍ RUDD John A.

1995-96 Neuropharmacological Investigations into the Role of Neurokinin Receptors in the Control of Emesis in the Suncus Murinus (MD95138)
✍ RUDD John A.

1995-96 Stimulus-response Coupling in Human Neutrophils; the Role of Prostaglandins (CU93602)
✍ WISE Helen ● JONES Robert Leslie

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*

1995-96 Development of an Enzyme-linked Immunosorbent Assay (ELISA) Using a Novel Monoclonal Antibody against 6 β -hydroxycortisol to Detect Enzyme Induction in Man (CU93613)
✍ YEUNG Hok Keung John

RESEARCH OUTPUTS AND PUBLICATIONS

- <P961709> **Lin, G.; Ivo P. Nnane and Lyaquatali A. Damani.** "Protective Effects of Glycyrrhizin and Glycyrrhetic Acid on Retrorsine-Induced Hepatotoxicity in Rats". *Journal of the 4th Military Medical University* vol.17 no.5, abstract no.008. Xian, China, 1996.09.01.
- <P961710> **Lau, H.Y.A.** "Frusemide: More Than a Diuretic". *Journal of the 4th Military Medical University* vol.17 no.5, abstract no.003. Xian, China, 1996.09.01.
- <P961711> **Rudd, J.A.; C.H.K. Cheng; R.J. Naylor; M.P. Ngan and M.K. Wai.** "Potential of Fentanyl to Act as a 'Broad Spectrum' Anti-Emetic Drug". *Journal of the 4th Military Medical University* vol.17 no.5, abstract no.012. Xian, China, 1996.09.01.
- <P961712> **Rudd, J.A.; C.C. Jordan and R.J. Naylor.** "The Action of the NK₁ Tachykinin Receptor Antagonist, CP99,994, in Antagonizing the Acute and Delayed Emesis Induced by Cisplatin in the Ferret". *British Journal of Pharmacology* vol.119, pp.931-936. UK, 1996.
- <P961723> **Nnane, Ivo P.; Ge Lin and Lyaquatali A. Damani.** "The Protective Effects of Glycyrrhizin Against Retrorsine-Induced Hepatotoxicity in Rats". *Proceedings of the 7th North American ISSX Meeting* vol.10, p.73. California, USA, 1996.10.20.
- <P961724> **Nnane, Ivo P.; Lyaquatali A. Damani; G. Lin and P.K. Kadaba.** "Metabolic and Pharmacokinetic Studies of a Novel Anticonvulsant, 2-(4-Chlorophenyl)Amino-2-(4-Pyridyl) Ethane in Rats". *Pharmaceutical Research* vol.13 no.9, p.S-508. USA, 1996.10.01.
- <P961745> **Lam, F.Y. and M.C.S. Wong.** "Characterization of Tachykinin Receptors Mediating Plasma Extravasation and Vasodilatation in Normal and Acutely Inflamed Knee Joints of the Rat". *British Journal of Pharmacology* vol.118, pp.2107-2114. UK, 1996.
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- <P961854> **Xie, Zhi-Hui and Helen Wise.** "Microscopic Examination of the Prostaglandin E₂-Stimulated Aggregation Response in HL-60 Cells". *Prostaglandins Leukotrienes and Essential Fatty Acids* vol.55 Supplement 1, p.91. UK, 1996.09.01.
- <P961855> **Wise, H. and B.S. Chow.** "Characteristics of Prostacyclin Receptors in Neuronal Cells". *Journal of the 4th Military Medical University* vol.17, p.4. Xian, China, 1996.09.01.
- <P961856> **Wise, Helen and Kevin B.S. Chow.** "Effect of Non-Prostanoid Prostacyclin Mimetics on Cyclic AMP Production by Neuronal SK-N-SH Cells". *Prostaglandins Leukotrienes and Essential Fatty Acids* vol.55 Supplement 1, p.35. UK, 1996.09.01.
- <P961883> **Jones, R.L.; Y.M. Qian; H. Wise; H.N.C. Wong; H.W. Chan; W.W.L. Lam; J.K.S. Ho and A.P.C. Yim.** "Relaxant Actions of Prostanoid and Non-Prostanoid Ip-Receptor Agonists on the Human Pulmonary Artery". *British Journal of Pharmacology (Proceedings Supplement)* vol.119, p.193P. England, 1996.
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- <P962284> **Wise, Helen.** "The Inhibitory Effect of Prostaglandin E₂ on Rat Neutrophil Aggregation". *Journal of Leukocyte Biology* vol.60, pp.480-486. USA, 1996.10.
- <P962285> **Qi, Ai-dong and Yiu Wa Kwan.** "Modulation by Extracellular ATP of L-Type Calcium Channels in Guinea-Pig Single Sinoatrial Nodal Cell". *British Journal of Pharmacology* vol.119, pp.1454-1462. UK, 1996.

- <P962286> **Lin, G.; G. McKay and K.K. Midha.** "Characterization of Metabolites of Clozapine N-Oxide in the Rat by Micro-Column High Performance Liquid Chromatography/Mass Spectrometry with Electrospray Interface". *Journal of Pharmaceutical and Biomedical Analysis* vol.14, pp.1561-1577. UK, 1996.
- <P962287> **Lin, G.; M.C. Tsai; M. Mitterhauser; I.P. Nnane; L.A Damani and I. Zolle.** "Pharmacokinetics of 2-Bromo- and 2-Methoxy-Phenylmetyrapones in Rats". *Proceedings of the 8th Southeast Asian Drug Metabolism Workshop* p.P-03. Indonesia: Centre for Clinical Pharmacology and Drug Policy Studies, Gadjah Mada University, 1996.11.18.
- <P962347> **Ding, Kan; Ge Lin; Yee-Ping Ho; Tin Y. Cheng and Ping Li.** "Prederivatization and High-Performance Liquid Chromatographic Analysis of Alkaloids of Bulbs of *Fritillaria*". *Journal of Pharmaceutical Sciences* vol.85 no.11, pp.1174-1179. USA, 1996.11.
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- <P962558> **Jones, Robert L. and Y.M. Qian.** "Actions of Prostanoids on Human Pulmonary Blood Vessels". *Journal of the 4th Military Medical University* vol.17 no.5, Abstract no.011. Xian, China, 1996.09.
- <P962712> **Stenton, G.R. and H.Y.A. Lau.** "Inhibition of Rat Peritoneal Mast Cell Exocytosis by Frusemide: A Study with Different Secretagogues". *Inflammation Research* vol.45, pp.508-512. Basel, Switzerland, 1996.
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- <P962728> **Jones, R.L.; Y.-M. Qian and J.K.S. Ho.** "Relaxation of Human Intrapulmonary Arteries by the Non-Prostanoid Prostacyclin Mimetic BMY 45778". *Proceedings of the 7th Southeast Asian/Western Pacific Regional Meeting of Pharmacologists* pp.533-534. Manila: Philippine Society of Experimental & Clinical Pharmacology, 1996.
- <P963713> **Rudd, J.A.; Cheng, C.H.K.; Naylor, R.J.; Ngan, M.P. and Wai, M.K.** "Role of Fentanyl to Act as a 'Broad Spectrum' Anti-Emetic Drug". (CD-ROM) Presented in the 3rd Internet World Congress on Biomedical Sciences, organized by Riken Gene Bank & Internet Association for Biomedical Sciences. Japan, 1996.12.09.
- <P970208> **Yeung, J.H.K.; J.K.L. Wong and B.K. Park.** "Development of a Screening Method for Anti-6 α -Hydroxycortisol Antibody Using an Enzyme-Linked Immunosorbent Assay (ELISA) and Its Applications". *Methods & Findings in Experimental and Clinical Pharmacology* vol.19 no.2, pp.79-86. Spain, 1997.
- <P970366> **Rudd, John A. and Robert J. Naylor.** "The Actions of Ondansetron and Dexamethasone to Antagonise Cisplatin-Induced Emesis in the Ferret". *European Journal of Pharmacology* vol.322, pp.79-82. UK, 1997.
- <P970367> **Rudd, J.A.; Ngan, M.P. and Wai, M.K.** "Enantioselective Inhibition of Emesis in *Suncus Murinus* by CP-99,994 Is Likely to Be Mediated Centrally". *Proceedings of the 7th Annual Meeting of the European Neuropeptide Club* p.R5. Marburg, Germany, 1997.05.21.
- <P970428> **Lam, F.Y.** "Specific Tachykinin Receptors Mediate Substance P-Induced Coronary Vasodilatation in Guinea-Pigs". *Proceedings of the 7th Annual Meeting of the European Neuropeptide Club* p.L1. Marburg, Germany, 1997.05.21.

- <P970529> **Chan, C.L. and H.Y.A. Lau.** "Effects of Prostanoids on Immunologically Activated Rat Mast Cells". *Abstracts of the 26th Annual Meeting of the European Histamine Reserach Society* p.59. Spain, 1997.05.14.
- <P970554> **Jones, Robert L.; Yue-Ming Qian; Helen Wise; Henry N.C. Wong; Wai-Lun Lam; Ho-Wai Chan; Anthony P.C. Yim and Jonathan K.S. Ho.** "Relaxant Actions of Nonprostanoid Prostacyclin Mimetics on Human Pulmonary Artery". *Journal of Cardiovascular Pharmacology* vol.29, pp.525-535. USA, 1997.04.
- <P970608> **Stenton, G.R. and H.Y.A. Lau.** "Effects of Histamine Agonists and Antagonists on Rat Peritoneal Mast Cells". *Inflammation Research* vol.46 Supplement 1, pp.S15-S16. Basel, Switzerland, 1997.
- <P970609> **Lau, H.Y.A. and G.R. Stenton.** "Effects of Cyclo-Oxygenase Inhibitors on Mediator Release from Rat Peritoneal Mast Cells". *Abstracts of the 26th Annual Meeting of the European Histamine Research Society* p.81. Spain, 1997.05.14.
- <P970610> **Lau, H.Y.A. and C.M. Roche.** "Effects of Secretory Phospholipase A₂ Enzymes on Mast Cells of Rat, Guinea Pig and Human". *Inflammation Research* vol.49 Supplement 1, pp.S19-S20. Basel, Switzerland, 1997.
- <P970798> **Qi, Ai-Dong and Yiu Wa Kwan.** "Antagonism by Extracellular ATP of L-type Calcium Channel Currents Pre-Stimulated with Isoprenaline in Guinea-Pig Single Sinoatrial Nodal Cells". *Biophysical Journal: Abstracts of the 41st Annual Meeting of the Biophysical Society* vol.72, p.A371. New Orleans, USA, 1997.03.02.
- <P970799> **Qi, Ai-Dong and Yiu Wa Kwan.** "Involvement of Protein Kinase C in the Inhibition by Extracellular ATP of L-Type Calcium Channel Currents in Guinea-Pig Single Sinoatrial Nodal Cell". *Biophysical Journal: Abstracts of the 41st Annual Meeting of the Biophysical Society* vol.72, p.A-371. New Orleans, USA, 1997.03.02.
- <P971913> **Wise, H. and B.S. Chow.** "Rat Neutrophil Aggregation: The Role of Adhesion Molecules". *Asian Pacific Journal of Allergy and Immunology* vol.15, p.63. Hong Kong, 1997.02.01.

see also <P962348>, <P970255>

RESEARCH PROJECTS

Attitudes and Motivations of Pharmacy Students

- ✍ HO Suk San Susan
- ☐ 1 March 1997
- ❖ New Asia Student Campus Work Scheme, CUHK

According to 1995/96 and 1996/97 statistics, the Department of Pharmacy at The Chinese University of Hong Kong admitted students who had the highest averages among all applicants for various programmes at The Chinese University of Hong Kong. Since the pharmacy programme is relatively new (only started in 1992), it is of great interest to know why secondary school students are motivated towards pharmacy. Specifically, the researchers would like to have knowledge of the demographics, attitudes, beliefs and expectations of these students who have chosen pharmacy as their profession. A survey will be conducted on all current undergraduate pharmacy students to determine the factors that influence their choice of pharmacy as a career. A similar survey will be conducted in future years only on first year students to explore trends and changes in these factors. The results of the project will provide the researchers' department with a better understanding of the demographics and social characteristics of these students as well as their expectations of the programme and of the profession as a whole.
(MD96135)

Utilization of Antidiabetic Drugs in Hong Kong

- ✍ LEE Kwing Chin Kenneth ● CHAN Yan Keung Thomas (Clinical Pharmacology) ● CHAN W. K. Anthony*
- ☐ 1 August 1996
- ❖ CUHK Departmental Funding

Antidiabetic drug-induced hypoglycemia as a cause of acute medical admissions is more common in Hong Kong than in other countries. To determine if this higher incidence may be related to the frequent use of some sulphonylureas, in particular the long-acting agents, the researchers have studied the overall prescribing patterns in the public sector by reviewing the utilization of antidiabetic drugs in the general out-patient/general practice clinics and Hospital Authority public hospitals and affiliated specialist clinics.
(MD96195)

Antibiotic Utilization and Expenditure in a General Teaching Hospital in Hong Kong

- ✍ LEE Kwing Chin Kenneth ● CHAN Yan Keung Thomas (Clinical Pharmacology) ● LEE S. C. Benjamin*
- ☐ 1 August 1996
- ❖ CUHK Departmental Funding

Antibiotic expenditure accounts for a major share of a hospital's total drug budget. Before any cost-containment programs are possible, it is first necessary to know the antibiotic usage and composition of costs. The researchers plan to audit the use of these antibiotics in a teaching hospital. Based on such information and the published guidelines, they hope to draw up recommendations on the cost-effective use of antibiotics.
(MD96196)

A Study to Assess the Potential Danger of Poisoning in the Existing Packaging of Medicated Oils

- ✍ LEE Kwing Chin Kenneth ● CHAN Yan Keung Thomas (Clinical Pharmacology)
- ☐ 1 September 1996
- ❖ CUHK Departmental Funding

In view of the toxic potential of some medicated oils, the researchers plan to study the existing packaging of 10 commonly used preparations from Hong Kong and Singapore and identify areas for improvement with respect to the prevention of poisonings.
(MD96194)

The Screening of Traditional Chinese Medicine for Antimicrobial Activity

- ✍ LI Chi Keung Ronald ● ZHU Min
- ☐ 10 August 1996
- ❖ CUHK Departmental Funding

The use of Traditional Chinese Medicine (TCM) for the treatment of minor infections is common. However, the efficacy of these commonly used TCMs is not well studied. A screening test is performed using the agar dilution or microdilution techniques on 10-15 standard strains of aerobic bacteria to determine the antimicrobial activity of these TCMs.
(MD96186)

Molecular and Biological Characterisation of Resistance Formation in Gram Negative Clinical Isolates and Cost analysis of β -Lactam Antibiotics Commonly Used in Hong Kong

- ✍ LI Chi Keung Ronald ● CHAN Wai Chi ● LING Mei Lun Julia (Microbiology) ● CHENG Fun Bun Augustine (Microbiology)

□ 1 January 1997

❖ CUHK Research Committee Funding

Microbial resistance to antibiotics represents an enormous challenge in both the development of new antibiotics and their use in antimicrobial chemotherapy. Much evidence has suggested a casual relationship between antibiotic usage and resistance development. In this projects, the researchers will characterise the formation of resistance to β -lactam antibiotics in various standard and clinical strains of gram negative bacteria implicated in serious hospital infections, including *Enterobacter spp.*, *Pseudomonas spp.* and *Escherichia coli*. The induction potential of commonly used antibiotics will be analysed along with their antimicrobial activity and the cost associated with the use of antibiotics. It is hoped that the results will not only offer a cost-effective therapeutic justification for the use of these antibiotics, but will also help formulate a good approach to chemotherapy by selecting the antibiotics with relatively strong antimicrobial activity but a low potential to induce resistance development, thus improving the chance of eradicating the organisms while minimizing the possibility of resistance formation. The molecular basis of resistance induced by different β -lactam antibiotics will also be investigated through analysis of both the plasmid and chromosomal DNAs, as well as β -lactamase production and outer membrane permeability in the resistant strains. Information on the nature of the resistant phenotypes induced by different antibiotics should further assist in the choice of antibiotics in antimicrobial therapy.
(MD96086)

Mathematical Evaluations of Pharmacokinetic / Pharmacodynamic Estimators for Antimicrobial Chemotherapy

✍ LI Chi Keung Ronald ● RAYMOND Kenneth

□ 10 January 1997

❖ CUHK Departmental Funding

The use of pharmacokinetic / pharmacodynamic estimators to describe the efficacy of antimicrobial therapy has been extensive. However, these estimators such as AUC above MIC, time above MIC, area under the inhibitory curve (AUIC) and the peak to MIC ratio have been used to relate to the outcome measurements of antibiotic treatment. This project aims to investigate mathematically the rationale behind the application of these estimators by simulating the pharmacokinetic profiles under different levels of susceptibility. The theoretical use of these estimators will be explored.
(MD96187)

Development of an *in situ* Liver Perfusion Technique for Drug Metabolism Studies

✍ LI Chi Keung Ronald ● RAYMOND Kenneth ● ZHU Min

□ 10 January 1997

❖ CUHK Departmental Funding

The liver is the key organ in the body responsible for the elimination of many drugs. How well the liver functions can affect the elimination of these drugs which in turn modifies their dosage requirements. This project is designed to use an *in situ* liver perfusion technique to investigate drug elimination without the interference of extra-hepatic metabolism. In a pilot study, the effects of two rifamycins on the elimination of a Phase I metabolism marker will be studied.
(MD96188)

Impact of Protein Binding on the Antimicrobial Activity of Highly Protein Bound Antibiotic

✍ LI Chi Keung Ronald

□ 10 January 1997

❖ CUHK Student Campus Work Scheme

It is generally believed that free drug is the active moiety responsible for pharmacological activity for many agents. This project is conducted to evaluate the contribution of free drug to the antimicrobial effect of some highly protein bound antibiotics, i.e. β lactams. An *in vitro* culture system will be employed for this study.
(MD96189)

Influence of Metal Chelate Formation on the Efficacy of Oral and Intravenous Administration of Ciprofloxacin

✍ LI Chi Keung Ronald ● CHANG Sophie

□ 15 April 1997

❖ Bayer AG (Singapore)

Metal chelate formation is always the cause for poor oral bioavailability for the quinolone antibiotics. Antacids have been shown to significantly reduce the absorption of ciprofloxacin in the GI tract. To date, investigations have focused on physical incompatibility. However, the pharmacodynamic implications of this incompatibility have not been addressed. This study will examine the impact of metal cations on the efficacy of oral and intravenous ciprofloxacin.
(MD96185)

Assessing the Pharmacokinetics and Pharmacodynamics of Drugs with Non-linear, Input Rate-dependent Dispositions

- ✍ RAYMOND Kenneth ● LI Chi Keung Ronald
 ☐ 1 January 1997
 ❖ CUHK Research Committee Funding

Verapamil, an antianginal, antihypertensive agent with antiarrhythmic properties has a most unusual pharmacokinetic profile in that it exhibits input rate-dependent (absorption-dependent) pharmacokinetics. That is, the faster the drug is absorbed the less the activity of the drug. In addition it has stereoselective activity with the R-isomer being less active than the S-isomer. Because of this input-rate dependent pharmacokinetics it is difficult to compare the amount of drug absorbed from different formulations since a slower absorbing tablet (e.g. a sustained-release formulation) will be absorbed at a different rate and possibly in a different amount when compared to a traditional (faster absorption) conventional tablet. It has also been suggested that these absorption mechanisms also affect the ratio of the R/S isomers eventually absorbed and possibly their metabolic disposition.

The researchers have already developed sophisticated computer pharmacokinetic models which allow the simulation of blood levels following traditional (input-rate independent) dosage forms administration. The purpose of this grant request is to further expand these models to gain a better understanding of the clinical effects of drugs such as verapamil which have nonlinear and non-standard disposition profiles. (MD96087)

Study on Antiulcer Effect of *Hippophae Rhamnoides*

- ✍ ZHU Min ● SONG Jing Mei*
 ☐ 3 January 1997
 ❖ CUHK Departmental Funding

In order to search for new antiulcer agents, seeds of *Hippophae rhamnoides* (Fam. Elaeagnaceae) were employed in this study. *H. rhamnoides* is commonly used for the treatment of gastric disorders, stomachache, blood clot, abnormal menstruation and burn in Mongolia and Tibet, China. Pharmacological studies showed the seed extract of *H. rhamnoides* having liver protection, free radical clearance, myocardium strength and burn healing effects. Antiulcer effect of *H. rhamnoides* was investigated in this study. Seeds of *H. rhamnoides* were extracted by hexane and the chemical ingredients were examined by GC-MS. The extract was given to Sprague-Dawley rats against a number of ulcer models including ethanol induced gastric acute damage, pylorus-ligated model, a chronic stomach ulcer model

induced by acetic acid, stress and NSAIDs induced gastric lesion. Mechanism of protective and healing effect of *H. rhamnoides* are investigated by measuring gastric acid output, pepsin secretion, mucus and protein content, gastric motility, mucosal blood flow, production of endogenous prostaglandins and sulfhydryls, etc. Antioxidative effect will be also investigated. The active ingredients of *H. rhamnoides* will be isolated and identified. (MD96150)

Quality Control of *Ganoderma* (Lingzhi) Products

- ✍ ZHU Min ● CHANG Qi*
 ☐ 17 February 1997
 ❖ Vita Green Health Products Co Ltd

Ganoderma species are medicinal fungi used as nontoxic medicines. In Chinese culture, Lingzhi, composed of major species of *Ganoderma*, has been regarded as a panacea, curing all kind of diseases. Modern pharmacological studies of Lingzhi demonstrated that it can be used for the treatments of chronic bronchitis, asthma, neurasthenia, insomnia, amnesia, primary hypertension, coronary heart diseases, arrhythmia, stroke, hyperlipidaemia, thrombosis, female endocrine disorder, menstrual disorder, chronic hepatitis, gastric disease and duodenal ulcer, allergic disorders, dysuria, arthritis and rheumatism. Moreover, it was found to prevent and mitigate cancers. Therefore, many products derived from Lingzhi are developed and marketed. However, quality control of these products is still a problem and no analytical method has been established for this purpose. The fungi appear to act as chemical complex, and partial active ingredients are highly water soluble which are difficult to be isolated to pure entities. Thus, it is hard to obtain control compounds for assuring the quality. In this project, an alternative method is developed, i.e. isolating *Ganoderma* into different fractions based on their physical and chemical properties; screening activities of each fraction by animal tests and biochemical analysis; establishing a series of analytical methods to analyze the active fractions quantitatively and, if possible, isolating mark compounds in the active fractions; finally, using mark compounds and active chemical complex as control substances in the quality assurance process. (MD96151)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition	Title/Investigators
1995-96	Development and Assessment of Sustained-release Microcapsules of Rifampicin (MD95220)

- ✍ CHOW Hee Lum Albert
- 1995-96 Assessment of Pharmacy Graduates' Need for Further Education (MD95239)
✍ HO Suk San Susan
- 1995-96 The Effects of Metformin on Insulin Sensitivity and Lipid Regulation in Chinese NIDDM Patients (MD95215)
✍ LEE Kwing Chin Kenneth ● TOMLINSON Brian (Clinical Pharmacology) ● CHAN Chung Ngor Juliana (Medicine) ● ARUMANAYAGAM Manoharan (Chemical Pathology) ● CRITCHLEY Julian A.J.H. (Clinical Pharmacology)
- 1993-94 A Single Dose Pharmacokinetics/Pharmacodynamics Study of Metoprolol in Chinese Subjects: Comparative Assessments with Caucasians (MD94018)
✍ LI Chi Keung Ronald ● DAMANI Lyaquatali A. ● TOMLINSON Brian (Clinical Pharmacology) ● TUCKER Geoffrey T.* ● LENNARD Martin S.* ● RAYMOND Kenneth ● CRITCHLEY Julian A.J.H. (Clinical Pharmacology)
- 1995-96 Effects of Prolonged Bacterial Growth Suppression Demonstrated by Binary Antibiotic Systems: Study of *in vitro* and *in vivo* Correlations Using a Pharmacokinetic/Pharmacodynamic Approach (CU95623)
✍ LI Chi Keung Ronald ● RAYMOND Kenneth ● LING Mei Lun Julia (Microbiology) ● CHENG Fun Bun Augustine (Microbiology)
- 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 (Clinical Pharmacology) ● CRITCHLEY Julian A.J.H. (Clinical Pharmacology)
- 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
- 1995-96 The Cytoprotective Effects of *Radix linderae* against Ethanol Induced Gastric Damages in Rats (MD95191)
✍ ZHU Min ● LUK Chiu Tong

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RESEARCH PROJECTS

Immunolocalization and Functional Studies of VEGF Receptors on Ovarian Macrophages

- ✉ AU Chak Leung
- ☐ 1 September 1996
- ❖ CUHK Research Committee Funding

The present study uses immunohistochemical staining and the technique of liposome-mediated macrophage depletion to identify the presence of VEGF receptors on ovarian macrophages. Specific markers will also be employed to determine whether the localization of VEGF receptors is related to a specific subset(s) or activation state of the macrophages. Once the above facts have been established, further experiments will be performed to investigate the functional significance of VEGF actions on ovarian macrophages. These include its direct effect in the recruitment of monocytes, and its indirect role, through maintaining or stimulating the ovarian macrophage population, to support normal folliculogenesis, ovulation and luteolysis. Furthermore, the possible co-operativity between VEGF and macrophage-derived angiogenic factors in the control of ovarian angiogenesis will be examined by monitoring the level of endothelial cell proliferation in VEGF-treated and macrophage-depleted ovaries. These studies may indicate that there is a paracrine or autocrine control of ovarian macrophage activities by VEGF. (MD96092)

Local Paracrine/Autocrine Control of Epididymal Anion Secretion by Vasoactive Peptides

- ✉ CHAN Hsiao Chang ● WONG Patrick Yee Ding ● CHEW Cheng Siew Boon ● KO Wing Hung
- ☐ 1 September 1996
- ❖ Research Grants Council

The epididymis is thought to be important for sperm maturation by creating an optimal microenvironment on which transformation of an immature sperm to one capable of movement and fertilization depends. Disruption of the microenvironment such as by defective epididymal electrolyte and fluid secretion could lead to obstructive azoospermia as seen in cystic fibrosis, Young's syndrome and some other unexplained cases of male infertility. It is this indispensable role of the epididymis that has been given rise to the "epididymal approach", an antifertility strategy based on intervention of sperm function at a post-testicular level. Therefore, the regulation of epididymal electrolyte and fluid secretion has been the main focus of our research.

Previous work from the researchers' laboratory has suggested that anion secretion in the epididymis may be subject to local paracrine/autocrine control in addition to neural and humoral regulation. A number of vasoactive peptides such as angiotensin II and endothelin have been shown to stimulate anion secretion by the rat epididymal epithelium. It remains to be elucidated whether these peptides could be produced locally in the epididymis and what precise roles these peptides play in regulation of epididymal secretion. It is the goal of the present study, to investigate local paracrine/autocrine control of epididymal secretion by vasoactive peptides including angiotensin II, endothelin and atrial natriuretic peptide (ANP). Regional distribution and expression of these peptides will be studied using immunohistochemical technique and *in situ* hybridization. Identification of receptor subtypes will be studied pharmacologically using the short-circuit current technique employing specific receptor agonists and antagonists. Localization of receptor subtypes in the epididymal epithelium will also be demonstrated by immunostaining using antibodies against specific receptor subtypes. Detail regulatory mechanisms of epididymal anion secretion by these peptides will also be explored using the patch-clamp as well as the short-circuit current techniques. The results of the proposed project should provide new understanding of local paracrine or autocrine regulation of epididymal anion secretion, which may provide theoretical basis for new strategy of male contraception. (CU96612)

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

- ✉ FISCUS Ronald R.
- ☐ 1 September 1996
- ❖ Research Grants Council

Calcitonin gene-related peptide (CGRP), a neuropeptide in nerves innervating most blood vessels, is a potent vasodilator and potential mediator of inflammation and endotoxin shock. CGRP causes both endothelium-dependent and endothelium-independent vasorelaxations, dependent on type of blood vessel. The researchers' studies with rat aortic rings have shown that CGRP activates a dual signal transduction mechanism involving both cAMP and cGMP in smooth muscle. Both cyclic nucleotide responses to CGRP require intact, healthy endothelium and enhanced release of nitric oxide (NO). Exogenous NO potentiates CGRP-induced relaxations and cAMP elevations in aortic rings (without endothelium), suggesting that NO may act by either enhancing synthesis or inhibiting metabolism of cAMP. The proposed project will

further investigate the mechanism of CGRP and NO interactions in both normal blood vessels and in vessels taken from endotoxin shock animals. The HYPOTHESES to be tested are: (1) CGRP and NO cause synergistic vasorelaxant responses via NO-induced: a) potentiation of adenylate cyclase activation by CGRP, b) inhibition of cAMP metabolism (i.e. inhibition of type III [cGMP-inhibited] phosphodiesterase), thus enhancing accumulation of cAMP, or c) potentiation of CGRP-induced lowering of cytosolic Ca²⁺ concentrations, in vascular smooth muscle cells, and (2) elevated levels of NO in smooth muscle from endotoxin shock animals potentiates CGRP-induced vasorelaxations, thus contributing to hypotension and vascular problems of endotoxin shock. The results of this study will provide valuable new information about vasodilator mechanism of two important physiologic and pathologic regulators, and should lead to the development of new, more efficacious therapies for treating endotoxin shock. (CU96644)

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

- ✉ FISCUS Ronald R.
- 1 January 1997
- ❖ CUHK Research Committee Funding

Pathology of stroke involves inadequate blood flow to certain regions of brain, leading to ischaemia and neuronal damage. The damage is believed to involve excessive release of glutamate (i.e. glutamate toxicity) and subsequent over-production of nitric oxide (NO). NO-induced neurotoxicity appears not to involve cyclic GMP (cGMP), the recognized signal transduction mechanism mediating many NO-induced physiological responses. Instead, the researchers laboratory has shown that activation of cGMP/protein kinase G (PKG) pathway in hippocampal neurons actually leads to protection against glutamate toxicity. The proposed project will investigate the mechanism of this neuroprotective effect in neurons. The WORKING HYPOTHESES to be tested are: (1) elevation of cGMP and activation of PKG in neurons leads to protection against toxicity of glutamate and NO, (2) this mechanism represents an intrinsic protective mechanism in neurons exposed to glutamate and NO, and (3) neuroprotection involves PKG-catalyzed phosphorylation of transcription factors and activation of neuroprotective genes. Involvement of cGMP/PKG in protection of neurons during glutamate and NO toxicity will be assessed using blockers of PKG activation. Gene expression will be assessed by Northern blot analysis. Results of this project should provide valuable new information about cellular/molecular mechanisms

involved in enhancing the survival of neurons during brain ischaemia of stroke. (MD96093)

Effects of Neurotoxins on Signal Transduction in Central Synapses of the Rats

- ✉ LEUNG Man Sing
- 1 October 1996
- ❖ CUHK Research Committee Funding

Lesions in the central monoaminergic neurons are known to cause neurological disorder such as Parkinson's disease, schizophrenia and motor dysfunction. Monoaminergic neurons such as serotonergic (5-HT), noradrenergic (NA) and dopaminergic (DA) in the new born rats can be selectively destroyed by neurotoxins such as 5,7-dihydroxytryptamine (5,7-DHT) and 6-hydroxydopamine (6-OH-DA). 5,7-DHT can deplete both 5-HT and NA; 6-OH-DA can deplete both NA and DA. Desmethylimipramine (DMI) pretreatment can be used to protect NA neurons from the toxic actions of these neurotoxins. The heterotrimeric G-proteins are membrane receptor linked signal transducers. Any alteration in the different isoforms of G-proteins by any factors will affect neurotransmission as well as cellular functions. In this pilot study, after different period of application of the neurotoxins, their effects on the signal transduction mechanisms in different parts of the brain will be studied. The different areas of the brain will be dissected out, i.e. cerebral cortex, basal ganglia, hippocampus, cerebellum and brain stem. Part of the tissue is homogenized for the semi-quantitative study of different isoforms of membrane bound G-proteins using Western Immunoblotting techniques after SDS-Polyacrylamide gel electrophoresis. Changes of the three monoamines can be monitored by HPLC-EC detection. Morphological changes of 5-HT, NA and DA neurons are examined by immunohistochemical methods to see whether 'chemical degeneration' will affect the development of G-proteins in neonatal rats. (MD96094)

The Gene Expression and Regulation of the Renin-angiotensin II System in the Rat Epididymis

- ✉ LEUNG Po Sing
- 1 March 1997
- ❖ CUHK Research Committee Funding

The renin-angiotensin II system (RAS) contains several important components namely, the precursor angiotensinogen, the enzymes renin and angiotensin converting enzyme, their products, angiotensin I and angiotensin II, together with the specific angiotensin

receptors. The concept of the tissue RAS is that its components are produced locally in the tissue and it acts in a paracrine/autocrine/intracrine fashion to regulate tissue functions. Recently, a tissue RAS has been proposed in the rat epididymis based on the observation of several components of RAS. This local RAS may be important in regulation of epididymal functions.

In this project, the gene expression of the RAS components in the rat epididymis is investigated using reverse transcriptase polymerase chain reaction (RT-PCR) and *in-situ* hybridization (ISH). Specifically designed primers for the RAS components including angiotensinogen, renin and angiotensin II receptors subtypes (AT_{1a}, AT_{1b} and AT₂) are synthesized. The total RNA is extracted from the epididymis using the acid guanidinium thiocyanate-phenol-chloroform protocol. The extracted RNA is then suspended in RNase free water. The tissue mRNA is isolated from the total RNA using oligo-dT column. The tissue mRNA (40µg) is subjected to first strand cDNA synthesis using oligo-dT primers or random hexamers and reverse transcriptase. After first strand cDNA synthesis, the reaction mixture is heated at 95°C for 5 min. 1/10 volume of the mixture is directly used for amplification. PCR is carried out in the presence of specific primers for RAS components. The amplified mixture is finally analyzed on 2% agarose gel electrophoresis. The localization of mRNA for angiotensinogen and renin is achieved by digoxigenin labelled riboprobes. The cDNA for angiotensinogen and renin are employed as templates for RNA probe preparation. The cDNA is first linearized by their respective restriction enzymes for antisense and sense RNA probes, which are synthesized *in vitro* using the T₃ and T₇ polymerases respectively. The digoxigenin labelled riboprobes is purified by repeated ethanol precipitation in the presence of lithium chloride. The riboprobes are finally analyzed using gel electrophoresis and these probes are then used for ISH.

The present research project is aimed to investigate the expression of the RAS system in the rat epididymis. The possible regulation of the RAS expression may be important for epididymal function which may provide new grounds for controlling male fertility.

(MD96117)

An Electrophysiological Approach To Study Sertoli Cell - Germ Cell Interaction

✉ WONG Patrick Yee Ding

☐ 1 March 1997

❖ CUHK Research Committee Funding

Although a lot is known about the role of the Sertoli cells in the regulation of spermatogenesis in the mammalian testis, little is known of the way in which germ cells affect the functions of the Sertoli cells. A

large body of evidence has accumulated to suggest that germ cells isolated from the seminiferous tubules release specific molecules which serve as signals of communication with the Sertoli cells. In this way, germ cells may participate in the regulation of spermatogenesis by acting through the Sertoli cells.

The aim of the project is to study chloride/fluid secretion by cultured Sertoli cells and the effect of germ-cell specific factors, isolated from germ cell conditioned media, on secretion. It is hoped that this study will increase our understanding of the cross talk between Sertoli cell and germ cells. In a wider context, the study will explore a new avenue of contraceptive research aiming at interfering with fluid production by the testis.

(MD96118)

Role of a K Channel (Kv1.3) in T-lymphocyte Activation

✉ YAO Xiaoqiang

☐ 1 April 1997

❖ CUHK Research Committee Funding

Potassium channels are essential for a variety of fundamental cell processes. Kv1.3 is a critical K⁺ channel in the activation and proliferation of T-lymphocytes. An increase in Kv1.3 current is required for the activation of T- lymphocytes. Inhibitors of Kv1.3 channel also inhibit mitogen-induced T-lymphocyte proliferation and activation. However, the molecular mechanism that mediates the increase in Kv1.3 current is not understood. The researchers have previously identified a novel gain-of-function mutation in rabbit Kv1.3 that results in a 20 fold increase in expressed K⁺ current. Here they plan to study the molecular mechanism (the contributing channel properties, and the role of protein phosphorylation and cytoskeleton) of the gain-of-function mutation and to determine whether a similar mechanism is involved in the T-lymphocyte activation. Their study will lead to the better understanding in the molecular mechanism of T-lymphocyte activation and immune response. The study on inhibitors of Kv1.3 may eventually help developing drugs for treatment of graft rejection and inflammation.

(MD96116)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
1995-96	Control of Testicular Microvasculature by Vascular Endothelial Growth Factor (CU95646) ✉ AU Chak Leung ● LEE Will M.*

- 1995-96 Local Regulation of Sperm and Epididymal Ion Channels by Epididymal Microenvironment: Study of Mechanisms Essential for Sperm Maturation (CU94605)
 ✎ CHAN Hsiao Chang ● WONG Patrick Yee Ding ● SHI Yu Liang*
- 1995-96 Study of Epithelial Electrolyte Transport (MD95029)
 ✎ CHAN Hsiao Chang ● WONG Patrick Yee Ding ● CHEW Cheng Siew Boon ● KO Wing Hung
- 1995-96 Mechanism of Cyclic GMP Release From Neural Cells and the Relationship to Activation of Cyclic GMP-Dependent Protein Kinase (MD95142)
 ✎ FISCUS Ronald R.
- 1995-96 Ionic Mechanisms of Action of cGMP- and CAMP-elevating Vasodilators (CU95669)
 ✎ HUANG Yu
- 1995-96 Endothelium-Dependent Relaxation of Rat Aorta and Mesenteric Artery by Chloride Channel Blockers (MD95143)
 ✎ HUANG Yu
- 1995-96 Interactions Between Autonomic Signal Transduction Pathways in Epithelial Cells (MD95038)
 ✎ KO Wing Hung ● WILSON Stuart MacDonald*
- 1995-96 Electrophysiological and Microspectrofluorimetric Studies of Cultured Human and Equine Sweat Gland Epithelial Cells (CU95611)
 ✎ KO Wing Hung ● WONG Patrick Yee Ding
- 1995-96 Regulation of Intracellular pH (pH_i) in Sweat Gland Epithelial Cells Using Dual Emission Laser Scanning Confocal Microscopy (MD95140)
 ✎ KO Wing Hung
- 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)
- 1994-95 Acid-Based Transport in Cultured Polarized Epithelia from the Rat Epididymis (MD95041)
 ✎ WONG Patrick Yee Ding
- 1995-96 Studies of Intracellular Calcium Homeostasis in Cultured Epididymal Cells of the Rat (CU93601)
 ✎ WONG Patrick Yee Ding
- 1995-96 Molecular Determinants of the Inhibitory Synaptic Transmission at an Identified Central Synapse (CU94631)
 ✎ YUNG Wing Ho
- 1995-96 Mechano-electric Transduction Currents in Merkel Cell Receptors (CU95612)
 ✎ YUNG Wing Ho ● BAUMANN Klaus Ingo
- 1995-96 The Role of ATP-Sensitive Potassium Channels in the Hypoxic Response of Central Neurons (MD95141)
 ✎ YUNG Wing Ho

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- <P953564> **Zhang, Lubo; Donald C. Dyer; Ronald R. Fiscus; Zoran Grujic and Xian Wang.** "5-Hydroxytryptamine Induces Endothelium-Independent Relaxations of Sheep Pulmonary Vein: Role of Cyclic Nucleotide". *European Journal of Pharmacology* vol.280, pp.335-337. The Netherlands, 1995.07.

- <P961654> **Huang, Yu and P.Y.D. Wong.** "Inhibitory Effect of ATP-Sensitive K⁺ Channel Regulators on Forskolin-Stimulated Short-Circuit Current Across the Isolated Mucosa of the Rat Colon". *Journal of Cellular Physiology* vol.168, pp.678-683. USA, 1996.09.01.
- <P962034> **Chan, Hsiao Chang and P.Y.D. Wong.** "Paracrine/Autocrine Regulation of Anion Secretion in the Epididymis: Role of Angiotensin II". *Biological Signals* vol.5, pp.309-316. Basel, Switzerland, 1997.02.19.
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- <P962145> **Huang, Y.; Y.W. Chung and P.Y.D. Wong.** "CA²⁺ - Activated k⁺ Channels Recorded from the Apical Membrane of Freshly Isolated Rat Epididymal Epithelium". *Molecular Biology of the Cell* (Abstracts of the 6th International Congress on Cell Biology & 36th American Society for Cell Biology Annual Meeting). vol.7, p.254a. USA, 1996.12.
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- <P962398> **Ko, W.H.; H.C. Chan and P.Y.D. Wong.** "Anion Secretion Induced by Capacitative Ca²⁺ Entry Through Apical and Basolateral Membranes of Cultured Equine Sweat Gland Epithelium". *The Journal of Physiology* vol.497 no.1, pp.19-29. UK, 1996.
- <P962583> **Leung, K.S.; Ye, G.L. and Yung, W.H.** "Presynaptic Effect of Baclofen on Rat Striaonigral Pathway *in vitro*". *Proceedings of the 1st FAONS Congress & IBRO Regional Congress* p.A70. Thailand, 1996.10.
- <P962586> **Baumann, Klaus I.; Eliza Chan; Zdenek Halata; Solomon S. Senok and Wing-Ho Yung.** "An Isolated Rat Vibrissal Preparation with Stable Responses of Slowly Adapting Mechanoreceptors". *Neuroscience Letters* vol.213, pp.1-4. Ireland, 1996.07.
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- <P962859> **Ko, W.H.; W.O. Fu; P.Y. Leung; S.B.C. Chew; H.C. Chan and P.Y.D. Wong.** "Purinergic Regulation of Electrogenic Anion Secretion by Primary Cultures of Sertoli Cells from Immature Rats". *International Meeting on Gastroenterology, Endocrinology and Reproduction* p.34. Hong Kong: The University of Hong Kong, 1996.12.09.
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see also <P962512>, <P962513>, <P962588>, <P970253>, <P970356>, <P970750>, <P970813>, <P972048>

RESEARCH PROJECTS

Evaluative Study of the Services of Non-Subvented Voluntary Drug Treatment and Rehabilitation Agencies

- ✉ CHEN Char Nie ● LEE Tak Shing Dominic ● LEUNG Yip Shing ● WING Yun Kwok ● LEE Sing
- ☐ 1 January 1996
- ❖ Social Welfare Department, Hong Kong Government

Hong Kong takes pride for her multi-modality approach in curbing drug abuse problems. Among the non-government organisations, there is a group of agencies that employ a "Christian therapeutic approach" in helping drug abusers to quit their addiction. They are not yet included in the Government's subvention system and, in the past, have been funded predominantly by overseas religious denominations. After the Governor's Second Summit Meeting in May this year, it was thought essential to further understand the operation of these agencies to allow the Government to consider including them in the subvention system. For this reason, a workable study protocol to look into various aspects of operation of these agencies is urgently needed. (MD96190)

Pharmacokinetics of Tricyclic Antidepressant Treatment: An Integrated Phenotype and Genotype Approach

- ✉ CHIU Fung Kum Helen ● WING Yun Kwok ● CHOW Lok Yee
- ☐ 1 March 1997
- ❖ CUHK Research Committee Funding

Tricyclic antidepressants (TCA) have been the mainstay treatment of depressive disorder. However, inter-individual and cross-ethnic variability has been consistently reported in the therapeutic and side effect profiles of these drugs. Imipramine, one of the commonly used TCAs, is mainly metabolised by liver cytochrome enzymes P450 especially CYP2D6. By using debrisoquine test, the hydroxylation status (phenotype of CYP2D6) of the subjects can be characterised. Whereas Caucasians have more poor metabolisers (PM, 6-10%), Chinese has only 1% (PM). This is in contrast to the clinical experience that Chinese requires less dosage of imipramine and the metabolism of imipramine is slower in Chinese than Caucasians. The latest advance of pharmacogenetics help to solve the puzzle. By using RFLP and PCR, it has been determined that Chinese differs from Caucasians at the site of mutations of

CYP2D6 which leads to slower metabolism of imipramine, albeit less percentage of PM. Thus, the researchers aim to correlate the plasma level of imipramine to the metabolism as well as the phenotypes and genotypes of CYP2D6 in the clinical population for the first time in Hong Kong Chinese. This will lay an important foundation for future study in using the pharmacokinetic and pharmacogenetic information in predicting the blood level and clinical responses. A rational and scientific-based prescription can be established then. (MD96114)

Dementia Home Care Project - Training for Demented Patient and Carer in a Territory Wide Level

- ✉ CHIU Fung Kum Helen ● LI Siu Wah* ● CHU Dana*
- ☐ 1 April 1997
- ❖ Health Care & Promotion Fund, Hospital Authority

In Hong Kong, the aging of the population is a concern. According to Hong Kong Government's Census, 1994, the percentage of elderly population above age 65 will increase from 9.7% in 1994 to 11.3% in 2000. Alzheimer's disease is predominantly a disease of the elderly. However, it affects not only the patients themselves but also their family members. Taking care of demented patients is a serious problem in many communities. The Dementia Home Care Project aims at helping to solve this serious problem.

- (1) to provide knowledge on dementia and management techniques of being a carer, to teach and to help them in coping with the patients effectively so as to relieve their anxiety and pressure in taking care of elderly patients.
- (2) to arouse public awareness on the problem of dementia in the elderly through educational programme.
- (3) to give social and psychological support to the patients and their family caregivers through the joint effort of professionals from different fields to improve the quality of life of demented patients. (MD96020)

Schizophrenia and the Microdeletion 22q11 in a Chinese Population

- ✉ CHOW Lok Yee ● WAYE Mary Miu Yee (Biochemistry) ● GARCIA BARCELO Maria (Biochemistry)
- ☐ 1 September 1996
- ❖ CUHK Research Committee Funding

Schizophrenia is a common and disabling psychiatric disorder with genetic factor being found to be the most consistently replicated etiological factor. Using

the candidate gene approach, Karayiorgou and coworker reported that 2 out of 100 schizophrenic patients harboured the microdeletion at chromosome 22q11 which has been initially attributed to the cause of Velo-Cardio-facial syndrome (VCFS). Patients with VCFS have been reported to have 10-20 times increase in risk of developing schizophrenia compared to general population. The mechanism by which the 22q11 microdeletion mediate the increase in risk of schizophrenia in VCFS remains unknown. Also the significance of the occurrence of the 22q11 microdeletion in schizophrenic patients needs further evaluation. It is not known whether the finding of Karayiorgou et al can be generalized to psychiatric settings in other populations. The researchers have recently found the first Chinese schizophrenic patient associated with VCFS. Thus, a replicative study of screening the 22q11 microdeletion in a randomly selected representative sample of schizophrenia in a different ethnic group such as Chinese will allow them to examine whether the genetic locus responsible for susceptibility to schizophrenia lies at the 22q11 region. It will give them information regarding the extent to which the 22q11 microdeletion is responsible for genetic susceptibility to schizophrenia in the general population and facilitate the identification of the gene(s) causing schizophrenia.

(MD96082)

Genetic Association Studies of Bipolar Affective Disorder

✉ LEE Tak Shing Dominic

☐ 1 January 1997

❖ CUHK Research Committee Funding

It has been established that bipolar affective disorder (BPD) (*synn.* manic depressive disorder) has a major genetic component in its aetiology. However, genetic linkage studies have produced confusing results. A complementary approach using association studies may help to clarify this confusion. The Department of Psychiatry has collected 140 BPDs over the years, which is an ideal cohort for genetic association studies. The researchers propose to collaborate with the psychiatric genetics group of the Cambridge University and to combine two cohort groups to conduct association studies. In particular, they would also like to explore a recent findings of the Cambridge group: a positive association between BPD and monoamine oxidase A locus. They would also like to study other candidate genes, including trinucleotide repeat-containing genes, human ciliary neurotrophic factor gene, serotonin transport gene, and mitochondria DNA sequences variants using association strategies. This collaboration is particularly powerful because the confirmation of a genetic association in two different ethnic groups provides robust support for a candidate gene.

(MD96083)

Apolipoprotein E Genotype in Chronically Institutionalized Geriatric Schizophrenic Patients in a Chinese Population

✉ UNGVARI Gabor Sandor ● CHIU Fung Kum Helen ● CHOW Lok Yee ● MAK Ying Tat (Chemical Pathology)

☐ 1 September 1996

❖ CUHK Research Committee Funding

Approximately 10-20% of schizophrenic patients have a chronic progressive course which results in an end-state resembling dementia in terms of cognitive impairment. Recent studies suggest that this subgroup of schizophrenic may have a higher risk of suffering from Alzheimer's disease although the evidence is inconclusive. Research on the relationship between late-life schizophrenia and dementia is important given the anticipated increase in life expectancy in the elderly schizophrenic patients. Apolipoprotein E4 (ApoE4) is now well established as a risk factor for Alzheimer's disease. It is not known whether the postulated increase in risk for Alzheimer's disease in schizophrenic patient with severe cognitive impairment is also mediated by ApoE4. Using a large sample of clinically well-defined subgroup of chronic schizophrenic patients with severe cognitive deficit, the researchers' study will allow a critical examination of the relation between ApoE4 and 'schizophrenic dementia'.

(MD96084)

Quantitative Cerebral Anatomy in Mood Disorders and Neurasthenia

✉ WING Yun Kwok ● CHAN Yu Leung (Diagnostic Radiology & Organ Imaging) ● LAM Wai Man Wynn (Diagnostic Radiology & Organ Imaging)

☐ 1 October 1996

❖ CUHK Research Committee Funding

The progress of psychiatry and the understanding of the mental illness is often limited by the lack of suitable tool in the investigation of the underlying brain and mind pathology. With the availability of more sophisticated brain imaging methods, psychiatric disorders are increasingly found to be associated with a number of previously undetectable changes in brain morphologies. The study of the cerebral anatomy of patients with schizophrenia has shown a consistent pattern of ventricular enlargement and focal temporal lobe atrophy in a subgroup of patients. Recently, researchers' attention has also extended to mood disorders. Though early studies were not well controlled and limited by the small number of subjects, recent studies and use of meta-

analysis have revealed a rather consistent pattern of abnormalities in mood disorders when comparing to age and sex- matched control subjects. These include ventricular enlargement, sulcal prominence, subcortical focal white matter abnormalities (1-2). However, a number of questions remain unanswered. For example, the etiologic and pathophysiological significance of these abnormalities, the specificity issue and the association of brain pathologies with the subtype of mood disorder (unipolar vs bipolar), age of onset of illness, gender effect and prognosis of illness have been unclear. Moreover, there has never been any imaging study on neurasthenia which is a very common psychiatric condition in Chinese societies. The concept of neurasthenia is controversial and opinions are divided on whether it is a variant of depressive disorder or a separate entity. By studying the anatomical anomalies in neurasthenia, this controversy may be clarified. (MD96085)

The Use of Sleep and Neuroendocrine Changes as Biological Probes of Depression and Neurasthenia in Chinese Subjects in Hong Kong

- ✉ WING Yun Kwok ● LEE Sing ● CHEN Char Nie ● CHOW Chun Chung Francis (Medicine)
- ☐ 1 November 1996
- ❖ Research Grants Council

Depression is a universal and very common psychiatric disorder which carries conspicuous morbidity and mortality. Whereas Western studies on its biological correlates are extensive, similar investigations in Chinese subjects are extremely scanty despite their obvious implications on the etiology and treatment of the disorder. Besides, the lower lifetime prevalence of depression in Chinese societies (1.29/2.44% for Hong Kong male and female) compared to the West has led to a number of etiological postulations. One popular hypothesis is that Chinese people tend to 'somatise' their emotions into physical symptoms. Consequently, many of them present instead as neurasthenia which is often considered a somatised and under-treated form of depression. On the other hand, based on both historical evidence and clinical similarity, the suggestion has been made that neurasthenia is in fact synonymous with 'chronic fatigue syndrome'. By using carefully translated semi-structured clinical diagnostic interviews and well validated operational criteria for depression and neurasthenia and a set of sleep and neuroendocrine measurements, the researchers aim to clarify for the first time in Chinese subjects the intriguing and long-debated relationship between depression and neurasthenia. Not only will the Chinese database of clinical-biological information to be obtained allow cross-cultural comparison to be made, but the study will also lay the foundation for establishing a research model in cross-

cultural psychiatry. At a practical level, the biological changes to be found will help predicting treatment response, shed light on the etiology of depression and neurasthenia, and serve as biological markers in improving the validity of their classification. (CU96676)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition	Title/Investigators
1995-96	Pharmacokinetics, Dosage and Therapeutic Plasma Levels of Imipramine in Chinese Depressed Patients (MD92109) ✉ CHIU Fung Kum Helen ● CHAN Kelvin Kam Chuen (Pharmacology) ● WING Yun Kwok ● LEE Sing ● CHEN Char Nie
1995-96	A Longitudinal Study of Thyroid Changes among Chinese Psychiatric Patients on Long-term Lithium Therapy in Hong Kong (CU92614) ✉ LEE Sing ● WING Yun Kwok ● AHUJA Anil Tejbhan (Diagnostic Radiology & Organ Imaging) ● CHOW Chun Chung Francis (Medicine) ● SHEK Chi Chung Anthony (Chemical Pathology)
1995-96	A Controlled Study of Serum and Erythrocyte Folate Levels in Chinese Inpatients with Major Depression in Hong Kong (MD95135) ✉ LEE Sing ● WING Yun Kwok
1995-96	A Comparison of the Drug Abuse Situation in Hong Kong with Selected Countries (MD95254) ✉ LEE Tak Shing Dominic ● NG Kee On* ● CHAN Calais* ● LEUNG Chi Ming ● CHEN Char Nie
1995-96	A Family Study of Chinese Narcolepsy in Hong Kong (MD95152) ✉ WING Yun Kwok ● CHEN Char Nie
1995-96	Understanding Adolescent Project (SS94024) ✉ WONG Chung Kwong ● CHOI Yuen Wan* ● LAU Tak Fai Joseph (Centre for Clinical Trials & Epidemiological Research) ● LAI Yee Ching Kelly ● OBORNE

David* ● LEUNG Yip Shing ●
HOH Ying* ● WAND Rox*

RESEARCH OUTPUTS AND PUBLICATIONS

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see also <P962093>, <P962736>, <P963814>, <P970061>, <P970214>, <P970252>, <P970404>, <P971355>, <P971357>

RESEARCH PROJECTS

Neo-adjuvant Chemotherapy in Squamous Oesophageal Cancer: Prediction of Chemoresponse Using Biopsy Sample before Chemotherapy

✉ CHAN Chi Wai Angus ● CHUNG Sheung Chee Sydney ● IP Sin Ming ● LAU Yun Wong James ● METREWELI Constantine (Diagnostic Radiology & Organ Imaging) ● SUEN Wang Ming Michael (Anatomical & Cellular Pathology) ● JOHNSON Philip James (Clinical Oncology)

□ 1 January 1996

❖ Research Grants Council

Most patients with squamous cell carcinoma of the oesophagus present with locally advanced disease and occult metastases. Despite an improved operative mortality, 5 years survival rate following surgery remains poor. The majority of patients who underwent successful resection still die of distant metastases. Chemotherapy is the only current treatment that can control local and distant disease. Further survival benefit may be accomplished with adjuvant chemotherapy. Cis-platin based multidrug regimen has the best reported tumour response rate of 65% with documented complete remission in some cases. And yet 35% of patients will not respond to the chemotherapy. The survival of this subgroup of patients may be jeopardized by the prolonged course of chemotherapy, the unwanted toxicity of chemo-agents and the delay in receiving potentially curative resection. If non-responders can be selected out prior to chemotherapy it would be of great clinical impact. To date there is no specific method that can predict the chemo-response of tumour. The researchers propose to evaluate the presence of multidrug resistance gene (*mdr 1*), P-glycoprotein, glutathione S-transferase (*GST- α*) and tumour DNA, ploidy expression before chemotherapy and correlate these with the clinical, radiological and pathological documentation of tumour response. (CU96649)

A Study of Expression of Prostate Secretory Protein of 94 Amino Acid and its Alternative Transcripts in Normal, Hyperplastic and Neoplastic Human Prostate

✉ CHAN Siu Foon Peter ● WONG Wai Sang ● CHAN Leung Franky (Anatomy)

□ 1 January 1997

❖ CUHK Research Committee Funding

Prostate cancer has become a major health problem in Western countries, its incidence is expected to increase in Eastern countries because of changes in

dietary habits, life-style and increased life expectancy. Prostate acid phosphatase (PAP), Prostate specific antigen (PSA) and prostatic secretory protein of 94 amino acids (PSP94) are the three predominant proteins secreted by the prostate. While PAP and more recently PSA has been used as prostate tumour markers, the biologic functions of PSP94 is yet unknown. PSP94 has been shown to inhibit FSH secretion from the pituitary, to inhibit prostate growth and to suppress the growth of a rat model of prostate cancer (Dunning R3327G rat tumour).

The main objective of this study is to investigate the gene expression and distribution of PSP94 and its alternative transcripts in normal, hyperplastic and neoplastic human prostates by conventional and RT-PCR *in-situ* hybridization. The information obtained may be useful in future determination of any potential use of PSP94 and its alternative-spliced form PSP57 as tumour markers and therapeutic use for prostate cancer. (MD96095)

To Investigate the Clinical Usefulness of Arginase, Amino Acid Profile and Sialic Acid as Tumour Markers for Breast Cancer

✉ CHAN Sun Yin Eric ● PANG Chi Pui Calvin (Chemical Pathology) ● LAM Ping Kuen ● KING Walter Wing Keung

□ 1 January 1997

❖ CUHK Research Committee Funding

Breast cancer is the second most common cancer among the Chinese women in Hong Kong. Among 346 breast cancer patients who underwent mastectomy at the Prince of Wales Hospital, only 11% patients were detected diagnosed as clinical stage I¹. In order to improve the early detection of breast cancer and to have an accurate tumour burden monitoring during treatment, the researchers investigate the clinical usefulness of combination of serum arginase, plasma free amino acid pattern, serum total and lipid-associated sialic acid as biochemical markers for breast cancer. (MD96096)

Stress Responses and Endotoxaemia in Patients with Generalised Peritonitis: A Randomised Comparison between Laparoscopic and Open Surgery

✉ CHUNG Sheung Chee Sydney ● LAU Yun Wong James

□ 1 July 1996

❖ CUHK Research Committee Funding

In elective surgery, laparoscopic approach is associated with attenuated stress responses and acute phase reactions as a result of less tissue trauma when

compared to the conventional open approach. The use of laparoscopic surgery is now extended to acute surgical conditions complicated by peritonitis. In these septic patients, the theoretical advantage of laparoscopic surgery in reducing stress may not be apparent. In addition, endotoxaemia from CO₂ pneumoperitoneum in patients with peritonitis is a theoretical concern. The researchers sought to compare stress responses and endotoxaemia in patients with generalised peritonitis randomised to receive laparoscopic or open surgery. At surgery, undiluted peritoneal fluid is obtained for quantitative bacterial and endotoxin assays to determine severity of peritoneal contamination. Serial blood samples are then taken for serum markers of inflammatory response (interleukin-6, C-reactive protein and cortisol) and endotoxin assay. The study not only quantitates stress related to laparoscopic surgery in the presence of sepsis. The differential stress responses and endotoxaemia to laparoscopic or open surgery provide basis for use of laparoscopy in patients with peritonitis.
(MD96098)

A Prospective Study on the Prevalence of Helicobacter Pylori Infection in Patients with Perforated Duodenal or Juxtapyloric Ulcers

- ✉ CHUNG Sheung Chee Sydney ● LAU Yun Wong James
- 1 July 1996
- ❖ CUHK Research Committee Funding

While it is known that *Helicobacter pylori* causes uncomplicated peptic ulcer, its role in perforated peptic ulcer is undefined. The knowledge of HP association implicates a different management strategy; HP eradication should become the therapy of choice and acid reduction surgery is no longer indicated. In the current study, the researchers sought to determine the prevalence of HP in non-NSAiD associated perforated peptic ulcers. At surgery, peroral gastroscopy will be performed and antral biopsies taken for rapid urease test, HP culture and histology. Following a simple omental patch repair, patients are prescribed HP eradication drugs. A prospective follow-up of these patients is then conducted to examine the effect of HP eradication on ulcer recurrences and complications.
(MD96099)

The Prevalence of Helicobacter Pylori in the Peptic Ulcer Complication of Pyloric Stenosis: An Implication for Change in Management Strategy

- ✉ CHUNG Sheung Chee Sydney ● LAU Yun Wong James
- 1 October 1996
- ❖ CUHK Research Committee Funding

Helicobacter pylori causes uncomplicated duodenal or juxtapyloric ulcers. The prevalence of the organism in the ulcer complication of pyloric stenosis is however unknown. The use of hydrostatic balloon in the endoscopic dilatation of pyloric stenosis has claimed early success in the relief of obstruction but further ulcer complications are common despite acid suppression. With the knowledge of HP prevalence, endoscopic balloon dilatation followed by HP eradication in curing ulcer diathesis becomes a therapeutic option. In this study, the researchers sought to determine the association of HP infection and pyloric stenosis and to evaluate this new therapeutic option.
(MD96097)

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

- ✉ CHUNG Sheung Chee Sydney ● LEUNG Wai Keung* ● WU Justin* ● CHAN Lek Yuen* ● WONG Kin Hung* ● CHING Yuet Ling (Medicine) ● YUNG Man Yee ● SUEN Choi Ying Roamy
- 24 March 1997
- ❖ GlaxoWellcome Pharmaceutical Inc.

This is a multi-centre trial sponsored by Glaxo-Wellcome on the efficacy of a new anti-*Helicobacter* compound Rantidine Bismuth Citrate. Centres from Australia, Hong Kong, New Zealand, Philippines, Singapore and Thailand took part. A total of 300 patients will be recruited. The Prince of Wales Hospital recruited 19 patients for the study, 18 of whom have completed the follow-up. Analysis of the results will be carried out when all the centres have completed their follow-up.
(MD96184)

Influence of External Stent Texture on Early Medial and Neointimal Thickening in a Pig Model of Saphenous Vein Bypass Grafting

- ✉ IZZAT Mohammad ● YIM Ping Chuen Anthony ● HO Chin Ho Kenny
- 1 April 1997
- ❖ CUHK Research Committee Funding

The long term results of saphenous vein grafts are severely compromised by the high incidence of late vein graft failure. This is due to progressive neointimal formation and superimposed atheroma. To date there is no single intervention that can improve on these results. Recently, the senior researcher has published his research results, documenting significant reduction in neointimal

formation by "external stenting". This project is a continuation of this work. Two types of stents, one highly porous (Dacron) and the other non-porous (GoreTex) will be compared, using a pig model of saphenous vein grafting. Grafts will be analysed, the end points being neointimal formation and graft wall thickening. The aim of this project is to design a clinically applicable intervention that improves patients' outcome.
(MD96120)

Prognostic Factors of Breast Cancer among Women in Hong Kong

- ✉ KING Walter Wing Keung ● SUEN Wang Ming Michael (Anatomical & Cellular Pathology)
☐ 1 July 1996
❖ CUHK Research Committee Funding

Breast cancer is the second most common cause of cancer death among women in Hong Kong. The researchers have previously analyzed the clinical data of 346 patients with breast cancer who were treated with mastectomy at the Prince of Wales Hospital. The results showed that the tumour size, lymph node involvement status and histologically positive lymph node status were significant prognostic factors for both survival and disease-free survival. Although, these parameters provide clinical parameters for diagnosis and monitoring of breast cancer, none is of sufficient sensitivity and specificity. Recent studies, however, revealed potentially useful new diagnostic, and prognostic factors in tumour DNA aneuploid status, tumour cell proliferative activity, oncogene products, and tumour suppresser gene mutation status. The researchers propose to study the new prognostic factors in breast cancer tissue for the evaluation of treatment and indication of recurrence and survival of breast cancer among women in Hong Kong.
(MD96101)

Reconstitution of a Human Skin Equivalent Composed of Lyophilized Allogenic Dermis, Keratinocytes and Fibrin

- ✉ KING Walter Wing Keung ● LI Arthur K. C. ● LAM Ping Kuen
☐ 1 December 1996
❖ Research Grants Council

There is a continuing search for a durable and clinically applicable human skin equivalent in order to serve as a permanent wound cover for patients with life-threatening major burns. The researchers have previously successfully cultured human epithelial cells (keratinocytes) for clinical application using the 3T3 feeder layer technique. In a more recent animal study, they have also shown that cultured epithelial cell sheets when combined with

fibrin (a natural glue) and collagen membrane did not result in an increase in the survival of the cultured epithelial cells.

More recently, the researchers have developed a modified feeder layer culture system that allows *in-vitro* growth of epithelial cells on a neo-dermis. In this modified culture system, the epithelial cells and fibrin are first seeded onto freeze dried (lyophilized) allogenic dermis obtained from cadaver skin. Hence, subsequent damaging enzymatic separation of the cultured epithelial sheet from the culture dish (by Dispase) is not required, and the living skin equivalent may achieve better vascularization from the wound bed.

Therefore, the researchers seek to study in a nude mice model whether the modified feeder layer culture system growing epithelial cells anchored by fibrin onto allogenic dermis rendered less immunogenic by freeze drying will provide a clinically effective human skin equivalent as assessed by the graft take rate, the infection rate and histological evidence of keratinocyte differentiation and formation of basement membrane.
(CU96648)

The Induction of Apoptosis of Hepatic Cancer Cells by Polyunsaturated Fatty Acids

- ✉ LAU Wan Yee Joseph ● LAI Bo San ● LEOW Chon Kar
☐ 1 June 1997
❖ CUHK Research Committee Funding

Selective induction of apoptosis in tumour cells is a novel means of cancer therapy. However the pathways and mechanisms involved in the process of apoptosis in liver cancer cells are largely unclear. There were scattered evidence showing that polyunsaturated fatty acids are cytotoxic to cancer cells but minimally toxic towards normal nontransformed cells. The researchers postulate that polyunsaturated fatty acids are cytotoxic towards liver cancer cells by inducing apoptosis. Confirmation of this hypothesis will enable them to study the expressions of various proteins which are important in the pathways of apoptosis and form the basis for developing ways of using polyunsaturated fatty acids in the treatment of liver cancer.
(MD96119)

Repeat Endoscopic Treatment or Surgery in the Management of Rebleeding Peptic Ulcers After Initial Endoscopic Haemostasis: A Prospective Randomized Controlled Trial

- ✉ LAU Yun Wong James ● SUNG Joseph Jao Yiu (Medicine) ● CHUNG Sheung Chee Sydney ● CHAN Ka Leung Francis (Medicine)
☐ 1 April 1996

❖ CUHK Departmental Funding

In the management of bleeding peptic ulcers, endoscopic therapy has emerged as the primary treatment modality. Permanent haemostasis can be achieved in 90% of cases by endoscopic means alone. Rebleeding however occurs in about 10-15% of patients. A significant proportion of them are elderly frail patients with high surgical risks. Surgery as a rescue procedure carries a mortality of up to 45%. Avoiding surgery may therefore be desirable. Anecdotal experience suggest that repeat endoscopic therapy can be successful in some of these patients. The issue has become particularly relevant in the era of *Helicobacter pylori*. Its eradication often lead to cure of ulcers. In this study, the researchers compare repeat endoscopic therapy to surgery in patients who continue to bleed after endoscopic treatment. It is envisaged that repeat endoscopic treatment can reduce both short and long term morbidity and possibly mortality.
(MD96182)

Antiemesis Efficacy of Tropisetron: A Double-Blind Randomised Trial Comparison to a Metoclopramide-Based Regimen in Patients with Carcinoma of Oesophagus Receiving Cisplatin

✉ LAU Yun Wong James ● NG K.W.* ● CHUNG Sheung Chee Sydney
 □ 1 May 1996
 ❖ CUHK Departmental Funding

In patients with carcinoma of oesophagus, neo-adjuvant chemo-irradiation prior to surgery improves patient outcome. The chemotherapy regime in use consists of cisplatin and continuous infusion of 5-fluorouril. Cisplatin is regarded as the most emetogenic amongst cytotoxics. Chemotherapy induced nausea is distressing to patients and compounds the problem of poor feeding. Tropisetron is a selective 5-hydroxytryptamine-3 receptor antagonist. Given once daily, it is effective against cisplatin induced nausea. Tropisetron is compared against conventional high dose metoclopramide, dexamethasone and lorazepam cocktail in their respective antiemetic efficacy as well as extra-pyramidal side-effects.
(MD96149)

A Multicentre Prospective Randomised Comparison of Laparoscopic Versus Open Cholecystectomy in Acute Cholecystitis

✉ 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

□ 1 May 1996

❖ CUHK Departmental Funding

Laparoscopic cholecystectomy (LC) is now the procedure of choice in the elective treatment of symptomatic gallstones and chronic cholecystitis. The role of LC in acute cholecystitis however remains undefined. Acute cholecystitis, with inflammatory oedema and adhesions, has been considered a contraindication to LC. Recent uncontrolled series suggest that LC is safe in acute cholecystitis and if successful performed can lead to shorter patient convalescence. This randomised controlled trial, with participation of three major hospitals, compares LC with the current standard treatment of open cholecystectomy in patients with acute cholecystitis. Outcome parameters being measured are procedure related morbidity, analgesic requirement, hospital stay and convalescence.
(MD96183)

Accelerated Induction of Liver Cirrhosis by Tamoxifen Via the TGF- β - Lipocyte Axis - a Putative Pathway

✉ LEOW Chon Kar ● LAU Wan Yee Joseph ● LIEW Choong Tsek (Anatomical & Cellular Pathology) ● LAI Bo San
 □ 1 February 1997
 ❖ CUHK Research Committee Funding

The principal effector of fibrogenesis in early and advanced liver disease, is the hepatic lipocyte or Ito cell. Its continuing synthesis and secretion of collagen is driven by transforming growth factor β (TGF- β). Recent evidence showed that tamoxifen, a well known anti-oestrogen drug, may exert beneficial effects on breast cancer, osteoporosis, atherosclerosis and autoimmune disorders via TGF- β . The combination of tamoxifen and TGF- β 1 injections increased the apoptosis incidence in the preneoplastic foci in the rat liver. The researchers hypothesise that by giving tamoxifen to rats receiving thioacetamide, the process of hepatic fibrosis should be hastened and cirrhosis would develop at a much earlier stage. Confirmation of this hypothesis would allow development of pharmacological agents which could influence the action of TGF- β in the liver and enable therapeutic intervention for the treatment of hepatic fibrosis.
(MD96102)

Innovation Technology to Develop Human Cell Lines for Biomedical Applications and Biopharmaceutical Production

✉ LEUNG Mun Fai ● IP Nancy*
 □ 1 July 1996

- ❖ Industrial Support Fund, Industry & Technology Development Council

It is generally recognized that the production of human cell lines is essential for biotechnology research and development, as well as for neural and blood cell therapy. Most of the ongoing research projects involving human cells are either performed with cell lines of tumor origin or with primary cultures which are time-consuming and cannot be grown in large quantities. Furthermore, progress in gene and cell therapy involving neural transplantation as well as blood cell replenishment therapy has been hindered by the availability of large quantities of human neuronal cells and stromal cells, respectively. In addition, production for other types of cell lines applicable to other biotechnology-related industries are also in great demand. Examples include establishment of cell lines for the production of specific proteins and screening of therapeutic drugs. Any gene of interest, such as insulin or growth hormone, can be introduced into the cell lines for large-scale production; screening of actions of chemical compounds or Chinese herbal extracts can also be accomplished using the cell lines established. Other potential applications include isolation of specific yeast strain for improving the quality of fermentation products such as beer favor, and screening of effective algae culture for improving waste treatment. This proposal aims to develop an innovative technology involving the use of mutagenesis coupled with flow cytometry to efficiently produce large number of human cell lines for biotechnological applications. It will undoubtedly represent a major advance over current technology of using primary tissue cultures or cell lines of tumor origin. The primary focus is on the production of human neuronal cell lines and bone marrow stromal cell lines. Large quantities of these cells will be extremely valuable for neural and blood cell transplantation. The deliverables of this project will be the development of well characterized human clonal cell lines that can be produced in large quantities. Most significantly, the development of such an innovative technology in producing cell lines will enhance the status of Hong Kong biomedical/pharmaceutical industry in the world. (MD96192)

Does Intensive Rehabilitation Improve the Functional Outcome of Traumatic Brain Injury (TBI)?

- ✍ POON Wai Sang ● ZHU Xian Lun ● HSIANG John Keung ● CHAN Che Hin* ● IP Wei Chung* ● CHANG Wai Ching*
- ☐ 1 August 1996
- ❖ Health Services Research Fund, Hospital Authority

The demand on resources for neurorehabilitation is increasing. Appropriate outcome and cost-effectiveness evaluations are required. In association with this, a question remains concerning the appropriate degree of intensity needed for maximizing the effectiveness of rehabilitation for traumatic brain injury (TBI) patients. At present this intensity varies throughout the world from less than 1 hour to 7 hours per day. This project proposes to assess the effectiveness of an intensive rehabilitation program for TBI patients (as measured by patient functional outcome). Two groups of TBI patients receiving different intensity levels of rehabilitation at the early post-traumatic stage will be compared (Sample size: 34 vs 34). The study will control the quality of rehabilitation and personnel involved in the rehabilitation by keeping these the same in the two arms of the trial. The only factor allowed to vary will be the amount of service (one arm having double the amount service time as that provided by the other). The results of the study will be directly useful in determining appropriate resources for TBI rehabilitation, and has the potential to be applied to other fields of neurorehabilitation. (MD96006)

Neuropsychological Outcome after Mild Head Injury: Any Difference if the Injury is Work-related?

- ✍ POON Wai Sang ● NG Kee On (Psychiatry) ● HSIANG John Keung ● CHAN Kin Yuen (Psychiatry)
- ☐ 1 November 1996
- ❖ CUHK Research Committee Funding

Mild head injury, defined as Glasgow Coma Scale 13-15 with transient loss of consciousness, contributes over 90% of head injury admissions to hospital. More than 10% of mild head injury patients acquired their injury at work. Each year, there are enormous amounts of compensation given and productivity lost because of this seemingly mild, but significant injury. The results of the researchers pilot study on postconcussion syndrome following mild head injury demonstrated that work-related injury patients have significantly higher compensation and longer sick leave when compared with their non work-related injury counterparts. The reasons behind these findings remain uncertain. However, it is believed that prolonged recovery from mild head injury probably is the result of an interplay between a number of factors: organicity; subtle cognitive deficits or complex attentional processes (defined by specific neuropsychological testing); psychogenic factor and state of mental health (defined of General Health Questionnaire-30); and occupational nature and status (types of work; responsibilities etc). The aim of this project is to investigate the rate of recovery of work and non work-related patients after

mild head injury, and their relationship with the aforesaid factors.
(MD96100)

Molecular Expression of Hypothalamic Atrial Natriuretic Peptide (ANP) and Anti-diuretic Hormone (ADH) in Hyponatraemia Following Experimental Head Injury

✉ POON Wai Sang ● NG Ho Keung (Anatomical & Cellular Pathology) ● LOLIN Yvette Ivanka (Chemical Pathology) ● YEUNG Tok Fai Vincent (Medicine) ● COCKRAM Clive Stewart (Medicine)

☐ 1 January 1997

❖ CUHK Research Committee Funding

Acute hyponatraemia (low plasma sodium < 134 mmol/l) occurs in 33% of severe head injuries and can cause further damage to an already compromised central nervous system. Clinical studies have suggested that the majority of these cases of hyponatraemia are due to cerebral salt wasting, the minority Syndrome of Inappropriate secretion of Anti-Diuretic Hormone (SIADH). Cerebral salt wasting is associated with an elevated circulating atrial natriuretic peptide (ANP), causing excessive sodium loss in the urine, with resultant polyuria and dehydration, the rational treatment being salt and fluid replacement. With SIADH, however, there is fluid retention, and accordingly, the logical treatment is fluid restriction.

Meticulous clinical studies have helped the researchers to distinguish these two syndromes (requiring opposite fluid management) by the plasma/urine derived biochemistry, subsequently confirmed by circulating ANP and ADH concentrations. To further understand the primary pathophysiology of acute post-traumatic hyponatraemia, one has to look beyond the confines of clinical studies, to the molecular expression of ANP and ADH in the hypothalamus using a head injury model.

50 rats will be employed using the severe diffuse head injury model, of which it is estimated that 10 will die from the primary insult, and 12 will develop acute hyponatraemia, leaving 28 normonatraemic. Plasma/urine biochemistry, circulating ANP and ADH levels, ANP immunohistochemistry and *in situ* hybridisation in coronal brain section, and Northern blotting for ANP and ADH m-RNA expression in the hypothalamus will be compared between the hyponatraemic and normonatraemic animals.
(MD96103)

Effect of Radiotherapy on the Cochlear and the Central Auditory Conduction Pathway in Patients with Nasopharyngeal Carcinoma (NPC)

✉ VAN HASSELT Charles Andrew ● TONG Chi Fai Michael

☐ 1 July 1996

❖ CUHK Research Committee Funding

To investigate the effects of radiation on the auditory system in patients with NPC. To understand and monitor the progression of hearing problems in patients with NPC and to apply this information in future patient care and rehabilitation.
(MD96012)

A Double Blind Randomised Placebo-control Trial on the Efficacy of Peri-operative Zithromax as Prophylactic Antibiotic for Functional Endoscopic Sinus Surgery

✉ WOO Kong Sang John ● TONG Chi Fai Michael ● VAN HASSELT Charles Andrew ● KU Peter K. M.* ● CHANG Mei Kam Amy

☐ 1 October 1996

❖ Pfizer Corporation

Chronic Rhinosinusitis is one of the commonest nasal conditions encountered in specialist's practice. Patients with this problem are prone to have recurrent infections. The use of perioperative antibiotics is infrequently practiced in other parts of the world and observed less perioperative bleeding and faster healing in the majority of patients. So, the researchers believed that a well planned clinical trial is required to prove its efficacy. Zithromax is a broad spectrum antibiotic with a stable drug level maintained for more than one week. It would thus appear that the use of Zithromax is a logical choice to demonstrate any benefits of pre-operative antibiotic regime.
(MD96143)

The Functional Outcome of Sharp Dissection Versus Laser Surgery for Benign Disease of the Vocal Cords

✉ WORMALD Peter-John ● SOO Gordon* ● CHANG Mei Kam Amy

☐ 1 September 1996

❖ CUHK Departmental Funding

Traditional sharp dissection techniques have for years been accepted as the most effective method of surgically treating benign disease of the vocal cords. However, laser surgery of the cords has recently gained the popularity and has now achieved widespread acceptance. The superiority of either traditional sharp surgical dissection as apposed to

laser excision has yet to be clearly shown. A study looking at the randomization of cases between the two modalities is needed to objectively assess both forms of therapy.
(MD96142)

Differences in Prevalence, Phenotype characteristics and Antigenicity of Helicobacter Pylori Infection in Children: A Comparative Study between Hong Kong and Jiangsu

✉ YEUNG Chung Kwong ● CHEN Junshi* ● WU Yongning* ● CHUNG Sheung Chee Sydney ● SUNG Joseph Jao Yiu (Medicine) ● PANG Chi Pui Calvin (Chemical Pathology)

□ 1 October 1996

❖ CUHK Research Committee Funding

It has been firmly established that Helicobacter pylori infection plays an important role in the pathogenesis of various gastroduodenal diseases including gastritis, peptic ulcerations and gastric cancer. However, the predominant associated pathological condition seems to vary among different geographical locations. While there is a very strong correlation between H.pylori infection and peptic ulcer diseases in Hong Kong, the microorganism seems to be much more associated with gastric carcinoma in high prevalence areas for gastric cancer like Jiangsu Province in China. The aim of this project is to study the differences in prevalence and age distribution, phenotypic characteristics, environmental and dietary factors as well as the antigenicity of H.pylori infections between the two places. As recent data suggest that H.pylori infections are often established early in life, the researchers propose to recruit school children aged 7-15 years from both areas for this study. The results from this study may well provide important clues to the difference in pathogenesis and management strategy for peptic ulcer diseases and gastric cancer. Furthermore, the epidemiological data obtained will be crucial for further planning of population-wide screening and eradication (e.g. by vaccination) of H.pylori infection.
(MD96104)

Comparative Study of Clip Applier Versus Conventional Suturing for Vascular Anastomosis in a Porcine Saphenous Vein - Carotid Artery Interposition Graft Model

✉ YIM Ping Chuen Anthony ● IZZAT Mohammad ● HO Chin Ho Kenny

□ 1 August 1996

❖ CUHK Research Committee Funding

Objective: To evaluate the efficacy of clip applier versus conventional suturing for vascular anastomosis.

Material and Method: The porcine saphenous vein-carotid artery interposition graft model will be used. 10 female swine (body weight 30-40kg) will be used for this study. Under general anaesthesia, clip applier (VCS clip applier Autosuture, USSC) will be used on the left carotid and conventional suturing on the right. Time taken for completion of the anastomosis and any intraoperative complications noted. Animals will be sacrificed at 4 weeks and outcome measures include integrity of the anastomosis, histological and electron microscopy study of the anastomosis.
(MD96105)

A Comparative Study of the Effects of Wedge Lung Resection by Thoracoscopy Versus Thoracotomy on the Metabolic and Immunological Response in a Porcine Model

✉ YIM Ping Chuen Anthony ● HEWITT Peter ● HO Jonathan Kei Shing

□ 15 August 1996

❖ Research Grants Council

The clinical benefits of thoracoscopy over thoracotomy in terms of minimizing chest wall trauma and decreased post-operative morbidity are generally well established. However, the biological bases behind these improvements remain to be established. This is particularly relevant as thoracoscopy is increasingly being applied to resection of early lung cancer and mediastinal tumour. As immune surveillance is thought to be important in limiting the spread of tumour cells, any surgical technique that preserves immunity may improve overall results. If the hypothesis is correct that thoracoscopy can better preserve body immunity, it would have a major impact on current perspectives regarding treatment of intrathoracic malignancy.
(CU96658)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition Title/Investigators

1994-95 Biliary Drainage Decompression with Nasobiliary Catheter Versus Plastic Biliary Stent in Acute Suppurative Cholangitis - A Randomised Controlled Trial (MD95047)

✉ CHAN Chi Wai Angus ● CHUNG Sheung Chee Sydney ● SUNG Joseph Jao Yiu (Medicine) ● LI Ka Wah Michael ● NG Enders K. W.* ● LAU James Y. W.*

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)
- 1994-95 Antiemesis Efficacy of Trepisetron Against Cisplatin: A Randomized Trial Comparing with High Dose Metoclopramide (MD94120)
 ✍ CHUNG Sheung Chee Sydney ● LAU James Y. W.* ● CHAN Chi Wai Angus ● NG Enders K. W.*
- 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.
- 1995-96 Biological Modulation of Growth of Nasopharyngeal Carcinoma Cells by Human Recombinant Interferon-alpha and 13-cis Retinoic Acid (CU95665)
 ✍ KING Walter Wing Keung ● LI Arthur K. C. ● LAM Ping Kuen ● LIEW Choong Tsek (Anatomical & Cellular Pathology)
- 1995-96 Polytetrafluorethylene for Guided Tissue Support and Regeneration in Primary Closure of Cleft Palate Defects (MD95169)
 ✍ KING Walter Wing Keung ● CHAN Sun Yin Eric ● TO Wai Hei ● KUO Chi Chu
- 1993-94 Molecular Pathology and Treatment of Virus Related Hepatocellular Carcinoma (MD94015)
 ✍ LAU Wan Yee Joseph ● JOHNSON Philip James (Clinical Oncology) ● TAM Siu Lun John (Microbiology)
- LIEW Choong Tsek (Anatomical & Cellular Pathology) ● LEUNG Wai Yee Nancy (Medicine) ● LI Arthur K. C.
- 1994-95 Analysis of Allelic Loss of the RB Tumour Suppressor Gene in Hepatocellular Carcinoma by Polymerase Chain Reaction Based Allotyping (MD94106)
 ✍ LAU Wan Yee Joseph ● LI Arthur K. C.
- 1994-95 Analysis of Polymorphic Expression of the Glutathione S-Transferase α Gene by Polymerase Chain Reaction in Human Liver and Lung Cancer (MD94107)
 ✍ LAU Wan Yee Joseph ● HO Jonathan Kei Shing ● YIM Ping Chuen Anthony ● LI Arthur K. C.
- 1994-95 Autoregulation Monitoring Using Laser-Doppler Flowmetry on Patients with Head Injury (MD94149)
 ✍ POON Wai Sang ● HSIANG John Keung ● LAM Ming Kuen*
- 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*
- 1995-96 Efficacy of Ondansetron 4mg for Prevention of Nausea and Vomiting after Middle Ear Surgery (MD94167)
 ✍ TONG Chi Fai Michael ● KU Peter Ka Ming* ● LO Suk Yee ● VAN HASSELT Charles Andrew ● WOO Kong Sang John ● CHEN Phoon Ping (Anaesthesia & Intensive Care) ● YUE Virgil* ● PAK Martin Wai*
- 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 Otological Ear Drops on Myringoplasty for Chronic Suppurative Otitis Media (MD95233)
 ✍ VAN HASSELT Charles Andrew ● YUE Virgil* ● TONG Chi Fai Michael ● PAK Martin W.* ● KU Peter K. M.* ● CHANG Mei Kam Amy

- 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) ● 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 mTHPC-mediated 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
- 1995-96 Splitted Kidney Glomerular Filtration Rates (GFR) and Ofloxacin Excretions in Postobstructive Kidneys and Contralateral Normal Kidneys (MD95145)
 ✎ WONG Wai Sang ● CHAN Siu Foon Peter
- 1995-96 The Effect of α -adrenergic Blocker on Patients with Urinary Retention (MD95242)
 ✎ WONG Wai Sang ● CHAN Siu Foon Peter ● CHAN Lung Wai*
- 1995-96 A Prospective Study on the Process of Diagnosing Nasopharyngeal Carcinoma (MD95234)
 ✎ WOO Kong Sang John ● CHANG Mei Kam Amy
- 1994-95 The Role of Helicobacter Pylori Infection in Childhood Recurrent Abdominal Pain: A Prospective, Randomised, Placebo-Controlled Study (MD95036)
 ✎ YEUNG Chung Kwong ● LAU Chun Yuen (Paediatrics) ● CHUNG Sheung Chee Sydney
- 1995-96 The Development of Bladder Function and Micturition Control in Human Infants: A New Appraisal (CU95666)
 ✎ YEUNG Chung Kwong ● NG Pak Cheung (Paediatrics) ● HO Kwok Wah Crover (Psychiatry) ● LIU Kam Wing Kelvin ● LI Arthur K. C.
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 ✎ YIM Ping Chuen Anthony

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see also <P960290>, <P961629>, <P961680>, <P961731>, <P961754>, <P961777>, <P961804>, <P961806>, <P961822>, <P961857>, <P961861>, <P961874>, <P961883>, <P962175>, <P962191>, <P962195>, <P962272>, <P962294>, <P962328>, <P962401>, <P962430>, <P962492>, <P962526>, <P962551>, <P962552>, <P962622>, <P962656>, <P962728>, <P962762>, <P963194>, <P963254>, <P963882>, <P963883>, <P963884>, <P963899>, <P963906>, <P963949>, <P970051>, <P970061>, <P970116>, <P970126>, <P970127>, <P970136>, <P970158>, <P970185>, <P970214>, <P970303>, <P970328>, <P970382>, <P970417>, <P970429>, <P970430>, <P970554>, <P970580>, <P970769>, <P970846>, <P970853>, <P970939>, <P971025>, <P971038>, <P971039>, <P971040>, <P971099>, <P971120>, <P971121>, <P971254>, <P971408>, <P971603>, <P971606>, <P971608>, <P971609>, <P971630>, <P971651>, <P971882>, <P972106>

RESEARCH PROJECTS

A Comparison between the Effects of Percutaneous and Oral 17-Beta Oestradiol on Atheroma Formation and Vascular Reactivity in Cholesterol-Fed Ovariectomised Rabbits

✍ 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)

☐ 1 October 1996

❖ CUHK Research Committee Funding

The proposal is designed to establish whether percutaneous oestradiol gel, accurately measured and consistently applied to cholesterol-fed ovariectomised rabbits, prevents atheroma formation as effectively as orally administered oestrogens.

The proposal is also designed to demonstrate whether the percutaneously administered oestrogen beneficially effects the reactivity of a peripheral arteries measuring the resistance to flow in a peripheral artery of hypercholesterolaemic ovariectomised rabbits. The ability to demonstrate a reduction in resistance to flow would be supportive of cardioprotective effect of percutaneously administered oestradiol gel in HRT.

If the results of the study demonstrate a reduction in the formation of atheroma and a reduction in resistance to flow in the peripheral arteries, it will have major clinical significance. The study will have confirmed that the gels have the same protective effect against the development of cardiovascular disease to that of the orally administered oestrogens. This information would form the basis of an improved rationale for HRT in women.

(MD96039)

RESEARCH OUTPUTS AND PUBLICATIONS

<P963566> **James, A.E.** "Agricultural Support Services Project - Australian Aid Program". *Laboratory Animal Management Program* p.16. Australia: Hassell & Associates, Australia, 1996.07.30.

<P971462> **James, Tony.** "Laboratory Animal Science in Hong Kong". *ANZLAS Newsletter, Winter 1997* Winter. pp.8-10. 1997.

see also <P971421>

RESEARCH PROJECTS

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

- ✉ LAU Tak Fai Joseph ● MICHON John
(Ophthalmology & Visual Sciences)
- ☐ 1 December 1996
- ❖ Health Services Research Fund, Hospital Authority

Cross-sectional epidemiological study is the most appropriate approach to provide the principles and methods to assess the prevalence of eye diseases in the over 40 years of age population of Hong Kong and provide data for policy, planning and allocation of resources. Hong Kong has a large and increasing elderly population. Recently completed population-based studies in other countries have shown that the leading causes of visual impairment are age-related. Most of the eye diseases of the elderly are progressive and cause blindness, but with proper detection and management, these diseases and the associated blindness are largely preventable. The ultimate goal of this study is to have a comprehensive understanding of eye diseases in Hong Kong so that appropriate public health and research programs may be planned, executed and evaluated to decrease the burden of vision loss on the aging population. (MD96016)

Hong Kong AIDS Information Net Project

- ✉ LAU Tak Fai Joseph
- ☐ 1 December 1996
- ❖ Hong Kong Aids Trust Fund

With the great leap of computer and information technology, the world has recently entered an age of information. Information becomes popular among both policy makers and the general public. The Internet eventually plays a pivotal role in circulating information that is important to the public. Information about AIDS is a candidate for public interest and access, with a goal to reduce the risk of AIDS and instigate public support for persons with AIDS. To enable the transmission of information through the Internet, the proposed project initiates technology required to set up a Hong Kong AIDS Information Net. The specific aims of the Net is to (1) build a homepage for all governmental and non-governmental organisations that are working to fight against AIDS, and (2) convey up-to-date information including newspaper clippings, guides for HIV testing, counseling, and clinical services. So far, this project has obtained the generous contribution of the Health Department of the Government and eight non-

governmental organisations to the provision of information regarding AIDS. The project will thus feature multi-purpose information catering to both local and international needs for education and communication. It will perennially update information in the Net and provide annual maintenance even beyond its two-year initialization period. (MD96133)

Knowledge and Attitudes of Social Service Personnel II

- ✉ LAU Tak Fai Joseph ● CHEUNG Chau Kiu
(Medicine)
- ☐ 1 January 1997
- ❖ Hong Kong Council of Social Services

The study involves a mail survey of social service personnel in 1997. It represents a follow-up survey to the one initiated in 1994 and is going to collect data from about 3,000 social service personnel working in various setting. Issues on AIDS, concerning providing services to persons with HIV/AIDS and their families are critical for social service personnel. Inadequate knowledge, negative attitudes, and insufficient training would impair the effectiveness of social service delivery. The survey aims at assessing current experiences, knowledge, need for training, and attitudes regarding issues of AIDS among social service personnel. With these data, the study can chart change in these aspects from 1994 to 1997. The survey is collecting data from January, 1997 and will have results in June, 1997. (MD96130)

Qualitative Study of the APIs on AIDS

- ✉ LAU Tak Fai Joseph ● JONES Rodney*
- ☐ 1 January 1997
- ❖ CEPAIDS, Department of Health

The study involves focus group interviewing with people of various walks of life concerning announcement of public interest (APIs) related to issues of AIDS. For more than a decade, the Government and voluntary agencies have perennially released APIs to promote the public's prevention of AIDS and support for persons with HIV/AIDS. In response to the constant flux of issues of AIDS, APIs have been changing in focus. Furthermore, a variety of APIs is necessary to appeal to different people who have different needs and preferences. Matching an API with an audience's need is a thorny exercise. Whereas the mass survey method would not offer much help in such matching, focus group interviewing is apt to reveal down-to-earth information on an individual's preference and evaluation of specific APIs. A focus group consists

of 8 to 10 participants who can freely discuss about a focal issue. The premise of social facilitation enables the focus group to stimulate creative thinking and discussion that are untenable in individual interviews. The focus groups are going to discuss issues concerning preference and evaluation of some APIs currently released by the Government in order to identify effective elements and issues concerning efforts towards publicity and education on AIDS prevention. (MD96131)

Public Opinion on Child Abuse - A Follow-up Study

✉ LAU Tak Fai Joseph ● CHEUNG Chau Kiu (Medicine)

☐ 1 March 1997

❖ Hong Kong Government

The study involves a telephone survey of about 1,200 people randomly sampled from the residential population in 1997. It represents a follow-up survey to the one initiated in 1996. Child abuse appears to be an increasingly salient issue in Hong Kong. To prevent it, the Government and voluntary agencies have launched series of campaigns and services. Assessing public opinion concerning child abuse, including awareness of it, willingness to seek help, and evaluation of publicity effort comprises the focus of the survey. With these data, the study can track the annual change of public opinion, following a year of campaign effort. The survey is going to commence in March and will have results in August, 1997. (SS96042)

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

Edition	Title/Investigators
1994-95	Sentinel AIDS-related Behavioural Surveillance Project (SS94029) ✉ LAU Tak Fai Joseph ● NG Mun Hon* ● LEE Shui San* ● LEE Peter*

1995-96 Quality of Life Study for Cancer Patients in Hong Kong (MD94068)
✉ LAU Tak Fai Joseph ● SHAM J.* ● FIELDING R.* ● LEUNG Sing Fai (Clinical Oncology) ● CHAN Cecilia*

1995-96 The Community Research Programme on AIDS in Hong Kong (SS93014)
✉ LAU Tak Fai Joseph

1995-96 Public Attitudes towards Handicapped Persons in Hong Kong - A Benchmark Study for Evaluation (SS94023)
✉ LAU Tak Fai Joseph

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*

1995-96 Development of Chinese Version of WHOQOL Scale (HK Team) (MD95092)
✉ LAU Tak Fai Joseph ● LEUNG Kwok Fai*

1995-96 Public Attitude towards Handicapped Persons in Hong Kong - A One-year Follow-up Study (MD94163)
✉ LAU Tak Fai Joseph ● CHEUNG Chau Kiu (Medicine)

1995-96 Opinion Survey on Child Abuse (SS95049)
✉ LAU Tak Fai Joseph ● CHEUNG Chau Kiu (Medicine) ● CHING Ka Wai Vivian

1995-96 Need Assessment for AIDS Policy and AIDS Education in Workplace (MD95182)
✉ LAU Tak Fai Joseph ● TONG Fred* ● LI Patrick*

RESEARCH OUTPUTS AND PUBLICATIONS

<P961783> 林國威、張宇橋、劉德輝、梁淑芳. <兒童少年人體測量指標計算軟件>. 《兒童生長標準的製定與應用論文選編》(第二冊), 頁 16-17. 西安: 香港中文大學醫學院, 第四軍醫大學, 1996.11.01.

<P961784> 劉德輝、梁淑芳、伍超標、林國威、黃永堅、楊桂芬. <青春期橫斷面調查和縱向追蹤資料的研究分析>. 《兒童生長標準的製定與應用論文選編》(第二冊), 頁 14-15. 西安: 香港中文大學醫學院, 第四軍醫大學, 1996.11.01.

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RESEARCH PROJECTS

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
1995-96	Study on Bone Mineral Density and Biochemical Markers in Hong Kong Chinese Perimenopausal Women (MD95124) ✉ LEE Kwong Man Simon ● HO Chan Suzanne (Community & Family Medicine) ● WOO Jean (Medicine)

RESEARCH PROJECTS

Please refer to previous issues of *Research Projects Summary* for more details of the following ongoing research at the department:

<u>Edition</u>	<u>Title/Investigators</u>
1995-96	Cervical Screening in New Territories East: Prevalence of Unmet Need (MD95149) ✉ HAZLETT Clarke Blaine