

OUR VISION

The School's Vision is "To be amongst the best medical schools in the world" and is dedicated to integrating the closely linked missions of clinical excellence, research, and education to produce doctors that meet Singapore's current and future healthcare needs, as well as developing solutions to Singapore's healthcare problems.



Immunomodulatory and anticancer activities of polysaccharide-protein complex from *Lycium barbarum* L.

Cover image compliments of
Emeritus Prof Chan Soh Ha

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BEING AT THE **FRONTIERS OF MEDICINE**,
IT IS **OUR IMPETUS** TO
CONTRIBUTE TO THE COMMUNITY BY
MAKING THE LINK BETWEEN
BREAKTHROUGH RESEARCH
AND THE MEDICAL NEEDS OF SOCIETY,
AT THE SAME TIME **AIMING FOR EXCELLENCE** AND
CREATING IMPACT **BEYOND THE ORDINARY.**

FOREWORD



NUS

National University
of Singapore

YONG LOO LIN SCHOOL OF MEDICINE

OUR IMPETUS BEHIND EDUCATION, RESEARCH AND ENTREPRENEURSHIP

EDUCATING AND PROVIDING INSIGHTS INTO RESEARCH WHILE
LINKING RESULTS TO IMPROVE THE WAY WE PRACTICE MEDICINE

YONG LOO LIN



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YONG LOO LIN SCHOOL OF MEDICINE

FOREWORD



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FOREWORD



The National University of Singapore has a clear vision to be a globally oriented university with a dynamic community, imbued with a “no walls” culture and a spirit of enterprise which promotes the free flow of ideas and builds synergies between the processes of creating, imparting and exploiting knowledge.

To this end, the Yong Loo Lin School of Medicine aspires to achieve research with impact and be at the forefront of biomedical development and patient care by focusing on “all the way” research programmes. We envision projects which can potentially take an idea from basic research to disease-oriented research, launch patient-oriented research clinical trials, and be supported by health services research.

In 2006, we witnessed a tremendous national drive and focus on translational research, with the Singapore government renewing its support for the Biomedical Sciences (BMS) initiative, which was first launched in mid-2000. As a key part of the 2nd phase of its Biomedical Sciences Initiative from 2006-2010, the Government has earmarked S\$1.4B to support translational and clinical research (TCR) to bring basic BMS research discoveries into clinical application, from “bench” to “bedside”. Spearheading this effort are the Agency for Science, Technology and Research (A*STAR)’s Biomedical Research Council (BMRC) and the Singapore Ministry of Health’s National Medical Research Council (NMRC).

The School of Medicine has therefore restructured its research strategy to dovetail with the national strategic disease-oriented areas, with investigators forming multidisciplinary, cross-departmental and cross-faculty collaborative groups with particular focus on the following areas:

- a) Cancer,
- b) Cardiovascular/Metabolic Disorders,
- c) Neurosciences,
- d) Infectious diseases, and
- e) Eye diseases.

An International Advisory Panel visited our School from 20-23 February 2006. Departments presented key challenges and sought the Panel’s advice on issues of education and research. The Panel comprised Dr Ralph L Nachman, Professor and Chairman, Department of Medicine, Weill Cornell Medical Center, and Physician-in-Chief, New York Presbyterian Hospital - Cornell Campus, USA; Professor Edward Holmes, Vice Chancellor of Health Sciences and Dean of School of Medicine, University of California, San Diego, USA; and Professor Tak H Lee, Professor of Respiratory Medicine & Allergy, King’s College London, Guy’s Hospital, UK. The IAP report affirmed our School’s direction and noted that there is tremendous potential in the next 5-10 years to capitalize on the commitment to establish clinical excellence by leveraging on a strong programme in clinical research.

FOREWORD

2006 also saw the establishment of three new centres at the School of Medicine:

i) Health services research was given a boost in Singapore with the launch of the NUS Centre for Health Services Research in August 2006. This centre was the result of our School's collaboration with RAND Health, the health division of the internationally renowned US-based think-tank RAND Corporation. It aims to accelerate the development and implementation of health services research in Singapore. Housed within the School, the Centre for Health Services Research will conduct a needs assessment with the Ministry of Health, SingHealth and the National Healthcare group to identify urgent and major health services research needs and to ensure that our research is always relevant in addressing Singapore's healthcare problems.

ii) Another significant milestone in 2006 was the launch of Singapore's first academic centre for biomedical ethics on 27 October 2006. Helmed by Professor Alastair Campbell, the Chen Su Lan Centennial Professor in Medical Ethics, the NUS Centre for Biomedical Ethics will support the teaching, scholarship and research of bioethics in the fields of medicine, allied health and the life sciences in Singapore. It will serve as a national resource, complementing existing ethics units such as the Bioethics Advisory Committee, the Singapore Medical Association Ethics Committee, and the institutional review boards (IRBs). The Centre's early research efforts will encompass areas such as the ethics of stem cell therapy, the uses of human tissue in cultural contexts, and the bioethical issues associated with the challenges of an ageing population.

iii) Singapore's first Bachelor programme in Nursing by the Alice Lee Centre for Nursing Studies commenced at NUS in August 2006. More than 2,000 students applied for admission, from which 49 were selected. A further intake of 50 is planned for 2007-2008. With medical treatment growing increasingly complex and hospitals seeing more cases of patients with multiple chronic conditions such as heart diseases, diabetes and kidney failure, it is imperative for Singapore nurses to be trained to enter new paradigms of care and shoulder a greater proportion of the healthcare burden. The new NUS nursing degree will equip graduates to function effectively and independently in a 'high-tech' multi-disciplinary hospital environment, assume leadership and supervisory responsibilities in hospitals, take on educational roles in the community, and conduct research as evidenced-based practitioners.

Faculty achievements

To further spearhead translational research, Singapore welcomed renowned physician leaders Professor Edward Holmes and Judith Swain, who hold joint appointments at NUS and A*STAR. Professor Holmes was appointed Executive Deputy Chairman for Clinical Translational Sciences at the Biomedical Research Council of A*STAR, while Professor Swain was appointed as NUS Lien Ying Chow Professor of Medicine and founding Executive Director of the Singapore Institute for Clinical Sciences (SICS). SICS was established in 2006 to speed up the development of therapeutic and diagnostic tools for common diseases such as vascular disease and cancer. The Institute aims to attract, train and nurture clinician scientists as well as serve as a bridge linking basic biomedical research and clinical research conducted at A*STAR, NUS, NUH and other universities, hospitals and disease centres.

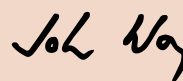
I would like to highlight a few of the research achievements of our faculty members. Led by Professor Donald Tan, the national research taskforce to investigate Fusarium keratitis cases linked to cosmetic contact lens wear was the first group in the world to publish findings on the fungal outbreak in the prestigious Journal of the American Medical Association. Researchers and scientists from several School of Medicine departments including Ophthalmology, COFM and Medicine (namely Associate Professors Aung Tin, Wong Tien Yin, Saw Seang Mei, Paul Tambyah and Adj Prof Roger Beuerman) contributed significantly to this taskforce. Initiated by the Singapore Eye Research Institute (SERI) and later coordinated through the Singapore National Eye Centre (SNEC), the group was the first to identify the epidemic of this potentially blinding condition among contact lens wearers. The taskforce was commended by the Minister of Health and the Prime Minister's Office for their national efforts and honoured with the Health Minister Awards on 10 July 2006.

Professor Barry Halliwell and Professor Alastair Campbell received NUS Centennial Professorship Awards from NUS President, Professor Shih Choon Fong during the State of University Address on 20 October 2006.

Also at the University level, Professor Lee Eng Hin (Department of Orthopaedic Surgery) was honoured with the University Outstanding Researcher Award, and Dr Leonard Ang (Department of Ophthalmology) was honoured with the University Young Researcher Award. These awards are given annually to recognize outstanding staff achievement and to stimulate quality research in the University. Prof Lee's research achievements include pioneering a study of mesenchymal stem cells for the repair and regeneration of chondral (articular cartilage) defects in adults and physal (growth plate) defects in long bones of children – now at the stage of clinical application – and the use of bioresorbable 3-D scaffolds as carriers for cells and growth factors to promote healing and repair of musculoskeletal tissues. Dr Ang has pioneered novel methods of ocular stem cell expansion and transplantation, including the use of a multi-step serum-free culture system for developing safe and effective bioengineered eye tissue-equivalents. His team was also the first to transplant autologous serum-free bioengineered ocular tissues successfully for the treatment of a variety of eye diseases.

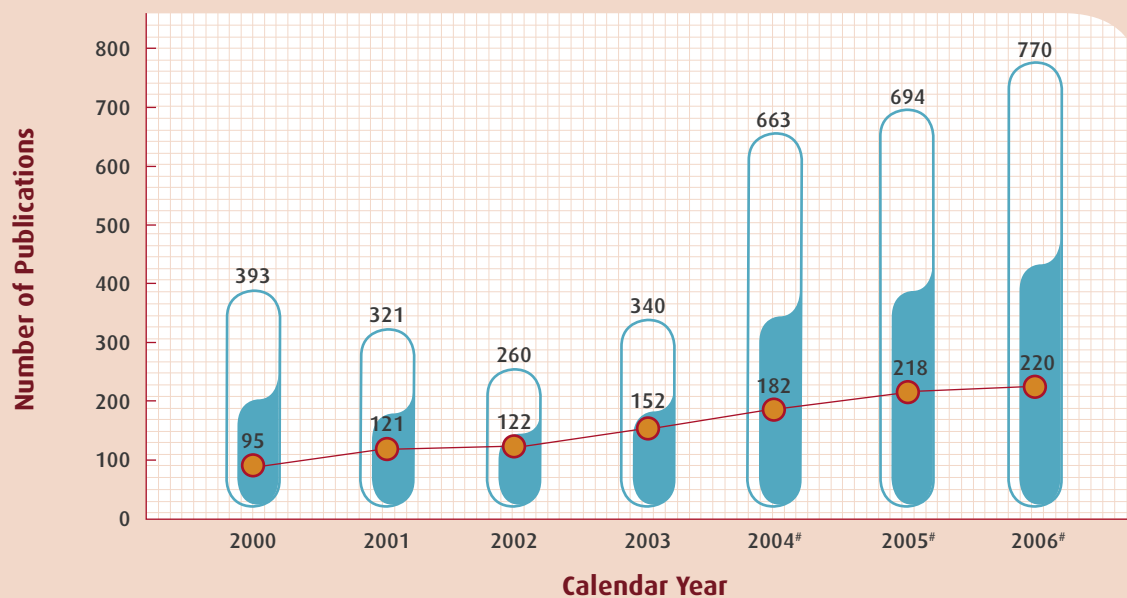
The School of Medicine continued to win strong funding support from external funding agencies, garnering over S\$36 million in research funding for FY2006. In 2006, the School also continued the upward trend of publishing in leading international journals, with the total number of international refereed journals increasing by almost 10%.

In conclusion, the year has been a very active and fruitful one for the School. These are exciting times in Singapore's academic and biomedical scene. With this array of research developments and infrastructure underway, we look forward to the transformation of our School into a world-class translational academic campus.



Professor John Wong
Dean
Yong Loo Lin School of Medicine

FOREWORD

Research Funding**Research Publication: Tier 1 (IF ≥ 4.5) indicated by line**

[#] Data calculated based on new Staff Research Publication System

● Tier 1

● Total Publications (International Refereed)

PROGRAMMES



NUS

National University
of Singapore

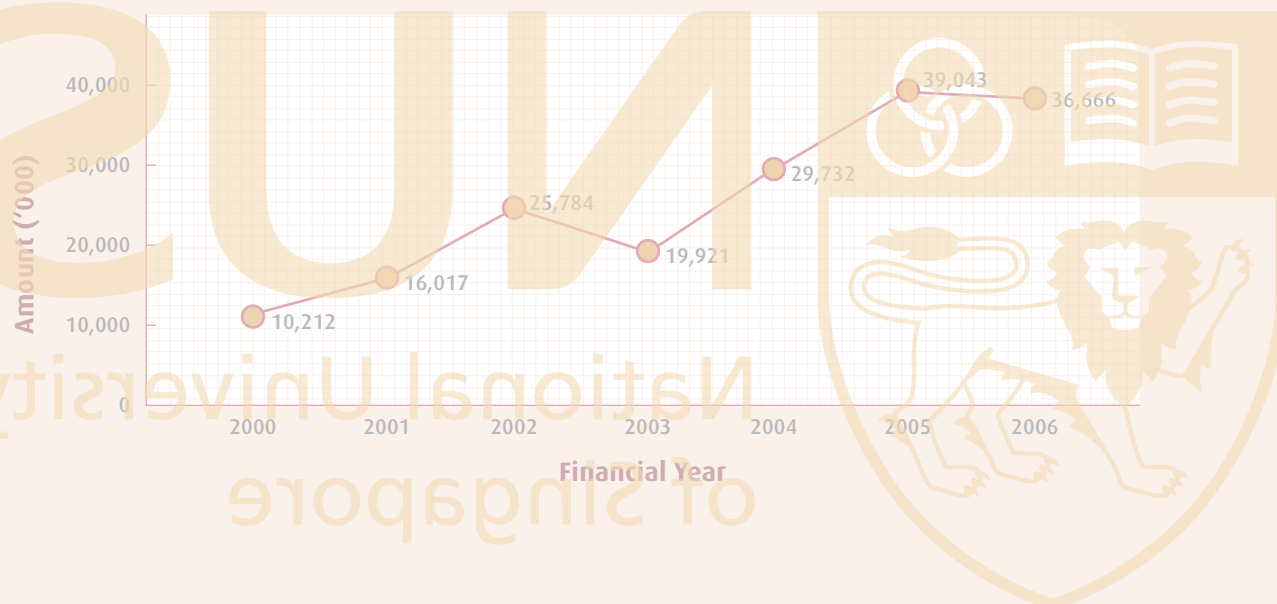
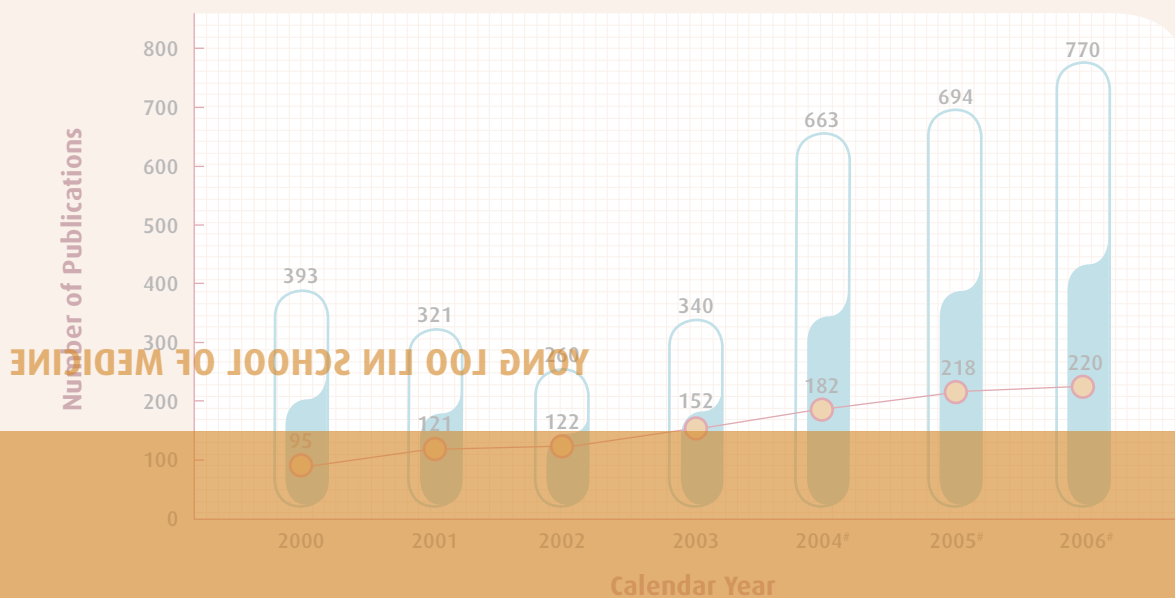
YONG LOO LIN SCHOOL OF MEDICINE

CONDUCTING
**BREAKTHROUGH
RESEARCH**

COMPREHENSIVE PROGRAMMES ENSURE THAT
OUR MEDICAL KNOWLEDGE IS APPLICABLE

FOREWORD

Research Funding

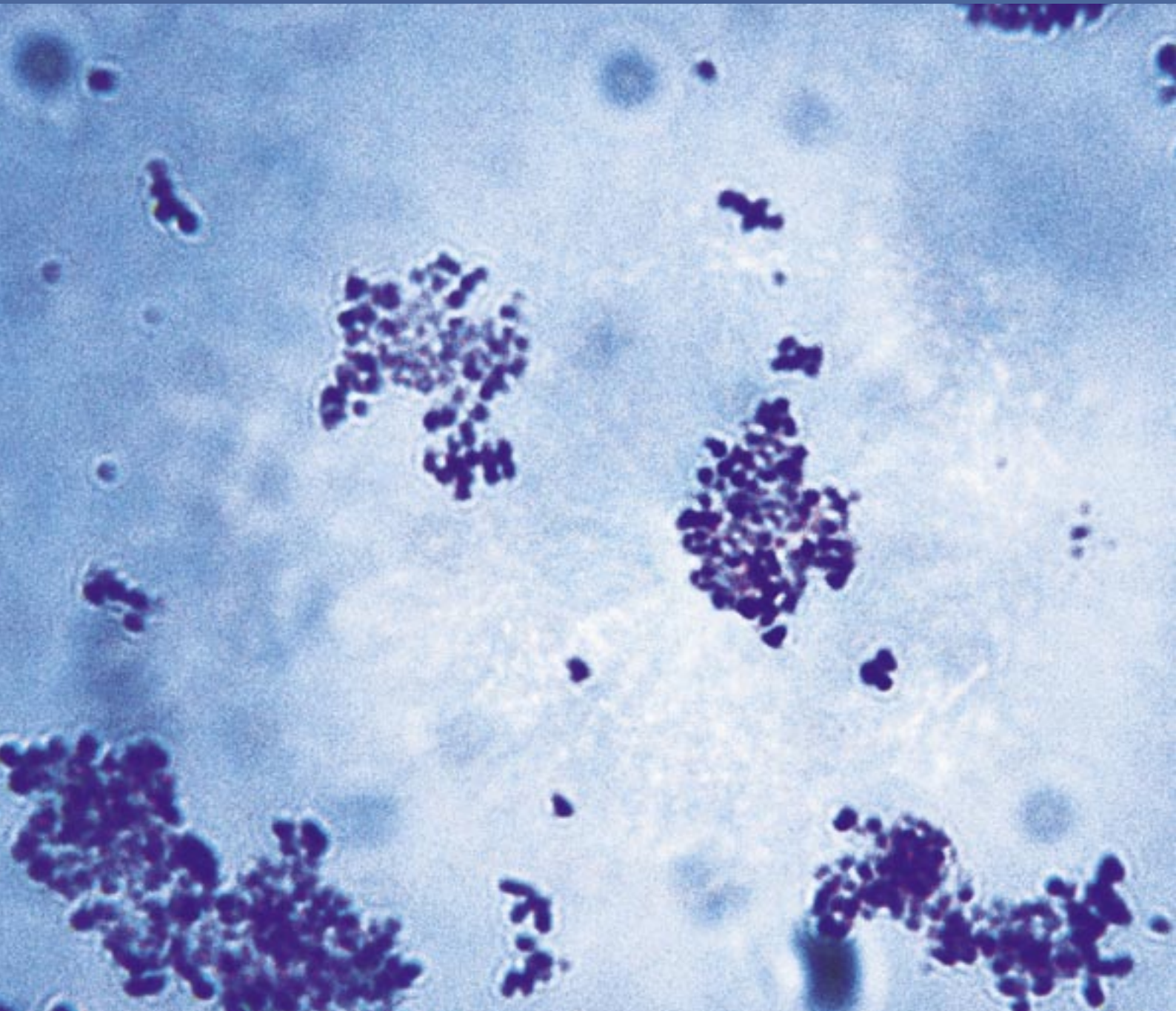
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* Data calculated based on new Staff Research Publication System

—●— Tier 1

— Total Publications (International Refereed)

PROGRAMMES



CONDUCTING **BREAKTHROUGH RESEARCH**

COMPREHENSIVE PROGRAMMES ENSURE THAT
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PROGRAMMES

Allergy Asthma and Immunology Research

http://medicine.nus.edu.sg/research/progrsch/allergy_asthma.shtml

Research theme

Immunopathogenesis of asthma and allergies towards advances in diagnostic and immunotherapeutic modalities.

Programme activities

- Collaborative research on the study of allergen NMR structure with The Institute of Biomedical Sciences, Structural Biology Division, Academia Sinica.
- Collaborative research project on production of oral vaccine for immunotherapy in transgenic plants with Professor Yu Su-May from Institute of Molecular Biology, Academia Sinica, Taiwan.
- Initiation and coordination of the regional multi-centre epidemiological studies of mite allergy in patients with asthma/rhinitis.
- Collaborative research with University of Otago, Dunedin New Zealand and Gadjah Maja University, Yogyakarta, Indonesia to carry out a comparative study of gut microbiota between urban Singapore and rural Indonesian (Yogyakarta) toddlers and determine its relationship with the development of allergic diseases.
- Collaborative research initiative on the protective effects of probiotics on allergic disease encompassing a double blind placebo controlled randomized clinical trial on the protective effects of probiotic supplementation in newborn infants, in-vitro study of the underlying immunoregulatory mechanisms of probiotics, and the protective/therapeutic potential of probiotic bacteria expressing recombinant dust mite allergens as a vehicle for allergen immunotherapy in mouse dust mite allergy model.
- Joint South East Asian studies on the epidemiology food allergy and allergic diseases in the young children in Singapore, Thailand and Indonesia.
- Weekly journal club and biweekly research seminars.
- Medical and Polytechnic attachment students working on research projects.
- Collaborative research with Assistant Professor Dr Lim Yaw Chyn, Department of Pathology on the mechanistic study of the stimulatory and adjuvant effects of a fungal immunomodulatory protein in tumor immunotherapy.

Research projects

- Mechanism of the pathogenesis of allergic diseases, focus on allergen and cell surface molecules interaction in skin fibroblast, lung epithelial, DC, Treg and B cells.
- Therapeutic and prevention modality with respect to studies on:
 - (a) DNA vaccine,
 - (b) Oral vaccine,

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- (c) Recombinant allergens-based immunotherapy, and
- (d) Development of new adjuvant for vaccines.
- The influence of environmental factors in the development of childhood allergies:
 - (a) A clinical trial on the effects of probiotics on atopic disease in babies at risk for atopy - The aim of this study is to assess the effect of early and sustained feeding of probiotics on the subsequent development of eczema and sensitization to allergens.
 - (b) A prospective study to compare the gut microbiota between two populations, one with high prevalence of allergy (Singapore) and one with low prevalence (Indonesia) in the first two years of life.
- A cross-sectional, population survey on the prevalence of food allergy in Singapore, Thailand and the Philippines.
- Comparative study on allergen sensitization in young children in Singapore, Jakarta and Bandung.
- A follow up cohort study on infantile wheezing to assess risk factors for persistence of wheeze.
- A population survey on drug allergy in Singapore children to assess prevalence and trend.
- A study on the effects of cold drinks on asthma symptoms.
- Impact of stress on symptoms and underlying immunologic mechanisms of allergic rhinitis.

Patents

US Provisional Patent Application No: BRC/P/04066/00/US.

Title: Recombinant Lactobacillus and use of the same. Filing date: 20-04-2006.

Member(s) of programme

Programme Coordinators:	Adj Assoc Prof Lee Bee Wah Prof Chua Kaw Yan Prof Van Bever HP
Members:	Assoc Prof Wang De Yun (Otolaryngology) Assoc Prof Lynette Shek Pei Chi Dr Cheong Nge Dr Liew Lip Nyin Dr Seow See Voon Dr Huang Chiung Hui Dr Yi Fong Cheng Dr Xu Hui Ms Seah Ching Ching Mr Soh Gim Hooi Ms Evelyn Loo Xiu Ling Ms Elaine Quah Phaik Ling Ms Terry Huang Ying Ting Ms Tan Teng Nging Ms Liew Lee Mei Mr Mah Ka Weng Ms Wen Hong Mei Ms Wong Wen Seen Ms Ding Ying Ms Judy Anthony Ms Kwek Poh Lian, Corinne

Gerontology Research Programme

<http://www.med.nus.edu.sg/pcm/research3.htm>

Research theme

Multidisciplinary programme of research on aging and health, aimed to increase understanding of factors influencing aging and age-related disease, by studying the transition from healthy aging through disease, illness, functional impairment and death, and identifying risk and protective factors for these outcomes, so as to identify healthcare strategies for the prevention and postponement of disability and improving the quality of life of the elderly.

Programme activities**Presentations/Conferences:**

Tze Pin Ng, Liang Feng, Peak Chiang Chiam, Ee Heok Kua. Acute Hospitalization in the Elderly: Relationship with Psychiatric Morbidity and Social Equity in Healthcare Access in Singapore. ISPOR 9th Annual European Congress, 28-31 October 2006, Copenhagen, Denmark.

YY Sitoh, WC Wong, NH Ismail, YO Leong, HC Lim, SH Seah, SH Chua, NM Matthew, TP Ng. Determinants of Health Related Quality of Life using EQ-5D in Community-dwelling Older Persons of Asian Descent. American Geriatrics Society Annual Scientific Meeting, 3-7 May 2006, Atlanta, USA.

SP Chan, YY Sitoh, WC Wong, EY Lee, IY Leong, N Hafizah, R Ramason, NM Matthew, TP Ng, SM Saw. Impaired Visual Acuity as a Risk Factor for Falls in Singapore Elderly Population. Australian Society for Geriatric Medicine Annual Scientific Meeting, 4-6 September 2006, Christchurch, New Zealand.

Wong WC, Sitoh YY, Ismail NH, Leong YO, Ramason R, Chan SP, Lim HC, Seah SH, Matthew NM, Ng TP. Factors Associated Fear of Falling in Community-dwelling Older Adults. 8th Scientific Meeting of the Society for Geriatric Medicine, 16-17 September 2006, Tan Tock Seng Hospital, Singapore. (Best Poster)

Feng Lei, Lisa Chuah, Ng Tze Pin. Homocysteine, Folate, Vitamin B-12 and Cognitive Performance in Older Chinese Adults: Findings from the Singapore Longitudinal Ageing Study. 8th Scientific Meeting of the Society for Geriatric Medicine, 16-17 September 2006, Tan Tock Seng Hospital, Singapore.

Liang Feng, Tze Pin Ng, Peak Chiang Chiam, Ee-Heok Kua. Mental Disorders and the Use of Complementary and Alternative Medicines in Asians. 8th Scientific Meeting of the Society for Geriatric Medicine, 16-17 September 2006, Tan Tock Seng Hospital, Singapore.

Ng TP (Invited Speaker). Studies of Cognitive Function and Impairment in the Singapore Aging Cohort Study. International Association of Research Universities Workshop on Aging, Longevity and Health, 4-6 October 2006, Copenhagen, Denmark.

Ng TP (Invited Speaker). Update on COPPD in Singapore. 12th Regional COPD Roundtable Meeting, 24 June 2006, Singapore.

Koh, CH G, K S Sanjiv, T P Ng, D Yong, NP Fong. Post Stroke Functional Recovery in Older Persons Occurs Mainly Within First 3 Months. 8th Scientific Meeting of the Society of Geriatric Medicine (Singapore), 16-17 September 2006, Tan Tock Seng Hospital, Singapore.

PROGRAMMES

Ng, T P. COPD Burden in Singapore. Launch of COPD Clinical Practice Guidelines Singapore, Saturday, 12 November 2006, Raffles Hotel, Singapore.

Ng, T P. Public Health Challenges of Mental Illness. Ministry of Health Public Health National Training Programme Public Health Lecture, 6 July 2006, College of Medicine, Singapore.

Ng, T P. Cognitive Impairment and Dementia Screening in the Elderly. Ministry of Health Public Health National Training Programme Public Health Lecture, 1 June 2006, College of Medicine, Singapore.

Ng, T P. Dementia and Cognitive Impairment in Singapore: Prevalence, Impact, Risk Factors, Correlates. Ministry of Health Public Health National Training Programme Public Health Lecture, 15 June 2006, College of Medicine, Singapore.

Ng, T P. Assessment of Physical Functional Status in the Elderly. Ministry of Health Public Health National Training Programme Public Health Lecture, 4 May 2006, College of Medicine, Singapore.

Ng, T P. Functional Disability in Elderly Singaporeans: Prevalence, Risk Factors and Impact. Ministry of Health Public Health National Training Programme Public Health Lecture, 18 May 2006, College of Medicine, Singapore.

Member(s) of programme

Programme Coordinator:	Assoc Prof Ng Tze Pin (Psychological Medicine)
Principal Investigators:	Prof Kua Ee Heok (Psychological Medicine) Assoc Prof Goh Lee Gan (COFM) Assoc Prof Tan Chay Hoon (Pharmacology) Prof Victor Goh (Obstetrics and Gynaecology) Dr Terry Tong (Obstetrics and Gynaecology) Assoc Prof Ko Soo Meng (Psychological Medicine) Dr Rajeev Kumar (Psychological Medicine) Assoc Prof Mike Chee (Duke-NUS University and SingHealth Cognitive Neuroscience Laboratory) Dr Lim Wee Shiong (Department of Geriatric Medicine, TTSH) Dr Chong Mei Sian (Department of Geriatric Medicine, TTSH) Assoc Prof Angela Chan (Sociology) Dr Steve Graham (Psychology) Assoc Prof Li Shu Chuen (Pharmacy) Reshmi Merchant (Geriatric Medicine, NUH) Dr Yap Keng Bee (Department of Geriatrics Medicine, AH) Dr Philip Yap (Department of Geriatric Medicine, AH) Dr Philip Eng (Respiratory Medicine Department, SGH) Dr Tan Boon Yeow (St Luke's Community Hospital)

Research Personnel:

Prof Tan Wan Cheng
(University of British Columbia, Canada)
Prof Bengt Winblad
(Karolinska Institute, Sweden)
Assoc Prof Lee Tih Shih
(Duke-NUS Graduate Medical school)
Assoc Prof Saw Seang Mei (SERI)
Assoc Prof Wong Tien Yin (SERI)
Dr Mathew Niti, Research Fellow
Feng Liang, Research Scholar
Feng Lei, Research Scholar
Ng Gim Yew, Research Scholar
Stella Ma Shwe Zin Nyunt,
Research Assistant and
Research Scholar
Jin Aizhen, Research Assistant
Li Bin Tao, Research Assistant
Ng Mei Yi, Psychologist
Susan Hin-Hiang,
Programme Administrator

Helicobacter pylori

http://medicine.nus.edu.sg/research/progrsch/helicobacter_pylori.shtml

Research theme

1. To study molecular mechanisms of pathogenesis of *H. pylori*.
2. To evaluate the use of probiotic/prebiotics as alternative therapeutic strategy.
3. To examine the survival strategy of *H. pylori* in the extragastric environment.
4. To investigate the relationship between *H. pylori* and gastric cancer.

Programme activities

1. Molecular mechanisms of *H. pylori* pathogenesis

The cytoplasmic enzyme 1 (CE1) was found to be strongly associated with patients having peptic ulcer disease ($p < 0.001$). Furthermore, it was shown to be associated with the vacuolating toxin (a well-studied virulence factor of *H. pylori*). The absence of CE1 resulted in reduced vacuolation of host cell *in vitro*. The team is investigating the host-pathogen interaction in relation to the role of CE1 in the pathogenesis of *H. pylori*-associated severe gastric diseases.

Through immuno-gold labeled TEM, we have confirmed the interaction of a surface localized enzyme (SE1) with CagA (another crucial virulence factor of *H. pylori*). This interaction was observed to take place only in the presence of host contact. The absence of SE1 does not affect the formation of the bacterial type IV secretion system (T4SS), but resulted in a substantial delay in CagA translocation into host cells and a reduced disruption of the tight junction barrier. The team is looking into the inter- and intra- protein-protein interactions to determine the probable potential role of SE1 in facilitating *H. pylori* invasion into the host gastric mucosa, leading to pathogenesis.

2. Alternative therapeutic strategy

Development of an effective alternative therapy is important with the increasing trend of antibiotic-resistance over the years. It has

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been shown in our studies that the “generally regarded as safe” microalgae and microalgae sulfated polysaccharides possess inhibitory activity against *H. pylori* adherence to gastric mucin. Preliminary *in vivo* study on BALB/c mice fed with prebiotics indicated a significant reduction of bacterial load in the stomach when these mice were challenged with *H. pylori*. It suggests that the prebiotics may potentially be used as anti-adhesive and bactericidal agents.

3. Extragastric survival strategy of *H. pylori*

Biofilm has been shown to play an important role in many chronic bacterial infections. Our preliminary work has shown that *H. pylori* biofilm formation begins as early as 3 days. The thickness of the biofilm and number of microcolonies were shown to increase with the age of the biofilm. The presence of live bacteria within the “aged” biofilm suggests a protective role of this film-like matrix against the harsh extragastric environment. It is hypothesized that biofilm formation by *H. pylori* could represent a facile microbial survival strategy where it exists in a dynamic equilibrium in the form of cell clusters, which will mature and detach to disseminate in a favourable growth condition.

4. *H. pylori* and gastric cancer

A prospective study on high-risk subjects is on-going to determine the correlation of *H. pylori* infection and the development of gastric cancer.

Member(s) of programme

Programme Coordinator: Assoc Prof Ho Bow (Microbiology)
Members: Assoc Prof Yeoh Khay Guan (Medicine)
Assoc Prof Ho Khok Yu (Medicine)
Assoc Prof Quak Seng Hock (Paediatrics)
Assoc Prof Teh Ming (Pathology)

Human and Molecular Genetics Research Programme

http://medicine.nus.edu.sg/research/progrsch/hum_mol_genetics.shtml

Research theme

To establish and develop genetic research and diagnostic facilities in cardiovascular, asthma, endocrine, neurometabolic, haematology/oncology, renal and developmental genetics, with regards to:

- Genetic epidemiology, including sequencing, mutation screening, and genotyping.
- Establishment of a cord blood bank resource representative of Singapore's three major ethnic groups.
- Karyotyping and gene mapping by linkage analysis and molecular cytogenetics.
- Molecular diagnostics and gene therapy.
- Functional genomics and pharmacogenomics.
- Animal models of human development and disease.

Programme activities

HMGRP Seminars

05 Apr 2006 Ng Kar Hui
“Getting to know the podocyte”

18 Apr 2006 Loo Pooi Eng
“Nonsense Mediated mRNA Decay in Beta-Thalassemia”
16 May 2006 Shirley Kham Kow Yin
“MA-SPORE Acute Lymphoblastic Leukemia 2003 Study: Preliminary Results”
20 Jun 2006 Tan Xueling
“Characterization of the Hepatitis B virus X (HBx) gene in hepatocellular carcinoma (HCC) patients”
15 Aug 2006 Chan Wei Loong
“Cloning of mini-gene constructs for gene repair in dystrophin”
17 Oct 2006 Dr Lee Yung Seng
“Mutations of the pro-opiomelanocortin gene associated with severe childhood obesity”

Member(s) of programme

Programme Coordinator: Dr Heng Chew Kiat
Members: Dr Caroline G Lee
Dr Goh Li Meng, Denise
Dr Lai Poh San
Dr Lee Yung Seng
Assoc Prof Loke Kah Yin
Prof Low Poh Sim
Assoc Prof Quah Thuan Chong
Assoc Prof Quek Swee Chye
Assoc Prof Samuel S. Chong
Dr Tay Kiat Hong, Stacey
Prof Yap Hui Kim

Lactic Acid Bacteria (LAB) Interest Group

<http://medicine.nus.edu.sg/research/progrsch/lab.shtml>

Research theme

Intestinal lactic acid bacteria as probiotics and vectors for gene therapy.

Programme activities

Members of the programme secured the following research grants.

1. Assoc Prof Bay BH (PI), Dr R Mahendran, Assoc Prof Lee YK. Effect of lactic acid bacteria in the tumorigenesis of bladder and breast cancer. Supported by NMRC.
2. Dr Lim CK (PI), Assoc Prof Lee Yuan Kun. Cloning of human genes into lactobacilli. Supported by SRS.
3. Assoc Prof Lee YK (PI), Assoc Prof Tan HM. Lactic acid bacteria as animal probiotics. Supported by Kemlin Industries (A) Pte Ltd.
4. Assoc Prof Lee YK (PI), Dr Lu JH. Host-bacteria and bacteria-bacteria interactions in human gastrointestinal tract. Supported by NMRC.
5. Assoc Prof Lee YK (PI), Prof J Kwang, Assoc Prof Ng ML, Dr Lim CK. Gene expression and colonization of lactic acid bacteria in gastrointestinal tract. Supported by NMRC.
6. Assoc Prof Lee YK (PI), Assoc Prof Bay Boon Huat, Dr R Mahendran. Modulation of the development and progression of cancer by lactobacilli. Supported by NMRC.

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7. Dr Ratha Mahendran (PI), Assoc Prof Bay Boon Huat, Assoc Prof Lee Yuan Kun. Modified lactobacilli as delivery vehicles for antigens for induction of local and system immunity. Supported by DSTA.
8. Assoc Prof Lee Yuan Kun (PI). Intestinal colonization and immunomodulation by probiotic microorganisms expressing antigens of pathogen. Supported by Microbiology Vaccine Initiative.

The LAB Interest Group is in collaboration with the following research groups:

1. **Asthma and Allergy Research Programme, NUS**
Development of prophylactic and therapeutic vaccines for asthma and allergy. Immune response to allergens in early childhood in relation to environmental factors.
2. **Edible Vaccine Group, NUS**
Intestinal colonization and immune-modulation by probiotic microorganisms expressing antigens of pathogens.
3. **Medical Nutrition Group, Karolinska Institute, Sweden**
Host-microbe cross-talk focuses on colon cancer.
4. **Functional Food Center, Turku University, Finland**
Bacterial adhesion and gene expression in human colonocytes: target for probiotic development.

Member(s) of programme

Programme Coordinator:	Assoc Prof Lee Yuan Kun (Microbiology)
Members:	Assoc Prof Bay Boon Huat (Anatomy) Dr George Yip (Anatomy) Dr Ratha Mahendran (Surgery) Assoc Prof Kesavan Esuvaranathan (Surgery) Dr Tan Hai Meng (Kemin Industries) Prof Jimmy Kwang (TTL) Assoc Prof Vincent Chow (Microbiology) Assoc Prof Lu Jinhua (Microbiology) Dr Chew Fook Tim (Biochemistry) Dr Lynette Shaek Pei Chi (Paediatrics) Prof Chua Kaw Yan (Paediatrics) Prof Sven Pettersson (Karolinska Institute Sweden)

Neurodegeneration

<http://medicine.nus.edu.sg/research/progrsch/neurodegeneration.shtml>

Research theme

To study factors which contribute to, or modulate, degeneration of the nervous system. Research is centered on the calcium hypothesis of aging and dementia, and examines factors that contribute to, or modulate calcium influx into neurons. The role of calcium dependent and free radicals in events leading to neurodegeneration, and the role of glial cells in propagating neuronal injury are also examined. In addition to calcium, an accumulation of iron and cholesterol oxidation products can also be toxic to neurons, and research is carried out, to elucidate iron and cholesterol metabolism in the brain.

Programme activities

Collaborative projects have been carried out between members of the group, resulting in several papers in premium journals, book chapters, and awards at international conferences. Individual members have also been awarded several grants for research on cell models of neurodegenerative diseases, and translational research, on the development of antioxidants to treat neurological disorders.

Member(s) of programme

Programme Coordinator:	Assoc Prof Ong Wei Yi
Members:	Prof Barry Halliwell Assoc Prof Lim Tit Meng Assoc Prof Benjamin Ong Kian Chung Assoc Prof Hanry Yu

Neuropsychopharmacology

<http://www.med.nus.edu.sg/research/progrsch/neuropsychopharmacology.shtml>

Research theme

The pharmacology of drugs that may exert neural, psychological and behavioural changes in animals and human.

Programme activities

The programme group conducted the seminar 21st Century Psychiatry Neuroscience & Psychiatric Education held on 19 September 2006 at The Regent Hotel. Assoc Prof Tan Chay Hoon presented the topic entitled Neuroscience in the pharmacotherapy of Schizophrenia.

Member(s) of programme

Programme Coordinator:	Assoc Prof Tan Chay Hoon
Members:	Assoc Prof Peter Wong Tsun-Hon (Pharmacology) Assoc Prof Lee How Sung (Pharmacology) Prof Kua Ee Heok (Psychological Medicine) Prof Calvin Fones Soon Leng (Psychological Medicine) Dr Zhu Yi-Zhun (Pharmacology) Dr Gavin Dawe (Pharmacology) Assoc Prof Ong Wei Yi (Anatomy)

Oxidants and Antioxidants Research Group

<http://www.med.nus.edu.sg/research/progrsch/oxidants.shtml>

Research theme

To study the molecular and cellular biology of the action of oxidants and antioxidants and their role in human disease and human nutrition.

Programme activities in 2006

1. Appointments

Prof Shazib Pervaiz was appointed as the Associate Editor for the journal *Cytometry A* and he is also in the Editorial Advisory Board for *Biochemical Journal* and Editorial Board for *International Journal of Biochemistry and Cell Biology*. Prof Pervaiz was also

PROGRAMMES

invited as a Raine Visiting Professor at the University of Western Australia, Perth, Australia in July 2006.

Assoc Prof Urs Alex Boelsterli was appointed as an Associate Editor for the international journal *Current Drug Metabolism* and he is also an Editorial Board Member for *Drug Metabolism Letters*.

2. Award

Prof Shazib Pervaiz was awarded the Faculty of Science Teaching Excellence Award.

3. Invited presentations

Prof Barry Halliwell

- International Anti-aging Medicine Symposium & Exposition, 21-23 April 2006, Florence, USA.
- Novartis Foundation Symposium "Dietary Supplements and Health", London, England, 9-11 May 2006. He was also part of the organizing committee.
- Asia-Pacific Society for Neurochemistry 2006 meeting, Singapore.
- 7th Association of Pacific Rim Universities (APRU) Doctoral Student Conference (DSC), July 2006, Singapore, 15-19 July 2006.
- 1st Symposium on Brain and Mind Research in the Asia/Pacific, Sydney, Australia, 14-16 August 2006. He was also the Chair of session.
- MHRI Cade Science Day, Melbourne, Australia, 15-18 November 2006.
- 17th International Symposium on ALS/MND, Yokohama, Japan, 30 November - 2 December 2006.
- Society for Free Radical Research Meeting, Perth, Australia, 1-4 December 2006.

Prof Shazib Pervaiz

- "Automated scanning cytometry: a powerful tool for multi-parameter analysis of drug-induced cell death." 4th International Workshop: Slide Based Cytometry in conjunction with 2006 International Symposium: Advances in Laser Scanning Cytometry, Leipzig, Germany, 27-29 April 2006.
- "Redox regulation of death signaling in cancer cells." New Zealand-NUS Cancer Symposium: "Apoptosis & Cancer Immunology and Genetic"-The frontier Science. Clinical Research Center, NUS, Singapore, 3 May 2006.
- "Glucose deprivation sensitizes leukemia cells to CD95-mediated apoptosis by decreasing intracellular superoxide anion, independent of Bcl-2." The 6th International Cell Death Symposium, "The mechanism of cell death in cancer and aging", Hotel do Frade, Angra dos Reis, Brazil, 2-5 June 2006.

Assoc Prof Marie-Veronique Clement

- "Reactive oxygen species cause or cure for apoptosis?" National Neuroscience Institute, Singapore, April 2006.
- "Reactive oxygen species cause or cure for apoptosis?" Singapore Eye Research Institute, Singapore, 29 May 2006.
- "Reactive oxygen species cause or cure for apoptosis?" School of Anatomy and Human Biology, The University of Western Australia 2006 Anatomy and human Biology seminar series, 12 July 2006.

Member(s) of programme

Programme Coordinators: Prof Barry Halliwell
Prof Shazib Pervaiz
Members: Prof Subroto Chatterjee
(Johns Hopkins Singapore)

Prof Ong Choon Nam
Prof Malcolm Paterson
Prof Alan Porter
Prof Sit Kim Ping
Prof Roland Stocker
Prof Frank Watt
Prof Philip Keith Moore
Assoc Prof Matthew Whiteman
Assoc Prof Tan Kwong Huat Benny
Assoc Prof Ong Wei Yi
Assoc Prof Kenneth Hughes
Assoc Prof Marie-Veronique Clement
Assoc Prof Urs Alex Boelsterli
Assoc Prof Lim Sai Kiang
Assoc Prof Shen Han Ming
Assoc Prof Markus Wenk
Dr Steve Cheung Nam Sang
Dr Jan Gruber
Dr Jeffrey Armstrong
Dr Rajasekhar Balasubramanian
Dr Andrew Jenner
Dr Lee Chung-Yung, Jetty
Dr Peter Colin Rose
Dr Wong Boon Seng
Dr Huang Dejian
Dr Ronan Kelly
Dr Alan Prem Kumar
Dr Andrea Lisa Holme
Dr Lee Shao Chin

Programme in Infectious Diseases

<http://www.med.nus.edu.sg/research/progrsch/infectious.shtml>

Research theme

Flaviviruses, Malaria, Enterobacteriaceae/Antibiotic resistance and Influenza and other Emerging Infections.

Programme activities

- Research Seminar on Pandemic Influenza co-chaired with Prof Fred Hayden, WHO, University of Virginia.
- Various ongoing research projects and collaborations which have led to 5-10 Tier 1 publications.

Member(s) of programme

Programme Coordinator: Assoc Prof Paul Anantharajah Tambyah
Members: Dr Sylvie Alonso
Assoc Prof Vincent TK Chow
Dr Chua Kim Lee
Assoc Prof Dale Fisher
Dr Gan Yunn Hwen
Prof P Gopalakrishnakone
Assoc Prof Ho Bow
Prof David Micheal Kemeny
Assoc Prof Evelyn S C Koay
Assoc Prof Lim Seng Gee
Dr Raymond Lin
Assoc Prof Lu Jinhua
Dr Paul A MacAry
Prof Mary Ng Mah Lee
Dr Ong Siew Hwa

PROGRAMMES

Assoc Prof Poh Chit Laa
Dr Seah Geok Teng
Assoc Prof Sim Meng Kwoon
Assoc Prof Sim Tiow Suan
Dr Kevin Tan Shyong Wei
Prof Donald Tan
Dr Mark B Taylor
Assoc Prof Wang De Yun
Dr Markus R Wenk
Assoc Prof Wong Mee Lian

Dr Janice Lee Mong Li
(Computer Science)
Assoc Prof Wynne Hsu
(Computer Science)

Singapore Epidemiology of Eye Diseases (SEED) Centre

<http://medicine.nus.edu.sg/research/progrsch/seed.shtml>

Research theme

This research group serves to initiate, promote and coordinate ophthalmic epidemiologic research in Singapore and in Asia. The program will provide a forum for generating new hypotheses, and the application of epidemiologic and statistical methods to test these hypotheses. The focus will be on major eye diseases of unique importance in Asia, such as myopia, angle-closure glaucoma, cataract, diabetic retinopathy, and other conditions. The program will centre on epidemiology and biostatistics, and will include research related to clinical epidemiology, genetic and molecular epidemiology research, evidence based medicine and outcomes research.

Specific aims

1. To determine the prevalence, incidence, risk factors and public health significance of blinding eye diseases in Singapore and Asia through the conduct of large scale epidemiological studies.
2. To foster international collaborations with other public health and ophthalmic institutes in Asia and worldwide.
3. To train Masters and PhD level students.
4. To conduct conferences, workshops and symposia in Singapore and internationally on ophthalmic clinical research, and epidemiologic and statistical methods.

Programme activities

For 2006, SEED has achieved several accomplishments:

1. Completion of the Singapore Malay Eye Survey (SIMES) of 3,300 Malay adults aged 40 to 80 years.
2. 11th International Myopia Conference, Fullerton Hotel, Singapore.
3. Commencement of STARS (Strabismus, Amblyopia and Refractive Error Study in Singapore Children) of 3,000 Chinese children aged 6 to 72 months.
4. On-going Singapore Cohort Study of the Risk Factors for Myopia (SCORM) project in schools.

Member(s) of programme

Programme Coordinators: Assoc Prof Saw Seang Mei (COFM)
Assoc Prof Wong Tien Yin (Ophthalmology)

Members: Prof Donald Tan (Ophthalmology)
Assoc Prof Tai E Shyong (COFM)
Assoc Prof Aung Tin (Ophthalmology)
Assoc Prof Ng Tze Pin (Psychiatry)
Prof David Koh (COFM)

Tissue Engineering

http://www.med.nus.edu.sg/research/progrsch/tissue_engine.shtml

Research theme

Repair and Regeneration of Musculoskeletal Tissues.

Programme activities

1. Isolation, Culture and Characterization of Mesenchymal Stem Cells (PI: Prof EH Lee)

MSCs can be derived from adipose tissue (AMSCs) as an alternative to bone marrow (BMSCs). We compared AMSCs and BMSCs in terms of their cell surface-marker expression, their differentiation potential and their expression profiles. Our studies showed that surface-marker expression could be used to isolate subpopulations of MSCs with enhanced colony formation capabilities. Using microarray technology, expression profiling showed that BMSC and AMSC express many common genes, however chondrogenic differentiation studies showed that BMSCs are superior in inducing chondrogenic differentiation to AMSCs. Comparison of the transcriptome profiles of AMSCs and BMSCs during directed differentiation into bone, cartilage and fat revealed an interesting bifurcation of pathways in both BMSCs and AMSCs in which osteogenesis and adipogenesis appear to be linked in a differentiation branch separate from chondrogenesis. Our data suggest that while a set of common genes may be needed for early differentiation into all three lineages, a different set of signature genes are associated with maturation into fully differentiated cells. The recruitment of different late differentiation factors explains and supports our conclusion that BMSCs can differentiate more efficiently into bone and cartilage whereas AMSC differentiate better into adipocytes.

2. Chondrogenic Differentiation of Mesenchymal Stem Cells (PI: Prof EH Lee)

The team has been studying the differentiation of chondrocytes for repair of articular cartilage as well as for repair of physal or growth plate cartilage. We have developed a novel growth factor free co-culture differentiation protocol to test the hypothesis that chondrocytes produce soluble factors that promote MSC differentiation to cartilage. Our data demonstrated that chondrogenic differentiation occurred in alginate encapsulated BMSCs which were physically isolated, but shared the same medium, from a mixed population of chondrocytes and BMSCs also in alginate. Further studies revealed that the factor secreted into the medium was TGF β .

We are using BMSCs to develop an *in vitro* model of physis or growth plate cartilage which will provide a valuable tool for studying the effects of different factors, conditions and chemicals on the this tissue. We have demonstrated that under defined conditions BMSCs can form heterogeneous tissues containing the different cell types found in normal physis, including immature chondrocytes, mature chondrocytes and hypertrophic

PROGRAMMES

chondrocytes. Mineralisation and apoptosis in the area containing hypertrophic chondrocytes was also seen as is characteristic of normal physis.

Chondrocytes of articular cartilage are maintained at an arrested differentiation stage with no progression to hypertrophy as in growth plate chondrocytes. Our team is developing an articular chondrogenic differentiation model using MSCs which will be used to study mediators that will influence initial chondrogenesis and/or hypertrophy chondrogenesis. The objective is to identify mediators that can control and stabilize the phenotype of MSC-derived chondrogenic cells, an essential criteria for the use of MSC-derived chondrogenic cells for articular cartilage tissue engineering. Employing small chemicals with perturbation effect, our initial results suggest that the beta-catenin signaling pathway plays multiple, and subtle roles along the different chondrogenic differentiation stages of MSCs. Perturbation of this pathway has the effect of preventing further hypertrophic development of chondrocytes. We are in the process of confirming this effect with gene-knockdown approach with the use of siRNA. We also investigated the effect of b-catenin pathway perturbation on explant cartilages, obtained from osteoarthritic patients that have undergone total knee replacement operation. Initial results suggest a role of this pathway in fibro- and hypertrophy development of OA cartilage.

3. Genetic manipulation of BMSCs

We have established lentiviral vector mediated stable overexpression or knock-down of target genes in MSCs. Targeting FKBP5, siRNA silencing of this gene resulted in a reduction adipogenic, chondro- and osteogenic differentiation of MSC, at both genetic and cellular levels. On the other hand, our overexpression results indicated an upregulated of differentiation. These results indicate that FKBP5 was involved in the three lineages differentiation. These approaches are currently employed to study a spectrum of genes identified in our earlier transcriptome profiling of AMSCs and BMSCs during 3 lineages differentiation.

4. The effect of extracellular matrix components in BMSC proliferation and differentiation using a micro-bead culture system (PI: Prof EH Lee)

Proliferation and differentiation of BMSCs *in vivo* is not only affected by signaling molecules, but also by extracellular matrix (ECM) components. This study investigated the effect of different cartilage matrix components on the proliferation and chondrogenic differentiation of BMSCs in a novel 3D alginate microbead-culture system. The microbeads were coated with either hyaluronic acid (HA), chondroitin sulfate (CS) or collagen type II (Col2) and BMSCs seeded onto the surface. Proliferation was seen to be enhanced in all three coated beads relative to uncoated beads. Under conditions that promote chondrogenesis, our data show that CS-coated microbeads were able to enhance chondrogenic differentiation of the MSCs relative to non-coated alginate beads and beads coated with HA or Col2, producing tissue that resemble hyaline cartilage. Studies are currently underway using glass surfaces coated with 3d chitosan nano-particles.

5. Tendon and Ligament (PI: Assoc Prof James Goh)

Cell seeding on knitted scaffolds often require a gel system, which is unstable in a dynamic situation. In order to solve this problem, the group fabricated a novel silk scaffold with weblike

silk microsponges formed in the openings of the knitted scaffold. Human bone marrow stromal cells (BMSCs) adhered and grew well on the novel scaffolds. Moreover, cellular function was more actively exhibited as evidenced by the significant higher expression of ligament specific marker (e.g., type I, III collagen and tenascin-C). The results indicated that the web-like silk microsponges formed in the openings of the knitted silk scaffold promoted cell proliferation and differentiation. The novel silk scaffold could be applied with promise in tissue engineering of ligaments. The novel scaffold has been used to reconstruct the anterior cruciate ligament (ACL) in a rabbit model. In addition, a four-chamber perfusion cum mechanical stimulation system was designed by the group to sustain cell viability and promote cell proliferation and tissue formation in-vitro. The focus is on growing BMSCs on silk coated, knitted silk scaffold for tissue engineering of anterior cruciate ligament.

6. Spine (PI: Prof Wong Hee Kit)

Under an agreement between the Department of Experimental Surgery, SGH, and the Department of Orthopaedic Surgery, NUS, pig operations were performed in SGH from November, 2006. So far, 31 pigs have undergone intervertebral spinal fusion with either autograft, scaffold + stem cell, or scaffold + BMP. X-rays, micro CT, biomechanical test and histological analysis will be carried out to assess for fusion. Only one pig was lost due to complications. Other operated pigs appeared to be healthy. These pigs will be sacrificed at 3, 6, and 12 months for assessment. X-rays will be taken before and immediately after the operation, as well as at an interval of 3 months post-operatively. The protocol for micro-CT has been set, and a trial biomechanical test is in preparation.

Member(s) of programme

Programme Coordinator:

Members:

Prof Lee Eng Hin
Assoc Prof James Goh Cho Hong (Secretary)
Prof Casey Chan
Prof Wong Hee Kit
Adj Assoc Prof Lim Beng Hai
Assoc Prof James Hui
Dr Wilson Wang
Dr Suresh Nathan
Assoc Prof Dietmar Werner Hutmacher
Adj Assoc Prof Simon Cool
Dr Jacqueline Frida Schmitt
Dr Ricky Lareu
Dr Liu Tongming
Dr Liu Haifeng
Dr Fan Hongbin
Dr Yang Kai
Dr Yang Zheng
Bharti Dewangan
Zhao Tianyun
Wu Yingnan
Jennifer Chong Sue Wee
Elaine To Chiou Yan
Siah Wan Ping
Khoo Hock Hee
Julee Chan Wai Kam
Yong Soon Chiong
Afizah Bte Mhd Hassan
See Kwee Hua
Tan Hwee San

Research Staff:

Laboratory Staff:

PROGRAMMES

Postgraduate Students in
Orthopaedic Surgery:

Joyce Tey (MSc)
Tan Heng Liang (PhD)

Collaborators from

National University Hospital:

Dr Alphonsus Chong
Dr Kevin Lee
Dr Lim Jit Kheng

Collaborators from Division
of Bioengineering, NUS:

Prof Teoh Swee Hin
Assoc Prof Toh Siew Lok
Assoc Prof Michael Raghunath
Assoc Prof Dietmar Huttmacher
Asst Prof Phan Toan Thang

UROP Student in
Orthopaedic Surgery:

Raghav Sundar

Venom and Toxin Research Programme

http://medicine.nus.edu.sg/research/progrsch/venom_toxin.shtml

Research theme

From Venoms to Drugs, From Toxins to Therapeutics.

Programme activities

Presentation of papers in conferences and International publications.

Patents

1. US continuation-in-part (CIP) patent application No. 11,414,719 (Filing date 28.04.2006). Title: Methods and compositions for treatment of arthritis and cancers. (INTRO Ref: GOPAL P 08-US/CIP).
2. US continuation-in-part (CIP) patent application No. 60,734,294 (Filing date 11.08.2005). Title: Development of bactericidal peptides against *Burkholderia pseudomalli* (INTRO Ref: GOPAL P 10-US/PRY-US).

Member(s) of programme

Programme Coordinator:

Prof P Gopalakrishnakone (Anatomy)

Members:

Prof K Jeyaseelan (Biochemistry)
Assoc Prof Khoo Hoon Eng
(Biochemistry)
K Rajasekar (DMERI, DSO)
Loke Weng Kiong (CCD, DSO)
Dr Maung Maung Thwin (Anatomy)
A Pachiappan (Anatomy)
Dr R Perumal Samy (Anatomy)
Dr R Saminathan (Anatomy)
Dr Gao Rong (Anatomy)
Feng Luo (Anatomy)

DEPARTMENTS



NUS

National University
of Singapore

YONG LOO LIN SCHOOL OF MEDICINE

THE EXPERTISE AT THE
FRONTIERS OF MEDICINE

THE DEDICATED TEAM BEHIND EACH MEDICAL FIELD
VERIFIES THE RELEVANCE OF RESEARCH TO SOCIETY

PROGRAMMES

Postgraduate Students in
Orthopaedic Surgery:

Joyce Tey (MSc)
Tan Heng Liang (PhD)

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National University Hospital:

Dr Alphonsus Chong
Dr Kevin Lee
Dr Lim Jit Kheng

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of Bioengineering, NUS:

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Assoc Prof Toh Siew Lok
Assoc Prof Michael Raghunath
Assoc Prof Dietmar Huttmacher
Asst Prof Phan Toan Thang

UROF Student in
Orthopaedic Surgery:

Raghav Sundar

Venom and Toxin Research Programme

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Programme Coordinator:

Prof P Gopalakrishnakone (Anatomy)

Members:

Prof K Jeyaseelan (Biochemistry)

Assoc Prof Khoo Hoon Eng

(Biochemistry)

Assoc Prof Lim EBN (DPO)

Loke Weng Kiong (CCD, DSO)

Dr Maung Maung Thwin (Anatomy)

A Pachiappan (Anatomy)

Dr R Perumal Samy (Anatomy)

Dr R Saminathan (Anatomy)

Dr Gao Rong (Anatomy)

Feng Luo (Anatomy)



DEPARTMENTS



THE EXPERTISE AT THE **FRONTIERS OF MEDICINE**

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DEPARTMENT OF ANAESTHESIA



INTRODUCTION

a) Pain research

Professor Lee Tat Leang and Dr Shinro Tachibana lead the work in pain research. They focus on identifying and characterization of novel neuropeptides involved in pain. We study the mechanisms of pain in which the peptides are involved, the processing pathway, and the other central nervous system effects. Our range of work includes developing quantification methods, antibody production, immunohistochemistry, and behavioral tests in animal models.

b) Airway research

Assoc Prof Eugene Liu and Dr Raymond Goy lead the evaluation of new devices and techniques for the management of difficult airways. Our team has completed both clinical and simulator studies of the Glidescope, the LMA CTrach systems, and the laryngeal tube. We are also studying the application of these systems in teaching medical students and trainee doctors. Our CTrach work received one of the best abstract awards at the International Anesthesia Research Society annual conference in March 2006, and our report was the first publication on this promising system.

c) Anaesthesia outcomes database

Dr Raymond Goy and Assoc Prof Eugene Liu work on quality of recovery and other outcomes after day surgery. This has highlighted

several problems, leading to changes in clinical practice, and the work has been presented to the Ministry of Health. Dr Ti Lian Kah leads the cardiac anaesthesia outcomes studies in collaboration with the Cardiothoracic and Vascular Department in National University Hospital. The database will generate research ideas both in basic and clinical studies to improve outcomes.



Anaesthesia research team

DEPARTMENT OF ANAESTHESIA

PROJECT DESCRIPTION

On-going Projects

Study of functional interaction between nociception and nocistatin in regulating pain perception pathways

Principal Investigator: Dr Kazi Ahsan Jamil
Collaborators: Assoc Prof Samuel S W Tay,
Dr Shinro Tachibana,
Prof Lee Tat Leang,
Assoc Prof Yong Eu Leong

Characterisation of clinically significant peptides present in human cerebrospinal fluid

Principal Investigator: Dr Shinro Tachibana
Collaborators: Prof Lee Tat Leang,
Assoc Prof Eugene Liu Hern Choon,
Dr Siau Chiang (NUH),
Dr Tessy Joseph,
Dr Kazi Ahsan Jamil,
Dr Sethuraman Rama,
Ms Lee Chun Mei

Re-evaluation of amino acids analysis in cerebrospinal fluid to find possible correlations with different pain states

Principal Investigator: Dr Shinro Tachibana
Co-Principal Investigator: Prof Lee Tat Leang
Collaborators: Dr Sethuraman Rama,
Assoc Prof Eugene Liu Hern Choon

Identification and characterization of nocistatin receptor protein

Principal Investigator: Dr Tessy Joseph
Collaborators: Dr Shinro Tachibana,
Prof Lee Tat Leang,
Dr Siau Chiang (NUH)

The effects of nocistatin on the central nervous system and the distribution of nocistatin receptors in the brain and spinal cord, in the mouse

Principal Investigator: Assoc Prof Eugene Liu Hern Choon
Collaborators: Dr Shinro Tachibana,
Prof Lee Tat Leang,
Assoc Prof Peter Wong

Learning with the human patient simulator: Is it necessary to be in the "Hot Seat" A pilot study

Principal Investigator: Dr Ti Lian Kah
Co-Principal Investigator: Assoc Prof Chen Fun Gee

Do medical students learn and retain the skill of endotracheal intubation better with directed or experiential learning?

Principal Investigator: Dr Ti Lian Kah
Co-Principal Investigator: Assoc Prof Chen Fun Gee

INTERNATIONAL PUBLICATION

Liu EHC, Goy RW, Chen EFG

An evaluation of poor LMA CTrach views with a fibreoptic laryngoscope and the effectiveness of corrective measures. *British Journal of Anaesthesia* (2006) 97(6):878-82. (United Kingdom).

Sethuraman R, Lee TL, Chui JW, Tachibana S

Changes in amino acids and nitric oxide concentration in cerebrospinal fluid during labor pain. *Neurochemical Research* (2006) 31(9):1127-33. (United States).

Lee TL

Unilateral bronchospasm after interpleural analgesia with bupivacaine. *Acta Anaesthesiologica Scandinavica* (2006) 50(4):518-9. (Norway).

Liu EHC, Nishiuchi Y, Kimura T, Tachibana S

Supraspinal nocistatin and its amide derivative antagonize the hyperalgesic effects of nociceptin in mice. *Neuroscience Letters* (2006) 397:59-63. (Ireland).

Liu EHC, Goy RW, Chen EFG

The LMA CTrach, a new laryngeal mask airway for endotracheal intubation under vision: evaluation in 100 patients. *British Journal of Anaesthesia* (2006) 96(3):396-400. (United Kingdom).

Ye Z, Liu EHC, Higgins JP, Keavney BD, Lowe GD, Collins R, Danesh J

Seven clotting gene polymorphisms in 64 968 cases of coronary disease and 90 398 controls: meta-analysis of 187 studies. *Lancet* (2006) 367:651-8. (United Kingdom).

Tessy J, Lee TL, Chou N, Nishiuchi Y, Kimura T, Jikuya H, Ou K, Yau CC, Tachibana S

Identification of mature nociceptin and nocistatin in human brain and cerebrospinal fluid by mass spectrometry combined with affinity chromatography and HPLC. *Peptides* (2006) 27(1):122-30. (United States).

Liu X, Lee TL, Wong PTH

Cyclooxygenase-1 inhibition shortens the duration of diazepam-induced loss of righting reflex in mice. *Anesthesia and Analgesia* (2006) 102:135-140. (United States).

STAFF PROFILE

Associate Professor & Head:	Chen Fun Gee
Professor:	Lee Tat Leang
Associate Professor:	Eugene Liu Hern Choon
Assistant Professor:	Ti Lian Kah
Senior Research Fellow:	Shinro Tachibana
Research Fellows:	Tessy Joseph Kazi Ahsan Jamil Sethuraman Rama
Research Assistant:	Lee Chun Mei

CONTACT INFORMATION

Contact Person:	Assoc Prof Eugene Liu Hern Choon
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Telephone:	6772-4207 6772-4208 6777-5702
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DEPARTMENT OF ANATOMY



INTRODUCTION

Research in the Department of Anatomy at the Yong Loo Lin School of Medicine has taken a bold step towards the development of new strategies to tackle the complexities of diseases and exploration of new treatment regimes. Some of the novel strategies include drug discovery from venoms & toxins, mapping of novel genes, exploitation of extracellular matrices and prognostic biomarkers for cancers and tailored cell cultures primed for target specific transplantation for age-related neurodegenerative diseases.

The synergy evolved from collaborations with intra- and inter-departmental, local and foreign researchers has resulted in several novel discoveries and high quality publications in reputable international journals. This symbiotic research culture developed by the department has metamorphosed over the years with great success through centralization and constant upgrading of facilities, thereby attracting like-minded researchers to forge ahead towards excellence in academic medicine.

PROJECT DESCRIPTION

Grants Awarded in 2006

Therapeutic leads from novel neurotransmitter-like molecules and voltage-gated ion channel toxins from scorpion venoms

Principal Investigator: Prof P Gopalakrishnakone
Co-Principal Investigator: Dr Selvanayagam Nirthanan (NNI)

Role of metallothionein in the prevention of diabetes-induced cardiac embryopathy

Principal Investigator: Assoc Prof Bay Boon Huat
Co-Principal Investigator: Assoc Prof Tay Sam Wah Samuel
Collaborator: Dr S Dinesh Kumar

GAMMA-RIMS as synaptic proteins for synaptic plasticity and neurotoxicity

Principal Investigator: Dr Liang Fengyi

The interactive responses between metastatic lung cancer cells and activated microglia - To study the mechanism involved in brain metastasis, dormancy and relapse of cancer cells

Principal Investigator: Dr He Beiping
Collaborator: Prof Alex Chang
(Oncology, Johns Hopkins S'pore)

DEPARTMENT OF
ANATOMY**Biological functions and pathological implications of CNS sirtuin 2: An oligodendroglia-specific tubulin/histone deacetylase**

Principal Investigator: Dr Liang Fengyi

Immune modulatory effects of transplanted bone marrow stromal cells on microglia in the treatment of mouse model of Parkinson's disease

Principal Investigator: Assoc Prof Tay Sam Wah Samuel

Co-Principal Investigator: Dr He Bei Ping

Collaborator: Ms Chao Yin Xia
(Graduate student/Anatomy)**The Y-box binding protein, YB-1 as a novel prognostic biomarker and predictor of chemoresistance in adjuvant chemotherapy for breast cancer and radioresistance in nasopharyngeal cancer**

Principal Investigator: Assoc Prof Bay Boon Huat

Co-Principal Investigator: Dr Tan Puay Hoon (SGH)

Collaborators: Dr Yap Wai Ming (SGH),
Dr George Yip,
Dr Ken Matsumoto (RIKEN, Japan),
Dr Masafumi Tsujimoto (RIKEN, Japan)**Exploration of novel proteins involved in memory function using jumping spider model**

Principal Investigator: Dr He Beiping

An interactive multimedia module to enhance independent learning in dental and medical students

Principal Investigator: Prof P Gopalakrishnakone

Collaborators: Mrs Kiruthika Ragupathi (CDTL, NUS),
Ms Yap Lee Yang Alena (CDTL, NUS)**Efficacy evaluation of antiarthritis peptide in animal models of rheumatoid arthritis**

Principal Investigator: Prof P Gopalakrishnakone

A peptide analogue phospholipase A2 inhibitor for treatment of rheumatoid arthritis

Principal Investigator: Prof P Gopalakrishnakone

Hypoxic damage in the developing hippocampus

Principal Investigator: Assoc Prof Charanjit Kaur

Molecular regulation of mammalian spinal neurulation: a genome-wide analysis

Principal Investigator: Dr George Yip Wai Cheong

Collaborator: Dr Andrew J Copp (Univ College London)

Analysis of heparan sulphation patterns as biomarkers of breast cancer and as regulators of tumour cell behaviour

Principal Investigator: Dr George Yip Wai Cheong

Collaborators: Dr Tan Puay Hoon (SGH),
Dr Martin Götte
(Münster Univ Hospital, Germany)**On-going Projects****Systematic in situ expression mapping of novel genes and molecular, functional characterization of area-/cell type-specific genes in the central nervous system**

Principal Investigator: Dr Liang Fengyi

Analysis of regulatory factor involved in neurotoxicity in neurodegenerative diseases

Principal Investigator: Dr S Thameem Dheen

Collaborators: Prof Ling Eng Ang,
Assoc Prof Tay Sam Wah Samuel**Role of the choroid plexus in the development of brain white matter damage (periventricular leukomalacia) following hypoxic injury in the neonatal brain**

Principal Investigator: Assoc Prof Charanjit Kaur

Collaborator: Dr Lu Jia (DMERI/DSTA)

Characterization of the biological roles of different heparan sulphate species in breast cancer development and metastasis

Principal Investigator: Dr George Yip Wai Cheong

Collaborators: Assoc Prof Bay Boon Huat,
Dr Tan Puay Hoon (SGH)**Effect of regimental running on spatial learning and memory in rats. Possible roles of endogenous trophic factors**

Principal Investigator: Assoc Prof Ng Yee Kong

Collaborators: Assoc Prof Peter Wong
(Pharmacology),
Mr Ang Eng Tat (PhD Student)**Interaction between aggregate-bearing neurons and microglial toxicity in the pathogenesis of adult-onset neurodegenerative diseases**

Principal Investigator: Dr He Beiping

Exercise induced glial reactions in the brain and their roles in relation to changes of cytokines

Principal Investigator: Assoc Prof Ng Yee Kong

Collaborators: Assoc Prof Peter Wong (Pharmacology),
Mr Ang-Eng Tat (PhD Student),
Ms Gan Le Ting (Lab Officer)**Immunohistochemical detection of prognostic biomarkers and predictors of response to adjuvant treatment in breast cancer**

Principal Investigator: Assoc Prof Bay Boon Huat

Co-Principal Investigator: Assoc Prof Tan Puay Hoon (SGH)

Collaborator: Dr George Yip

Molecular analysis of microglia functions in the rat brain

Principal Investigator: Dr S Thameem Dheen

Collaborators: Prof Ling Eng Ang,
Assoc Prof Tay Sam Wah Samuel**Identification of bactericidal peptides from the venoms of *Pseudechis australis* and *Bitis gabonica* for treatment of skin infection caused by *Staphylococcus aureus***

Principal Investigator: Prof P Gopalakrishnakone

Co-Principal Investigators: Assoc Prof Ho Bow (Microbiology),
Assoc Prof Vincent TK Chow
(Microbiology)**Molecular and morphological analysis of urinary bladder and its neural pathways following chronic bladder outlet obstruction**

Principal Investigator: Prof Ling Eng Ang

Co-Principal Investigators: Assoc Prof Chin Chong Min (Surgery),
Assoc Prof Ng Yee Kong

Collaborator: Dr Hu Jin

DEPARTMENT OF ANATOMY



Loading samples into a real-time RT-PCR machine.

Global gene expression analysis of cardiac neural crest cells exposed to maternal teratogenicity during development

Principal Investigator: Assoc Prof Tay Sam Wah Samuel
Collaborators: Dr S Thameem Dheen,
Dr S Dinesh Kumar

Functional characterization of crospp: a cytoskeleton-related oligodendroglia-specific novel protein

Principal Investigator: Dr Liang Fengyi
Collaborators: Dr Xiao Zhi Cheng (SGH),
Dr Feng Zhi Wei (NNI)

Role of diabetes mellitus and retinoic acid in the development of congenital heart defects in the mouse embryo

Principal Investigator: Assoc Prof Tay Sam Wah Samuel
Collaborator: Dr S Dinesh Kumar

Screening of ion channel therapeutics from the venoms of scorpion and conus snails

Principal Investigator: Prof P Gopalakrishnakone
Collaborator: Dr Gavin Stewart Dawe
(Pharmacology)

Chondroitin sulphate: a novel therapeutic agent for promoting cutaneous wound healing

Principal Investigator: Dr George Yip Wai Cheong
Collaborators: Assoc Prof Bay Boon Huat,
Assoc Prof SM Mochhala (DMERI),
Assoc Prof Lu Jia (DMERI)

Therapeutic potential of neuroprotective agents for traumatic brain injury

Principal Investigator: Prof Ling Eng Ang
Collaborator: Dr Lu Jia (DMERI)

Functional roles of crospp myelin protein in molecular specialization of the node of Ranvier

Principal Investigator: Dr Liang Fengyi
Co-Principal Investigator: Prof Ling Eng Ang

Screening of changes in the endogenous neurotrophic factors & their associated receptors in rat brains following regimented exercise

Principal Investigator: Assoc Prof Ng Yee Kong
Collaborators: Assoc Prof Peter TH Wong
(Pharmacology),
Dr Lu Jia (DMERI)

Role of brain oxysterols in neurodegeneration

Principal Investigator: Assoc Prof Ong Wei Yi
Co-Principal Investigator: Dr Andrew Jenner (Biochemistry)

Investigation on possible delayed cardiotoxicity arising from chronic exposure to clinically asymptomatic levels of VX nerve agent

Principal Investigator: Prof P Gopalakrishnakone
Collaborators: Mr Loke Weng Keong (CCD, DSO),
Dr Lee Fook Kay (CCD, DSO)

Maternal diabetes-induced changes in the anatomy and the global gene expression patterns during neural tube development

Principal Investigator: Dr ST Dheen

INTERNATIONAL PUBLICATIONS

Kaur C, Viswanathan S, Zhang Y, Ling EA

Hypoxia-induced astrocytic reaction and increased vascular permeability in the rat cerebellum. *Glia* (2006) 54:826-839. (United States).

Du HY, Li Y, Olivo M, Yip GWC, Bay BH

Differential up-regulation of metallothionein isoforms in well-differentiated nasopharyngeal cancer cells in vitro by photoactivated hypericin. *Oncology Reports* (2006) 16:1397-1402. (Greece).

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Lim CN, Ho BC, Bay BH, Yip GWC, Tan PH

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Metallothionein as a prognostic biomarker in breast cancer. *Experimental Biology and Medicine* (2006) 231:1516-1521. (United States).

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A missing factor in chip-based patch clamp assay: Gigaseal. *Journal of Physics* (2006) 34:187-191. (United Kingdom).

DEPARTMENT OF
ANATOMY

Talbot K, Cho DS, Ong WY, Benson MA, Han LY, Kazi HA, Kamins J, Hahn CG, Blake DJ, Arnold SE

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Farooqui AA, Ong WY, Horrocks LA

Inhibitors of brain phospholipase A2 activity: Their neuropharmacologic effects and therapeutic importance for the treatment of neurologic disorders. *Pharmacological Reviews* (2006) 58:591-620. (United States).

Buschdorf JP, Chew LL, Zhang B, Cao Q, Liang FY, Liou YC, Zhou Y, Low BC

Brain-specific BNIP-2-homology protein Caytaxin relocalises glutaminase to neurite terminals and reduces glutamate levels. *Journal of Cell Science* (2006) 119:3337-3350. (United Kingdom).

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Purification of antibacterial agents from *Tragia involucrata* - A popular tribal medicine for wound healing. *Journal of Ethnopharmacology* (2006) 11:99-106. (Ireland).

Huang E, Ong WY

Distribution of ferritin in the rat hippocampus after kainate-induced neuronal injury. *Experimental Brain Research* (2006) 161:502-511. (Germany).

Xue LP, Lu J, Cao Q, Kaur C, Ling EA

Nestin expression in Muller glial cells in postnatal rat retina and its upregulation following optic nerve transection. *Neuroscience* (2006) 143:117-127. (United States).

He BP, Wang JJ, Zhang X, Wu Y, Wang M, Bay BH, Chang AYC

Microglial differential reactions in response to brain metastasis of lung cancer. *Molecular Medicine* (2006) 12:161-170. (United States).

Wu CY, Kaur C, Lu J, Cao Q, Guo CH, Zhou Y, Viswanathan S, Ling EA

Transient expression of endothelins in the amoeboid microglial cells in the developing rat brain. *Glia* (2006) 54:513-525. (United States).

Wu CY, Lu J, Cao Q, Guo CH, Gao Q, Ling EA

Expression of 2',3'-cyclic nucleotide 3'-phosphodiesterase in the amoeboid microglial cells in the developing rat brain. *Neuroscience* (2006) 142:333-341. (United States).

Li ZH, Lu J, Tay SSW, Wu Y, Strong MJ, He BP

Mice with targeted disruption of neurofilament light subunit display formation of protein aggregation in motoneurons and down-regulation of complement receptor type 3 alpha-subunit in microglia in the spinal cord at their earlier age: a possible feature in pre-clinical development of neurodegenerative diseases. *Brain Research* (2006) 1113:200-209. (Netherlands).

Ang ET, Dawe GS, Wong PTH, Mochhala SM, Ng YK

Alterations in spatial learning and memory after forced exercise. *Brain Research* (2006) 1113:186-193. (Netherlands).



Preparing samples for gene expression analysis.

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Wound healing potential of *Tragia involucrata* extract in rats. *Fitoterapia* (2006) 77:300-302. (United Kingdom).

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Kaur C, Viswanathan S, Ang LS, Sunderasan L

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Tan CH, He X, Yang J, Ong WY

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Huang E, Ong WY, Go ML, Connor JR

Upregulation of iron regulatory proteins and divalent metal transporter-1 isoforms in the rat hippocampus after kainate induced neuronal injury. *Experimental Brain Research* (2006) 170:376-386. (Germany).

Ong WY, Patel SC, He X

Neuroprotective effect of apoD on hippocampal neurons after kainic acid-induced injury. *Journal of Neurochemistry* (2006) 96:77. (United States).

Kaur C, Viswanathan S, Foulds WS

Early response of neurons and glial cells to hypoxia in the retina. *Investigative Ophthalmology & Visual Science* (2006) 47:1126-1141. (United States).

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Up-regulation of metallothionein isoforms in keloid keratinocytes. *International Journal of Molecular Medicine* (2006) 17:385-389. (Greece).

Olivo M, Du HY, Bay BH

Hypericin lights up the way for the potential treatment of nasopharyngeal cancer by photodynamic therapy. *Current Clinical Pharmacology* (2006) 1:217-222. (Ireland).

Choy MS, Chan YG, Bay BH, Cheng HC, Cheung NS

PTEN is recruited to specific microdomains the plasma membrane during lactacystin-induced neuronal apoptosis. *Neuroscience Letters* (2006) 405:120-125. (Ireland).

Xue LP, Lu J, Cao Q, Hu S, Ding P, Ling EA

Muller glial cells express nestin coupled with glial fibrillary acidic protein in experimentally induced glaucoma in the rat retina. *Neuroscience* (2006) 139:723-732. (Japan).

Satake S, Song SY, Cao Q, Satoh H, Rusakov DA, Yanagawa Y, Ling EA, Imoto K, Konishi S

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Lu J, Mochhala S, Moore XL, Ng KC, Tan MH, Lee LKH, He BP, Wong MC, Ling EA

Adult bone marrow cells differentiate into neural phenotypes and improve functional recovery in rats following traumatic brain injury. *Neuroscience Letters* (2006) 398:12-17. (Ireland).

Ong WL, Jiang B, Tang N, Ling SF, Yeo JF, Wei SH, Farooqui AA, Ong WY

Differential effects of polyunsaturated fatty acids on membrane capacitance and exocytosis in rat pheochromocytoma-12 cells. *Neurochemical Research* (2006) 31:41-48. (United States).

Dinesh Kumar S, Tay SSW, Ling EA

Partial outlet obstruction enhances NADPH-diaphorase activity in the monkey (*Macaca fascicularis*) bladder: Light and electron microscopic studies. *Histology and Histopathology* (2006) 21:383-391. (Spain).

Fu J, Tay SSW, Ling EA, Dheen ST

High glucose alters expression of genes involved in proliferation and cell fate specification of embryonic neural stem cells. *Diabetologia* (2006) 49:1027-1038. (West Germany).

Kaur C, Viswanathan S, Dheen ST, Ling EA

Insulin-like growth factor-I and II expression and modulation in activated microglial cells by lipopolysaccharide and retinoic acid. *Neuroscience* (2006) 138:1233-1244. (United States).

Ng YK, Brailoiu GC, Dun SL, Ling EA, Yang J, Chang JK, Dun NJ

Beacon-immunoreactivity in the rat hypothalamus. *Journal of Neuroscience Research* (2006) 83: 1106-1117. (United States).

Yip GWC, Smollich M, Gotte M

Therapeutic value of glycosaminoglycans in cancer. *Molecular Cancer Therapeutics* (2006) 5:2139-2148. (United States).

He X, Jenner AM, Ong WY, Farooqui AA, Patel SC

Lovastatin modulates increased cholesterol and oxysterol levels and has a neuroprotective effect on rat hippocampal neurons after kainate injury. *Journal of Neuropathology and Experimental Neurology* (2006) 65:652-663. (United States).

Seidler DG, Faiyaz-ul-Haque M, Hansen U, Yip GWC, Zaidi SH, Teebi AS, Kiesel L, Gotte M

Defective glycosylation of decorin and biglycan, altered collagen structure, and abnormal phenotype of the skin fibroblasts of an Ehlers-Danlos syndrome patient carrying the novel Arg270Cys substitution in galactosyltransferase I (beta4GalT-7). *Journal of Molecular Medicine* (2006) 84:583-594. (United States).

Wong PTH, Qu K, Chimon GN, Seah ABH, Chang HM, Wong MC, Ng YK, Rumpel H, Halliwell B, Chen CPL

High plasma cysteine level may indicate poor clinical outcome in patients with acute stroke: possible involvement of hydrogen sulfide. *Journal of Neuropathology and Experimental Neurology* (2006) 65:109-115. (United States).

Perumal Samy R, Gopalakrishnakone P, Ignacimuthu S

Anti-tumor promoting potential of luteolin against 7,12-dimethylbenz(a)anthracene-induced mammary tumors in rats. *Chemico Biological Interactions* (2006) 164:1-14. (United States).

STAFF PROFILE

Professor & Head:

Professor:

Associate Professors:

Ling Eng Ang

P Gopalakrishnakone

Bay Boon Huat

Charanjit Kaur

Ng Yee Kong

K Rajendran

Ong Wei Yi

Tay Sam Wah, Samuel

Voon Chee Tet, Francis

DEPARTMENT OF ANATOMY

Assistant Professors:	He Beiping Liang Fengyi S Thameem Dheen Yip Wai Cheong, George
Teaching Assistant:	S Dinesh Kumar
Part-time Tutors:	Deepti Nayak Tan Kun Kiaang, Henry Gurmit Singh Wong Wai Chow
Adjunct Staff:	Leung King Chor, Thomas Yang Xiaohang Lu Jia Tan Puay Hoon Teng Feng Ru Xiao Zhicheng Lo Yew Long
Research Fellows:	Maung Maung Thwin Viswanathan Sivakumar R Perumal Samy
Research Assistants:	Ramasamy Saminathan Pachiappan Arjunan Fu Jiang Gao Qing Cheng Yu Juan Hu Jin Li Lv Li Zhaohui Tran Manh Hung



Mounting specimen for cutting in a cryocut.

CONTACT INFORMATION

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DEPARTMENT OF BIOCHEMISTRY



INTRODUCTION

The Department is well equipped for research. The main areas of research include:

- Reactive species and antioxidants in human health and disease, especially neurodegenerative diseases and cancer
- The role of mitochondria in cell death and disease
- Enabling technology for tissue engineering and drug discovery
- Genetics of drug response genes
- Liposome-mediated drug delivery
- Drug metabolism and transport
- Molecular neurobiology
- Cell death mechanisms
- Genetics of cancer development
- Proteomics & Lipidomics
- Intracellular sterol transport, triglyceride metabolism and lipotoxicity
- Protein folding, structure and inhibitor design by NMR spectroscopy
- Bioinformatics Databases; Bioinformatics Grid computing and workflow integration
- NP-complete problems in biology, sequence analysis, pattern recognition and transcription regulation
- Molecular biology of toxins
- Signal transduction
- Molecular mechanisms of mitotic events in cell division
- Burkholderia pseudomallei: Host pathogen interactions, multidrug resistance and anti-infectives discovery

The Department has established collaborative research with many overseas groups, other departments and research institutes within and outside NUS, with government departments and private industries. Staff members also hold joint appointments in University of Melbourne, University of London, Institute of Molecular and Cell Biology (IMCB), National Cancer Centre and Johns Hopkins University School of Medicine. Staff from institutions such as IMCB, Bioinformatics Institute, ES Cell International Pte Ltd, Singapore General Hospital, National Neuroscience Institute and the National Cancer Centre hold adjunct appointments in the Biochemistry Department.

DEPARTMENT OF BIOCHEMISTRY

PROJECT DESCRIPTION Grants Awarded in 2006

The influence of diet on colon disease

Principal Investigator: Dr Andrew Jenner

Lipid biomarkers for mycobacterial infections

Principal Investigator: Assoc Prof Markus R Wenk
Collaborator: Dr Verponie Dartois (NITD)

Towards understanding responses to adefovir therapy for chronic hepatitis B infection

Principal Investigator: Dr Tan May Chin Theresa

Lipid signalling during adult stem cell differentiation

Principal Investigator: Assoc Prof Markus R Wenk
Co-Principal Investigators: Assoc Prof Victor Nurcombe (IMCB),
Prof Edward A Dennis
(Univ of California)

An integrated proteomics and molecular modeling approach in understanding the pharmacological effects of rhubarb

Principal Investigator: Assoc Prof Chung Ching Ming
Co-Principal Investigators: Assoc Prof Chen Yuzong,
Prof Ong Choon Nam

Investigating the role of cdk5 in neuronal synaptic organization through phosphorylation of δ catenin

Principal Investigator: Dr Sashi Kesavapany

Evaluation of lipid pathways as potential mycobacterial targets

Principal Investigator: Assoc Prof Markus R Wenk

Dengue epitope vaccine, tetravalent & MHCII – targeted

Principal Investigator: Assoc Prof Tan Tin Wee
Co-Principal Investigators: Prof Thomas August (JHU),
Dr Vladimir Brusic,
Prof Shoba Ranganathan

N01 contract: Large scale antibody and T cell epitope discover program

Principal Investigator: Assoc Prof Tan Tin Wee
Co-Principal Investigator: Prof Thomas August (JHU)

Mitochondrial dynamics and cell death

Principal Investigator: Dr Jeffrey S Armstrong
Collaborator: Assoc Prof Boelsterli Urs Alex

Towards understanding responses to adefovir therapy for chronic hepatitis B infection

Principal Investigator: Dr Tan May Chin Theresa
Co-Principal Investigator: Assoc Prof Lim Seng Gee
Collaborator: Dr Shanthi Wasser

Ngr2's expression profile, signaling mechanisms and its roles in neuronal regeneration

Principal Investigator: Dr Tang Bor Luen

Bacterial virulence factors-function regulation, variation and interactions with host

Principal Investigator: Assoc Prof Leong Ka Yin (DBS)
Co-Principal Investigators: Dr Gan Yuun Hwen
Prof Ding Jeak Ling
Assoc Prof Zhang Lian Hui
Dr Patrick Tan

Role of microRNAs in liver cirrhosis and liver regeneration

Principal Investigator: Dr Tan May Chin Theresa
Co-Principal Investigators: Assoc Prof Lim Seng Gee,
Mr Ravishankar K Diddapur
Collaborators: Dr Shanthi Wasser
Assoc Prof Khoo Hoon Eng,
Sridhar Ganapathi Iyer

Halting neurodegeneration through the selective inhibition of aberrant cyclin dependent kinase 5 hyperactivity in vivo

Principal Investigator: Dr Sashi Kesavapany
Collaborator: Dr Harish C Pant

Mechanisms of vascular protection by haem oxygenase

Principal Investigator: Prof Barry Halliwell
Co-Principal Investigators: Prof Frank Watt,
Prof Roland Stocker,
Prof Peter Lay

Hepatitis B virus x protein (HBX) and hepatocellular carcinogenesis (HCC) - Characterization HBX in HCC patients and identification and downstream target of HBX

Principal Investigator: Assoc Prof Lee Guat Lay, Caroline
Co-Principal Investigators: Dr Ooi Peng Jin London Lucien,
Assoc Prof Tan Tin Wee

MicroRNAs and cell proliferation

Principal Investigator: Dr Tan May Chin Theresa
Co-Principal Investigators: Dr Deng Lih Wen,
Assoc Prof Tan Tin Wee

Identification and characterization of functionally important polymorphisms at the ABCC2 and ABCC3 gene loci

Principal Investigator: Assoc Prof Lee Guat Lay Caroline

Cellular functions of nogo -roles in membrane dynamics, neuroprotection and neuroregeneration

Principal Investigator: Dr Tang Bor Luen

Elucidation of the roles of a novel protein MLL5 in cell cycle regulation and tumor suppression

Principal Investigator: Dr Deng Lih Wen

On-going Projects

Oxidative stress in neuronal injury: Functional genomic and proteomic analysis in cultured neurones from genetically manipulated mice

Principal Investigator: Dr Steve Cheung Nam Sang

Towards a bioartificial kidney device

Principal Investigator: Prof Sit Kim Ping

DEPARTMENT OF BIOCHEMISTRY

Lipid profiling of mycobacteria bovis BCG during hypoxic dormancy response

Principal Investigator: Assoc Prof Markus R Wenk

Understanding the dynamic nature of the gradual unfolding of CHAB1 and designing function mimetics for protein-protein interaction between EphrinB2 and its binding partner

Principal Investigator: Dr Song Jianxing

The role of nogo and nogo-66 receptor in mammalian brain neurogenesis and neuroregeneration after injury

Principal Investigator: Dr Tang Bor Luen

Functions of small GTPases and their interacting partners in the brain

Principal Investigator: Dr Tang Bor Luen

Isolation and cloning of a novel ADP-ribosyl cyclase from CD38 knockout mouse

Principal Investigator: Assoc Prof Chang Chan Fong

The role of mitotic exit components in the development of C elegans

Principal Investigator: Dr Yeong Foong May

Lipidomics of neuronal membranes - identification of lipids involved in neurosecretion and neurodegenerative diseases

Principal Investigator: Assoc Prof Markus R Wenk

Establishing and identifying important dietary and TCM-based antioxidants in the human body

Principal Investigator: Prof Barry Halliwell

Biofilm formation by *Burkholderia Pseudomallei*

Principal Investigator: Dr Chua Kim Lee

Dengue epitope vaccine, tetravalent & MHCII – targeted

Principal Investigator: Assoc Prof Too Heng-Phon

Molecular dissection of apoptotic pathways in the fission yeast

Principal Investigator: Assoc Prof Yang Hongyuan Robert

Function characterization of amigo-1, a brain-enriched cell adhesion molecule with possible neurogenic roles

Principal Investigator: Dr Tang Bor Luen

Development of peptide inhibitors to HMGCoA reductase

Principal Investigator: Prof Jeyaseelan Kandiah
Co-Principal Investigator: Dr Arumugam Arunmozhiarasi

The Na⁺/H⁺ exchanger 1, NHE-1 gene expression, reactive oxygen species and tumor cells' response to apoptosis

Principal Investigator: Assoc Prof Marie-Veronique Clement

The role of mitochondrial superoxide in hyperglycemia-mediated signal transduction in the endothelium

Principal Investigator: Dr Jeffrey S Armstrong

Determination of the antioxidant uric acid and its oxidation products as specific biomarkers of oxidative stress in human studies

Principal Investigator: Prof Barry Halliwell

Lipidomics of membrane signalling as a tool in clinical prognostics

Principal Investigator: Assoc Prof Markus R Wenk

Genome-wide screening for genes that regulate cellular dynamics of lipid bodies in the budding yeast *Saccharomyces cerevisiae*

Principal Investigator: Assoc Prof Yang Hongyuan Robert

Biomarkers in stroke: Effects of novel venom components on MCAo induced cerebral ischemia in rat models

Principal Investigator: Prof Jeyaseelan Kandiah

Study to assess superoxide-mediated activation of the pro-survival kinase, AKT through a Na⁺/H⁺ exchanger 1-dependent activation of P13K and/or an oxidation

Principal Investigator: Assoc Prof Marie-Veronique Clement

Iron, atherosclerosis and neurodegeneration - A crucial role for iron and zinc in atherosclerosis and neurodegenerative diseases?

Principal Investigator: Prof Barry Halliwell

Genetic and immune determinants of pathogen virulence and host susceptibility in melioidosis

Principal Investigator: Dr Gan Yunn Hwen

Understanding the mechanistic links between late mitotic events & cytokinesis & cell separation using *Saccharomyces cerevisiae* as the model system

Principal Investigator: Dr Yeong Foong May

Nephrotoxicity of diclofenac sodium (voltaren)

Principal Investigator: Prof Sit Kim Ping

Genetic analysis of a lipopoptosis pathway in yeast

Principal Investigator: Assoc Prof Yang Hongyuan Robert
Co-Principal Investigator: Prof Shazib Pervaiz

Regulation of multidrug resistance protein (MRP) transporters by xenobiotics

Principal Investigator: Dr Tan May Chin Theresa

Elucidation of gene regulation mechanism in Cyr61 to understand down-regulation of its expression in hepatocellular carcinoma

Principal Investigator: Assoc Prof Lee Guat Lay, Caroline

Regulation of the Na⁺/H⁺ exchanger 1, NHE-1 gene expression by activation of PPARGgamma receptor in the human breast cancer cell line MCF-7

Principal Investigator: Assoc Prof Marie-Veronique Clement

Investigation of the association of MLL5 with CRC on cell cycle regulation and transcriptional activation

Principal Investigator: Dr Deng Lih Wen

Discovery of *B. pseudomallei* quorum sensing regulons using proteomics

Principal Investigator: Dr Chua Kim Lee

Aquaporin modulators from animal venom

Principal Investigator: Prof Jeyaseelan Kandiah

DEPARTMENT OF
BIOCHEMISTRY**Lipidomics of infectious diseases-novel molecular insights into host-pathogen interactions**

Principal Investigator: Assoc Prof Markus R Wenk

Elucidation of gene regulation mechanism of the fat10 gene which is upregulated in hepatocellular carcinoma

Principal Investigator: Assoc Prof Lee Guat Lay Caroline

***Burkholderia pseudomallei* multidrug efflux pumps**

Principal Investigator: Dr Chua Kim Lee

Host pathogen interaction in the infection by *Burkholderia pseudomallei*

Principal Investigator: Dr Gan Yunn Hwen

INTERNATIONAL PUBLICATIONS

Akram S, Teong HFC, Fliegel L, Pervaiz S, Clement MV

Reactive oxygen species-mediated regulation of the Na⁺/H⁺ exchanger 1 expression connects intracellular redox status with cells' sensitivity to death triggers. *Cell Death and Differentiation* (2006) 13:628-641. (United States).

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Nitric oxide-releasing flurbiprofen reduces formation of proinflammatory hydrogen sulfide in lipopolysaccharide-treated rat. *British Journal of Pharmacology* (2006) 147:966-974. (United Kingdom).

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Mitochondria: A target for cancer therapy. *British Journal of Pharmacology* (2006) 147:239-248. (United Kingdom).

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Mitochondrial Membrane Permeabilization: the sine qua non for cell death. *BioEssays* (2006) 28:253-260. (United Kingdom).

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Biochemical and physiological characterisation of a novel nitrosothiol formed from the gaseous mediators hydrogen sulfide and nitric oxide: Implications for cardiovascular disease. *Free Radical Research* (2006) 40(7):S49. (United Kingdom).

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Chao SP, Clement MV

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AMIGO and friends: An emerging family of brain-enriched, neuronal growth modulating, type I transmembrane proteins with leucine-rich repeats (LRR) and cell-adhesion motifs. *Brain Research Reviews* (2006) 51:265-274. (Germany).

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Chen MJ, Yap YW, Choy MS, Koh CHV, Seet SJ, Duan W, Whiteman M, Cheung NS

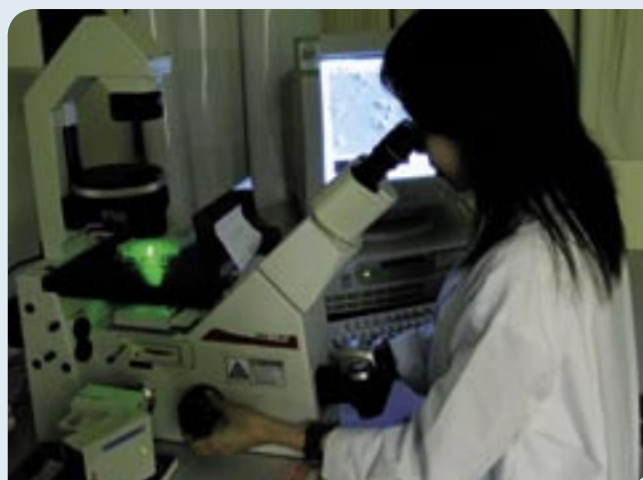
Early induction of calpains in rotenone-mediated neuronal apoptosis. *Neuroscience Letters* (2006) 397:69-73. (Ireland).

Chen Y, Tang BL

The amyloid precursor protein and postnatal neurogenesis/neuroregeneration. *Biochemical and Biophysical Research Communications* (2006) 341:1-5. (United States).

Chen Y, Teng FYH, Tang BL

Coaxing bone marrow stromal mesenchymal stem cells towards neuronal differentiation: progress and uncertainties. *Cellular and Molecular Life Sciences* (2006) 63(14):1649-1657. (Switzerland).



RA, Ms Yap Yann Wan at the DC500 Microscope

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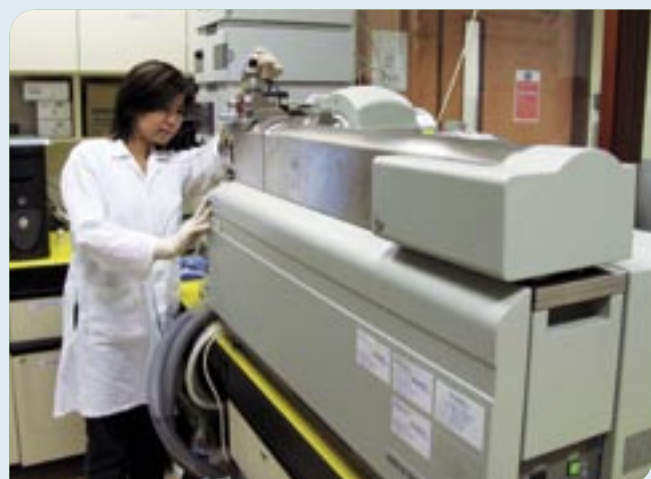
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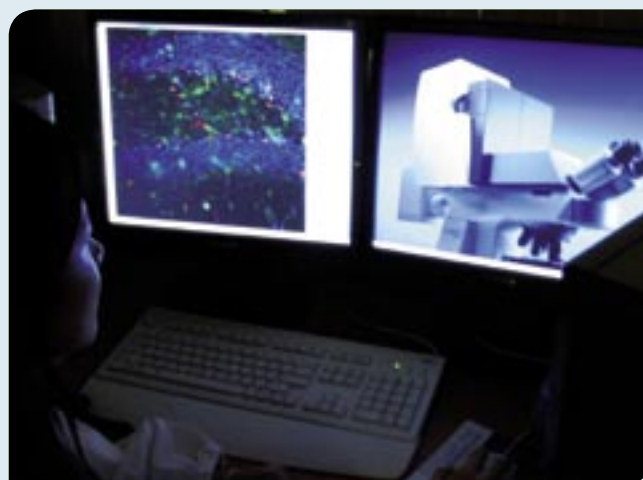
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DEPARTMENT OF COMMUNITY, OCCUPATIONAL & FAMILY MEDICINE

INTRODUCTION

In the year 2006, COFM had published more than one hundred papers in international refereed journals. There were more than 30 on-going and new research projects conducted in the department, and Centre for Molecular Epidemiology. Some highlights of our research activities are as follows:

- (i) **Molecular Epidemiology Research:** The aim of the Centre for Molecular Epidemiology (CME) is to discover gene-environment interactions for the promotion of public health. Common diseases of public health significance such as diabetes mellitus, cardiovascular disorders, and most cancers are multi-factorial involving complex gene-environment interactions. To elucidate the causes of disease, we need genetic and environmental exposure information. A prospective cohort study design is ideal as it reduces bias and participants in the study are not limited to survivors. CME received 5-year funding of \$12 million from BMRC to pool existing cohort studies and set up an epidemiologic infrastructure that promotes translational research. To this end, the Centre also works on infrastructural projects for population registers, record linkages and studies on public perceptions/education in genetics research.
- (ii) **Environmental and Occupational Health Research:** The main mission of the Centre for Environmental and Occupational Health Research is to elucidate and prevent environmental and occupational related health problems. It is made up of members of different disciplines to conduct credible upstream research and provide support and consultancy in the areas of chemical safety, and environmental and occupational health. It also provides training in the area of Environmental and Occupational Health. The Centre has close collaboration with various institutions in US and China, and is a member of the US National Institute of Environmental Health Sciences (NIEHS) Global Health Alliance.
- (iii) **Health Promotion Research:** Health promotion research has focused on the prevention of sexually transmitted infections (STIs) and HIV among sex workers and their clients in Singapore. One of the publications on the impact of condom use on STIs among brothel-based sex workers in Singapore was cited in the UN AIDS 2006 Report of the global AIDS epidemic as an example of a comprehensive HIV prevention intervention programme. In 2006, research on HIV and STI prevention was extended to adolescents and mainstream women with grants received from NMRC and AWARE. The survey on STI Management Practices by doctors, carried out in collaboration with and led by the Department of STD Control, has just been completed. We also collaborated with NUS Department of Medicine on a nationwide survey to determine barriers to recommend cancer screening

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among Singaporeans. The international collaborative research with University of Guelph, Canada on HIV prevention among indirect sex workers in Cambodia, received additional funding from the MAC AIDS Fund for its ongoing research.

- (iv) **Health Services Research:** The departmental team continues to build on its interest in health policy and evaluation research, with specific emphasis on comparative health systems and health financing. Much of this work is done in collaboration with international agencies like World Health Organization and World Bank.

In addition, some members are involved in helping to set up the School of Medicine's Centre for Health Services Research, which has a collaborative agreement with the US RAND Corporation. The Centre has identified some national-level projects, and work on them is progressing through the project teams. Some of the work done by the research fellows include cost-effectiveness and cost-utility analysis of specific treatment regimes and quality of life (QoL) measures in mental health, orthopaedic care and cancer treatment. International projects include validation of cross-cultural QoL instruments and pharmacoeconomic evaluations of certain treatments.

(v) Chronic Diseases Research

(a) Genetic Epidemiology of Diabetes Mellitus and Its Complications

Diabetes mellitus is a major public health problem in Singapore as well as in developed countries such as Europe, Japan and the USA. In the COFM Disease Genetics Laboratory, we are seeking to identify novel prognostic factors for this disease and its attendant complications. Following up on our 2005 meta-analysis of 47 studies totaling 14,727 subjects published in *Diabetologia* which implicated the angiotensin-I converting enzyme insertion/deletion polymorphism as a genetic marker for diabetic nephropathy, recent research in our laboratory found that detection of this gene-disease association can be greatly facilitated using a haplotype-based approach. Conducted in collaboration with the Joslin Diabetes Center, Harvard Medical School, this work has been published in the premier journal *Diabetes*. As another critical step forward for local diabetes research, the laboratory has taken the lead to establish the Singapore Diabetes Cohort Study. Working with the National Healthcare Group Polyclinics, Tan Tock Seng and National University Hospitals, this 5000-strong cohort will be an invaluable resource to dissect out gene-environment interactions in the etiology of diabetes, while offering an invaluable opportunity to seek out new biomarkers to track disease progression.

(b) Epidemiology of Eye Diseases

Myopia is a huge public health problem in urban Asian countries such as Singapore, Japan, Hong Kong and Taiwan. High myopia (myopia greater than -6.0 Diopters) may be associated with cataract, glaucoma, retinal degeneration and myopic macular degeneration. The Singapore Epidemiology of Eye Disease (SEED) program includes several large prevalence surveys and cohort studies, including the myopia epidemiologic studies, Singapore Cohort study of the Risk factors for Myopia (SCORM) with a 9-year follow-up of 2,000 children, and Strabismus, Amblyopia and Refractive error in Singapore children (STARS) study of 3,000 preschoolers. In the BMRC Research Grant Awards (June 2006 Exercise), the largest amount funded of

\$1,744,615 was awarded to a myopia study joint project between NUS and Singapore Eye Research Institute (SERI) headed by Assoc Prof Saw Seang Mei, Dept of COFM.

(c) Epidemiology of cardiovascular disease, hypertension, and chronic kidney disease

Cardiovascular disease is a major cause of death in developed countries, including Singapore. Similarly with the increase in prevalence rates of obesity and overweight, hypertension and kidney disease are becoming increasingly prevalent in developed countries, and are strong risk factors for subsequent cardiovascular disease and mortality. Our research group has a broad research interest in studying both traditional risk factors (such as smoking, overweight, and diabetes mellitus) and non-traditional risk factors (such as markers of inflammation, endothelial function, oxidative stress, and microvascular processes) in the development of cardiovascular disease, hypertension, and chronic kidney disease. We are involved in several local and overseas studies as Principal/Co-Investigator, including the Beaver Dam cohort, Blue Mountains Eye Study, Singapore Malay Eye Study, the Atherosclerosis Risk in Communities Study, and the Wisconsin Epidemiologic Study of Diabetic Retinopathy/ Cardiovascular Diseases in Diabetes (WESDR/WESCID). Several important findings have been published in high impact journals, including (1) showing for the first time that a combined exposure to current smoking and heavy drinking (>3 drinks/day) substantially increases the risk of developing kidney disease among community-dwelling adults, (2) plasma fibrinogen levels are associated with long-term risk of developing hypertension among men, (3) serum uric acid levels are positively related to the 10-year risk of developing hypertension, (4) that low-normal blood pressure levels, even lower than the currently recommended levels, have additional protective effect on the 16-year risk of development of kidney disease among subjects with type 1 diabetes.

(d) The Singapore Chinese Health Study

The Singapore Chinese Health Study is a collaborative research project between the Department and several research institutes in USA, including the Cancer Center in the University of Minnesota and the National Institute of Environmental Health Sciences in USA. The study was established between 1993 and 1998 by the recruitment of a residential cohort of roughly 63,000 Chinese men and women, who were aged 45-74 years, into the study. The main objective is to establish a stable cohort for long-term study of dietary, genetic and environmental determinants of cancer, and understand how these factors can play an etiological or protective role on the incidence of cancer. The information we can obtain from our studies, given the distinct genetic and lifestyle factors of our cohort members compared with other populations, will not only help us better understand the mechanisms of tumor development, but should also aid in developing prevention strategies. At present, we have made several noteworthy and novel scientific contributions of reports in over 40 international peer-reviewed publications, including protective roles of fish, soy, cruciferous vegetables and tea in cancer. Sub-studies arising from this cohort have also been established in collaboration with other international research institutes and research groups in USA and China, and received prestigious NIH grants. The Ministry of Health regards the Study as a significant undertaking in the field of epidemiology locally, and is actively collaborating with and supporting the Study.

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Analysis of parthenolide in chrysanthemum extract using Liquid-Chromatography with Mass Spectrophotometer.

(e) Cancer Epidemiology

Two case-control studies on cancer are currently in the field. Both are multi-centre collaborative efforts and seek to obtain epidemiologic data and biological specimens from patients seen in various healthcare institutions, and to use these to evaluate the interaction between specific genetic and environmental factors in carcinogenesis.

The Genes, Environment and Lung Cancer (GEL) study, funded by NMRC, aims to evaluate the role of estrogen and inflammatory pathways in lung cancer among Chinese women in Singapore. This study is being conducted in the National University Hospital, National Cancer Centre, Singapore General Hospital, Tan Tock Seng Hospital, and Changi General Hospital. Close to 900 patients have been recruited over the past 2 years, and this phase of the study will close in 2008.

The Singapore Lymphoma Study, funded by BMRC, began in 2005 and will run till 2010, with the aim of recruiting 500 cases and 1000 controls. Fieldwork is in progress in NUH, NCC, SGH, TTSH and the National Skin Centre. This study will examine a wide range of potential lifestyle and environmental factors that may influence the development of lymphomas, as well as possible genetic determinants of risk.

Over the past year, there have been a total of seven full-time staff supporting these projects; the team is also working with international consortia to establish collaborative studies, including pooled analyses.

(vi) Niche Area Research – Salivary Biomarkers

There is interest in the measurement of salivary biomarkers for several reasons. The collection of saliva is non-invasive, and thus more readily acceptable by patients and subjects, especially children. The collection of serial measurements is also more likely to be consented to, as compared to collection requiring invasive procedures e.g. venepuncture. A wide range of salivary biomarkers can be measured at present. These include toxins (e.g. Pb, Cd), hormones (e.g. cortisol, DHEA), various drugs and their metabolites (e.g. cotinine), DNA, and measures of mucosal function (e.g. immunoglobulins and enzymes). In 2006, the Salivary Biomarkers Group in COFM collaborated with the National Environmental Agency to use

saliva to determine the seroprevalence and proportion of undiagnosed past dengue infections in the community. The group also initiated research collaborations with the NUS Psychology Department to study the effects of exercise on cortisol stress response and the NUS Business School to study the relationship between salivary testosterone and cortisol with leadership traits. Research collaborations with NUS Paediatrics, NUS ENT and School of Design and Environment are ongoing to study the relationship between the environment and immunological responses to allergic diseases and stress.

Looking forward, the Department will continue to work on high-impact research in the post-clinical areas, and creating synergy with the clinical departments in creating cutting-edge research.

PROJECT DESCRIPTION Grants Awarded in 2006

Singapore Consortium of Cohort Studies

Principal Investigator: Prof Chia Kee Seng
Collaborators: Dr Tai E Shyong (SingHealth),
Prof Wong Tien Yin,
Dr Jeannette Lee,
Dr Daniel Ng,
Dr Lim Su Chi (AH),
Dr NV Ramani (MNI),
Dr Tang Wern Ee (NHGP)

Genetic and environmental risk factors for diabetic nephropathy among Singaporeans with type 2 diabetes mellitus: Role of inflammatory genes

Principal Investigator: Dr Daniel Ng Peng Keat

The genetics of high density lipoprotein cholesterol metabolism

Principal Investigator: Dr Tai E Shyong

Molecular epidemiology of nephropathy secondary to type 2 diabetes

Principal Investigator: Dr Lim Su Chi

The relationship between severely impaired activities of daily living (ADL) function and life expectancy

Principal Investigator: Dr Koh Choon Huat, Gerald
Co-Principal Investigators: Prof Koh Soo Quee David,
Prof Chia Kee Seng
Collaborators: Dr Chan Kim Ming (THKH),
Dr Fong Ngan Phoon (SLH),
Dr Tan Boon Yeow (SLH)

The relationship between inflammation, endothelial dysfunction, oxidative stress, micro-vascular function and chronic kidney disease (CKD)

Principal Investigator: Dr Anoop Shankar
Co-Principal Investigators: Prof Koh Soo Quee David,
Prof Chia Kee Seng
Collaborators: Prof F Javier Nieto (UW-Madison),
Prof Ronald Klein (UW-Madison),
Prof Barbara EK Klein (UW-Madison)

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Scanning for residue radioactive substance using pancake Geiger Counter.

Preschool refractive error, amblyopia and strabismus in Singapore study

Principal Investigator: Assoc Prof Saw Seang Mei
 Co-Principal Investigator: Assoc Prof Wong Tien Yin
 Collaborators: Prof David Koh,
 Prof Chia Kee Seng,
 Prof Rohit Varma (USC),
 Prof Paul Mitchell (UOS)
 Prof Joanne Katz (JHBSOPH)
 Dr Quah Boon Long (SNEC)
 Dr Sonal Farzavandi (SNEC)
 Dr Audrey Chia (SNEC)
 Dr Lam Pin Min (KKWACH)
 Dr Benjamin Chang (AH)
 Assoc Prof Au Eong Kah Guan (AH)
 Prof Donald TH Tan (SERI)
 Dr Yvonne Ling (SNEC)
 Dr Leo Seo Wei (TTSH)

Sexually transmitted infections and high risk sexual behaviours among adolescents in Singapore

Principal Investigator: Assoc Prof Wong Mee Lian
 Co-Principal Investigators: Prof Koh Soo Quee David,
 Assoc Prof Roy Chan KW
 Collaborators: Dr Tan Hiok Hee (DSC),
 Assoc Prof Shanta Emmanuel (MOH),
 Prof George Bishop,
 Dr Lim Fong Seng (NHG)

A qualitative study of attitudes and risk reduction behaviours of women (non-sex workers) with HIV-positive partners

Principal Investigators: Assoc Prof Wong Mee Lian,
 Ms Braema Mathiapparanam
 Co-Principal Investigators: Dr Priya Sen,
 Assoc Prof Leo Yee Sin,
 Assoc Prof Roy Chan

Improving ambulatory teaching of medical students: Identifying barriers to acceptance of student presence during medical consultations from all stakeholders (CDTL)

Principal Investigator: Dr Koh Choon Huat Gerald
 Co-Principal Investigators: Dr Cheong Seng Kwing,
 Dr Wong Teck Yee,
 Dr Raymond Seet (NUH),
 Dr Erle Lim (NUH)

Genes, gene-environment interactions and myopia in Singapore children

Principal Investigator: Assoc Prof Saw Seang Mei
 Co-Principal Investigators: Assoc Prof Eric Yap,
 Prof Roger Beuerman (SERI),
 Prof Chia Kee Seng,
 Prof Donald Tan (SERI),
 Dr Mark Seielstad (GIS),
 Dr Wong Yong Wee (SERI),
 Dr Nishanthi Viranga Eranga (SERI),
 Dr Ng Peng Keat Daniel,
 Prof Terri Young (Duke University),
 Dr Li Yi Ju (Duke University)

On-going Projects

Establishing a Singapore twin database for genomics research

Principal Investigator: Prof Chia Kee Seng
 Collaborators: Prof Chew Suok Kai (MOH),
 Prof Edison Liu (ASTAR),
 Dr Eric Yap (DSO),
 Prof Lee Hin Peng

Setting up an infrastructure for population-based case control studies in molecular epidemiology of cancer

Principal Investigator: Prof Chia Kee Seng

Setting up a record linkage facility for cancer studies within the Singapore Cancer Syndicate

Principal Investigator: Prof Chia Kee Seng

Follow up of the Singapore breast screening project: Efficacy, disease progression and mammographic density

Principal Investigator: Prof Chia Kee Seng
 Collaborators: Dr Ng Fook Cheong (SGH),
 Prof Stephen Duffy (WIPM),
 Dr Rupert Jakes (UK MRC),
 Dr Gao Fei (NCC)

Discovering ethnic differences in gene-environment interaction

Principal Investigator: Prof Chia Kee Seng
 Collaborators: Assoc Prof Manuel Salto-Tellez (NUH),
 Dr Tan Puay Hoon (SGH)

Dissection of the signalling pathways in reactive nitrogen species-induced cell death

Principal Investigator: Dr Shen Han Ming

Saliva as a reliable source of genomic DNA for modern genetic studies

Principal Investigator: Dr Ng Peng Keat Daniel
 Collaborators: Prof Koh Soo Quee David,
 Prof Chia Kee Seng

Luteolin sensitizes trail-induced apoptosis in human cancer cells: Molecular mechanisms and potential application

Principal Investigator: Dr Shen Han Ming
 Collaborators: Dr Duan W,
 Prof Ong Choon Nam,
 Dr ZG Liu

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Singapore Cardiovascular Cohort Study

Principal Investigator: Dr Jeannette Lee
 Collaborators: Dr Tai ES (SGH),
 Dr Tan CE (Gleneagles Hosp),
 Prof Chia KS,
 Dr Chew SK (MOH),
 Dr Heng D (MOH),
 Dr Sethi S (NUH),
 Assoc Prof Hughes K,
 Assoc Prof Wong TY

The Singapore lymphoma study: a multi-center investigation of the etiologic and prognostic determinants of lymphoid malignancies in Singapore

Principal Investigator: Assoc Prof Adeline Seow
 Co-Principal Investigators: Assoc Prof Chia Sin Eng,
 Dr Benjamin Mow (NUH),
 Dr Lee Khai Mun (NUH),
 Dr Leonard Tan (NUH),
 Dr Tan Suat Hoon (NSC),
 P Kuperan (TTSH),
 Dr Tan Soo Yong (SGH),
 Dr Ng Siok Bian (NUH),
 Dr Wong Gee Chuan (SGH),
 Dr Susan Loong (NCC),
 Dr Miriam Tao (NCC)

A prospective study of antioxidant biomarkers in the etiology of coronary heart disease

Principal Investigator: Prof Ong Choon Nam
 Co-Principal Investigators: Prof Chia Kee Seng,
 Dr Koh Woon Puay
 Collaborator: Prof Yuan Jian Min (UOM)

Critical roles of TNF signaling molecules in reactive nitrogen species-induced cell death

Principal Investigator: Dr Shen Han Ming
 Collaborators: Dr M Whiteman,
 Dr Song Zhiwei,
 Dr ZG Liu

Incidence of irritable bowel syndrome development in a general practice clinic following the use of antibiotics

Principal Investigators: Assoc Prof Wong Mee Lian,
 Assoc Prof Gwee Kok Ann
 Co-Principal Investigator: Dr Jason Yap Soo Kor

Lung cancer in Singapore Chinese women: The role of estrogens & their interaction with genetic & environment factors (the genes, environment & lung cancer (GEL) study)

Principal Investigator: Assoc Prof Adeline Seow
 Co-Principal Investigators: Dr Philip Eng (SGH),
 Dr Hui Kok Pheng (CGH),
 Dr Lim Tow Keang (NUH/NUS),
 Dr Elaine Lim (NUH/NUS),
 Dr Alan Ng (TTSH),
 Dr Poh Wee Teng (CGH),
 Dr Teh Ming (NUH/NUS),
 Dr Chuah Khoon Leong (SGH)
 Collaborators: Dr Ng Peng Keat Daniel,
 Dr Liu Jianjun (GIOS)

The relationship between inflammation, endothelial dys-function, oxidative stress, microvascular function and chronic kidney disease(ckd) a population-based case-control study

Principal Investigator: Dr Anoop Shankar
 Co-Principal Investigators: Prof Koh Soo Quee David,
 Prof Chia Kee Seng

Luteolin and its analogues as chemosensitizers in cancer chemotherapy

Principal Investigator: Dr Shen Han Ming
 Collaborators: Prof Ong Choon Nam,
 Dr Lu Yixin

The relationship between severely impaired activities of daily living (ADL) function & life expectancy

Principal Investigator: Dr Koh Choon Huat Gerald
 Co-Principal Investigators: Prof Chia Kee Seng,
 Prof Koh Soo Quee David
 Collaborators: Dr Chan Kim Ming (AMKTHKH),
 Dr Fong Ngan Phoon (SLH),
 Dr Tan Boon Yeow (SLH)

Salivary biomarkers research

Principal Investigator: Prof Koh Soo Quee David
 Co-Principal Investigators: Assoc Prof Daniel Goh (NUS/NUH)
 Assoc Prof Tham Kok Wai,
 Dr Koh Choon Huat Gerald,
 Dr Lynette Shek (NUS/NUH)
 Dr Chew Fook Tim
 Collaborators: Assoc Prof Chia Sin Eng,
 Assoc Prof Stephen Hsu,
 Adj Assoc Prof Mabel Yap (HPB),
 Dr Chan Kim Ming (AMKH),
 Dr Fong Ngan Phoon (SLH),
 Dr Tan Boon Yeow (SLH),
 Dr Daniel Fung (IOMH),
 Dr Goh Chee Leok (NSC)

Genetic & environmental risk factors for diabetic nephropathy among Singaporeans with type 2 diabetes mellitus: Role of inflammatory genes

Principal Investigator: Dr Ng Peng Keat Daniel



Graduate research students examining human cancer cells treated with anti-cancer agents.

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Collaborators: Prof Koh Soo Quee David,
Prof Chia Kee Seng,
Dr Helen Leong (NHGP),
Assoc Prof Shanta Emmanuel (NHGP),
Dr Winston Kon (TTSH),
Dr Stanley Liew (NUH)

Changes in the refractive components in Myopia and Emmetropic Eyes: The teenage years

Principal Investigator: Assoc Prof Saw Seang Mei
Co-Principal Investigator: Prof Donald Tan
Collaborators: Dr Louis Tong,
Dr Chua Wei Han,
Dr Allan Fong,
Prof Chia Kee Seng,
Dr Daniel Ng Peng Keat,
Prof Koh Soo Quee, David,
Dr Joanne Katz,
Dr Richard Stone

The Singapore Chinese Health Study

Principal Investigators: Dr Koh Woon Puay,
Prof Lee Hin Peng
Co-Principal Investigators: Prof Mimi Yu (USA),
Assoc Prof Yuan Jian Min (USA)

Follow-up II Phase of The Singapore Chinese Health Study

Principal Investigators: Dr Koh Woon Puay,
Prof Mimi Yu (USA),
Prof Lee Hin Peng,
Assoc Prof Yuan Jian Min (USA),
Dr Stephanie London (USA)

Dietary and genetic determinants of mammographic density

Principal Investigators: Prof Anna Wu (USA),
Prof Mimi Yu (USA),
Dr Koh Woon Puay,
Prof Lee Hin Peng

Dietary factors in the etiology of colorectal cancer

Principal Investigator: Assoc Prof Yuan Jian Min (USA),
Co-Principal Investigators: Dr Koh Woon Puay,
Prof Gao WT (China),
Prof Mimi Yu (USA),
Dr R Turesky (USA)

Exploring demand for health research by Singapore Policy Makers: an empirical approach

Principal Investigator: Assoc Prof Lim Meng Kin
Co-investigators: Asst Prof Wong Teck Yee,
Asst Prof Cheong Seng Kwing



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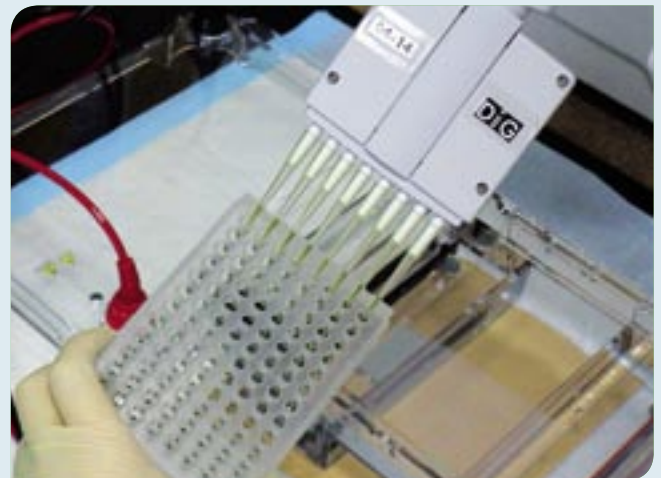
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Joint Associate Professors:

Research Fellows:

Research Assistants:

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Tan Huiling
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Adjunct Associate Professors:	Chan Kum Wah Roy Cheong Pak Yean Chew Suok Kai Hughes, Kenneth Lee Hock Siang Lee Kim Hock Lionel Lim Lean Huat Tai E Shyong Tan Say Beng Wilder-Smith Annelies Yap Mei Poh Mabel Yap Peng Huat Eric
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DEPARTMENT OF DIAGNOSTIC RADIOLOGY

INTRODUCTION

2006 saw further expansion of our interests in medical image computational analysis and processing, with a number of publications on tumour segmentation and biomechanical modeling, and new projects in medical informatics developing with collaborators from Electrical and Computer Engineering and the School of Computing at NUS. In addition, research into serial brain volumetry in normals, and segmentation of differential component renal enhancement features from MR images has been progressing well.

At the end of 2006/early 2007, members of our department were PI's on major grants awarded to NUS to pursue development of software modules for segmentation of tissues and organs from clinical medical images, to assist with treatment planning.

Other research in clinical imaging using new techniques continued accrual, and were reported at a number of conferences internationally. Dr Sudhakar Venkatesh was the lead author on scientific presentations which won no fewer than 4 awards, both locally and internationally.

A major theme we have developed over the last few years is the noninvasive assessment of response to therapy using medical imaging, which are steadily accruing case material:

- Segmentation and quantitation of tumour volumes on MRI and multi-slice CT

- Diffusion weighted MRI scans to evaluate the efficacy of liver cancer ablation techniques performed by interventional radiology
- Dynamic contrast enhanced MRI (DCE-MRI) and metabolic molecular imaging with Tc99m-sestamibi to evaluate the response of breast cancers to neoadjuvant chemotherapy
- MRI and MR arthrography for evaluation of success of articular cartilage repair in the knee after autologous mesenchymal stem cell therapy

We were fortunate to collaborate with the world-rekowned scientist Prof Britton Chance from the University of Pennsylvania, who visited our department for 5 months over 2006/2007, while his team conducted near infrared optical breast imaging research with patients from the National University Hospital. This will continue in 2007.

In 2006 we also began collaboration with the Department of Chemistry to develop novel radiopharmaceuticals for nuclear isotope imaging. This is a new field for our department but is critical for future research in molecular imaging diagnosis.

At a preclinical level, research into MRI of human fetal stem cell lines from our collaborators in fetal medicine, labeled with magnetic polymer-encapsulated nanoparticles developed by collaborators from Chemical Engineering at NUS and NTU continued, show promising results from in vitro measurements and imaging. In vivo experiments in animal models will be used for longitudinal studies with MRI over the next year.

DEPARTMENT OF DIAGNOSTIC RADIOLOGY

Finally, we made significant strides in developing online teaching modules for medical students and trainees in Radiology, and have expanded the range of online teaching resources. We are collaborating to develop integrated radiological anatomy and pathology teaching as part of the revised curriculum. We will continue to grow this area in 2007, converting much of our film and slide libraries into digital resources to form a strong base of material for online teaching and assessment for the School of Medicine in the future.

PROJECT DESCRIPTION

Grants Awarded in 2006

Anatomic modeling of the human head from non-ionising radiation imaging modalities for orthodontic treatment and jaw surgery

Principal Investigators: Assoc Prof Kelvin Foong Weng Chiong,
Dr Ong Sim Heng
Co-Principal Investigator: Dr Goh Poh Sun

Simulation-based design of implants in bone-spinal disc surgery

Principal Investigator: Prof Teoh Swee Hin
Co-Principal Investigators: Dr Ong Sim Heng,
Dr Wong Hee Kit
Collaborators: Assoc Prof Wang Shih-Chang,
Dr Yan Chye Hwang,
Dr Chui Chee Kong

Segmentation, structural modelling and stimulation of the aorta and liver for clinical decision-making and treatment planning

Principal Investigators: Assoc Prof Wang Shih Chang,
Assoc Prof Ashraf Kassim,
Assoc Prof Leow Wee Kheng,
Dr Tian Qi (A*STAR),
Prof Teoh Swee Hin
Co-Principal Investigators: Dr Borys Shuter,
Dr Chui Chee-Kong
Collaborators: Assoc Prof Peter Robless,
Dr Ravishankar Diddapur

On-going Projects

64-slice CT in staging and segmentation of nasopharyngeal carcinoma

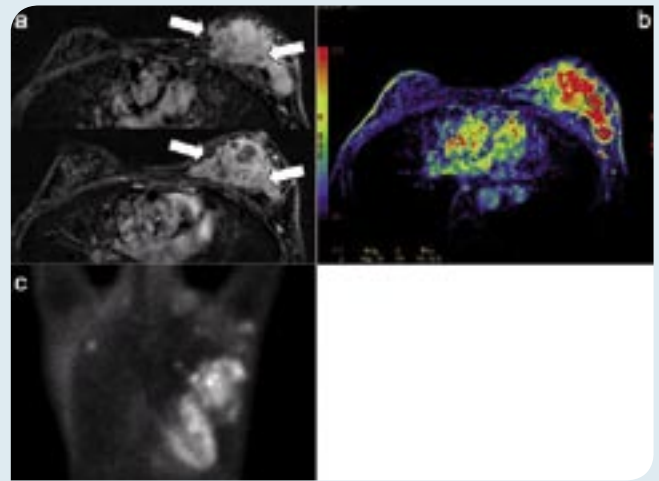
Principal Investigator: Assoc Prof Vincent Chong Fook Hin
Co-Principal Investigators: Dr Loh Kwok Seng,
Dr Lu Jiade Jay,
Assoc Prof Khoo Boon Kheng James

Automated segmentation, quantitative parameter measurements and visualisation of tumour on contrast-enhanced MRI for computer aided diagnosis & evaluation

Principal Investigator: Assoc Prof Wang Shih-Chang
Co-Principal Investigator: Assoc Prof Ashraf Kassim
Collaborators: Dr Ong Sim Heng,
Dr Borys Shuter

Abdominal organ segmentation, registration and quantitation for clinical decision-making

Principal Investigators: Assoc Prof Wang Shih-Chang,
Assoc Prof Ashraf Kassim
Co-Principal Investigators: Assoc Prof Leow Wee Kheng,
Dr Tian Qi,
Dr Borys Shuter



Patient with advanced breast cancer prior to neoadjuvant chemotherapy. **a)** DCE-MRI shows strongly enhancing tumour replacing the entire left breast cone (arrows). **b)** Colour parametric map showing intensely and rapidly enhancing tumour as red pixels. **c)** Tc99m-sestamibi image showing extensive isotope-avid tumour on the left with axillary nodal metastases on the same side and on the contralateral side

Collaborators: Dr R Diddapur,
Dr Peter Robless,
Prof David Stringer,
Dr Yvonne Ho Yi-Wan

Application of advanced MRI sequences for the understanding of brain physiology and pathology

Principal Investigator: Dr Yeh Ing Berne
Co-Principal Investigators: Assoc Prof Wang Shih Chang,
Dr Borys Shuter
Collaborators: Dr Chong Lai Mun June,
Mr Au Christopher

Cysteine-based tailoring of peptide radiopharmaceuticals and probes

Principal Investigators: Assoc Prof Hor Tzi Sum Andy,
Dr Saw Maung Maung
Co-Principal Investigator: Assoc Prof Wang Shih-Chang
Collaborators: Dr Lear Martin James,
Dr Yvonne Ho Yi-Wan,
Dr Borys Shuter,
Dr Hong Ming Hui,
Dr Yang YK,
Dr Yang YY

Development of in-house prepared kits for 90Yttrium- DOTA labeled anti-CD20 and 99mTc - Annexin V

Principal Investigator: Dr Saw Maung Maung
Co-Principal Investigator: Assoc Prof Wang Shih-Chang
Collaborator: Dr Yvonne Ho Yi-Wan

Development of automated image reconstruction and segmentation methods for tumour and organ volumetry

Principal Investigator: Assoc Prof Wang Shih-Chang
Co-Principal Investigator: Assoc Prof Ashraf Kassim

Development of Cardiovascular MRI and MRA in NUH

Principal Investigator: Assoc Prof Wang Shih-Chang

DEPARTMENT OF DIAGNOSTIC RADIOLOGY

Development of paramagnetic nanoparticles for bio-imaging at cellular level

Principal Investigator: Assoc Prof Wang Shih-Chang
Co-Principal Investigators: Dr Borys Shuter,
Dr Zhang Yong

Development and validation of highly efficient nanoparticle contrast agents for cellular labelling and targeting using MR

Principal Investigator: Assoc Prof Wang Shih-Chang
Co-Principal Investigator: Assoc Prof Mahesh A Choolani
Collaborator: Dr Borys Shuter

Efficacy of optical breast imaging for differentiating benign from malignant breast disease

Principal Investigator: Assoc Prof Wang Shih-Chang
Co-Principal Investigator: Assoc Prof Britton Chance
Collaborator: Dr Visjna Reynolds

Evaluation of brain function before and after standard chemotherapy for early breast cancer

Principal Investigator: Assoc Prof Wang Shih-Chang
Co-Principal Investigator: Dr Yeh Ing Berne

Evaluation of clinical efficacy and optimisation of visualisation and reconstruction methods in multi-detector CT pulmonary angiography in clinically suspected cases of pulmonary embolism

Principal Investigator: Dr Sudhakar K Venkatesh
Collaborators: Dr Goh Poh Sun,
Assoc Prof Wang Shih-Chang,
Dr Lynette Teo Li San

Evaluation of utility of diffusion MR Imaging in the loco-regional treatment of hepatocellular carcinomas and metastatic lesions of the liver

Principal Investigator: Dr Sudhakar K Venkatesh

Establishing normal standard of radiographic bone ages in Asian children

Principal Investigator: Assoc Prof Wang Shih-Chang
Co-Principal Investigators: Prof David Stringer,
Assoc Prof James Hui

Imaging-based tumour volumetric analysis

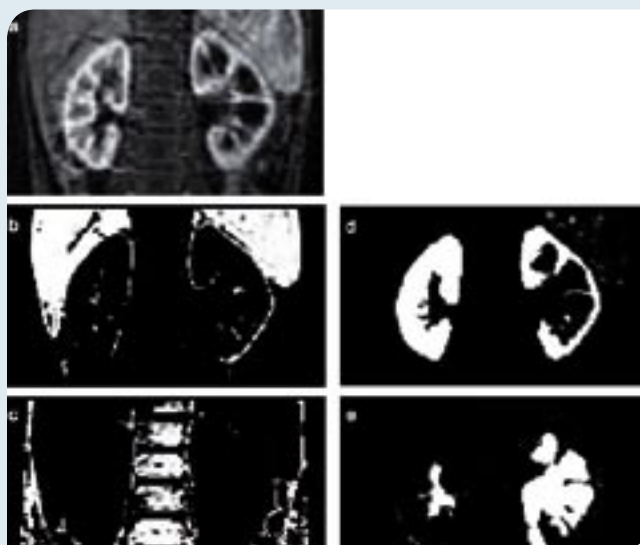
Principal Investigator: Assoc Prof Vincent Chong Fook Hin
Co-Principal Investigators: Dr Ma Kai Kuang,
Dr Khoo Boon Kheng,
Dr Thng Choon Hua

MMWEB - Multimedia Medical Conceptual Web for intelligent information access

Principal Investigator: Assoc Prof Leow Wee Kheng
Collaborators: Dr Bernard PL Chan,
Dr Erle CH Lim,
Assoc Prof Wang Shih-Chang

MRI techniques and imaging findings of the knee after autologous chondrocyte implantation (ACI)

Principal Investigator: Dr Yvonne Ho Yi-Wan
Co-Principal Investigator: Assoc Prof Wang Shih-Chang
Collaborators: Dr Tony Stanley A,
Assoc Prof James Hui



Segmentation of the 3D MR images of the abdomen using PCA-EM cluster analysis. *a)* 2D slice in 3D volume *b)* liver, spleen *c)* other vascular tissue *d)* functioning kidney tissue *e)* kidney pelvis. In images *b* to *e*, brightness reflects the probability of belonging to a tissue class.

MR venography in the evaluation of hemodialysis patients with upper limb swelling

Principal Investigator: Dr Goh Poh Sun
Co-Principal Investigator: Assoc Prof Wang Shih-Chang

Noninvasive detection of acute lower gastrointestinal bleeding using multiphasic multidetector CT after inconclusive endoscopy

Principal Investigator: Dr Goh Poh Sun

Prospective randomised comparative evaluation of proximal valve and distal valve peripherally inserted central catheter (PICCs) under radiological guidance

Principal Investigator: Dr Sudhakar K Venkatesh

Prospective evaluation of staging of gastric carcinoma with dual phase dynamic CT with water filling

Principal Investigator: Dr Sudhakar K Venkatesh

Silicon-based and microwave-driven fluorination of bioactive molecules

Principal Investigators: Dr Martin James Lear,
Dr Maung Maung Saw

Volumetric modelling of the muscles of mastication in humans from magnetic resonance imaging

Principal Investigator: Assoc Prof Kelvin Foong Weng Chiong
Co-Principal Investigator: Dr Ong Sim Heng
Collaborators: Dr Goh Poh Sun,
Dr Wieslaw Nowinski,
Dr Hu Qingmao

INTERNATIONAL PUBLICATIONS

Ong CK, Chong FHV

Imaging of tongue carcinoma. *Cancer Imaging* (2006) 6:186-93. (United Kingdom).

DEPARTMENT OF DIAGNOSTIC RADIOLOGY

Lim JK, Ang KC, Wang SC, Prem kumar V

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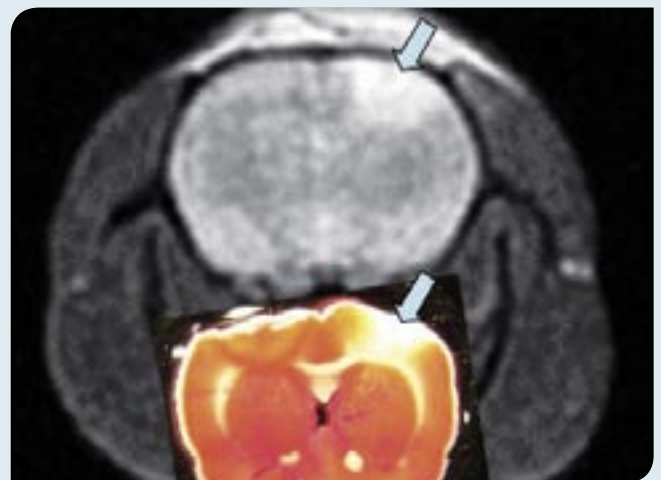
Cranioplasty after Trephination using a Novel Biodegradable Burr Hole Cover: Technical Case Report. Neurosurgery (2006) 58(1 Suppl): ONS-E176. (United States).

STAFF PROFILE

Associate Professor & Head:	Wang Shih-Chang
Professor:	Lenny Tan Kheng Ann
Associate Professor:	Chong Fook Hin, Vincent
Assistant Professors:	Goh Poh Sun
	Sudhakar K Venkatesh
	Borys Shuter
Senior Lecturer:	
Senior Research Fellow	
(Joint Appointment with	
Chemistry, NUS):	Maung Maung Saw
Professor (Joint Appointment	
with Bioengineering):	Colin Sheppard
Research Fellow:	Fan Quli
Research Engineer:	Eddy Lee Shoo Ming

CONTACT INFORMATION

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MRI and corresponding brain slice after TTC infusion of a rat with an induced cortical stroke in the left hemisphere (arrows). This model will be used for stem cell homing and tracking experiments after cellular labelling with novel iron based nanoparticles.

DEPARTMENT OF MEDICINE

INTRODUCTION

Research in the Department of Medicine is anchored across all of its Divisions. The Department concentrates on being a focus of translational & clinical research both locally in Singapore as well as internationally, and has important collaborations with many of the leading basic science institutes (Institute of Molecular and Cell Biology, IMCB, Genome Institute of Singapore, GIS, A*STAR) across Singapore.

Gastroenterology contributes to the Singapore Gastric Cancer Consortium, a national coalition of leading clinicians and scientists working on gastric cancer research. The specific research projects are: (1) Improving early detection of gastric cancer; (2) Improving biologic understanding of gastric carcinogenesis; (3) Molecular epidemiology of gastric cancer risk; (4) Improving treatment by well-designed clinical trials combined with gene expression profiling of tumours. International collaborations include the International Cancer Biomarker Consortium and the Asia-Pacific Working Group on Gastric Cancer. The other research foci are functional gastrointestinal disorders, and novel investigative applications such as robotic diagnostic devices. For hepatology, basic research is mainly on hepatitis B with focus on the immunopathology (structural biology of core particle, cccDNA, splice variants are all being investigated). Clinical research foci include the natural history of HBV with characterisation of viral activity following HBeAg seroconversion, and the outcome of therapy in treated patients.

Respiratory & Critical Care division has put in place several active outcome research programs: (1) rapid molecular diagnosis of tuberculosis, (2) optimal management of pleural sepsis, (3) improving asthma control in a national intervention program, (4) bundle interventions to improve clinical outcomes in COPD, (5) minimally and most cost-effective diagnosis and staging of lung cancer, (6) optimal liberation from mechanical ventilation, and (7) cost-effective management of pneumonia in the elderly (minimizing mortalities & hospital days).

Endocrinology division continues to investigate ethnic differences in the patterns and complications of diabetes mellitus. Importantly, an exciting and new collaboration has been started with the Department of Surgery and the Department of Immunology on the immunology of umbilical cord stem cells, and potential gene therapy of diabetes.

The **Infectious disease** group at NUS is part of the Infectious Diseases Themed Group and the Infectious Diseases Interdisciplinary Program which involves extensive collaboration across NUS (with Departments of Mathematics, Computer Science, Biological Sciences and Microbiology) and Research Institutes (IMCB, IBN, GIS), together with industry. The main areas of interest are antimicrobial resistance, device associated infections, emerging infectious diseases including avian and pandemic influenza.

The division of **Neurology** has achieved much success in “niche-related” work in the field of peripheral nerve disease diagnostics

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and treatment and is poised to deliver important translational work in this area in the field of diabetic and other polyneuropathies. There is a thriving collaboration with bioengineering as well as clinical and basic science departments. Stroke research has a strong base in clinical trials and is starting to implement promising new treatments with sophisticated transcranial Doppler techniques which are linked to diagnostics of brain embolism in ischemic stroke.

Cardiology runs active research programs investigating the mechanics of cardiac function, pathophysiology of valvular heart disease, clinical importance of cardiac biomarkers especially natriuretic peptides, genetics of atrial fibrillation and detection of premature atherosclerosis. A number of prospective studies investigating the importance of vascular stiffness and ventriculovascular coupling in the pathogenesis of heart disease were initiated. Apart from multidisciplinary collaborations within NUS and NHG, the Division also conducts research with investigators at Singapore General Hospital, Bioengineering, NTU and partners in industry.

PROJECT DESCRIPTION
Grants Awarded in 2006

Identifying and categorizing the genes for carbapenem and inducible-cephalosporin resistance in local pathogenic Gram-negative bacilli

Principal Investigator: Dr Hsu Li Yang
Co-Principal Investigator: Assoc Prof Dale Fisher
Collaborator: Assoc Prof Paul A Tambyah

Hypertension genes in Chinese adults with obesity and the metabolic syndrome (HYGENE-COMS)

Principal Investigator: Prof Oh Min Sen, Vernon
Collaborators: Assoc Prof Thai Ah Chuan,
Dr Chionh Siok Bee,
Dr Liew Choon Fong Stanley,
Dr J J Mukherjee,
Dr Ho Kheng Thye,
Dr Yap Peng Huat Eric,
Prof Stephen Harrap

Outpatient Parenteral Antibiotic Therapy (OPAT) - Medical Capability Development Fund (MCDF)

Principal Investigator: Assoc Prof Dale Andrew Fisher

Cardiovascular risk, osteoporosis and psychosocial well-being: An association or a casual link?

Principal Investigator: Dr Anselm Mak
Co-Principal Investigator: Assoc Prof Peter Ashley Robless
Collaborators: Assoc Prof Ling Lieng Hsi,
Dr Roger Ho Chun Man,
Assoc Prof Koh Dow Rhoon,
Dr Leung Pui Lam Bernard

Serum levels of Protein S100B, anti N-Methyl-D-Aspartate receptor antibodies and functional magnetic resonance imaging in patients with neuropsychiatric systemic lupus erythematosus - A prospective study

Principal Investigator: Dr Anselm Mak
Co-Principal Investigators: Dr Steven Graham,
Assoc Prof Koh Dow Rhoon,
Dr Yeh Ing Berne,
Dr Roger Ho Chun-Man



Ms Tong Koh Jong using the cryomicrotome to prepare frozen sections.

Validation of surrogate measures in Irritable Bowel Syndrome, IBS: Experimental measures of pain, functional MR-imaging and endogenous pain modulation in IBS: correlations with clinical disease activity with and without medication

Principal Investigator: Assoc Prof Ho Khek Yu
Co-Principal Investigators: Prof Clive Wilder-Smith,
Assoc Prof Yeoh Khay Guan
Collaborators: Dr Song Guang Hui,
Dr Steven Graham,
Dr Yeh Ing Bern

Further development and experimental trials of a robotic system to enhance therapeutic GI endoscopic procedures

Principal Investigator: Dr Louis Phee Soo Jay (NTU)
Co-Principal Investigator: Assoc Prof Ho Khek Yu

Community acquired methicillin-resistant *S. aureus* and penicillin non-susceptible *S. pneumoniae* carriage in healthy children attending day care centres

Principal Investigator: Assoc Prof Paul A Tambyah

GCEP II: Extension to Establishment of a Gastric Cancer Epidemiology, Clinical and Genetics Programme (GCEP) cohort study of patients at high risk of gastric cancer

Principal Investigator: Assoc Prof Yeoh Khay Guan
Co-Principal Investigators: Assoc Prof Ho Khek Yu,
Prof Yoshiaki Ito
Collaborators: Dr Andrea Rajnakova (NUH),
Dr Christopher Jen Lock Khor (NUH),
Prof Fock Kwong Ming (CGH),
Dr Ooi Choon Jin (SGH),
Assoc Prof Wong Wai Keong (SGH),
Dr Andrew Wong (SGH),
Dr Wong Heng Yu (TTSH),
Dr Kosei Ito,
Assoc Prof Teh Ming,
Assoc Prof Manuel Salto-Tellez,
Dr Richie Soong Chuan Teck,
Dr Robert Hewitt,
Assoc Prof Ho Bow,
Prof Chia Kee Seng,
Dr Lim Yoon Pin,
Dr Patrick Tan (NCC)

DEPARTMENT OF MEDICINE

Identification of novel genetic determinants of atrial fibrillation in an Asian population

Principal Investigator: Dr Chen Lin Yee
Co-Principal Investigators: Prof Chia Kee Seng,
Assoc Prof Ling Lieng Hsi

Left ventricular dysfunction in a pacemaker population: Relation to pacing mode, mechanical dyssynchrony and N-terminal pro-B-type natriuretic peptide levels

Principal Investigator: Assoc Prof Ling Lieng Hsi
Collaborators: Dr Hazel Penafiel,
Dr Yong Quek Wei

Functional assessment of anthracycline cardiomyopathy using NT pro-BNP and myocardial strain rate

Principal Investigator: Dr Raymond CC Wong
Co-Principal Investigator: Assoc Prof Ling Lieng Hsi

Liver epithelial progenitor cells and their therapeutic potential

Principal Investigator: Dr Dan Yock Young

Optimising human hepatocytes from marginal livers for cellular therapeutics from 2006-2009

Principal Investigator: Dr Dan Yock Young

A clinical and molecular study of *Acinetobacter baumannii* at a tertiary public hospital in Singapore

Principal Investigator: Dr Limin Wijaya (SGH)
Co-Principal Investigator: Dr Hsu Li Yang

Methicillin-resistant *Staphylococcus aureus* and *Streptococcus pneumoniae* carriage in healthy children attending day care centres

Principal Investigator: Assoc Prof Paul Tambyah
Co-Principal Investigator: Dr Hsu Li Yang

Spot prevalence of antibiotic resistance in Singapore hospitals, and evaluation of in-vitro antibiotic synergy in multi-resistant gram-negative bacilli using a pharmacodynamic model

Principal Investigator: Dr Tan Thean Yen
Co-Principal Investigator: Dr Hsu Li Yang

Early infectious diseases physician consultation for better outcomes from *Staphylococcus aureus* bacteraemia

Principal Investigator: Assoc Prof Paul Anantharajah
Co-Principal Investigator: Assoc Prof Dale Fisher

A phase 1/2 dose escalation study of a vero cell derived whole virus H5N1 influenza vaccine in healthy volunteers aged 18-45 years

Principal Investigator: Assoc Prof Paul Anantharajah
Co-Principal Investigator: Assoc Prof Dale Fisher

Costing MRSA and its control in a large hospital with highly prevalent disease

Principal Investigator: Assoc Prof Dale Fisher

A phase 3 double-blind, randomised study to evaluate the safety and efficacy of BAL8557 versus a Caspofungin followed by Voriconazole regimen in the treatment of Candidaemia and other invasive candida infections

Principal Investigator: Dr G D Mills
Co-Principal Investigator: Assoc Prof Dale Fisher

Retrospective study of fatal cases of Dengue Haemorrhagic Fever and Dengue Shock Syndrome at NUH

Principal Investigator: Assoc Prof Dale Fisher

On-going Projects

Intra-gastric balloon for treatment of non-alcoholic steatohepatitis (NASH)

Principal Investigator: Assoc Prof Ho Khek Yu
Co-Principal Investigators: Dr Lee Yin Mei,
Prof Cheah Jin Seng,
Dr Jimmy So
Collaborators: Tay Han Yong,
Lim Su Lin

Development of an early phase clinical trials oncology program at The Cancer Institute (National Healthcare Group-NHG), in conjunction with the cancer therapeutics research group (CTRG)

Principal Investigator: Assoc Prof Chen Chien-Shing
Co-Principal Investigators: Prof Jean-Paul Deslypere,
Prof John Wong

Clinical evaluation of novel biological markers for the prediction of severe acute pancreatitis

Principal Investigator: Assoc Prof Ho Khek Yu
Collaborators: Assoc Prof Madhav Bhatia,
Dr Mark Fernandes,
Dr Ravi Shankar

Development of the transplantation material medical research centre at NUS/NUH: Therapeutic applications in haematological malignancies and solid tumors

Principal Investigator: Assoc Prof Chen Chien-Shing
Co-Principal Investigators: Dr Tan Lip Kun,
Dr Ping Law

Differentiation of human embryonic stem cells (HESC) into pneumocytes: Co-culture of HESC with foetal lung tissue

Principal Investigator: Elaine Lim
Co-Principal Investigator: Assoc Prof Wong Poo Sing

The functional genomic characterization of trip-br integrator function

Principal Investigator: Dr Sim Khe Guan
Co-Principal Investigator: Dr Stephen Hsu I-Hong

Cancer therapeutic animal model program for pre-clinical testing in NUS/NUH

Principal Investigator: Assoc Prof Chen Chien-Shing
Co-Principal Investigators: Assoc Prof Hanry Yu,
Prof Yong Eu Leong

Determinants of premature atherosclerosis in patients with systemic lupus erythematosus in Singapore

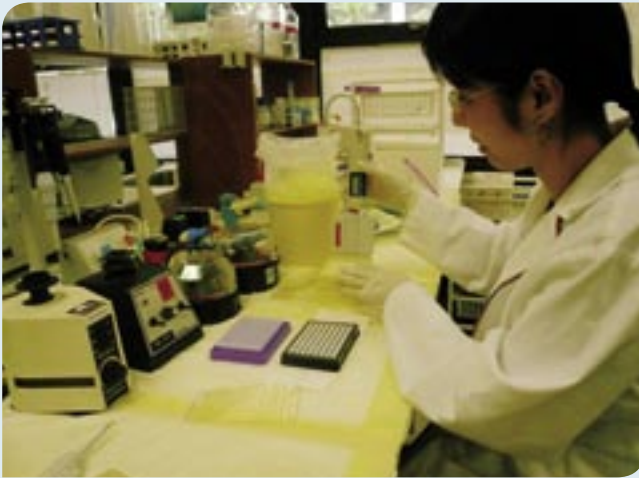
Principal Investigator: Assoc Prof Peter Ashley Robless
Co-Principal Investigators: Dr Anselm Mak,
Assoc Prof Ling Lieng Hsi,
Dr Sheila Vasoo

Molecular genetics and clinical characterisation of young onset diabetes - screening for mutations in maturity-onset diabetes of the young genes

Principal Investigator: Dr Liew C F Stanley (NUH)
Co-Principal Investigator: Assoc Prof Thai Ah Chuan

Prevalence of reversible endocrine causes of hypertension in type 2 diabetic patients with poorly controlled blood pressure

Principal Investigator: Dr Jagat Jothi Mukherjee (NUH)
Co-Principal Investigator: Prof Lim Pin

DEPARTMENT OF
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Ms Chua Boon Ming setting up a 96-well plate for PCR.

To investigate if there is a difference in the insulin response to oral and intravenous glucose (measures of pancreatic beta-cell function) between non-diabetic healthy normal young men of different ethnic groups living in Singapore

Principal Investigator: Dr Liew C F Stanley (NUH)
Co-Principal Investigator: Prof Lee Kok Onn
Collaborator: Dr Stephen Wise (Lilly-NUS)

To describe the characteristic features of Asian diabetics, and investigate for any unique differing features

Principal Investigator: Assoc Prof Thai Ah Chuan

Central processing and intestinal reaction to visceral and physical stressors in healthy controls and IBS patients

Principal Investigator: Assoc Prof Ho Khek Yu
Co-Principal Investigator: Prof Clive Wilder Smith
Collaborators: Assoc Prof Yeoh Khay Guan,
Dr Song Guanghui

Identification of novel biomarkers for the screening of gastric cancer in Singapore

Principal Investigator: Assoc Prof Yeoh Khay Guan
Co-Principal Investigator: Assoc Prof Ho Khek Yu

Optical bioimaging of premalignant lesions in the gastrointestinal tract: Development of endoscope-based Raman spectroscopy and NIR autofluorescence imaging technique

Principal Investigator: Dr Huang Zhiwei
Co-Principal Investigators: Prof Sheppard Colin,
Assoc Prof Harvey Lui,
Assoc Prof Ho Khek Yu,
Assoc Prof Shen Ze Xiang,
Assoc Prof Teh Ming,
Dr Zheng Wei,
Dr Hai Shan Zeng

Gastric Cancer Biomarker Discovery I (GASCAD I)

Principal Investigator: Assoc Prof Yeoh Khay Guan
Collaborators: Prof Hew Choy Leong,
Assoc Prof Maxey Chung,
Dr Richie Soong Chuan Teck,
Dr Lim Yoon Pin,
Dr Zhu Feng,
Assoc Prof Teh Ming,
Dr Lance Miller (GIS)

Gastric Cancer Biomarker Discovery II (GASCAD II)

Principal Investigator: Assoc Prof Yeoh Khay Guan
Co-Principal Investigator: Dr So Bok Yan Jimmy (NUH)
Collaborators: Prof Hew Choy Leong,
Assoc Prof Maxey Chung,
Dr Lim Khong Hee (TTSH),
Prof Yoshiaki Ito,
Dr Lim Yoon Pin,
Dr Zhu Feng,
Assoc Prof Teh Ming,
Dr Lance Miller (GIS),
Dr Gunaretnam Rajagopal (BII),
Mr Wong Chee Hong (BII)

Pilot study of the use of confocal endomicroscopy in resected gastric cancer tissue (and supplementary study: Study of the utility of confocal endoscopy in gastric cancer patients)

Principal Investigator: Assoc Prof Yeoh Khay Guan
Co-Principal Investigators: Assoc Prof Ho Khek Yu,
Dr Emily Shen
Collaborators: Dr Andrea Rajnakova (NUH),
Dr Christopher Jen Lock Khor (NUH),
Dr So Bok Yan Jimmy (NUH),
Assoc Prof Teh Ming,
Assoc Prof Manuel Salto-Tellez,
Dr Robert Hewitt

The expression of RUNX3 and other molecular markers in human gastrointestinal tract and its malignancy

Principal Investigator: Assoc Prof Yeoh Khay Guan
Collaborators: Prof Yoshiaki Ito,
Dr Yang Shu

Study of colonoscopic data over a 6-mth period - Review of colonoscopic findings and patient demographics

Principal Investigator: Assoc Prof Yeoh Khay Guan

Asian Colorectal Adenoma Database: A six month collection of colonoscopic data

Principal Investigator: Assoc Prof Yeoh Khay Guan

Colorectal Adenoma Reminder Programme (CARP)

Principal Investigator: Assoc Prof Yeoh Khay Guan

Genetics of Acute Myocardial Infarction

Principal Investigator: Dr Adrian Low Fatt Hoe

Non-traditional cardiovascular risk factors

Principal Investigator: Dr Adrian Low Fatt Hoe

HBV quasispecies evolution during HBeAg seroconversion and antiviral therapy

Principal Investigator: Assoc Prof Lim Seng Gee
Co-Principal Investigator: Dr Shanthi Wasser

To identify the epitopes of HBeAg seroconversion

Principal Investigator: Assoc Prof Lim Seng Gee
Co-Principal Investigator: Dr Shanthi Wasser

Analysis of splice variants of HBV

Principal Investigator: Assoc Prof Lim Seng Gee
Co-Principal Investigator: Dr Shanthi Wasser

DEPARTMENT OF MEDICINE

Expression profiling and gene silencing in hepatocellular carcinoma

Principal Investigator: Assoc Prof Lim Seng Gee

Co-Principal Investigator: Dr Shanthi Wasser

Establishment of an animal model for chronic hepatitis B infection

Principal Investigator: Assoc Prof Lim Seng Gee

Co-Principal Investigator: Dr Shanthi Wasser

To characterise host and viral factors between patients with clinical liver disease (abnormal LFTs, cirrhosis and HCC) compared to those without liver disease (hepatitis B carriers) in chronic hepatitis B patients

Principal Investigator: Assoc Prof Lim Seng Gee

Co-Principal Investigator: Dr Shanthi Wasser

To systematically evaluate the contributions of the core promoter and the completed genome in the regulation and fidelity of HBV viral replication

Principal Investigator: Assoc Prof Lim Seng Gee

Co-Principal Investigator: Dr Shanthi Wasser

A-STAR HBV Immunovirology Programme for 3 years from August 2005 to May 2008, comprising the following projects: (a) HBV quasispecies evolution during HBeAg serconversion. (b) To identify the B cell epitopes for HBeAg serconversion. (c) To determine the structural changes in core particle during HBeAg serconversion. (d) To determine changes in polymerase fidelity associated with increased quasispecies diversity. (e) To determine the molecular requirements for cccDNA formation. (f) To characterize the role of splice variants in clinical HBV disease. (g) Expression profiling and gene silencing in hepatocellular carcinoma. (h) Establishment of an animal model for chronic hepatitis B infection

Principal Investigator: Assoc Prof Lim Seng Gee

A-STAR HBV Cohort Study for 3 years from August 2005 to May 2008, with the main objective for characterizing the prognostic factors for different clinical phenotypes of chronic hepatitis B, together with immune and viral factors that lead to HBV-related events

Principal Investigator: Assoc Prof Lim Seng Gee

Development of multi-functional ingestible microcapsule

Principal Investigator: Dr Louis Phee Soo Jay (NTU)

Co-Principal Investigator: Assoc Prof Ho Khek Yu

High resolution brain functional MR-imaging (fMRI) for the characterization of abnormal pain perception and response in functional bowel disease

Principal Investigator: Prof Clive Wilder-Smith

Co-Principal Investigator: Assoc Prof Ho Khek Yu

Collaborator: Dr Song Guang Hui

Exploring the efficacy and mechanism of action of a probiotic in irritable bowel syndrome

Principal Investigator: Assoc Prof Ho Khek Yu

Cost effectiveness modeling of HBeAg serconversion

Principal Investigator: Dr Dan Yock Young

The potential of liver progenitor cells

Principal Investigator: Dr Dan Yock Young

Is the inanimate environment of Intensive Care Units an important reservoir facilitating the development of nosocomial infection? A study facilitated by a unit's relocation at National University Hospital, Singapore

Principal Investigator: Assoc Prof Dale Fisher

Functional assessment of severe organic mitral regurgitation using N-terminal pro-brain natriuretic peptide, myocardial strain rate imaging and heart rate variability

Principal Investigator: Assoc Prof Ling Lieng Hsi

INTERNATIONAL PUBLICATIONS

Salto-tellez M, Peh BK, Ito K, Tan SH, Chong PY, Han HC, Tada K, Ong WY, Soong CTR, Voon DC, Ito Y

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Seet CSR, Lim ECH

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Lim ECH, Seet CSR, Ong BKC

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Symptoms associated with electrophysiologically verified carpal tunnel syndrome in Asian patients. *Journal of Hand Surgery - British and European Volume* (2006) 31(3):326-330. (United Kingdom).

Wilder-smith EPV

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Khor WB, Aung T, Saw SM, Wong TY, Tambyah PA, Tan AL, Beuerman RW, Lim L, Chan WK, Heng WJ, Lim J, Loh RSK, Lee SB, Tan DT

An outbreak of *Fusarium* keratitis associated with contact lens wear in Singapore. *JAMA - Journal of the American Medical Association* (2006) 295:2867-73. (United States).

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DEPARTMENT OF
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Lim ECH, Seet CSR, Ong BKC

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STAFF PROFILE

Associate Professor & Head:	Ho Khek Yu
University Professor:	Lim Pin
Professors:	Burgunder, Jean-Marc (Visiting Professor) Cheah Jin Seng (Professorial Fellow) Chia Boon Lock (Professorial Fellow) Holmes, Edward Lee Kok Onn Lim Tow Keang Liu Edison (seconded to GIS) Oh Min Sen, Vernon Swain, Judith Tan Chorh Chuan Wilder-Smith, Clive (Visiting Professor) Wong Eu Li, John Young, Archibald (Parkway Visiting professor)
Adjunct Professors:	Copeland, Neal Feng Pao Hsii Jenkins, Nancy Sir David Lane Ito, Yoshiaki
Associate Professors:	Chen Chien-Shing Fisher, Dale Andrew Kueh Yan Koon (Assoc Professorial Fellow) Lee Jon Choon, Evan Lim Seng Gee Lim Yean Teng Ling Lieng Hsi Ong Kian Chung, Benjamin Tambyah, Paul Anantharajah Thai Ah Chuan Wilder-Smith, Einar Yeoh Khay Guan
Adjunct Associate Professors:	Boey Mee Leng Fong Kok Yong Gwee Kok Ann Kong Hwai Loong Lee Kang Hoe Loong Si Chin Tan Huay Cheem Thumboo, Julian Wise, Stephen D Chen Lin Yee Hsu Li Yang Lam Su Ping, Carolyn Lee Yin Mei Lim Chuen Hian, Erle Lim Hsuen, Elaine Low Fatt Hoe, Adrian Mak, Anselm Seet See Cheong, Raymond Teo Boon Wee Wai Chun Tao, Desmond
Assistant Professors:	



Ms Yeo Soh Bee conducting research on the genetics of hypertension.

Adjunct Assistant Professors:	Bertoletti, Antonio Chew Chin Hin Li Baojie Wong Soon Tee
Senior Research Scientist:	Md Matiullah Khan
Research Scientist:	Shanthi Wasser
Research Fellows:	Lim Min Chin Sim Khe Guan Palaniyandi Senthilnathan Song Guanghui Xie Zhigang Zhang Shenli Zhang Wencai Zhou Jianbiao
Research Assistants:	Chan Yoke Ying, Regina Choong Pei Feng Jasinghe V Janakakumara Lee Guan Huei Lim Shan Poon Lai Fong Xie Zhigang Yang Maolin, Christopher Yip Yeok Ping, Robyn Donaldson, Annabelle Hsu I-Hong, Stephen Feng Shengquan
Visiting Fellows:	
Visiting Scientist:	

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A close-up photograph of a petri dish containing a bacterial culture on a pink agar medium. The culture shows several distinct, dark, circular colonies of varying sizes, some of which are arranged in a streaked pattern. The petri dish is tilted, and the lighting creates a soft glow on the agar surface.

DEPARTMENT OF MICROBIOLOGY

INTRODUCTION

Microbiology and Immunology are central disciplines in the development of life sciences in Singapore. The Department of Microbiology is committed to serve Singapore's growing needs in research, industry and professional services. The Department of Microbiology aims to deliver:

- High quality, internationally competitive research
- Excellence of undergraduate teaching and post graduate training
- Exploitation of intellectual property
- Support for the development of Singapore's emerging biotechnology sector
- Advisory services to various governmental statutory bodies
- Editorial input to quality academic journals
- Advisory services to industry

History and background

The Department of Microbiology was formed by the merger of the Departments of Bacteriology (founded 1925) and Parasitology (founded 1950) in 1974. Traditionally the department has had strength in Parasitology, Bacteriology and Virology. Subsequently Immunology in the Department expanded in the areas of vaccine development and cancer immunology. Over the past eight years, nine immunologists have joined the Department to create additional strengths in Dendritic and T cell biology, innate immunity and lung

immunology. The Department currently receives over S\$12 million in competitive research grants. The Department is committed to excellence and in 2006 staff published 17 papers in journals with an impact factor of greater than 5 including papers in Nature Immunology and Science. The present day Department seeks to integrate immunology with infectious and inflammatory diseases through the Office of Life Sciences Immunology Programme to deliver world class science in infection and immunity.

PROJECT DESCRIPTION

Grants Awarded in 2006

Dengue vaccine: Use of *Lactococcus lactis* as a live oral and nasal delivery system

Principal Investigator:	Dr Sylvie Alonso
Co-Principal Investigator:	Assoc Prof Chow Tak Kwong Vincent
Collaborator:	Prof David Michael Kemeny

Survival of *Mycobacterium tuberculosis* inside the phagolysosomes of activated macrophages: relevance for persistence, drug susceptibility and vaccine efficiency

Principal Investigator:	Dr Sylvie Alonso
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Interaction between *Burkholderia pseudomallei* and the Innate Immunity.

Principle Investigator:	Prof Chan Soh Ha
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DEPARTMENT OF MICROBIOLOGY

Innate Immunity and Host-Pathogen Interaction: The molecular interaction of pathogen recognition receptors (PRRs)

Principal Investigator: Prof Ding Jeak Ling
Co-Principal Investigator: Assoc Prof Ho Bow

Helicobacter pylori biofilm formation - A survival strategy and probable role in transmission

Principal Investigator: Assoc Prof Ho Bow

Asthma mouse: generation of Blomia tropicalis and Dermatophagoides pteronyssinus CD4 T cell receptor transgenic mice for investigation of the asthmatic lung model

Principal Investigator: Prof David Michael Kemeny
Co-Principal Investigators: Prof Chua Kaw Yan
Assoc Prof Fred Wong Wai-Shiu

Immunocompetent mouse-adapted flavivirus: A model for antiviral testing

Principal Investigator: Prof Ng Mah Lee Mary

A genetic approach to study post-translational histone modifications in yeast and human tissue culture cells

Principal Investigator: Dr Norbert Lehming

Investigation of the class A macrophage scavenger receptor (SR-AI) in microbial recognition and sensing

Principal Investigator: Assoc Prof Lu Jinhua

Mycobacterial HSP70 cross-presentation: Defining the role of DC-T lymphocyte interactions and G-protein coupled receptor(s)

Principal Investigator: Dr Paul A Macary
Co-Principal Investigators: Dr Tan Suet Mien, NTU
Dr Lina Lim Hsiu Kim, NUS

The role of dengue virus non-structural protein 1 (NS1) in the pathogenicity of the dengue virus infection

Principal Investigator: Prof Ng Mah Lee Mary

Characterising the domain II protein of flavivirus envelope protein as a protective immunogen in flavivirus infection

Principal Investigator: Prof Ng Mah Lee Mary

Molecular and cellular characterization of blastocystis programmed cell death: identification of novel genes and pathways

Principal Investigator: Dr Kevin Tan
Co-Principal Investigators: Assoc Prof Lim Chwee Teck
Dr Mark B Taylor

Modulation of phagocytosis in dendritic cells by aspirin: through its effects on the expression and distribution of molecules of the endosomal membrane trafficking machinery

Principal Investigator: Dr Wong Siew Heng

On-going Projects

Development of live recombinant vaccine against avian influenza virus: Use of Bordetella pertussis as a nasal deliver vehicle

Principal Investigator: Dr Sylvie Alonso

Development of vaccine against dengue virus

Principal Investigator: Assoc Prof Chow Tak Kwong Vincent



The persistence and universal prevalence of Herpes Viruses such as Human Cytomegalovirus (huCMV) and Epstein-Barr Virus (EBV) indicates that these viruses have developed an evolutionary survival advantage. It is known that Herpes Viruses employ a number of mechanisms to switch off protective immune responses in infected hosts. The principal goal of my laboratory is to develop new targeting strategies for Herpes viruses that bypass viral immune evasion mechanisms. This involves improving our understanding of the pathophysiology of Herpes Virus infections combined with a study of viral interactions with host immune cells. We are particularly interested in heat shock proteins (Hsp's) as molecular vehicles for inducing anti-viral responses. Hsp's are remarkable for their ability to prime the innate immune system and to exert specificity for viruses, which is derived from their peptide binding/chaperoning activity.

Development of live recombinant vaccines against enterovirus 71: Use of Bordetella pertussis as delivery system

Principal Investigator: Assoc Prof Chow Tak Kwong Vincent
Co-Principal Investigator: Dr Sylvie Alonso

Vaccine initiative programme

Principal Investigator: Assoc Prof Chow Tak Kwong Vincent

Innate immunity against microbial infection: development of biomedical sensors and anti-inflammatory anti-sepsis strategies for human healthcare

Principal Investigator: Prof Ding Jeak Ling
Co-Principal Investigator: Assoc Prof Ho Bow

Development of anti-adhesive for use in the prevention and/or eradication of Helicobacter pylori infections

Principal Investigator: Assoc Prof Ho Bow

Characterization of a novel CD8 T-cell mediated immunoregulatory pathway that prevents type I (IGE) hypersensitivity and systemic lupus erthematosus (SLE)

Principal Investigator: Prof David Michael Kemeny

Modulation of the development and progression of cancer by lactobacilli

Principal Investigator: Assoc Prof Lee Yuan Kun

Intestinal colonization and immuno-modulation by probiotic microorganisms expressing antigens of pathogens

Principal Investigator: Assoc Prof Lee Yuan Kun

Establishment of a comprehensive picture of the transcription process with the help of the split-ubiquitin system

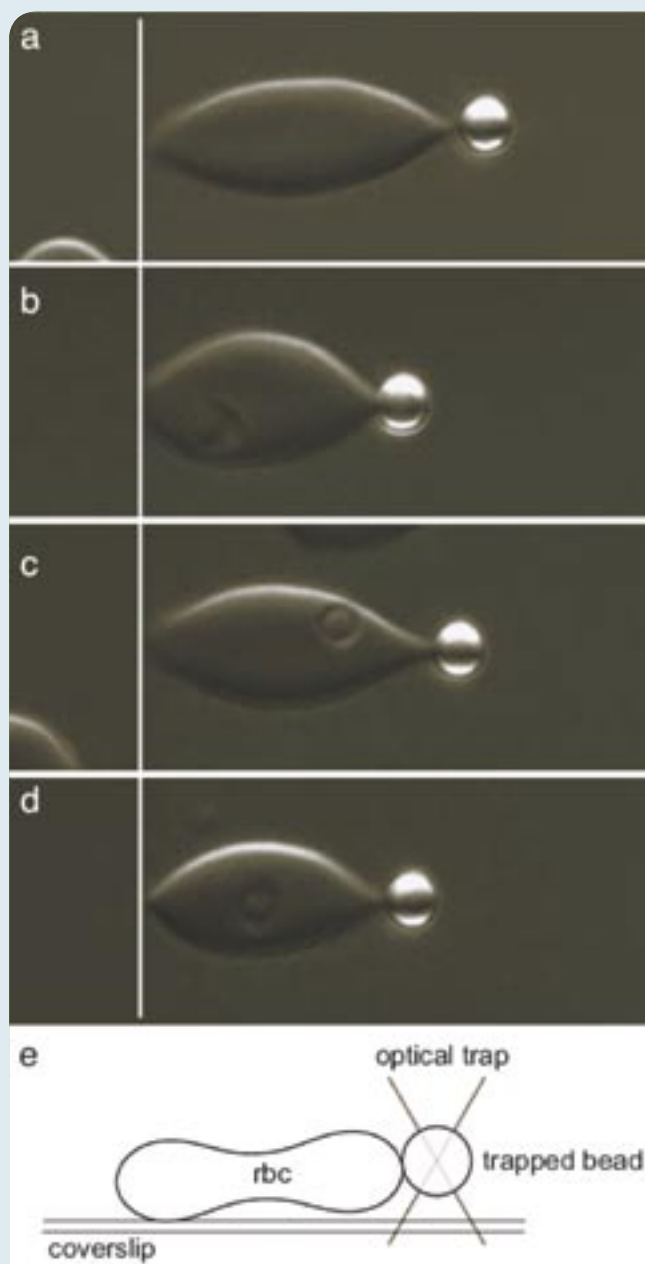
Principal Investigator: Dr Norbert Lehming

In vivo analysis of the human transcription machinery with the help of the human split-ubiquitin system

Principal Investigator: Dr Norbert Lehming

Building a platform for receptor- targeted antigen delivery strategies

Principal Investigator: Assoc Prof Lu Jinhua

DEPARTMENT OF
MICROBIOLOGY

Optical microscopy images of RBCs stretched by using optical tweezers. (a-d) Representative RBCs stretched uniaxially with a 100-pN force. The *resA1-KO* Pf-RBC (c) shows deformability similar to parasite-free RBCs (a) whereas wild-type *resA1* (b) and *resA1*-rev Pf-RBCs (d) display similar decreased deformability. Stiffness values are determined from the entire force versus displacement response of each cell. (e) A schematic representation of a side view of an optical tweezers stretch test where a RBC is stretched by holding it at the coverslip surface and at the trapped bead.

Understand the roles of beta₂ microglobulin in dendritic cell macropinocytosis and assess its role as a potential enhancer for subunit vaccines

Principal Investigator: Assoc Prof Lu Jinhua

Mechanisms of C1q contribution to the prevention of systemic lupus erythematosus (SLE)-like diseases: Insight from unique mechanism of C1q biosynthesis

Principal Investigator: Assoc Prof Lu Jinhua

Structural and functional study of flavivirus attachment domain(s) and the cellular receptor(s)

Principal Investigator: Prof Ng Mah Lee Mary

Peptide nucleic acid (PNA) as antiviral therapy for enterovirus 71

Principal Investigator: Assoc Prof Poh Chit Laa

Development of an outer membrane protein vaccine for *Klebsiella pneumoniae*

Principal Investigator: Assoc Prof Poh Chit Laa

Development of vaccine against enterovirus 71 (EV71)

Principal Investigator: Assoc Prof Poh Chit Laa

Dendritic cell targeting in vaccine development

Principal Investigator: Dr Seah Geok Teng

Immune correlates of latent tuberculosis

Principal Investigator: Dr Seah Geok Teng

Anti-malarial drug discovery from natural product extracts

Principal Investigator: Assoc Prof Sim Tiow Suan

Novel strategies to improve the efficacy of antibacterial and adjunctive therapies of acute and chronic bacterial infections

Principal Investigator: Dr Mark B Taylor

Generation of purified recombinant malaria proteins and development of transgenic bacteria and yeast cell lines

Principal Investigator: Dr Kevin Tan

Tuberculin skin test reactivity and peripheral blood mononuclear gamma interferon responses to *Mycobacterium tuberculosis* specific proteins in medical and nursing students

Principal Investigator: Dr Seah Geok Teng

Co-Principal Investigator: Clinical Assoc Prof Wang Yee Tang (TTSH)

An in vitro bacterial-dendritic cells (bed) environment for gut immunoregulation study

Principal Investigator: Dr Wong Siew Heng

INTERNATIONAL PUBLICATIONS

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(* = Equal first authors)

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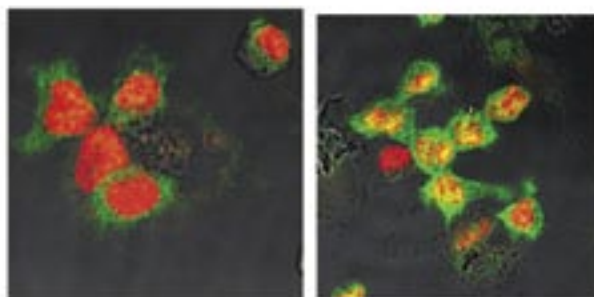
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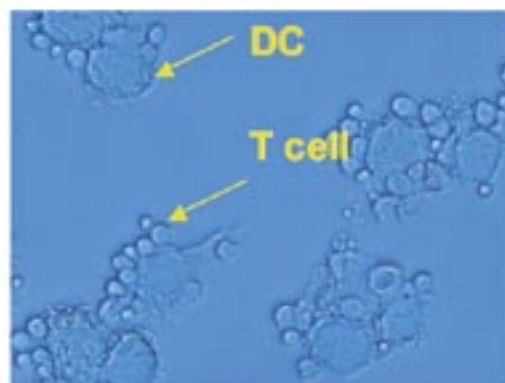
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Nuclear translocation of Rel-A



Un-stimulated

1µM CpG and anti-MHC-I



Human DC + CD8 T cells

Interactions between CD8 T cell and dendritic cells are central to initiation of host immunity against viruses and intracellular bacteria. CD8 T cells are primed by dendritic cells that regulate their growth and function. CD8 T cells signal back to dendritic cells to regulate CD4 T cell responses. The images above are taken from work investigating the interaction between CD8 T cells and dendritic cells. The upper image shows trans nuclear migration of rel-A to the nucleus of the dendritic cells following stimulation with the bacterial product CpG and anti-MHC class I. The lower image is of CD8 T cells and dendritic cell co-cultured in a mixed lymphocyte response.

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Adjunct Professor:

Adjunct Associate Professors:

Adjunct Assistant Professors:

Research Fellows:

GEM4 Postdoctoral Fellow:

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Gong Min
Lui Sook Yin
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DEPARTMENT OF OBSTETRICS & GYNAECOLOGY

INTRODUCTION

The highlight of this year is the remarkable research achievements made by our Maternal-Fetal Medicine Division. The main areas of research in Maternal-Fetal Medicine are diagnostic biomarkers discovery, and breastfeeding and persistent organic pollutants research.

MATERNAL-FETAL MEDICINE

- Dr Mahesh Choolani, Dr Jerry Chan and team have had substantial publications in 2006, including non-invasive prenatal diagnosis of alpha thalassaemia using fetal DNA from maternal plasma and rapid prenatal diagnosis. In particular, an abstract titled *Non-invasive prenatal exclusion of haemoglobin (Hb) bart's hydrops fetalis (SEA/SEA) using fetal DNA from maternal plasma* won the Young Scientist Award in the 13th International Conference Prenatal Diagnosis and Therapy in Kyoto, Japan.

In the rapid prenatal diagnosis arena, two international peer reviewed articles were accepted and published in *Clinical Chemistry* and *Molecular Human Reproduction*. This paper describes rapid prenatal diagnosis of the very common genetic disorder alpha thalassaemia using a one-day rapid protocol. Another advance is the ultra rapid prenatal diagnosis for chromosomal abnormalities using FAST FISH.

- Dr Jerry Chan, a bright young Assistant Professor, has published two important publications on *Human fetal mesenchymal stem cells* and described how *Galectin-1 induces skeletal muscle differential in human fetal mesenchymal stem cells and increases muscle regeneration*.
- Dr Chong Yap Seng continues his research on breastfeeding with major publications and new research grants obtained in 2006. This is part of the Department's efforts to understand the biology of lactation and to promote breastfeeding.

An interesting new development in 2006 was the formation of new research collaboration with the Liggins Institute of New Zealand. This collaboration in the field of developmental biology was with Professor Peter Gluckman and includes associate institutes in Cambridge and the University of Southampton. Despite the short gestation, the collaboration has resulted in a successful grant application and a publication in the *Lancet*.

REPRODUCTIVE ENDOCRINOLOGY

- Professor Yong Eu Leong continues his drug discovery programme based on traditional Chinese herbal medicine. A new dimeric progestogenic compound Diligustilide was isolated from the rhizome of the traditional Chinese medicine herbal *Ligusticum chuanxiong*. Diligustilide was found for the first time to have

DEPARTMENT OF OBSTETRICS & GYNAECOLOGY

progestogenic effect and would therefore be useful for treatment of women with menstrual disorders and for uterine cancer. This novel compound is the unique dimeric structure, and animal experiments show that it exerts progestogenic activity following oral administration. Using cell-based assays, the group managed to document a new methodology to study summated progestogenic activity of this compound in animal models paving the way for human application and use. This work has resulted in two patents.

- Furthermore, his team has identified and characterized flavonoids from two traditional Chinese herbs that can activate the PPAR family of receptors. These compounds have therapeutic use for diabetes and dyslipidemia.

EMBRYOLOGY

- Professor Bongso and Dr Mark Richards' team continue their work on human embryonic stem cells and describe the transcription profiling using novel SAGE technology.
- Our adjunct staff, Professor Ng Soon Chye, have contributed using mouse models on the profile of gene expression in mouse and embryos and following exposure of cumulus cell nuclei to porcine ooplasmic extract.

CONTRACEPTION

- Professor Kuldip and Dr Vanaja published on the incidence of actinomyces infection in Singapore women using intrauterine contraceptive devices and this was published in the prestigious journal, Contraception.

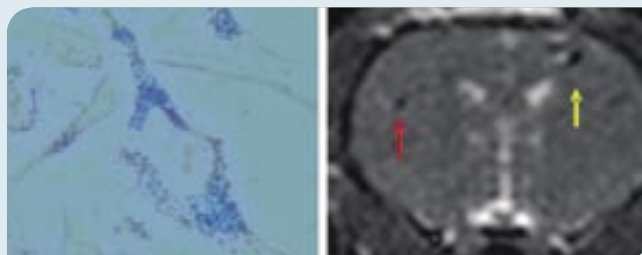
SEXUAL DYSFUNCTION

- Professor P G Adaikan and team continue with their work on erectile dysfunction publishing on the mechanisms of direct relaxant effect of various drugs on the corpus cavernosum. Productive collaboration with Pharmacology resulted in several important publications on the novel gasotransmitter hydrogen sulphide in erectile dysfunction.

GYNAECOLOGIC ONCOLOGY

- Ovarian cancer ranks as the top killer among the different gynaecological malignancies in Singapore. The Ovarian Cancer Research program in the Department headed by Dr Choolani focuses on two main areas:
 - Understanding the biology of ovarian cancer which could result in the identification of potential early diagnostic markers for this highly insidious disease;
 - Development of diagnostic kits for ovarian cancer.

For the above purpose the team have used a suite of genomic and proteomic techniques to identify potential markers from sera and cystic fluid which could facilitate early diagnosis of ovarian cancer. The team has identified a promising marker for distinguishing benign cancer from malignant cancer. Data from their study carried out with Associate Professor Ilancheran have shown for the first time the presence of a protein which has the potential to serve as a diagnostic marker in cystic fluid of patients presenting with epithelial ovarian cancer. A patent application is pending based on this finding.



In vivo tracking of stem cells via MRI visualization of fetal mesenchymal stem cells labelled with microgel iron oxide particles (blue particles in cytoplasm of cells 1A) demonstrated the migration of cells from the right hemisphere (low echo area, red arrow) to the left hemisphere (low echo area, yellow area) after induction of a stroke on the left hemisphere of a rat.

In addition to the above strategies, the team also focuses on the enrichment strategies for low abundance cancer markers associated with cell cycle which plays a key role in the development and progression of ovarian cancer. The team has successfully established a regional tissue repository network with the Department as the headquarters for the region.

- Dr Stephen Koh and team published an article describing the association between Fibrinogen, von Willebrand Factor, Antithrombin III and D-dimer levels and survival outcome in ovarian cancer.

PROJECT DESCRIPTION Grants Awarded in 2006

Novel therapeutic potential of endogenous hydrogen sulphide modulation in erectile dysfunction

Principal Investigator:	Prof Adaikan P Ganesan
Co-Principal Investigator:	Prof Philip K Moore
Collaborator:	Dr Srilatha Balasubramanian

Alternative novel approaches for the production of tissues from human embryonic stem cells (hESCs) for transplantation and cancer therapy

Principal Investigator:	Prof Ariff Bongso
Co-Principal Investigator:	Dr Mark Richards
Collaborator:	Dr Fong Chui Yee

Biology of umbilical cord blood mesenchymal stem cells

Principal Investigator:	Dr Jerry Chan Kok Yen
Co-Principal Investigator:	Dr Mahesh Choolani

Endodermal differentiation of human fetal mesenchymal stem cells

Principal Investigator:	Dr Jerry Chan Kok Yen
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The utility of fetal mesenchymal stem cells and polycaprolactone-tricalcium phosphate scaffolds for bone tissue engineering

Principal Investigator:	Dr Jerry Chan Kok Yen
Co-Principal Investigators:	Prof Teoh Swee Hin, Dr Mahesh Choolani

DEPARTMENT OF OBSTETRICS & GYNAECOLOGY

Intrauterine gene therapy of haemophilia in a non-human primate model

Principal Investigator: Dr Jerry Chan Kok Yen
Co-Principal Investigators: Dr Mahesh Choolani,
Dr Waddington Simon
(Imperial College London, UK),
Dr Amit Nathwani
(University College London, UK),
Prof Nicholas Fisk
(Imperial College London, UK),
Prof Adaikan P Ganesan
Collaborators: Dr Donald Peebles
(University College London, UK),
Assoc Prof Arijit Biswas,
Dr Michael Themis
(Imperial College London, UK),
Assoc Prof Quah Thuan Chong

Metoclopramide to augment lactogenesis II in diabetic women: a randomized controlled trial

Principal Investigator: Dr Citra Nurfarah bte Zaini Mattar (NUH)
Co-Principal Investigator: Dr Chong Yap Seng
Collaborators: Dr Mark D Cregan (Univ of W Australia),
Assoc Prof Mary Rauff

Karyotypic stability and telomere dynamics of human fetal mesenchymal stem cells

Principal Investigator: Dr Mahesh A Choolani
Co-Principal Investigator: Dr Jerry Chan Kok Yen
Collaborators: Dr Sukumar Ponnusamy,
Prof Nicholas M Fisk
(Imperial College London, UK)

Ovarian Cancer Research Collaboration: prognostic haemostatic markers and human tissue kallikrens for survival outcome in ovarian cancer

Principal Investigator: Dr Mahesh A Choolani
Collaborator: Dr Koh Chee Liang Stephen

Enhancing enrichment of fetal primitive erythroblasts from maternal blood: Development of novel MEMS devices to deplete adult anucleate erythrocytes

Principal Investigator: Dr Mahesh A Choolani
Co-Principal Investigators: Assoc Prof Arijit Biswas,
Assoc Prof Jackie Yi-Ru Ying (IBN)

Chiral separation and characterization of bioactive enantiomer of novel phytoprogestin Dihydrodiligustilide

Principal Investigator: Dr Gong Yinhan
Collaborator: Dr Li Jun

Development of rapid molecular fluorescence excitation-emission spectroscopy system for non-invasive, in vivo detection of precancerous and cancerous tissue in the cervix

Principal Investigator: Dr Huang Zhiwei
Co-Principal Investigators: Assoc Prof A Ilancheran,
Assoc Prof Teh Ming,
Dr Jeffrey Low Jen Hui (NUH)

A phase III, double-blind, randomized, controlled study to evaluate the safety, immunogenicity and efficacy of GlaxoSmithKline Biologicals' HPV-16/18L1/AS04 vaccine administered intramuscularly according to a three-dose schedule (0, 1, 6 month) in healthy adult female subjects aged 26 years and above

Principal Investigator: Assoc Prof A Ilancheran

Evaluation of chloride channel blockers in diabetes induced erectile dysfunction in rabbit

Principal Investigator: Ms Lau Lang Chu

Transfer of persistent organic pollutants between mother and fetus in Singapore

Principal Investigator: Assoc Prof J P Obbard
Co-Principal Investigators: Dr Chong Yap Seng,
Dr A Loganath

Is there a role for the novel gasotransmitter, hydrogen sulphide in female sexual function/dysfunction

Principal Investigator: Dr Srilatha Balasubramanian

Gene expression profiling prenatal molecular karyotype for trisomy 21

Principal Investigator: Dr Su Lin Lin
Co-Principal Investigator: Dr Mahesh Choolani
Collaborators: Dr Narasimhan Kothandaraman (NUH),
Assoc Prof A Biswas

Preimplantation genetic screening to improve pregnancy rates in poor prognosis ART patients

Principal Investigator: Assoc Prof P C Wong
Collaborators: Assoc Prof Samuel S Chong,
Ms Joyce Mathew (NUH),
Mr Arnold S C Tan

On-going Projects

A pilot study of cancer diagnosis in the cervix using near-infrared Raman spectroscopy and multivariate techniques

Principal Investigator: Dr Huang Zhiwei
Co-Principal Investigator: Assoc Prof A Ilancheran

Characterisation of low molecular weight tumor specific markers for ovarian cancer from serum of ovarian cancer patients

Principal Investigator: Assoc Prof A Ilancheran
Co-Principal Investigators: Dr Mahesh Choolani,
Dr Khalil Razvi,
Dr Narasimhan Kothandaraman (NUH)

New approaches to deriving human embryonic (hES) cell lines and their evaluation for pharmaceutical drug screening, cancer studies and germ cell development

Principal Investigator: Prof Ariff Bongso
Co-Principal Investigator: Dr Mark Richards
Collaborators: Dr Fong Chui Yee,
Assoc Prof Chan Woon Khiong

Transcriptome analyses of human embryonic stem cells using SAGE

Principal Investigator: Prof Ariff Bongso
Co-Principal Investigator: Dr Mark Richards
Collaborators: Dr Fong Chui Yee,
Assoc Prof Chan Woon Khiong

DEPARTMENT OF OBSTETRICS & GYNAECOLOGY

Advances in pharmacotherapy of sexual medicine

Principal Investigator: Prof Adaikan P Ganesan

Role of hydrogen sulphide as a novel modulator of penile erection and in the pathogenesis of erectile dysfunction

Principal Investigator: Prof Adaikan P Ganesan
Co-Principal Investigator: Prof Keith Philip Moore
Collaborator: Dr Srilatha Balasubramanian

Development of autologous corporal tissue for male erectile dysfunction

Principal Investigator: Prof Adaikan P Ganesan
Collaborators: Dr Dietmar W Huttmacher,
Dr Henry Yu

Studies on the role of cytokines on placental trophoblasts of normotensive women and in pregnancies complicated by pre-eclampsia

Principal Investigator: Dr Annamalai Loganath
Co-Principal Investigator: Assoc Prof Wong Yee Chee

Intrapartum fetal monitoring with fetal electrocardiogram

Principal Investigator: Assoc Prof Arijit Biswas
Collaborator: Dr Chong Yap Seng

Endodermal differentiation of human fetal mesenchymal stem cells

Principal Investigator: Dr Jerry Chan Kok Yen
Co-Principal Investigator: Dr Mahesh Choolani

Metoclopramide to aid establishment of breastfeeding after delivery: A randomized controlled trial

Principal Investigator: Ms Chan Yah Shih (NUH)
Co-Principal Investigator: Dr Chong Yap Seng
Collaborators: Dr Citra Nurfarah bte Zaini Mattar (NUH),
Assoc Prof Mary Rauff

The influence of maternal ethnic group and diet on breast milk fatty acid content and its potential effect on development of allergy in the offspring

Principal Investigator: Dr Chong Yap Seng
Collaborators: Dr Chng Seo Yi (NUH),
Prof Birgitta Strandvik (Goteborg University),
Em Prof Lars Ake Hanson (Goteborg University),
Dr Marina Korotkova (Goteborg University),
Dr Gong Yinhan,
Dr Mabel Deurenberg Yap (HPB),
Prof Hugo Van Bever

Early and regular breast milk expression to help establish lactation after preterm and term delivery: A randomized controlled trial

Principal Investigator: Dr Chong Yap Seng
Co-Principal Investigator: Dr Steven Ng (NUH)
Collaborators: Dr Citra Nurfarah bte Zaini Mattar (NUH),
Assoc Prof Mary Rauff,
Dr Chan Yiong Huak,
Dr Mark D Cregan (Univ of W Australia)

Perinatal exposure to organochlorine pesticides and polychlorinated biphenyls in Singapore

Principal Investigator: Dr Chong Yap Seng
Collaborators: Assoc Prof J Obbard,
Dr Annamalai Loganath

Genetic epidemiology of preclampsia

Principal Investigator: Dr Chong Yap Seng
Collaborators: Assoc Prof Samuel Chong,
Assoc Prof Arijit Biswas,
Dr Heng Chew Kiat,
Dr Caroline G Lee

Fatigue Matrix II

Principal Investigator: Prof Goh Hng Hang Victor
Collaborators: Miss Yin Hui-Qin (DMERI/DSO),
Mr Lim Chin Leong (DMERI/DSO)

Genetics as risk factors for osteoporosis and fracture in Singapore

Principal Investigator: Prof Goh Hng Hang Victor
Co-Principal Investigator: Dr Tong Yoke Yin Terry
Collaborator: Assoc Prof Yap Eric (DMERI/DSO)

Evaluation of haemostatic prognostic markers and human Kallikrein Biomarkers for survival outcome in Indonesian women with ovarian cancer

Principal Investigator: Dr Mahesh Choolani
Collaborator: Dr Koh Chee Liang Stephen

Human fetal mesenchymal stem cells for intrauterine treatment of mucopolysaccharidoses

Principal Investigator: Dr Mahesh Choolani
Co-Principal Investigator: Dr Jerry Chan Kok Yen

Development and validation of highly efficient Nanoparticle contrast agents for cellular labelling and targeting using MRI

Principal Investigator: Assoc Prof Wang Shih-Chang
Co-Principal Investigator: Dr Mahesh Choolani

The application of female centre care methodology to the development of a mobile health communication unit for women

Principal Investigator: Dr Yen Ching-Chiuan
Co-Principal Investigator: Dr Mahesh Choolani

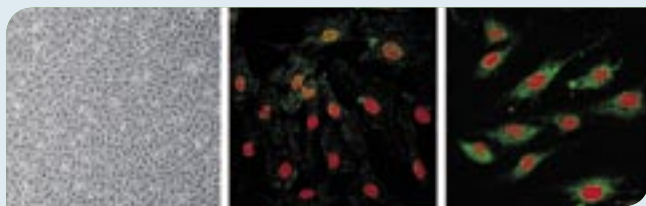
Enhancing enrichment of fetal primitive erythroblasts from maternal blood by identification of unique fetal surface antigens and the development of a novel MEMS device to deplete adult anucleate erythrocytes

Principal Investigator: Dr Mahesh Choolani
Co-Principal Investigators: Dr Victor Samper (IBN),
Assoc Prof Arijit Biswas,
Dr Narasimhan Kothandaraman (NUH)

Non-invasive prenatal diagnosis using fetal erythroblasts derived from first trimester maternal blood

Principal Investigator: Dr Mahesh Choolani
Collaborators: Assoc Prof Arijit Biswas,
Assoc Prof A C Roy

DEPARTMENT OF OBSTETRICS & GYNAECOLOGY



Fetal endothelial progenitors assumes the typical cobble stone morphology in culture (A), and express von Willibrand Factor (b) and CD133 (c).

Rapid diagnosis of common aneuploidies (chromosome x, y, 13, 18 and 21) using quantitative fluorescence polymerase chain reaction

Principal Investigator: Dr Mahesh Choolani

Antenatal preparation of postnatal counselling - a randomised controlled trial to compare strategies for improving breastfeeding rates

Principal Investigator: Assoc Prof Mary Rauff
Collaborators: Ms Chan Yah Shih (NUH),
Dr Chong Yap Seng,
Dr Su Lin Lin,
Dr Chang Yiong Huak

Ultra-rapid prenatal diagnosis using uncultured amniocytes

Principal Investigator: Dr Su Lin Lin
Co-Principal Investigator: Dr Mahesh Choolani
Collaborators: Dr Chan Yiong Huak,
Assoc Prof Arijit Biswas,
Dr Sukumar Ponnusamy,
Ms Ho Sze Yee Sherry

Effect of oestrogens on intracellular cAMP and cGMP pathways in rat erectile tissue

Principal Investigator: Dr Srilatha Balasubramanian

A multinational, multicenter, randomized, double-blind parallel group, placebo-controlled clinical trial to investigate safety and efficacy of tibolone (Org OD14) in women with climacteric symptoms and a history of breast cancer

Principal Investigator: Assoc Prof P C Wong
Collaborators: Dr A Anupriya A (NUH),
Dr Philip Lau (NUH)

Molecular mechanisms whereby non-protein small molecules are recruited to chromatin and their role as co-regulatory molecules for hormone-mediated steroid/nuclear receptor signalling

Principal Investigator: Prof Yong Eu Leong
Co-Principal Investigators: Dr Gong Yinhan,
Dr Shen Ping

Role of estrogen receptor alpha/beta and phyto-flavonoids in treatment of uterine fibroids

Principal Investigator: Prof Yong Eu Leong

Identification and characterisation of phyto-flavonoids for their use as novel therapeutic agents for uterine fibroids

Principal Investigator: Prof Yong Eu Leong

Pre-clinical studies using hormone-responsive bioassays as surrogate biomarkers to measure selective estrogen receptor modulator (SERM) activity in serum following oral administration of flavonoid-enriched traditional Chinese herbal extracts

Principal Investigator: Prof Yong Eu Leong
Collaborators: Dr Sheng Ping,
Dr Gong Yinhan

Study of herbal medicines - John Hopkins University-National University of Singapore Center for Research Complementary and Alternative Medicine (Planning Grant) (PICRC). United States National Institutes of Health, National Center for Complementary and Alternative Medicine (NIH-NCCAM)

Principal Investigator: Prof Yong Eu Leong
Collaborators: Prof Ong Choon Nam,
Dr Hong Yan (Temasek Life Sciences),
Dr Goh Boon Cher (NUH),
Dr Ronan Kelly,
Dr Steven Wise (Eli Lilly -NUS)

Molecular mechanisms of synergistic action, and clinical effectiveness of compounds from the herb, sz, on androgen and estrogen-receptor function

Principal Investigator: Prof Yong Eu Leong
Collaborator: Assoc Prof Paul Heng Wan Sia

INTERNATIONAL PUBLICATIONS

Chong YS, Mattar CN

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Lim LS, Shen P, Gong Y, Yong EL

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Loganath A

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DEPARTMENT OF OBSTETRICS & GYNAECOLOGY

Tong GQ, Heng BC, Tan LG, Ng SC

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Chan J, O'Donoghue K, Gavina M, Torrente Y, Mehmeta H, Stewart H, Watt, DJ, Morgan JE, Fisk NM

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Kueh J, Mark R, Ng SW, Chan WK, Bongso TA

The search for factors in human feeders that support the derivation and propagation of human embryonic stem cells: Preliminary studies using transcriptome filing by SAGE. *Fertility and Sterility* (2006) 85:1843-01846. (United States).

Chan J, Cabrol D, Ingemarsson I, Marsal K, Moutquin JM, Fisk NM

Pragmatic comparison of beta2-agonist side effects within a randomised controlled trial for tocolysis. *European Journal of Obstetrics Gynecology And Reproductive Biology* (2006) 128:135-141. (Ireland).

Lau LC, Adaikan PG

Mechanisms of direct relaxant effect of sildenafil, tadalafil and vardenafil on corpus cavernosum. *European Journal of Pharmacology* (2006) 541(3):184-90. (Netherlands).

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Srilatha B

Possible role for the novel gasotransmitter hydrogen sulphide in erectile dysfunction. *European Journal of Pharmacology* (2006) 535(1-3):280-282. (Netherlands).

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Li J, Raghavan B, Ng ML

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Lau LC, Adaikan PG

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Su LL, Chong YS

Common modalities for routine antepartum fetal monitoring: are they evidence-based? *Singapore Med J* (2006) 47(10):830-6.

STAFF PROFILE

Associate Professor & Head:
Professors:

P C Wong
Kuldip Singh
Yong Eu Leong

Associate Professors:

Arijit Biswas
A Ilancheran
Mary Rauff
Wong Yee Chee

Assistant Professors:

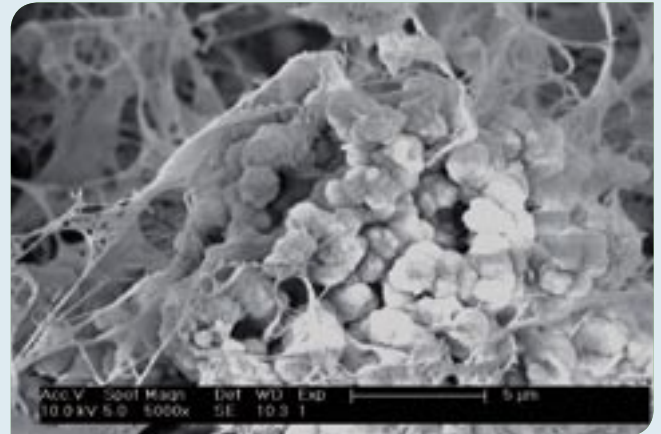
Chong Yap Seng
Mahesh Choolani
Fong Yoke Fai
Su Lin Lin
Chan Kok Yen Jerry

Research Professors:

Gong Yinhan
Fong Chui Yee
Ariff Bongso
Victor Goh Hng Hang
P Ganesan Adaikan

DEPARTMENT OF OBSTETRICS & GYNAECOLOGY

Senior Research Fellow: Loganath Annamalai
Research Fellows: Leena A Gole
Mark Richards
Shen Ping
Ponnusamy Sukumar
Tong Yoke Yin, Terry
Lau Lang Chu
Srilatha Balasubramanian
Kalamegam Gauthaman
Yang Lei
Li Jun
Praveen Kumar
Koh Chee Liang Stephen
Research Assistants: Li Qing Qing
Aradhana Rani
Chen Zhen Cheng, Clarice
Ye Chaopeng
Ho Sze Yee Sherry
Adjunct Professor: Ng Soon Chye
Adjunct Associate Professor: Philippe Jacques Taupin



Scanning electron micrograph of calcium nodules deposited by fetal mesenchymal stem cells after induction of osteogenic differentiation in a three dimensional bioactive scaffold.

CONTACT INFORMATION

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DEPARTMENT OF OPHTHALMOLOGY

INTRODUCTION

Department of Ophthalmology continues to work very closely with the Singapore Eye Research Institute (SERI), an NUS affiliated national research institute, as all NUS Dept of Ophthalmology staff play key roles in SERI, our national body for ophthalmic and vision research. The Department's research has elevated to a new horizon, with augmented cross-departmental and cross-faculty collaborations, collaborative studies within eye departments from both medical clusters, and many overseas institutions. This report focuses on specific research achievements by NUS Department of Ophthalmology staff in 2006.

Summary of research achievements in 2006

In 2006, 24 new research grants were secured by department staff. There were 53 ongoing research projects which focus on major eye diseases of specific regional relevance, including myopia, glaucoma, ocular surface stem cells, ocular infections, retinal vascular disorders, and cataract surgery. A total of 80 scientific papers in peer reviewed international journals with a mean impact factor (2005) of 3.96 were published. This represents the best publication output in terms of quality from the department to date.

Our fulltime faculty won no less than 8 awards for research, including the Minister for Health Award for outstanding performance in Public Health - Outbreak of Fusarium Keratitis (Investigating team

led by Prof Donald Tan), the Singhealth Outstanding Publication Award (Research team led by Assoc Prof Aung Tin), a Distinguished Achievement Award (Prof Donald Tan), a University Awards 2006 - Young Researcher Award (Dr Leonard Ang), The Commonwealth Minister of Health Award for Excellence in Medical Research, Australia and 2 research awards from Alcon & Novartis respectively (Assoc Prof Wong Tien Yin).

Research Highlights in 2006

- 1. Aborting global outbreak of contact lens-related fungal keratitis**
In January 2006, Professor Donald Tan led a SERI team of researchers in a nation-wide epidemiological study to determine the cause of a recent outbreak of severe fusarium keratitis in contact lens wearers in Singapore, which resulted in the discovery that the outbreak was related to the use of a specific contact lens solution - B&L MoistureLoc. A world-wide alert from Singapore led to the discovery of other cases in the US, Malaysia and Brunei, and ultimately culminated in a world-wide recall of the product within 3 months of the investigation, aborting further cases of blindness globally. The study was published in the April issue of the Journal of the American Medical Association (JAMA)¹, and the group have a further case-control study in press in the Archives of Ophthalmology, further implicating another related contact lens product which is currently still in world-wide use. Prof Tan was awarded with the first Minister for Health Award: For Outstanding Performance in Public Health.

DEPARTMENT OF
OPHTHALMOLOGY

¹ Khor W.B, Aung T., Saw S.M., Wong T.Y., Tambyah P.A., Tan A.L., Beuerman R.W., Lim L., Chan W.K., Heng W.J., Lim J., Loh R.S., Lee S.B., Tan D.T.H. An outbreak of *Fusarium* keratitis associated with contact lens wear in Singapore. *JAMA* 2006; 295(24):2867-2873

2. Gene discovery for Congenital Hereditary Endothelial Dystrophy

In July 2006, the SERI genetics group [led by Assoc Prof Aung Tin and (NUS Adjunct) Dr Eranga Vithana] worked with Professor Donald Tan to identify a new gene (SLC4A11) for Congenital Hereditary Endothelial Dystrophy (CHED), based on genetic material obtained in our first case from a corneal transplant patient operated by Prof Tan in Myanmar. This resulted in a publication in *Nature Genetics*², and two Singhealth research awards for Assoc Prof Aung Tin and Dr Vithana.

² Vithana EV, Morgan P, Sundaresan P, Ebenezer N, Tan DT, Anand S, Khine KO, Venkataraman D, Yong V, Salto-Tellez M, Venkataraman A, Guo K, Heemadevi B, Mohamad M, Srinivasan M, Prajna V, Khine M, Casey JR, Inglehearn C, Aung T. Mutations in Na-borate co-transporter SLC4A11 cause recessive Congenital Hereditary Endothelial Dystrophy, CHED2. *Nature Genetics*, 2006; 38: 755-7.

3. SiMES – Singapore Malay Eye Study

SiMES is a large-scale population based study to assess the causes and risk factors of blindness and visual impairment in our Malay community, over a 3 year period. Funded by the National Medical Research Council, SiMES examined 3,200 Malay adults aged between 40 to 80 years, and at this point, all study subjects have been recruited, and data analysis is underway. The Principal Investigator for SiMES, is Assoc Prof Wong Tien Yin, while, Co-PIs assisting Assoc Prof Wong are Assoc Prof Saw Seang Mei and Prof Donald Tan. SiMES will be the first large-scale survey of its kind to be conducted for a Malay community in the world. SiMES will provide important and previously unavailable public health information on the frequency of the most important eye diseases affecting Malay Singaporeans, which will aid in strategic planning of cost-effective public health policies in ophthalmology which may ultimately reduce blindness and visual disability in our ageing population.

PROJECT DESCRIPTION

Grants Awarded in 2006

A prospective clinical trial to evaluate the safety and effectiveness of the AcuFocus™ ACI 7000 in presbyopic subjects Progression

Principal Investigator: Prof Donald Tan
Collaborators: Dr Chan Wing Kwong (SNEC),
Dr Wee Tze Lin (SNEC),
Dr Chua Wei Han (SNEC)

Ahmed vs Baerveldt comparison study

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Collaborators: Dr Maria Cecilia Aquino (NUH),
Dr Grace Dizon (NUH)

An 8-Week, multicenter, masked, randomized trial (with an 18-week Masked Extension) to assess the safety and efficacy of 700mg and 350mg dexamethasone posterior segment drug delivery system (DEX PS DDS) applicator system compared with sham DEX PS DDS applicator system in the treatment of non-infectious ocular inflammation of the posterior segment in patients with intermediate uveitis

Principal Investigator: Assoc Prof Chee Soon Phaik
Collaborators: Dr Lim Wee Kiak (SNEC),
Dr Bobby Cheng (SNEC)

Birth parameters, blood pressure and retinal vascular changes in children

Principal Investigator: Assoc Prof Wong Tien Yin
Collaborator: Assoc Prof Saw Seang Mei

Case-control study on the risk factors for fungal keratitis in contact lens users

Principal Investigator: Prof Donald Tan
Collaborators: Assoc Prof Saw Seang Mei,
Assoc Prof Wong Tien Yin,
Assoc Prof Aung Tin,
Dr Lim Li (SNEC),
Adj Prof Roger Beuerman,
Dr Chan Wing Kwong (SNEC),
Dr Khor Wei Boon (SNEC)

Comparison of safety and efficacy of Brinzolamide/Timolol fixed combination vs COSOPT® in patients with open-angle glaucoma or ocular hypertension

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Collaborators: Dr Maria Cecilia Aquino (NUH),
Dr Cheng Jin Fong (SNEC)

Contact lens in pediatrics (CLIP) in an Asian population study

Principal Investigator: Dr Lim Li (SNEC)
Co-Principal Investigator: Prof Donald Tan
Collaborators: Dr Khoo Chong Yew (SNEC),
Dr Quah Boon Long (SNEC),
Dr Por Yong Ming (SNEC)

Cultivated ocular surface epithelial transplantation for the treatment of severe cornea and ocular surface disease (COSET)

Principal Investigator: Dr Leonard Ang
Collaborators: Prof Donald Tan,
Adj Prof Roger Beuerman,
Dr Ti Seng Ei (SNEC),
Dr Por Yong Ming (SNEC),
Dr Do Phuc Tien (SERI),
Dr Maung Zaw Moe Thein (SERI)

Development of new procedure for corneal transplantation and corneal surgery using a femtosecond laser – Human eye bank corneal studies

Principal Investigator: Prof Donald Tan
Collaborators: Adj Prof Roger Beuerman,
Dr Howard Cajucom-Uy (SNEC)

Efficacy and safety of a systematic switch from latanoprost to travoprost for glaucoma patients

Principal Investigator: Assoc Prof Aung Tin

DEPARTMENT OF OPHTHALMOLOGY

Evaluation of anterior segment OCT for angle closure diagnosis

Principal Investigator: Assoc Prof Aung Tin

Evaluation of ocular surface inflammation

Principal Investigator: Adj Prof Roger Beuerman
Collaborators: Prof Donald Tan,
Dr Zhou Lei (NUS Adjunct),
Dr Liu Shou Ping (SERI)

Gene and protein profiling and the selection of limbal stem cell markers

Principal Investigator: Dr Li Jing (NUS Adjunct)
Co-Principal Investigator: Adj Prof Roger Beuerman
Collaborators: Prof Donald Tan,
Dr Zhou Lei (NUS Adjunct),
Dr Wong Yong Wee (SERI),
Dr Ti Seng Ei (SNEC)

Multicenter prospective study to investigate the pattern of Vogt Koyanagi Harada disease in South East Asia

Principal Investigator: Assoc Prof Chee Soon Phaik
Collaborators: Dr K Bacsal (SNEC),
Dr Sivamalar,
Dr Lim Wee Kiak (SNEC),
Dr Bobby Cheng (SNEC),
Dr Lennard Thean (NUH)

Pilot study to evaluate the efficacy of Neurovision's NVC™ - vision correction technology for the improvement in visual acuity in myopic children and slowing of myopia

Principal Investigator: Prof Donald Tan
Co-Principal Investigator: Dr Chua Wei Han (SNEC)
Collaborators: Dr Allan Fong (SNEC),
Assoc Prof Saw Seang Mei

Preschool refractive error, amblyopia, and strabismus in Singapore study

Principal Investigator: Assoc Prof Saw Seang Mei
Co-Principal Investigator: Assoc Prof Wong Tien Yin

Quantitative proteomics of tear biomarkers for dry eye

Principal Investigator: Adj Prof Roger Beuerman
Collaborators: Dr Zhou Lei (NUS Adjunct),
Prof Donald Tan

Retinal vascular caliber as a predictor of retinopathy in type 1 diabetes

Principal Investigator: Assoc Prof Wong Tien Yin
Collaborators: Assoc Kim Donaghue
(University of Sydney),
Assoc Prof Alicia Jenkins
(University of Melbourne)

Singapore Eye Disease Study (SEDS) – The Indian/Chinese cohort

Principal Investigator: Assoc Prof Wong Tien Yin
Collaborators: Assoc Prof Saw Seang Mei,
Prof Donald Tan,
Assoc Prof Aung Tin,
Dr Tai E Shyong (SGH)

Singhealth Post-Doctoral Fellowship Recruitment Award

Principal Investigator: Assoc Prof Aung Tin



Normal retina.

Sources of conjunctival stem cells

Principal Investigator: Adj Prof Roger Beuerman
Collaborators: Dr Liu Shao Hui Andrea (SNEC),
Dr Li Jing (NUS Adjunct),
Prof Donald Tan,
Assoc Prof Chee Soon Phaik,
Prof Yann Barrandon (EPFL)

Sydney Paediatric Eye Study

Principal Investigators: Prof Paul Mitchell
(University of Sydney),
Prof Varma R
(University of Southern California),
Dr Rose K (University of Sydney),
Assoc Prof Gole G
(University of Queensland),
Assoc Prof Wong Tien Yin

Use of anterior segment optical coherence tomography (AS-OCT) as a new method of evaluating filtering blebs after trabeculectomy surgery in eyes with glaucoma

Principal Investigator: Assoc Prof Aung Tin
Co-Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Collaborator: Dr Mandeep Singh (NUH)

On-going Projects

A multicentre randomised clinical trial of laser treatment plus intravitreal triamcilon for diabetic macular oedema

Principal Investigator: Assoc Prof Mark Gillies
(University of Sydney)
Co-Principal Investigators: Assoc Prof Ian McAllister (UWA),
Assoc Prof Wong Tien Yin

A multi-centre, investigator-marked, randomised, parallel, 6-month study (with treatment extended to 12 months) of the safety & efficacy of lumigan 0.03% ophthalmic solution compared with latanoprost 0.005% ophthalmic solution administered adjunctively with timolol ophthalmic solution, in patients with glaucoma or ocular hypertension

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Collaborators: Dr Ho Ching Lin (SNEC),
Dr Wong Hong Tym (TTSH)

DEPARTMENT OF OPHTHALMOLOGY



Dilating eyes of patient for checkup.

A prospective comparison of primary angle closure: Glaucoma vs primary open angle glaucoma in Singapore

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Collaborators: Dr Jovina See (NUH),
Dr Gus Guzzard (UK),
Dr Wong Hon Tym (TTSH),
Assoc Prof Saw Seang Mei,
Assoc Prof Aung Tin,
Dr Robert Ritch (US),
Dr David Garway-Heath (UK)

A search for quantitative trait loci in angle closure glaucoma

Principal Investigator: Assoc Prof Aung Tin

A six-month phase 3, multicenter, masked, randomized, sham-controlled trial (with six-month open-label extension) to assess the safety and efficacy of 700mg and 350mg dexamethasone posterior segment drug delivery system (DEX PS DDS) applicator system in the treatment of patients with macular edema following central retinal vein occlusion or branch retinal vein occlusion

Principal Investigator: Assoc Prof Chee Soon Phaik
Collaborator: Dr Bobby Cheng (SNEC)

A study to assess the affect of glaucoma on postural control with age matched normal subjects

Principal Investigators: Assoc Prof Paul Chew,
Dr Valerie Peres (CNRS)
Collaborator: Dr Noor Shabana (NUS)

A twelve-month, multicenter, randomised, double-masked study to evaluate the efficacy and safety of once-daily instillation of travoprost 0.004%/Timolol 0.5% and Latanoprost 0.005%/Timolol 0.5% eye drops in subjects with open-angle glaucoma or ocular hypertension

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Co-Principal Investigator: Dr Steve Seah (SNEC)
Collaborators: Dr Lennard Thean (NUH),
Dr Clement Tan (NUH),
Dr Lim Boon Ang (SNEC),
Dr Joseph Manuel (NUH),
Dr Loon Seng Chee (NUH),
Dr Yeong Suet Ming (NUH)

Anterior segment optical coherence tomography: A new method of evaluating the drainage angle of eyes with glaucoma

Principal Investigator: Assoc Prof Aung Tin
Co-Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Collaborators: Dr Scott Smith (Cole Eye Institute,
Cleveland Clinic, US),
Dr David Friedman
(Wilmer Eye Institute)

Assessment of fibrin glue (Tisseel) in pterygium surgery and other forms of ocular surface reconstruction

Principal Investigator: Prof Donald Tan
Collaborators: Dr Leonard Ang,
Dr Por Yong Ming (SNEC)

Combined phacoemulsification and glaucoma implant surgery versus combined phacoemulsification and trabeculectomy: A randomized controlled trial

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Co-Principal Investigator: Dr Cecilia Aquino (NUH)
Collaborators: Dr Grace Dizon (NUH),
Dr Jovina See (NUH)

Comparison of the quality of vision provided by Pfizer Z9000 three-piece silicone posterior chamber intraocular lens and alcon laboratories MA60 acrysof three-piece acrylic posterior chamber intraocular lens

Principal Investigator: Assoc Prof Chee Soon Phaik
Collaborators: Dr Chua Wei Han (SNEC),
Dr Por Yong Ming (SNEC)

Contact diode micropulse laser transscleral cyclophotocoagulation for severe glaucoma

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Co-Principal Investigator: Dr Leonard Yip Wei Leon (TTSH)
Collaborator: Dr Anna Tan (NUH)

Detection of early glaucoma in myopic optic nerve heads of East Asians using the heidelberg retina tomograph II

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Collaborators: Dr Zheng Ce (NUS),
Dr Wong Hon Tym (TTSH),
Dr David Garway-Heath (UK)

Diurnal variations in intraocular pressure in primary angle closure

Principal Investigator: Assoc Prof Aung Tin
Collaborators: Dr Wong CY (SNEC),
Dr Govindasamy C
(Sankara Nethralaya, Chennai, India)

DEPARTMENT OF OPHTHALMOLOGY

Early retinal vessel changes in diabetes and the metabolic syndrome

Principal Investigator: Assoc Prof Wong Tien Yin
Co-Principal Investigators: Assoc Prof Jonathan Shaw (IDI),
Prof Paul Mitchell
(University of Sydney),
Prof Hugh Taylor (CERA)

Epidemiological study of the metabolic syndrome and microangiopathies in Asians

Principal Investigator: Dr Lim Su Chi (AH)
Co-Principal Investigator: Assoc Prof Wong Tien Yin
Collaborator: Assoc Prof Tai E Shyong (SGH)

Evaluation of anterior chamber depth measurement using IOL master as a method of detecting occludable anterior chamber angles in Chinese residents of Singapore

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Co-Principal Investigator: Assoc Prof Aung Tin

Inflammation, immunity and risk factors for cardiovascular disease in Chinese, Malays and Indians living in Singapore

Principal Investigator: Assoc Prof Tai E Shyong (SGH)
Co-Principal Investigator: Assoc Prof Wong Tien Yin
Collaborator: Dr Lim Su Chi (AH)

Investigating the genetic basis of primary angle closure glaucoma

Principal Investigator: Assoc Prof Aung Tin
Co-Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Collaborators: Dr Seah SKL (SNEC),
Dr Eranga Vithana (NUS Adjunct)

Linkage analysis of Singaporean primary angle closure glaucoma pedigrees to identify a genetic locus for the condition

Principal Investigator: Assoc Prof Aung Tin
Collaborators: Assoc Prof Paul Chew,
Dr Steve Seah (SNEC),
Dr Eranga Vithana (NUS Adjunct)

Molecular analysis of PRPF31 and CA4 genes in retinitis pigmentosa patients from Singapore

Principal Investigator: Dr Eranga Vithana (NUS Adjunct)
Co-Principal Investigator: Assoc Prof Aung Tin
Collaborator: Dr Adrian Koh (SNEC)

Multi-Centre Retinal Stroke Study

Principal Investigator: Assoc Prof Wong Tien Yin

Multi-Ethnic Study of Atherosclerosis – Eye Study (MESA-Eye)

Principal Investigators: Prof Ronald Klein (UW),
Assoc Prof Wong Tien Yin

Off label use of avastin (bevacizumab) intravitreal injection for the treatment of cystoid macular oedema secondary to uveitis

Principal Investigators: Assoc Prof Chee Soon Phaik,
Dr Lee Mun Wai (SNEC)
Collaborators: Dr Lim Wee Kiak (SNEC),
Dr Bobby Cheng (SNEC)

Prevalence of uveal effusion and plateau iris in angle closure: An ultrasound biomicroscopic study

Principal Investigator: Assoc Prof Aung Tin
Collaborators: Dr Lee KY (SNEC),
Dr Hoh Sek Tien (SNEC),
Dr Baskaran M (SNEC),
Dr Kumar RS (SNEC)

Prevention of myopia development in kindergarten children by early correction of astigmatism

Principal Investigator: Dr Fan DS (CUHK)
Co-Principal Investigator: Assoc Prof Wong Tien Yin

Prophylactic laser iridotomy for eyes with narrow drainage angles: A randomized controlled trial

Principal Investigator: Assoc Prof Aung Tin
Collaborators: Prof Paul Foster
(Institute of Ophthalmology &
Moorfields Hospital, UK),
Dr Seah SKL (SNEC),
Assoc Prof Paul Chew,
Dr Chan YH (NUS),
Dr Wong Hon Tym (TTSH),
Dr Aliza Jap (SNEC)

Prospective clinical trial comparing HOYA AF-1 (UY) YA-60BBB intraocular lens and alcon acrysof natural intraocular lens

Principal Investigator: Assoc Prof Chee Soon Phaik
Collaborators: Dr Ti Seng Ei (SNEC),
Dr K Bacsai (SNEC)

Retinal arteriolar signs and cardiovascular disease in an Australian cohort

Principal Investigator: Assoc Prof Wong Tien Yin
Co-Principal Investigators: Prof Paul Mitchell
(University of Sydney),
Prof Andrew Tonkin
(Monash University)

Retinal microvascular abnormalities: are they related to endothelial dysfunction?

Principal Investigator: Assoc Prof Jonathan Shaw (IDI)
Co-Principal Investigator: Assoc Prof Wong Tien Yin

Retinal microvascular signs and cardiovascular disease in type 2 diabetes

Principal Investigator: Assoc Prof Wong Tien Yin

Retinal microvascular signs in acute stroke: Associations with stroke subtype & prognosis

Principal Investigator: Assoc Prof Wong Tien Yin
Co-Principal Investigators: Assoc Prof Saw Seang Mei (NUS),
Assoc Prof Wong Meng Cheong (SGH)
Collaborators: Dr Chang Hui Meng (SGH),
Dr Deidre de Silva (SGH)

Retinal vascular caliber as a predictor of retinopathy in type 1 diabetes

Principal Investigator: Assoc Prof Wong Tien Yin
Co-Principal Investigators: Assoc Prof Kim Donaghue
(University of Sydney),
Assoc Prof Alicia Jenkins
(University of Melbourne)

DEPARTMENT OF OPHTHALMOLOGY

Retinal vascular signs as predictors of systemic disease outcomes: 10-year evolution in a population-based cohort

Principal Investigators: Prof Paul Mitchell
(University of Sydney),
Dr Wang Jie Jin
(University of Sydney),
Assoc Prof Wong Tien Yin,
Dr Smith W
(University of Newcastle, Australia)

Retinal vessel imaging & cardiovascular risk prediction

Principal Investigator: Assoc Prof Wong Tien Yin
Collaborators: Prof Ronald Klein
(University of Wisconsin),
Prof Paul Mitchell
(University of Sydney),
Assoc Prof Wynne Hsu
(School of Computing),
Dr Janice Lee (School of Computing)

Risk and determinants of fatal and non fatal coronary heart disease in the Melbourne collaborative cohort study

Principal Investigators: Prof John McNeil (Monash University),
Dr Harrap S
(University of Melbourne, Australia),
Dr Welborn T
(University of Melbourne, Australia),
Assoc Prof Wong Tien Yin,
Dr Liew D (Monash University),
Dr Diana Magliano (Monash University)

Selective laser trabeculoplasty for primary angle closure glaucoma: A pilot study

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Co-Principal Investigator: Dr Winifred Nolan (NUH)
Collaborator: Dr Maria Cecilia Aquino (NUH)

SGH Stem Cell Research Group Block Grant

Principal Investigator: Prof Donald Tan
Collaborator: Dr Leonard Ang

Singapore Consortium for Antimicrobial Peptides (SCAMP)

Principal Investigator: Adj Prof Roger Beuerman
Collaborators: Prof Donald Tan,
Dr Zhou Lei (NUS Adjunct),
Dr Eric Yap (DMRI),
Dr Li Jing (NUS Adjunct),
Assoc Prof Chandra Verma
(Bioinformatics Institute),
Assoc Prof Poh Chit Laa
(Microbiology, NUS),
Assoc Prof Chee Soon Phaik

The effect of low energy laser iris surface therapy (LIST) on the intraocular pressure in chronic angle closure glaucoma

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Co-Principal Investigator: Dr Cecilia Aquino (NUH)

The ex vivo expansion of ocular surface epithelial cells for transplantation – novel use of cord blood and fetal fibroblasts and stem cells

Principal Investigator: Dr Leonard Ang
Co-Principal Investigator: Prof Donald Tan
Collaborators: Adj Prof Roger Beuerman,
Dr Chen Pei Hsin (SERI),
Dr Christine Yap (SGH),
Dr Tan Hak Koon (SGH)

The identification of genes causing corneal endothelial dystrophies

Principal Investigator: Assoc Prof Aung Tin
Co-Principal Investigator: Prof Donald Tan
Collaborators: Dr Neil Ebenezer (UCL),
Dr Eranga Vithana (NUS Adjunct)

The localization of functional characterization of ocular CD38: A study of its role in the calcium signaling processes in the human eye

Principal Investigator: Assoc Prof Chang Chan Fong (NUS)
Collaborators: Dr Chng Hiok Hee (TTSH),
Dr Khoo KM (TTSH),
Assoc Prof Chee Soon Phaik

The pathophysiological and clinical significance of retinal microvascular signs in acute stroke

Principal Investigator: Prof Richard Lindley (WH)
Co-Principal Investigators: Assoc Prof Wong Tien Yin,
Dr Wang Jie Jin (University of Sydney),
Prof Paul Mitchell
(University of Sydney),
Dr Victor Fung (Royal Melbourne)

The prevalence rates of myopia and other refractive errors in Singapore adults aged 21 years and above: The Singapore cohort study

Principal Investigator: Assoc Prof Saw Seang Mei
Collaborators: Assoc Prof Wong Tien Yin,
Assoc Prof Tai E Shyong (SGH),
Dr Lim Su Chi (AH),
Dr Jeanette Lee
(NUS School of Computing),
Prof Donald Tan

The Retinal Vascular Imaging Centre (RetVIC)

Principal Investigator: Assoc Prof Wong Tien Yin

The Singapore Malay Eye Study: Collection of blood for blood chemistry and genetic association studies

Principal Investigator: Assoc Prof Wong Tien Yin
Co-Principal Investigators: Assoc Prof Saw Seang Mei,
Prof Donald Tan
Collaborators: Assoc Prof Aung Tin,
Assoc Prof Tai E Shyong (SGH)

The Singapore Malay Eye Survey (SiMES)

Principal Investigator: Assoc Prof Wong Tien Yin
Co-Principal Investigators: Assoc Prof Saw Seang Mei,
Prof Donald Tan
Collaborators: Assoc Prof Aung Tin,
Assoc Prof Tai E Shyong (SGH)

DEPARTMENT OF OPHTHALMOLOGY

Tissue engineering of conjunctival stem cells

Principal Investigator: Prof Donald Tan
Co-Principal Investigator: Dr Leonard Ang
Collaborator: Adj Prof Roger Beuerman

Tissue engineering of ocular surface epithelial stem cells – The development of a conjunctival tissue equivalent for clinical transplantation

Principal Investigator: Prof Donald Tan
Co-Principal Investigator: Dr Leonard Ang
Collaborators: Prof Teoh Swee Hin (Engineering, NUS),
Adj Prof Roger Beuerman,
Dr Li Jing (NUS Adjunct)

To investigate the HLA typing and its prognostic significance in VKH patients in Singapore

Principal Investigator: Dr Bobby Cheng (SNEC)
Co-Principal Investigator: Assoc Prof Aung Tin
Collaborators: Dr Lim Wee Kiak (SNEC),
Assoc Prof Chee Soon Phaik

Ultrasound biomicroscopy investigation of pseudo-accommodation in 1 CU humanoptics accommodative intra ocular lens

Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Co-Principal Investigator: Dr Wang Jenn Chyuan (NUH)

Use of anterior segment optical coherence tomography (AS-OCT) as a new method of evaluating filtering blebs after trabeculectomy surgery in eyes with glaucoma

Principal Investigator: Assoc Prof Aung Tin
Co-Principal Investigator: Assoc Prof Paul Chew Tec Kuan
Collaborator: Dr Mandeep Singh (NUH)

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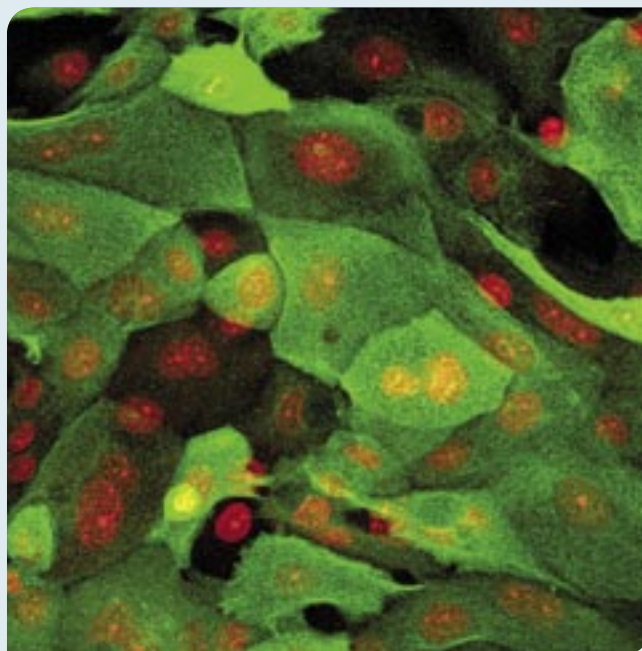
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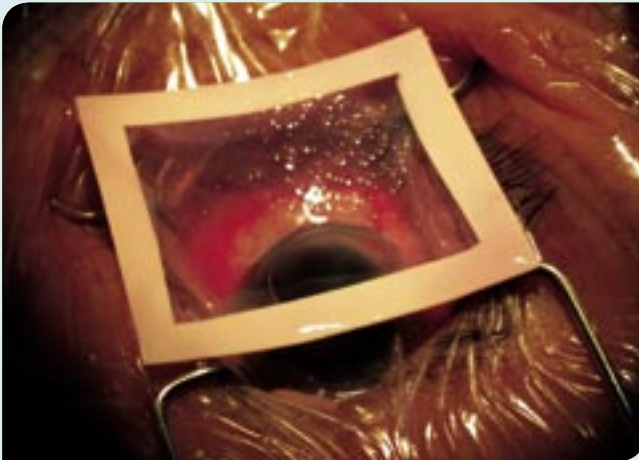
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DEPARTMENT OF
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DEPARTMENT OF OPHTHALMOLOGY

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STAFF PROFILE

Professor & Head:	Tan Tiang Hwee, Donald
Associate Professors:	Chew Tec Kuan, Paul Chee Soon Phaik Saw Seang Mei (secondary appointment) Wong Tien Yin Aung Tin
Assistant Professors:	Ang Pek Kiang, Leonard Anoop Shankar (secondary appointment)
Adjunct Professor:	Roger W Beuerman
Adjunct Associate Professor:	Au Eong Kah Guan
Adjunct Assistant Professors:	Eranga N Vithana Luu Chi Dzung Zhou Lei
Research Assistants:	Li Jing Cheng Ziyuan Gao Jiong Mya Sandar Ng Bee Fang Foong Wai Ping, Athena Ting Jeum Ngit, Steven Low Mavis
Management Support Officers (Research):	Nur Kamilah Binte Mohd Sharip Siti Nur Fatimah Bte Johari Haslina Binte Hamzah Muhamad Fauzi Bin Mat Isa Ho Huey-Shi, Maisie

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DEPARTMENT OF ORTHOPAEDIC SURGERY



INTRODUCTION

The Department of Orthopaedic Surgery has continued to develop core expertise and facilities in research. We have built up a strong infrastructure for orthopaedic research activities and our faculty members are actively involved in spearheading the university wide NUS Tissue Engineering Program. With this commitment to continuing research and application of knowledge to be translated into novel clinical applications, our surgeons and faculty are recognized locally and in the region, as pioneers in their areas of interest. In 2006, Prof Lee Eng Hin was awarded both the Faculty and NUS Outstanding Researcher Award for his pioneering work in the study of mesenchymal stem cells for the repair and regeneration of chondral defects in adults and physal defects in long bones of children. Assoc Prof James Hui received the BMRC Senior Clinician Scientist Award to enable him to focus on his research which involves the use of cell based therapy and injectable supplements for the repair of cartilage defects in knee joints. Our faculty members and staff also won a number of awards at the national and international level for excellence in research. Dr Suresh Nathan was awarded the Researcher Investigator Scientist Enabler (RISE) grant from the National Healthcare Group and a Health Service Development (HSDP) grant from the Ministry of Health. At the 29th Singapore Orthopaedic Association Annual Scientific Meeting, Dr Wilson Wang won the Singapore Orthopaedic Association-Bioengineering Society (SOA-BES) Prize for Best Bioengineering Paper while our Spine Group

won the Young Orthopaedic Investigator Award. The department has continued to establish research collaborations with overseas groups, other departments and research institutes. We secured 10 new grants in competitive research funding amounting to more than S\$2 million. This includes a grant under the 1st Singapore Stem Cell Consortium Grant Call to identify novel signalling pathways in chondrogenic differentiation of adult and embryonic human stem cells, a Biomedical Research Council grant to develop and evaluate novel methods to enhance the biocompatibility and osseointegration of commonly used implant biomaterials and a start-up grant to establish a musculoskeletal cancer registry in Singapore. The research output from the department has been remarkable, with 58 papers published in international peer reviewed journals, out of which more than 40 papers are in a Tier 2 journal and above.

PROJECT DESCRIPTION

Grants Awarded in 2006

Development of xeno-/serum free medium to improve the safety and quality of human chondrocytes culture for clinical autologous chondrocyte implantation

Principal Investigator:
Collaborators:

Prof Lee Eng Hin
Assoc Prof Hui Hoi Po James,
Dr Andre Choo (BTI),
Dr Steve Oh (BTI)

DEPARTMENT OF ORTHOPAEDIC SURGERY

Effects of dynamic tension on degenerated human annulus fibrosus and nucleus pulposus cells – An in-vitro study

Principal Investigator: Dr Hee Hwan Tak
Collaborator: Prof Wong Hee Kit

Retrograde flow venous flaps – A potentially reliable resurfacing tool?

Principal Investigator: Assoc Prof Lim Yu-Tang Aymeric
Co-Principal Investigator: Dr Maybelle Tan Phui-San (NUH)

Instability analysis of aging based on 3D proximal femur model

Principal Investigator: Dr Lee Taeyong
Collaborators: Prof Das De Shamal,
Assoc Prof Goh Cho Hong James

The limb salvage surgery patient at home - A systematic cross-sectional survey of patients with musculoskeletal malignancies in remission

Principal Investigator: Dr Saminathan Suresh Nathan

The influence of the vascularity and intrinsic permeability of the cartilaginous endplate on normal and degenerate discs in animal models of intervertebral disc compression and distraction

Principal Investigator: Dr Hee Hwan Tak
Collaborators: Prof Wong Hee Kit,
Dr Lee Taeyong

Chondrogenic differentiation of human stem cells: Characterising and defining the cellular and molecular mechanisms and the establishment of stable cellular phenotypes for cartilage regeneration

Principal Investigators: Prof Lee Eng Hin,
Dr Yang Zheng
Co-Principal Investigators: Dr Thomas Lufkin (GIS),
Assoc Prof Hui Hoi Po James,
Dr Liu Tongming
Collaborators: Dr Bing Lim (GIS),
Dr Cao Tong,
Dr Jacqueline Frida Schmitt

Biocompatibility and antimicrobial activity of orthopaedic implant biomaterials with novel surface modifications

Principal Investigator: Dr Wang Ee Jen Wilson
Co-Principal Investigator: Prof Neoh Koon Gee
Collaborator: Prof Das De Shamal

Muscle derived stem cells (MDSCS) for limb lengthening in rabbit model

Principal Investigator: Assoc Prof Hui Hoi Po James
Collaborator: Prof Lee Eng Hin

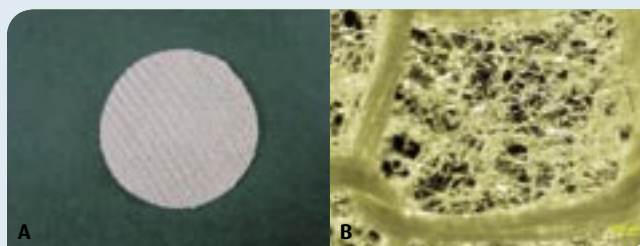
Surface modification and functionalization of bone-related implant biomaterials to enhance biocompatibility and promote osseointegration

Principal Investigator: Dr Wang Ee Jen Wilson
Co-Principal Investigator: Prof Neoh Koon Gee
Collaborator: Prof Das De Shamal

On-going Projects

Factor of safety in ligaments: A study of the physiological strains of ligaments relative to its ultimate load

Principal Investigator: Assoc Prof James Goh
Collaborator: Prof K Satku



3-D silk scaffold made from knitted silk scaffold and aqueous silk fibroin solution (A) photograph of the scaffold which was cut to fit 6-well multiplate; (B) phase contrast view of the scaffold (magnification X 40), showing the porous structure formed by freeze-dried silk solution.

Multisensory skin flap planning assistant using a virtual model of patient- specific biomechanics and blood supply

Principal Investigator: Adj Assoc Prof Lim Beng Hai
Collaborators: Dr Lim Kian Meng,
Dr Chew Chee Meng,
Assoc Prof Teo Chee Leong,
Dr Chen Chao Yu Peter

A study on fusion performance of the novel contoured spinal fixation device in conjunction with stem cells and bone morphogenetic proteins in lumbar interbody fusion

Principal Investigator: Prof Wong Hee Kit
Collaborators: Assoc Prof Goh Cho Hong James,
Assoc Prof Dietmar Hutmacher

Tissue engineering approaches to the repair and regeneration of anterior cruciate ligament

Principal Investigator: Assoc Prof Goh Cho Hong James
Co-Principal Investigators: Prof Lee Eng Hin,
Adj Prof Casey Chan,
Assoc Prof Toh Siew Lok,
Assoc Prof Hui Hoi Po James

Tissue engineering in musculoskeletal tissues: Characterizing and defining the cellular and molecular mechanisms and their role in tissue integration

Principal Investigator: Prof Lee Eng Hin
Collaborators: Assoc Prof Goh Cho Hong James,
Assoc Prof Hui Hoi Po James,
Dr Saminathan Suresh Nathan,
Dr Lim Sai Kiang (GIS),
Assoc Prof Cao Xinmin (IMCB),
Dr Li Jun

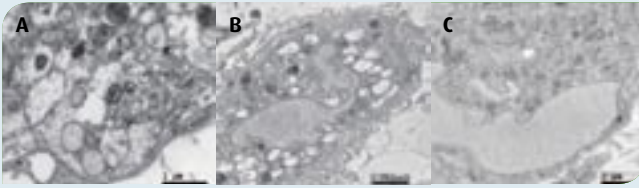
The study of gene-enhanced bone marrow mesenchymal stem cells for articular cartilage repair in pig model

Principal Investigator: Prof Lee Eng Hin
Collaborators: Assoc Prof Goh Cho Hong James,
Dr Li Baojie (IMCB)

Gene expression in sustained lumbar spinal nerve root compression neuropathy: An evaluation of novel gene detection techniques in an experimental animal model

Principal Investigator: Prof Wong Hee Kit
Collaborators: Assoc Prof Too Heng Phon,
Dr He Beiping

DEPARTMENT OF ORTHOPAEDIC SURGERY



A: Control AF cell without compression and tension.

B: Compressed AF cell only.

C: 10% Tensioned AF cell after compression, showing some granules within cell.

The equibiaxial cyclic tensile stress at a rate of 1 Hz with 10% strain suggested a capability of increasing proteoglycan and collagen synthesis of compressed annulus fibrosus (AF) cells.

Determining the moment arms and lines of action of skeletal muscles that cross the forearm axis

Principal Investigator: Dr Barry P Pereira

Construction and validation of a dynamic 3D Finite Element (FE) model of the tibiofemoral joint

Principal Investigator: Assoc Prof Goh Cho Hong James

Co-Principal Investigator: Dr Lee Vee Sin Peter (DMERI)

Mechanical analysis of human facet joints after artificial disc replacement

Principal Investigator: Prof Wong Hee Kit

Collaborator: Assoc Prof Goh Cho Hong James

The role of angiogenic growth factors in articular cartilage and bone

Principal Investigator: Dr Wang Ee Jen Wilson

Collaborators: Dr Lingaraj Krishna (NUH),
Prof Zheng Ming Hao (UWA)

Assessment of insufficiency fractures and incident knee osteoarthritis in pre and post-menopausal women using dual energy x-ray absorptiometry

Principal Investigator: Prof Shamal Das De

Collaborators: Dr Wang Ee Jen Wilson,
Prof K Satku

Enhancement of meniscus repair using mesenchymal stem cells in a porcine model

Principal Investigator: Assoc Prof Hui Hoi Po James

Collaborators: Prof Lee Eng Hin,
Assoc Prof Goh Cho Hong James,
Dr Andrew Dutton (NUH)

The role of intramuscular innervation in the functional recovery of lacerated skeletal muscles after repair – investigating morphological and molecular changes after repairing the intramuscular nerve branch

Principal Investigator: Dr Barry P Pereira

Co-Principal Investigator: Prof V Prem Kumar

RNAi for tendon healing: Synthetic small interfering RNA decrease type V collagen synthesis for growing larger collagen fibrils

Principal Investigator: Assoc Prof Goh Cho Hong James

Co-Principal Investigators: Dr Ricky Lareu,
Dr Ouyang Hongwei (Zhejiang U, China)
Collaborators: Dr Andrew Thomson (GIS),
Dr Isidore Rigoutsos (IBM, NY, USA)

Adult stem cell research as a cure for diabetes funded from Central Initiatives Fund

Principal Investigator: Prof Lee Eng Hin

Co-Principal Investigator: Adj Assoc Prof Lim Mey Lee Susan

Intraarticular therapy of encapsulated hyaluronan with chondroitin sulfate or mesenchymal stem cells for osteoarthritis of the knee

Principal Investigator: Assoc Prof Hui Hoi Po James

Collaborator: Prof Lee Eng Hin

A detailed investigation of the intra-muscular anatomy and physiology of skeletal muscles to maximize the role and potential of neuromuscular compartments for novel surgical procedures in limb reconstruction

Principal Investigator: Prof V Prem Kumar

Co-Principal Investigators: Dr Barry P Pereira,
Assoc Prof Lim Yu-Tang Aymeric

Development of a tissue engineered bone substitute for bridging a large weight bearing cortical bone defect. An experimental study in adult

Principal Investigator: Assoc Prof Nather Abdul Aziz

The effects of graft enhancement using autologous mesenchymal stem cells on osteointegration and the minimum graft length of hamstring tendon grafts in a porcine model of anterior cruciate ligament reconstruction

Principal Investigator: Assoc Prof Hui Hoi Po James

Collaborator: Prof Lee Eng Hin

Characterisation of mesenchymal stem cells isolated from animal and human tissues

Principal Investigator: Assoc Prof Hui Hoi Po James

Collaborators: Dr Saminathan Suresh Nathan,
Prof Lee Eng Hin,
Assoc Prof Goh Cho Hong James,
Prof Das De Shamal

Design and development of a system to apply hydrostatic pressure stimuli to regulate cell metabolism in cultures used in musculoskeletal tissue

Principal Investigator: Dr Wang Ee Jen Wilson

Collaborator: Prof K Satku

INTERNATIONAL PUBLICATIONS

Ling ZX, Kumar VP

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DEPARTMENT OF ORTHOPAEDIC SURGERY

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Hui HP, Lee EH

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DEPARTMENT OF
ORTHOPAEDIC SURGERY

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Lim AYT, Sebastin SJ
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DEPARTMENT OF ORTHOPAEDIC SURGERY

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Characterization of osteogenically induced adipose tissue-derived precursor cells in 2-dimensional and 3-dimensional environments. *Cells Tissues Organs* (2006) 182(1):1-11. (Switzerland).

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Lim BH, Loh SY

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Philips JE, Hutmacher DW, Guldborg RE, Garcia AJ

Mineralization capacity of Runx2/Cbfa1-genetically engineered fibroblasts is scaffold dependent. *Biomaterials* (2006) 27(32):5535-5545. (United Kingdom).

Schantz JT, Lim TC, Ning C, Teoh SH, Tan KC, Wang SC, Hutmacher DW

Cranioplasty after trephination using a novel biodegradable burr hole cover: a technical case report. *Neurosurgery* (2006) 58(1 Suppl):ONS-E176, discussion ONS-E176. (United States).

Song SJ, Hutmacher D, Nurcombe V, Cool SM

Temporal expression of proteoglycans in the rat limb during bone healing. *Gene* (2006) 379:92-100. (Netherlands).

Zhou YF, Sae-Lim V, Chou AM, Hutmacher DW, Lim TM

Does seeding density affect in vitro mineral nodules formation in novel composite scaffolds? *Journal of Biomedical Materials Research A* (2006) 78(1):183-93. (United States).



Bone mineral density (BMD) image of the knee.

STAFF PROFILE

Professor & Head:

Emeritus Professor:

Professors:

Adjunct Professor:

Associate Professors:

Assistant Professors:

Adjunct Associate Professors:

Adjunct Assistant Professor:

Research Fellows:

Research Assistants:

Wong Hee Kit

Robert Pho

Lee Eng Hin

K Satkunanantham

Shamal Das De

V Prem Kumar

Casey Chan

Aziz Nather

James Goh

James Hui

Aymeric Lim

Andre van Wijnen

(Visiting Professor)

Hee Hwan Tak

Wilson Wang

Suresh Nathan

Dietmar Hutmacher

(joint appointment)

Khong Kok Sun

Lim Beng Hai

Victor Nurcombe

Simon McKenzie Cool

Barry Pereira

Detlef Olaf Alexander Schumann

Guo Xi-Min

Jacqueline Frida Brown

Fan Hongbin

Kerrie Tang

Liu Haifeng

Liu Tongming

Ni Guoxin

Ren Xiafei

Ricardo Rodolfo Lareu

Tan Phui-Shan Maybelle

Yang Zheng

Ouyang Hongwei

Zhang Jituan

Bharti Dewangan

Chong Sook Yee

Christopher Lam Xu Fu

Ho Hoan Nghia

DEPARTMENT OF ORTHOPAEDIC SURGERY

Lewis Tan Hark Chuan
Kolencheril Raphael Beena
Ivy Seah
Ramruttun Amit Kumarsing
Rashidah Sakban
Sujeevini Jeyapalina
Toh Wei Seong
Wu Yingnan
Yang Kai
Zhao Tianyun
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DEPARTMENT OF OTOLARYNGOLOGY



INTRODUCTION

The strategy of the Otolaryngology Department is to develop focused areas of research based on the research questions which are founded on relevant clinical questions. We have also expanded our research interests into clinical application of genetic predisposition and gene-environmental interaction on disease expression the above disease processes. Our major research areas include:

A. HEAD AND NECK CANCER – NASOPHARYNGEAL AND THYROID CANCER RESEARCH

1. Evaluation of screening program of siblings of NPC patients.
2. Assessment of value of plasma EBV DNA in screening for NPC.
3. Development of classification of trismus in irradiated NPC patients.
4. Conduct of phase I and II trials of c225 in NPC.
5. Conduct of phase III trials of tirapazimine in chemoradiation of head and neck squamous cell carcinoma (part of international trial sponsored by Sanofi-Aventis).
6. Tissue engineered prefabricated vascularised bone flap – a feasibility study.
7. Minimally Invasive approaches to Thyroid Surgery.
8. Quality of Life Research in Thyroid Cancer.
9. Surgical Cost and Benefit studies in Head and Neck Surgery.
10. Detection of RET/PTC expression and its' role as a molecular and prognostic marker in our local patients with papillary thyroid carcinoma.

B. Rhinologic & Immunology

1. Association between polymorphisms of candidate genes and atopy and allergic rhinitis in Singapore population.
2. Clinical manifestation of food allergy: a double-blind placebo-controlled food challenge (DBPCFC) study.
3. Clinical and immunologic effects of sublingual immunotherapy in patients with persistent allergic rhinitis: a double-blind, placebo controlled study.
4. Epigenetic alterations and gene expression profiles in human nasal polyps and chronic rhinosinusitis.
5. The role of fungus in allergic rhinitis.
6. Environmental Control Measures in Persistent Allergic Rhinitis.
7. Impact of stress on symptoms and underlying immunologic mechanisms of allergic rhinitis.
8. Computational Modeling of Geometrical Configuration on Human Nose and its Related Physiologic Functions in Health and Disease.

C. Paediatric otolaryngology

1. Genetic hearing loss and clinical correlates.
2. Auditory Processing Disorder.
3. The Role of Microbes in Rhinitis and Otitis Media with Effusion.
4. Development of a scientific questionnaire for "Caregiver experience in Pediatric Hearing Impairment".
5. Biodegradable Airway Stent for Laryngotracheal Airway Stenosis.

DEPARTMENT OF
OTOLARYNGOLOGYPROJECT DESCRIPTION
Grants Awarded in 2006

The detection of early nasopharyngeal carcinoma using a screening programme for siblings of affected patients

Principal Investigator: Dr Thomas Loh Kwok Seng
 Co-Principal Investigator: Prof Chan Soh Ha
 Collaborators: Assoc Prof Tan Kim Siang Luke,
 Dr Goh Boon Cher,
 Dr Lu Jiade Jay,
 Dr Hsieh Wen-Son,
 Dr Wong Seng Cheong Alvin

Impact of stress on symptoms and underlying immunologic mechanisms of allergic rhinitis

Principal Investigator: Assoc Prof Wang De Yun
 Co-Principal Investigators: Assoc Prof Chia Sin Eng,
 Prof Pontus Stierna
 Collaborators: Prof Koh Soo Quee David,
 Ms Ng Ah Ching Vivian

Computational modeling of geometrical configuration on human nose and its related physiologic functions in health and disease

Principal Investigator: Assoc Prof Wang De Yun,
 Co-Principal Investigators: Assoc Prof Lee Heow Pueh,
 Assoc Prof Vincent Chong,
 Assoc Prof K Rajendran

On-going Projects

Pathogenesis of nasal polyposis: role of leukotrienes in recruitment and activation of CD8+ T cells.

Principal Investigator: Assoc Prof Wang De Yun
 Collaborators: Dr Lim Yaw Chyn,
 Dr Pang Yoke Teen (NUH)

Cochlear delivery of neurotrophic factors by gene transfer through an intact round window membrane for treatment of profound hearing loss

Principal Investigator: Dr Ruan Run Sheng
 Collaborator: Dr Ge Ruowen

EBV DNA (RT-PCR) predictor of nasopharyngeal cancer. Early detection of nasopharyngeal cancer with EBV Dual

Principal Investigator: Assoc Prof Tan Kim Siang Luke
 Collaborators: Dr Winson Hsieh,
 Dr Loh Woei Shyang

Clinical and immunologic effects of sublingual immunotherapy in patients with persistent allergic rhinitis: A double-blind, placebo controlled study

Principal Investigator: Assoc Prof Wang De Yun
 Collaborators: Dr Pang Yoke Teen,
 Dr Chan Yiong Huak

Tissue engineered prefabricated vascularised bone flaps

Principal Investigator: Assoc Prof Tan Kim Siang Luke
 Collaborators: Assoc Prof Dietmar W Hutmacher,
 Assoc Prof Wang De Yun,
 Dr Kenneth Oo

Genotypic and phenotypic correlations of hereditary non-syndromic hearing loss in Singapore: Connexin 26, Connexin 30, Pendrin and A1555G mutations

Principal Investigator: Dr Lynne Lim
 Co-Principal Investigator: Dr Denise Goh
 Collaborator: Assoc Prof Evelyn Koay

The role of fungus in allergic rhinitis

Principal Investigator: Dr Chao Siew Shuen
 Collaborators: Assoc Prof Wang De Yun,
 Dr Raymond Ngo

Environmental control measures in persistent allergic rhinitis

Principal Investigator: Dr Chao Siew Shuen
 Collaborator: Assoc Prof Wang De Yun

Allergens for diagnosis, treatment and control of dust mite allergy

Principal Investigator: Dr Chew Fook Tim
 Co-Principal Investigator: Assoc Prof Wang De Yun
 Collaborators: Dr Pang Yoke Teen (NUH),
 Dr Mok Yu Keong,
 Dr Markus R Wenk,
 Dr Mona Iancovici Kidon

The role of microbes in non-allergic

Principal Investigator: Dr Lynne Lim
 Collaborators: Prof Rylander Ragnar,
 Assoc Prof Wang De Yun,
 Dr Chao Siew Shuen

INTERNATIONAL PUBLICATIONS

Soo R, Wu J, Aggarwal A, Tao Q, Hsieh W, Putti TC, Tan KB, Soon WL, Lai YF, Mow B, Hsu SI, Loh KS, Tan KSL, Tan BOP, Goh BC
 Celecoxib reduces microvessel density in patients treated with nasopharyngeal carcinoma and induces changes in gene expression. *Annals of Oncology* (2006) 17(11):1625-1630. (Switzerland).

Low WK, Tan GK, Li S, Chua WC, Goh LK, Wang DY
 Dose-dependant radiation-induced apoptosis in a cochlear cell-line. *Apoptosis* (2006) 11:2127-2136. (United Kingdom).

Li J, Yang C, Li H, Wang X, Goh SH, Ding JL, Wang DY, Leong KW
 Cationic Supramolecules Composed of Multiple Oligoethylenimine-Grafted beta-Cyclodextrins Threaded on a Polymer Chain for Efficient Gene Delivery. *Advanced Materials* (2006) 18(22):2969-2974. (Germany).

Multi-Authors, Wang DY

Pharmacologic and anti-IgE treatment of allergic rhinitis ARIA update (in collaboration with GA2LEN). *Allergy* (2006) 61(9):1086-1096. (Denmark).

Low WK, Toh ST, Wee J, Fook-Chong MC, Wang DY

Sensori-neural hearing loss after radiotherapy and chemo-radiotherapy: a single blinded randomised study. *Journal of Clinical Oncology* (2006) 24(12):1904-1909. (United States).

DEPARTMENT OF OTOLARYNGOLOGY

Liang XH, Cheung W, Heng CK, Liu JJ, Li CW, Lim B, Wang DY

CD14 promoter polymorphisms have no functional significance and are not associated with atopic phenotypes. *Pharmacogenetics* (2006) 16(4):229-236. (United States).

Hao J, Pang YT, Wang DY

Inflammatory cell patterns in nasal polyps and paired middle turbinate. *Otolaryngology - Head and Neck Surgery* (2006) 134:267-275. (United States).

Wong AS, Soo RA, Lu JJ, Loh KS, Tan KS, Hsieh WS, Shakespeare TP, Chua ET, Lim HL, Goh BC

Paclitaxel, 5-fluorouracil and hydroxyurea concurrent with radiation in locally advanced nasopharyngeal carcinoma. *Ann Oncol* (2006) 17(7):1152-7.

Ma X, Lu JJ, Loh KS, Shakespeare TP, Thiagarajan A, Goh BC, Tan KS

Role of computed tomography imaging in predicting response of nasopharyngeal carcinoma to definitive radiation therapy. *Laryngoscope* (2006) 116(12):2162-5.



Participant undergoing skin testing for inhalant allergy.

STAFF PROFILE

Associate Professor & Head:	Tan Kim Siang, Luke
Clinical Professor:	Yeoh Kian Hian
Associate Professor:	Wang De Yun
Assistant Professors:	Thomas Loh
	Lynne Lim
	Chao Siew Shuen
	Loh Woei Shyang
Adjunct Assistant Professor:	Ruan Run Sheng

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	Singapore 119074



DEPARTMENT OF PAEDIATRICS

INTRODUCTION

Research in the Department of Paediatrics is focused in three major areas: Human Genetics, Immunology and Allergy, and Paediatric Oncology.

The Human Genetics Research Group aims to establish and develop genetic research and diagnostic facilities in cardiovascular, endocrine (adrenal disease and obesity), neuromuscular, neurometabolic, haematology-oncology, hepatobiliary (Alagille's syndrome) and renal genetics, with regards to:

- Genetic epidemiology, including sequencing, mutation screening, and genotyping.
- Establishment of a cord blood bank resource representative of Singapore's three major ethnic groups
- Karyotyping and gene mapping by linkage analysis and molecular cytogenetics
- Molecular diagnostics and gene therapy
- Functional genomics and pharmacogenomics
- Animal models of human development and disease

The Neuromuscular and Neurogenetic Research Group is currently focused on the following areas of translational research:

- **Molecular therapy for Duchenne and Becker muscular dystrophy**
The use of aminoglycosides in inducing mutation read-throughs in Duchenne muscular dystrophy
Development of antisense oligonucleotide therapy

- **Mutation screening for mitochondrial disorders**
Genotype and phenotype correlation of mitochondrial mutations in mitochondrial encephalomyopathies
Screening of mitochondrial mutations in children with non-syndromic hearing loss
Investigating the association between mitochondrial haplogroups and sporadic Parkinson's Disease in Singapore Chinese
Mitochondrial sequence variations in the D-loop region of patients with acute childhood leukemia
- **Studying genotype and phenotype correlations in rare neurogenetic disorders**
Studying a rare mild phenotype of aromatic amino decarboxylase deficiency in a family
Investigating the cholesterol and cholesterol oxidation products in Niemann Pick disease Type C patients and the npc1 mouse model

The human genetics team working on zebrafish in a multinational collaboration effort has identified a genetic mutation as the cause of a congenital craniofacial birth defect, cranio-lenticulo-sutural dysplasia, which affects one in every 500 to 1,000 newborns. The mutation closes off a pathway that is vital to the transport of cellular proteins and, in doing so, significantly alters normal growth patterns of skeletal and connective tissue. This collaboration included well-known scientists, Simeon Boyadjiev Boyd from University of California, Davies, whose team were able to map the defect to a particular region of human chromosome 14 and find the exact

DEPARTMENT OF PAEDIATRICS

mutation in gene SEC23A using genetic linkage studies, Lelio Orci from the University of Geneva, Switzerland, a recognized leader on cell morphology; Randy Schekman and Chris Fromme from the University of California, Berkeley, who used biochemical characterization of the mutant cells to precisely pinpoint the mechanism leading to cranio-lenticulo-sutural dysplasia; and Samuel Chong from the Human Genetics Research Group of NUS, who inactivated the corresponding gene in zebrafish and was able to produce very similar skeletal defects. This mutation inactivated the SEC23A protein, an integral component of the COPII-mediated secretory pathway, a critical intracellular pathway that moves proteins from one part of a cell to another. For individuals with cranio-lenticulo-sutural dysplasia, this transition is defective resulting in accumulation of the proteins in the endoplasmic reticulum. These results have been published in the October issue of *Nature Genetics* 2006.

The Immunology and Allergy Research Group has 2 major laboratories:

The Paediatric Allergy Laboratory whose main areas are as follows:

- Prevention and treatment of asthma and allergic diseases, where the focus is on the optimization of DNA vaccines for allergic diseases. This includes a collaboration with Professor Yu Su-May from Institute of Molecular Biology, Academia Sinica, Taiwan on the production of oral vaccine for immunotherapy in transgenic plants.
- Immunopathogenesis of asthma and allergic diseases, where the focus is on allergen and cell surface molecules interaction in skin fibroblast, lung epithelial, DC, Treg and B cells.
- Collaborative research on the study of allergen NMR structure with The Institute of Biomedical Sciences, Structural Biology Division, Academia Sinica.
- Study of immunoregulatory proteins and their application in treatment of allergic diseases.
- Further research and development on *Blomia tropicalis* mite allergens with reduced allergenicity and the generation of hypoallergenic recombinant mite proteins as immunotherapeutic reagents.
- Evaluation of the protective/therapeutic effects of recombinant *Lactobacillus* expressing dust mite allergen Der p2 (L.casei /Der p2) using a murine allergy model and to perform *in vivo* and *in vitro* studies to elucidate the mechanisms of probiotics on the induction of T regulatory and effector cells network in these mice. The group has filed a US patent based on this work (BRC/P/04066/00/US).
- The influence of environmental factors in the development of childhood allergies:
 - (a) Collaborative Research initiative on the protective effects of probiotics on allergic disease encompassing a double blind placebo controlled randomized clinical trial on the protective effects of probiotic supplementation in newborn infants, *in vitro* study of the underlying immunoregulatory mechanisms of probiotics, and the protective/therapeutic potential of probiotic bacteria expressing recombinant dust mite allergens as a vehicle for allergen immunotherapy in mouse dust mite allergy model.
 - (b) Collaborative research with University of Otago, Dunedin New Zealand and Gadjah Maja University, Yogyakarta, Indonesia to carry out a comparative study of gut microbiota between urban Singapore and rural Indonesian (Yogyakarta) toddlers and determine its relationship with the development of allergic diseases.
 - (c) A follow up cohort study on infantile wheezing to assess risk factors for persistence of wheeze.

The Paediatric Renal and Transplant Immunology Research Laboratory focuses on the following:

- Immunopathogenesis of nephrotic syndrome, in particular minimal change disease. The Group has developed an *IL-13* transfection rat model of minimal change-like nephropathy, which won the Young Scientist Award at the World Congress of Nephrology, 2005
- Immunogenetics of familial nephritis. The reported work on NPHS2 mutations in Singapore Chinese patients with nonfamilial steroid-resistant nephrotic syndrome won the International Travel Grant Winner awarded by the American Association for Clinical Chemistry (AACC) at its annual meeting in San Diego, USA in July 2007. CA 15.7.07 – 19.7.07.
- Infections in solid organ transplantation

The Paediatric Oncology Research Group has as its main focus research in childhood leukemias. They currently focus on both childhood acute lymphoblastic and myeloid leukaemias through a multi-faceted, multi-centre treatment trials using the Malaysia-Singapore Study Group frame work.

This unique collaboration involving 4 centres in Singapore and Malaysia allowed us to increase the enrollment rates to the studies.

The Ma-Spore ALL 2003 study has enrolled more than 250 patients over 4 years and preliminary analysis showed very good event-free survival of 79% at 4 years in the group. More importantly, we demonstrated that tailoring therapy according to early response to therapy allows us to deliver the optimal chemotherapy intensity. For 36% of patients with an excellent early response, decreasing the intensity of therapy did not adversely impair the treatment outcome. We recently reported that there is a higher frequency of high risk Philadelphia positive acute lymphoblastic leukaemia in Asian population (6%) compared to Western cohorts (2-3%). There are also ethnic differences involving other subtypes.

The Ma-Spore AML 2006 study was piloted in 2005 and launched group-wide in 2006. An interesting pattern of AML subtypes that is different from the Western population is seen.

PROJECT DESCRIPTION

Grants Awarded in 2006

Pre-implantation genetic diagnosis

Principal Investigator: Assoc Prof Samuel Chong
Co-Principal Investigator: Dr Christine Yap (SGH)

Development of a universal microarray format for multiplexed genotyping of candidate genes for coronary artery disease

Principal Investigator: Dr Heng Chew Kiat
Co-Principal Investigator: Dr Robert Yang Yong Yuan

Prevalence of peanut, tree nut and seafood allergy among children in 3 Asian countries: A cross-sectional population-based study

Principal Investigator: Dr Lynette Shek
Co-Principal Investigators: Dr Pasuree Sangsupawanich (Prince of Songkla Univ, Thailand),
Dr Elizabeth Morales (Univ of Santo Tomas Hospital, Philippines)
Collaborators: Assoc Prof Lee Bee Wah,
Dr Stefan Ma (MOH)

DEPARTMENT OF PAEDIATRICS

Obesity Gene Study (OGS): Uncovering genetic variations which predispose to human obesity and obesity-related complications

Principal Investigator: Dr Lee Yung Seng
Collaborators: Assoc Prof Loke Kah Yin,
Assoc Prof Samuel Chong

A risk-stratified multicentre childhood acute myeloid leukemia study using the modified MRC AML 10 backbone with anthracycline reduction, and minimal residual disease and cardiomyopathy assessments

Principal Investigator: Dr Allen Yeoh
Collaborators: Dr Tan Ah Moh (KKH),
Assoc Prof Quah Thuan Chong,
Assoc Prof Hany Arrifin
(Paeds, Univ Malaya),
Assoc Prof Quek Swee Chye,
Assoc Prof Ling Lieng Hsi,
Dr Tan Poh Lin,
Dr Kuperan Ponnudurai (TTSH),
Dr Chan Yiong Huak

Mechanistic study of the stimulatory and adjuvant effects of a fungal immunomodulatory protein in tumor immunotherapy

Principal Investigator: Prof Chua Kaw Yan
Collaborators: Dr Lim Yaw Chyn,
Dr Seow See Voon,
Dr Kuo I-Chun

The identification and evaluation of cystic fibrosis transmembrane conductance regulator (CFTR) gene mutations and polymorphisms in Asians with chronic pulmonary disease

Principal Investigator: Assoc Prof Daniel Goh
Collaborators: Assoc Prof Sam Chong,
Dr Lynette Shek,
Dr Nicola Ngiam,
Dr Chng Seo Yi (NUH),
Assoc Prof Jessie DeBruyne
(Paeds, Univ Malaya Medical Centre, KL)

Screening of mitochondrial mutations in children with non-syndromic hearing loss

Principal Investigator: Dr Tay Kiat Hong Stacey
Co-Principal Investigator: Dr Lynne Lim
Collaborators: Dr Goh Li Meng, Denise,
Dr Lai Poh San

Altered molecular regulation of cholesterol metabolism in an IL-13 gene overexpression model of minimal change-like nephropathy

Principal Investigator: Dr Wei Changli
Co-Principal Investigator: Prof Yap Hui Kim
Collaborators: Assoc Prof Lee Guat Lay Caroline,
Assoc Prof Khoo Hoon Eng,
Prof Stanley C Jordon,
Dr Gilbert SC Chiang

On-going Projects

Characterisation of the genetics and complications of childhood obesity in Singapore

Principal Investigator: Dr Lee Yung Seng
Collaborators: Assoc Prof Loke Kah Yin,
Dr Rose Vaithinathan (SHS, MOH),
Dr Paul Deurenberg
(Wageningen Univ, Nether),
Dr Saw Seang Mei (COFM, NUS)

Retroviral-mediated strategies for in vivo expression reporting and isolation of novel zebrafish genes important in human development and disease

Principal Investigator: Assoc Prof Chong Siong-Chuan Samuel
Collaborators: Assoc Prof Caroline Lee,
Dr Ethylin W Jabs

Single Nucleotide Polymorphisms (SNPs) in the Mdr1 gene in the three ethnic groups in Singapore - Correlating Polymorphisms/Haplotypes with drug transport in search of functional SNPs

Principal Investigator: Assoc Prof Chong Siong-Chuan Samuel
Collaborators: Assoc Prof Caroline G Lee,
Prof Edmund Lee

Genetic polymorphisms of the IL-13 gene and IL-13 receptor complex genes in minimal change nephrotic syndrome of childhood

Principal Investigator: Prof Yap Hui Kim
Collaborators: Assoc Prof Chong Siong-Chuan Samuel,
Dr Cheung Wai Wilson

A Singapore nation-wide study in childhood acute lymphoblastic leukemia incorporating minimal residual disease based risk-stratification pharmacogenomic study of thiopurine methyltransferase deficiency and establishment of a cell bank

Principal Investigator: Dr Yeoh Eng Juh Allen
Collaborators: Assoc Prof Quah Thuan Chong,
Dr Tan Poh Lin (NUH),
Dr Tan Ah Moy (KKH),
Dr Heng Chew Kiat,
Dr Li Chi Kong (HK),
Dr Dario Campana (St Jude, USA),
Dr Pui Ching Hon (St Jude, USA)

Establishment of a national Paediatric Oncology Group (Singapore) [POG(S)] comprising of an experimental therapeutics/clinical trial and outcome consortium, a central research laboratory and cancer and tissue bank in Singapore

Principal Investigator: Dr Yeoh Eng Juh Allen
Collaborators: Assoc Prof Quah Thuan Chong,
Dr Tan Ah Moh (Paeds, KKH),
Dr Chan Mei Yoke (Paeds, KKH),
Dr Chui Chan Hon (Paeds, KKH)

DEPARTMENT OF PAEDIATRICS

Influence of probiotics on atopy, atopic disease and immunological responses - A randomised double-blind, placebo-controlled clinical trial

Principal Investigator: Dr Lynette Shek
Co-Principal Investigator: Dr Marion M Aw
Collaborators: Assoc Prof Lee Bee Wah,
Assoc Prof Abu Rauff,
Dr Chong Yap Seng,
Assoc Prof Saw Seang Mei,
Dr Dawn Lim,
Assoc Prof Lee Yuan Kun,
Assoc Prof Chua Kaw Yan,
Dr Steven Ng (NUH)

Molecular characterization of mutant DAX-1 protein in X-linked adrenal hypoplasia congenita: A study of 3 novel mutations

Principal Investigator: Assoc Prof Loke Kah Yin
Collaborator: Dr John C Achermann

BioMEMS for cells characterization

Principal Investigator: Dr Heng Chew Kiat
Collaborator: Assoc Prof Poenar Daniel Piu (NTU)

Screening of mitochondrial DNA and nuclear DNA gene mutations in patients with mitochondrial encephalomyopathies

Principal Investigator: Dr Stacey Tay
Co-Principal Investigators: Dr Lai Poh San,
Prof Low Poh Sim
Collaborator: Dr Yee Woon Chee (NNI)

Th2 cytokines in minimal change nephrotic syndrome - in vivo and in vitro study of the underlying molecular mechanisms

Principal Investigator: Prof Yap Hui Kim
Co-Principal Investigator: Dr Wei Chang Li
Collaborators: Assoc Prof Caroline Lee,
Dr Lu Jin Hua (NUMI, NUS),
Prof Stanley C Jordan (UCLA),
Dr Gilbert SC Chiang (Pathology, SGH)

The influence of fever on early life wheeze: creating a predictive index for identifying wheezy infants at risk of persistent wheeze and likely asthma at preschool age

Principal Investigator: Prof Van Bever Hugo P S
Co-Principal Investigators: Assoc Prof Daniel Goh,
Dr Chng Seo Yi,
Ms Tan Teng Nging

A longitudinal study on infectious risks and immune response to vaccination in Singapore infants enrolled in a placebo-controlled, randomised study of probiotic supplementation

Principal Investigator: Dr Marion Aw
Co-Principal Investigator: Dr Lynette Shek
Collaborator: Dr Steven Ng Chin Yuen (NUH)

A study on the paediatric prevalence of adverse drug reaction and drug allergy in Singapore

Principal Investigator: Prof Van Bever Hugo P S
Co-Principal Investigators: Dr Lynette Shek,
Ms Tan Teng Nging
Collaborator: Adj Assoc Prof Lee Bee Wah



Research staff maintaining fish system in the zebrafish core facility.

Genetics of pediatric renal diseases

Principal Investigator: Prof Yap Hui Kim
Collaborators: Dr Goh Li Meng Denise,
Assoc Prof Samuel Chong SC,
Dr Tan Puay Hoon (Pathology, SGH),
Dr Gilbert Chiang (Pathology, SGH),
Dr Ng Kar Hui (Paeds, NUH)

Homologous recombinant gene correction of dystrophin mutations using a novel fusion protein nuclear transfer system

Principal Investigator: Dr Yee Woon Chee
Co-Principal Investigator: Dr Lai Poh San

Development of antisense oligonucleotides for molecular therapy of duchenne muscular dystrophy

Principal Investigator: Dr Dwi Pramono
Co-Principal Investigator: Dr Lai Poh San

Programme for molecular genetics in neuromuscular diseases

Principal Investigator: Dr Yee Woon Chee
Co-Principal Investigator: Dr Lai Poh San

Functional studies of mutant melanocortin receptors due to novel mutations of the melanocortin-3 receptor gene and melanocortin-4 receptor gene causing obesity in humans

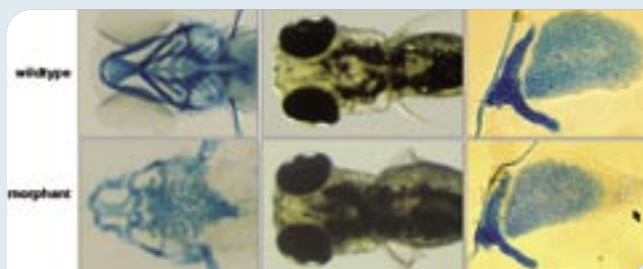
Principal Investigator: Dr Lee Yung Seng
Collaborator: Assoc Prof Loke Kah Yin

Characterization of the mechanism of albumin premeability in childhood minimal change nephrotic syndrome

Principal Investigator: Prof Yap Hui Kim
Collaborator: Assoc Prof Harry Yu

Characterization of molecular events involved in the immunosuppressive action of px-3.102 - a bioactive extract from a Chinese herb

Principal Investigator: Prof Yap Hui Kim
Collaborators: Assoc Prof Lee Guat Lay Caroline,
Assoc Prof Ang Siau Gek,
Assoc Prof Lai Yee Hing

DEPARTMENT OF
PAEDIATRICS

Zebrafish sec23a morphants with defects analogous to the human cranio-lenticulo-sutural-dysplasia syndrome phenotype. Malformation/dysgenesis of the head cartilages (left), and kinked pectoral fins (middle) as a result of a larger non-cartilaginous fin segment at the distal edge (right, arrow).

Prevalence of allergic symptoms and atopy in 2 diverse populations in south East Asia, and a comparative evaluation of the influence of environmental microbial factors

Principal Investigator: Prof Van Bever Hugo P S
Collaborators: Dr Dawn Lim,
Adj AP Lee Bee Wah,
Prof Chua Kaw Yan,
Ms Tan Teng Nging (Paediatrics),
Prof Ho Bow (Microbiology),
Prof Malkeet Singh (Microbiology),
Prof Karnen Garna Baratwidjaja
(FOM, Univ Indonesia)

Characterization and evaluation of the functional significance of the unregulated dec-1 gene in children with steroid-responsive nephrotic syndrome (SRNS) in relapse

Principal Investigator: Prof Yap Hui Kim
Collaborators: Dr Wei Chang Li,
Assoc Prof Lee Guat Lay Caroline,
Dr Gong Wei Kin

Molecular basis of nonsense-mediated mRNA decay (NMD) in beta-thalassemia

Principal Investigator: Assoc Prof Chong Siong-Chuan Samuel
Collaborators: Dr Denise Goh,
Assoc Prof Caroline G Lee

Development of prophylactic and therapeutic vaccines for asthma and allergic diseases

Principal Investigator: Prof Chua Kaw Yan
Collaborators: Adj Assoc Prof Lee Bee Wah,
Dr Rane Lim,
Dr L Shek,
Assoc Prof Daniel Goh,
Dr Cheong Nge,
Dr Denise Goh,
Dr Liew Lip Nyin,
Dr Dawn Lim,
Dr Thomas August (John Hopkins),
Dr Sven Pettersson
(Karolinska Inst. Sweden),
Dr Bengt Bjorksten
(Karolinska Inst. Sweden),
Assoc Prof Lee Yuan Kuan
(Microbiology, NUS),
Dr Lu Jinhua (NUMI, NUS),
Dr Wang De Yun (ENT, NUS)

Hepatitis B immune status in children - a decade after mass vaccination

Principal Investigator: Prof Quak Seng Hock
Collaborators: Dr Lai Poh San,
Dr Marion Aw,
Dr Andrea Yeo

Genomic and in situ expression analyses of the zebrafish homologs of twist, the gene mutated in saethre-chotzen syndrome

Principal Investigator: Assoc Prof Chong Siong-Chuan Samuel
Collaborators: Dr Ethylin W Jabs (John Hopkins Univ),
Dr Akihiko Koga
(Biology, Nagoya Univ, Japan)

Establishment and validation of a preimplantation genetic diagnosis program in Singapore

Principal Investigator: Assoc Prof Chong Siong-Chuan Samuel
Collaborator: Dr Christine Yap (O&G, SGH)

Continuation group grant for POG(S) database development, pharmacogenomics in childhood Acute Lymphoblastic Leukaemia (ALL), and collaborative study on treatment protocols for AML

Principal Investigator: Dr Yeoh Eng Juh Allen
Collaborators: Assoc Prof Quah Thuan Chong,
Dr Tan Ah Moh (Paeds, KKH),
Dr Chan Mei Yoke (Paeds, KKH),
Dr Chui Chan Hon (Paeds, KKH)

The role of interleukin 13 in the pathogenesis of minimal change nephrotic syndrome and its underlying molecular mechanisms

Principal Investigator: Dr Wei Changli
Co-Principal Investigator: Prof Yap Hui Kim
Collaborators: Assoc Prof Lu Jinhua (NUMI, NUS),
Assoc Prof Caroline Lee,
Prof Stanley C Jordan (UCLA),
Dr Tan Puay Hoon (Pathology, SGH),
Dr Gilbert SC Chiang (Pathology, SGH)

International genetic epidemiology oral clefts

Principal Investigator: Assoc Prof Samuel Chong
Collaborators: Prof Lim Thiam Chye,
Dr Denise Goh Li Meng,
Assoc Prof Kelvin WC Foong
(Dentistry, NUS)

Application of aminoglycosides in inducing mutation read-throughs for molecular therapy in duchenne muscular dystrophy patients

Principal Investigator: Dr Lai Poh San
Co-Principal Investigators: Prof Low Poh Sim,
Dr Stacey Tay KH

Automated mutations/snp lab-on-a-chip devices for molecular diagnostics and genomic research

Principal Investigator: Assoc Prof Samuel Chong
Co-Principal Investigators: Assoc Prof Caroline Lee,
Dr Liu Wen Tso (Civil Engineering, NUS),
Dr Dieter Trau
(Chemical & Biomolecular, NUS)
Collaborator: Dr Feng Han Hua
(Institute of Microelectronics)

DEPARTMENT OF PAEDIATRICS

Evaluation of the effect of a low density gas (helium) in the alleviation of upper airway obstruction in children with obstructive sleep apnea syndrome

Principal Investigator: Assoc Prof Goh Yam Thiam Daniel
Co-Principal Investigators: Dr Chng Seo Yi (Paeds, NUH),
Dr Ng Kar Hui (Paeds, NUH)
Collaborator: Prof Carole L Marcus
(Ped Pulmonology,
Children's Hosp of Philadelphia)

Evaluation of allergy related genes - exploiting genetic differences in closely related substrains of balb/c mice with diverse responses to allergens

Principal Investigator: Dr Denise Goh Li Meng
Co-Principal Investigator: Prof Chua Kaw Yan

Cord blood mononuclear cell responses to probiotics as a predictor for and potential therapeutic tool in allergic diseases

Principal Investigator: Dr Lynette Shek Pei-Chi

Developing new molecular signatures for disease prognostication for childhood acute lymphoblastic leukemia using gene expression profiling

Principal Investigator: Dr Yeoh Eng Juh Allen

Genetics of cardiovascular disorders

Principal Investigator: Dr Heng Chew Kiat

A 2 year prospective study of stool microbiota in 2 diverse cohorts of Asian (Singaporean and Indonesian) newborns its influence on allergy development

Principal Investigator: Adj Assoc Prof Lee Bee Wah
Collaborators: Prof Chua Kaw Yan,
Dr Marion Aw,
Prof YatiSoenarto
(Univ of Gadjah Mada),
Dr Sumadion (Univ of Gadjah Mada),
Prof Hugo PS Van Bever,
Dr Dawn Lim Li Chern,
Dr Lynette Shek Pei-Chi

Lactobacilli-based oral vaccine: a model to study the induction and role of regulatory cells in the ablation of allergic diseases

Principal Investigator: Assoc Prof Chua Kaw Yan

INTERNATIONAL PUBLICATIONS

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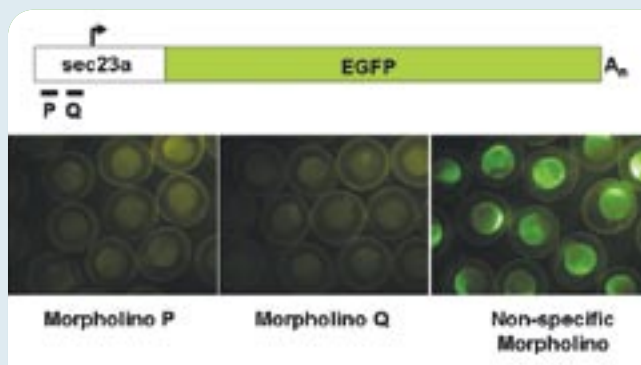
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Effective translational inhibition of sec23a by antisense morpholinos. Translation of an in-frame fusion sec23a-EGFP transcript in zebrafish embryos is effectively blocked by morpholino P or Q.

STAFF PROFILE

Associate Professor & Head:
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Quak Seng Hock
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Low Poh Sim

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Hugo PS van Bever
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Quek Swee Chye
Daniel Goh Yam Thiam
Chua Kaw Yan

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Research Associate Professor:

Adjunct Associate Professors:

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Ng Kar Hui
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Stacey Tay Kiat Hong
Lynette Shek Pei Chi
Allen Yeoh Eng Juh
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Assistant Professors:

Senior Research Fellows:

Research Fellows:

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Heng Chew Kiat
Chen Hui
Cheong Nge
Huang Chiung Hui
Liew Lip Nyin
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Tan Teng Nging
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Wang Zihua
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Yi Fong Cheng

DEPARTMENT OF PAEDIATRICS

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	Koh Chor Hui, Vivien
	Lai Kin Wai, Danny
	Li Zhi Mei
	Lye Hui Jen
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	Soh Gim Hooi
	Tan Li Kiang
	Wang Jingbo
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	Yeo Hui Joo, Sharon
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DEPARTMENT OF PATHOLOGY

INTRODUCTION

Academic Pathology remains very much at the cross-roads between basic science and the clinical practice. We are, therefore, at the centre of the translational research endeavours that our institution in particular, and the national biomedical research initiative as a whole, is thoroughly pursuing.

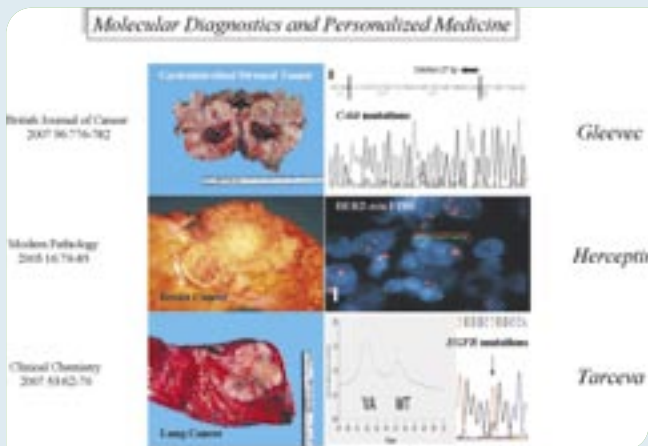
To continue with this challenge, the Department of Pathology has kept pace with this evolution, completing the setting up of the necessary infrastructure to do so. Our department, through its own laboratories or those developed in collaboration with other institutions, allows a broad range of biological interrogations of cells and tissues, as well as facilitates the validation on biomarkers and the transfer of technology and knowledge into the clinical setting. Again, this highlights the unique strategic situation of academic Pathology in Translational and Clinical Molecular Research.

The Department of Pathology is keeping an output of more than 60 published articles per year. In 2006, however, there has been a considerable shift in the specific weight of these publications. Our department has led or taken part in publications in journals such as *Nature Genetics*, *Blood*, *Cancer Research*, *Journal of Immunology*, *Bioinformatics*, *Oncogene*, *Clinical Pharmacology and Therapeutics*, *Antiviral Therapy*, *Pharmacogenetics*, *Leukemia*, and *Carcinogenesis*, apart from a significant publication body in the main Pathology and

Cytology journals. This outstanding productivity highlights, once again, a dual role in Pathology-based research and research in the molecular basis of diseases.

Part of this success is epitomised in our grant funding. With more than 45 grants and an ongoing amount of grant money of over \$5 million, our department is in a position of surpassing our previous research output, and maintaining long-standing research operations such as the Special Histology Laboratory, the Experimental Pathology Unit and the Molecular Diagnosis Centre. Last year saw the emergence of the Diagnostic Molecular Oncology Centre, a joint effort of our department with the Oncology Research Institute.

Due to the encompassing nature of pathology, the research interests and activities of our faculty cover a broad range that includes basic science, translational research, and clinical research, deriving benefit from synergistic opportunities related to intra-disciplinary, multi-disciplinary, inter-disciplinary and trans-disciplinary interactions. Many of our staff actively collaborate with fellow researchers at the NUS Oncology Research Institute (indeed, some hold joint appointments with this institute), with colleagues in the Medical, Science and Engineering faculties, as well as with principal investigators at the A-STAR research institutes at the Biopolis research hub, with special focus on the biology, genetics and immunology of cancer, and validation of new molecular markers in cancer diagnostics and therapy. Special links with institutions from the “other cluster”,

DEPARTMENT OF
PATHOLOGY

Molecular Diagnostics in the Era of Personalized Medicine.

such as the National Cancer Centre, the Singapore Eye Research Institute, and the Singapore General Hospital, have led to the publication of high-impact factor articles and further strengthened the “cross-collaboration” in Singapore. In recent years, the research in tumour biology, the traditional strength of our department, has evolved to include analysis of neoplasia at all levels of involvement: molecular, nuclear, cell membrane, intracellular, and matrix, and the identification and analysis of neoplastic events and the application of novel therapies.

In essence, we understand that we have a double mission as far as research is concerned, namely a) to develop our own, pathology based-research; and b) to establish the necessary operational frameworks to allow others to link into clinical materials and clinical information, in order to facilitate the bridge between basic and translational research. In this regard, 2006 has been a good year in the pursuit of these endeavours.

PROJECT DESCRIPTION
Grants Awarded in 2006

Role of lipid mediators, leukotriene B4 and lipoxin A4, as inflammatory and immune modulators in Hodgkin lymphoma

Principal Investigator: Dr Lim Yaw Chyn
Collaborators: Assoc Prof Chong Siew Meng (UAE University),
Assoc Prof Tan Kim Siang Luke

Pathological features, molecular characteristics and their prognostic implications in gastrointestinal endocrine cell tumors

Principal Investigator: Assoc Prof M Priyanthi Kumarasinghe
Co-Principal Investigator: Dr Wang Shi
Collaborators: Assoc Prof Manuel Salto-Tellez,
Dr Richie Soong

Expansion of the molecular pathology/biomarker initiative in Singapore

Principal Investigator: Assoc Prof Manuel Salto-Tellez
Co-Principal Investigators: Assoc Prof Teh Ming,
Dr Richie Soong,
Dr Thomas C Putti,
Assoc Prof M Priyanthi Kumarasinghe,
Dr Ng Sok Bian (KKCWH),
Dr Lim-Tan Soo Kim (KKCWH),
Dr Chew Sung Hock (KKCWH),
Dr Hwang Wei Sek (KKCWH),
Dr Victor Lee Kwan Min (KKCWH),
Dr Robert E Hewitt,
Prof Chia Kee Seng

A tissue microarray-based sarcoma study: molecular and immunochemical profiling of these tumors

Principal Investigator: Dr Nga Min En
Co-Principal Investigator: Assoc Prof Manuel Salto-Tellez

Immunohistochemical study of novel biomarkers in prostate and bladder carcinomas

Principal Investigator: Assoc Prof Teh Ming
Co-Principal Investigators: Assoc Prof Manuel Salto-Tellez,
Dr Thomas P Thamboo

Evidence of association of EBV, CMV and HPV with breast cancer

Principal Investigator: Dr Thomas C Putti
Collaborators: Assoc Prof Evelyn S C Koay,
Dr Keith Ong

The role of RUNX3 in columnar cell lesions of breast

Principal Investigator: Dr Thomas C Putti
Collaborators: Dr Lau Quek Choon,
Dr Kosei Ito,
Assoc Prof Manuel Salto-Tellez

Methylated genes as predictive markers of recurrent ductal carcinoma in situ

Principal Investigator: Dr Thomas C Putti
Collaborators: Dr Lau Quek Choon,
Assoc Prof Manuel Salto-Tellez,
Prof Saraswati Sukumar

Advanced test order management system

Principal Investigator: Assoc Prof Sunil K Sethi
Co-Principal Investigators: Dr Linus Tham (NHG),
Assoc Prof Danny Poo

Keratoacanthomas and squamous cell carcinomas: elucidation of biomarker immunoexpression and identification of novel molecular signatures by proteomics

Principal Investigator: Dr Tan Kong Bing
Co-Principal Investigator: Prof Lee Yoke Sun
Collaborators: Dr Zhang Daohai,
Assoc Prof Evelyn S C Koay

DEPARTMENT OF PATHOLOGY

Individual-based modelling on the spread of infectious diseases in Singapore

Principal Investigator: Prof Wong Lim Soon
Co-Principal Investigators: Dr Fu Xiuju (IHPC),
Dr Goh Liping (IHPC),
Dr Harold Soh (IHPC),
Dr Stefan M A (MOH),
Dr Xiao Gaoxi (NTU),
Dr Cheng Tee Hiang (NTU)

Development of rapid molecular fluorescence excitation-emission spectroscopy system for non-invasive, in vivo detection of precancerous and cancerous tissue in the cervix

Principal Investigator: Dr Huang Zhiwei
Co-Principal Investigators: Assoc Prof A Ilancheran,
Assoc Prof Teh Ming,
Dr Jeffrey Low (NUH)

Characterization of liver sinusoid endothelial cell capillarization during hepatocellular carcinoma development

Principal Investigator: Assoc Prof Ge Ruowen
Co-Principal Investigator: Assoc Prof Teh Ming

The role of leukotriene B4 in malignant lymphoma growth and survival

Principal Investigator: Dr Lim Yaw Chyn
Collaborators: Dr Leonard Tan (SGH),
Assoc Prof Chong Siew Meng
(UAE University)

Mechanistic study of the stimulatory and adjuvant effects of a fungal immunomodulatory protein in tumor immunotherapy.

Principal Investigator: Prof Chua Kaw Yan
Collaborators: Dr Lim Yaw Chyn,
Dr Seow See Voon,
Dr Kuo I-Chun

On-going Projects

HER-2/*neu*-mediated phosphoproteomic profiles in breast cancer cell lines: identification of phospho- and/or dephosphorylated proteins by switching on/off the HER-2/*neu* signalling pathway

Principal Investigator: Dr Zhang Daohai
Collaborator: Assoc Prof Evelyn S C Koay

Proteomics analysis of HER-2/*neu*-linked differentially expressed proteins and phosphorylation patterns in the tumour microenvironment

Principal Investigator: Assoc Prof Evelyn S C Koay
Co-Principal Investigator: Dr Zhang Daohai
Collaborators: Dr Thomas C Putti,
Prof Hew Choy Leong,
Assoc Prof Chang Chan Fong

Novel receptor-ligand interactions that mediate tumour cell adhesion to endothelial cell from different organ sites

Principal Investigator: Dr Lim Yaw Chyn
Co-Principal Investigator: Assoc Prof Teh Ming

Development of a cell tracking programme for the analysis of cell-cell (cell-protein) interactions under defined flow conditions

Principal Investigator: Dr Lim Yaw Chyn
Collaborators: Assoc Prof Tay Cho Jui,
Assoc Prof Quan Chenggen

Molecular Information Arrays (MIA) – High-throughput constructions of annotated frozen and paraffin tissue microarrays, linked to clinico-pathological relational databases, to support clinical translational and epidemiologic trials, and to validate new molecular markers

Principal Investigator: Assoc Prof Manuel Salto-Tellez
Co-Principal Investigators: Assoc Prof Teh Ming,
Dr Richie Soong,
Dr Thomas C Putti,
Dr Tan Kong Bing,
Dr Robert E Hewitt

Immunoperoxidase study of the antigenic profile of the esophageal mucosa in Barrett's esophagitis

Principal Investigator: Dr Nga Min En
Co-Principal Investigator: Assoc Prof Teh Ming
Collaborator: Dr Liu Qiang

Molecular determinants of acute renal allograft rejection

Principal Investigator: Dr Thomas P Thamboo
Co-Principal Investigators: Assoc Prof Teh Ming,
Dr Richie Soong,
Dr Lim Yaw Chyn

Investigating the genomics of new strains of virulent community-acquired *Staphylococcus aureus* isolated in Singapore

Principal Investigator: Dr Raymond Lin (NUH)
Co-Principal Investigator: Assoc Prof Evelyn S C Koay
Collaborators: Dr Koh T H (SGH),
Dr Hsu L Y (SGH),
Dr Ooi Eng Eong (DSO),
Dr Nancy Tee (KKCWH)

Characterizing plasmid-mediated quinolone resistance associated with the *qnr* gene in bacteria as a new resistance threat in Singapore

Principal Investigator: Dr Raymond Lin (NUH)
Co-Principal Investigator: Assoc Prof Evelyn S C Koay
Collaborator: Dr Jeanette Teo (NUH)

Whole genome sequencing in influenza viruses

Principal Investigator: Dr Raymond Lin (NUH)
Co-Principal Investigator: Assoc Prof Evelyn S C Koay
Collaborator: Dr Jeanette Teo (NUH)

Sequencing of novel HLA Class 1 alleles in the local Singaporean population

Principal Investigator: Dr Mickey Koh (CTM)
Co-Principal Investigator: Assoc Prof Evelyn S C Koay
Collaborators: Ms Phang Chew Yen (CTM),
Dr Diana Teo (CTM)

DEPARTMENT OF
PATHOLOGY**Predictive significance of 5-fluorouracil enzymes in Asians and Caucasians**

Principal Investigator: Dr Richie Soong
 Co-Principal Investigator: Assoc Prof Manuel Salto-Tellez
 Collaborators: Assoc Prof Barry Iacopetta (UWA),
 Dr Ross Soo (NUH)

Clinical relevance of thymidylate synthase gene variants

Principal Investigator: Dr Richie Soong
 Co-Principal Investigators: Dr Liu Yanqun (SGH),
 Dr Ross Soo (NUH)
 Collaborators: Assoc Prof Manuel Salto-Tellez,
 Dr Nilesh Shah,
 Dr Goh Boon Cher (NUH),
 Assoc Prof Barry Iacopetta (UWA),
 Dr Ho Kok Sun (SGH)

Infrastructure for developing gastrointestinal cancer prognostic and predictive markers

Principal Investigator: Dr Richie Soong
 Co-Principal Investigators: Assoc Prof Manuel Salto-Tellez,
 Dr Ross Soo (NUH),
 Dr Liu Yanqun (SGH),
 Dr Simon Ong (NCC),
 Dr Yap Wai Ming (SGH)

Pattern spaces: theory, algorithms and applications

Principal Investigator: Prof Wong Lim Soon

A personalized and adaptive literature curation system for biomedical sciences

Principal Investigator: Dr Patrick Tan (NCCS)
 Co-Principal Investigators: Dr Lim Yun Ping (BII),
 Dr Martti Tammi,
 Assoc Prof Tan Tin Wee,
 Prof Wong Lim Soon,
 Dr Ng See Kiong (I²R),
 Dr Su Jian (I²R)

A study of genes whose expressions are co-regulated with that of AMPA receptors of excitatory synapses

Principal Investigator: Dr Tang Bor Luen
 Co-Principal Investigators: Prof Wong Lim Soon,
 Dr Allen Chong

Development of computerised registry systems

Principal Investigators: Dr Robert E Hewitt,
 Mr Tan Kee Peck (NHG)
 Collaborators: Prof John Wong,
 Prof Yong Eu Leong,
 Prof Chia Kee Seng,
 Dr Michael Back (NUH),
 Dr Jimmy So (NUH),
 Dr Robert Lim Seng Cheong (NUH),
 Dr Tchoyson Lim (NNI),
 Dr Ng Wai Hoe (NNI),
 Dr Denis Cheong (TTSH),
 Dr James Tan (TTSH)

Establishing PI-centred cancer repositories and associated bioinformatics systems

Principal Investigator: Dr Robert E Hewitt
 Collaborators: Prof Yong Eu Leong,
 Assoc Prof Teh Ming,
 Assoc Prof Sunil Sethi,
 Assoc Prof Manuel Salto-Tellez,
 Dr Thomas Putti

The role of RUNX-3 as a tumour suppressor in human colorectal cancer

Principal Investigator: Dr Robert E Hewitt
 Co-Principal Investigator: Dr Kosei Ito
 Collaborators: Dr Masafumi Inoue (IMCB),
 Assoc Prof Teh Ming

Involvement of the CC3 metastasis suppressor gene in colorectal and breast cancer progression

Principal Investigator: Dr Robert E Hewitt
 Collaborators: Dr Masafumi Inoue (IMCB),
 Dr Lau Quek Choon,
 Dr Zhang Daohai,
 Assoc Prof Evelyn S C Koay

Tissue Repository Programme

Principal Investigator: Dr Robert E Hewitt

Phase II study of docetaxel combined with ketoconazole in the first-line treatment of locally advanced or metastatic breast cancer patients with measurable primary breast tumours

Principal Investigator: Dr Lee Soo Chin (NUH)
 Co-Principal Investigators: Dr Goh Boon Cher (NUH),
 Dr Lim Siew Eng (NUH),
 Dr Philip Iau,
 Dr Benjamin Mow (NUH),
 Prof John Wong,
 Dr Thomas C Putti,
 Dr Tan S H (NSC),
 Dr Chin T M (NUH),
 Dr Wong C I (NUH),
 Dr B Chuah (NUH)

Cyclooxygenase-2 expression in nasopharyngeal carcinoma: immunohistochemical findings and potential implications

Principal Investigator: Dr Tan Kong Bing
 Collaborator: Dr Thomas C Putti

Response of leukemia cells to drug (Genistein) treatment

Principal Investigators: Assoc Prof Chen Chien-Shing,
 Dr Zhang Daohai
 Collaborator: Assoc Prof Evelyn S C Koay

Preliminary studies to test the clinical relevance of the metastasis-suppressing gene in the progression of colorectal and breast cancer towards a metastatic phenotype

Principal Investigator: Dr Robert E Hewitt
 Collaborator: Dr Emma Shtivelman
 (California Pacific Medical Center
 Research Institute)

DEPARTMENT OF PATHOLOGY

Maintenance of telomere-chromosome integrity by DNA repair/recombination and DNA damage signalling factors in mammalian cells: Role of breast cancer genes

Principal Investigator: Dr Prakash Hande
Co-Principal Investigator: Dr Thomas C Putti

Technetium-99m sestamibi scintimammography for the prediction of multidrug resistance expression and neoadjuvant chemotherapy response in locally advanced/metastatic breast cancer: correlation with dynamic MRI, gene expression and genotyping studies

Principal Investigator: Dr Yvonne Ho (NUH)
Co-Principal Investigators: Assoc Prof Wang S C,
Dr Lee S C (NUH),
Dr Philip Iau,
Dr Thomas C Putti

Prevalence of the founder *BRCA1* mutation C2845insA in Singapore Malay breast and ovarian patients unselected for family history

Principal Investigator: Dr Philip Iau
Co-Principal Investigator: Dr Thomas C Putti

Physiopathological animal models of disease

Principal Investigator: Assoc Prof M Salto-Tellez
Collaborator: Dr Lim Sai-Kiang

Knowledge discovery from biological & clinical data

Principal Investigators: Dr Wynne Hsu,
Prof Wong Lim Soon
Co-Principal Investigators: Dr Lee Mong Li,
Mr Ken Sung,
Mr Ng See Kiong (I²R),
Mr Li Jinyan (I²R),
Dr Vladimir Brusic (I²R),
Dr Vladimir Bajic (I²R)

Disease-related protein database of colorectal cancer: Identification of tumour-related proteins by proteomic studies

Principal Investigators: Dr Zhang Daohai,
Assoc Prof Evelyn S C Koay
Collaborator: Assoc Prof Teh Ming

Biomarkers that regulate metastatic potential in colorectal cancer cells: the role and regulation of *CXCR4* and *beta1* integrins

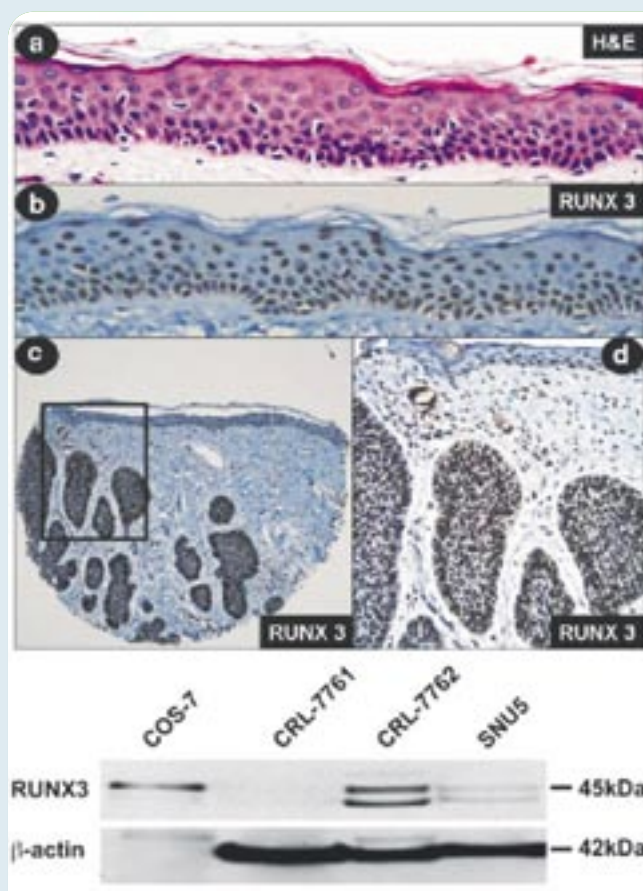
Principal Investigator: Assoc Prof Hooi Shing Chuan
Co-Principal Investigators: Dr Lim Yaw Chyn,
Dr Lim Hsiu Kim Lina

Effects of nanoparticles on the functional integrity of endothelial cells

Principal Investigator: Dr Yung Lin Yue, Lanry
Co-Principal Investigator: Dr Lim Yaw Chyn

Mechanisms of basophil activation and recruitment during allergic inflammation and anaphylaxis

Principal Investigator: Dr Lim Hsiu Kim Lina
Collaborator: Dr Lim Yaw Chyn



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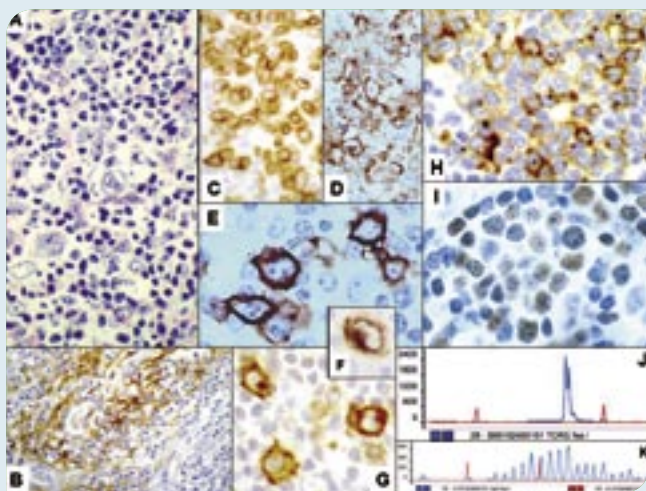
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DEPARTMENT OF
PATHOLOGY

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STAFF PROFILE

Associate Professor & Head:
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Aileen Wee
Alexander R Chang
Wong Lim Soon

Adjunct Professor:
Professorial Fellows:

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K Shanmugaratnam
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Lee Yoke Sun

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Sunil K Sethi
Marian Priyanthi Kumarasinghe
Manuel Salto-Tellez

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Assistant Professors:

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Thomas C Putti
Robert E Hewitt

Lim Yaw Chyn
Richie Soong
Tan Kong Bing
Thomas P Thamboo
Nga Min En

Adjunct Assistant Professor:
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Lim Joe Thuan
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DEPARTMENT OF PATHOLOGY

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DEPARTMENT OF PHARMACOLOGY



INTRODUCTION

The Department plays a leading role in both basic and clinical pharmacology research. Three major areas of research form the focus of the research efforts of the Department of Pharmacology. These include Pharmacogenetics and Pharmacokinetics, Neuropharmacology, Immunopharmacology and Cardiovascular Pharmacology. Members of the Department work together in these general areas and in close collaboration with staff in other Departments, elsewhere in Singapore, and also overseas. The longer term strategic aim of the research undertaken is to elevate the quality of research output, increase the emphasis on translational research and maintain a successful and competitive research focus.

Specific research topics of interest in the current year include, (i) the effect of genetic variables in determining variability to drugs in cardiovascular disease, (ii) optimization of anti-cancer drug therapy from a pharmacokinetics perspective, (iii) gene and protein expression and involvement of local hormones, hormones and neurotransmitters in inflammation, (iv) neuroprotective drugs and their clinical evaluation, (v) pharmacological mediators of anxiety and the response to psychoactive drugs, (vi) evaluation of novel derivatives of des-aspartate angiotensin I in cardiovascular and metabolic disease states, (vii) therapeutic uses of agents derived from natural products, (viii) physiological and pathophysiological significance of hydrogen sulphide in physiological responses of

the cardiovascular system and in vascular and heart disease, (ix) toxicological effects of drugs on liver function and (x) regulation of glutamate receptor subunit function and expression.

PROJECT DESCRIPTION

Grants Awarded in 2006

Anti-diabetic actions of angiotensin IV

Principal Investigator: Assoc Prof Sim Meng Kwoon

Anti-rhinoviral action of des-aspartate-angiotensin I

Principal Investigator: Assoc Prof Sim Meng Kwoon

Co-Principal Investigator: Assoc Prof Vincent Chow Tak Kwong

Interaction of amyloid precursor protein (APP) with sodium channels

Principal Investigator: Dr Gavin Dawe

Investigation of noradrenergic modulation of long-term potentiation of hippocampo-prefrontal cortical projections

Principal Investigator: Dr Gavin Dawe

Negative modulation of beta adrenergic receptor function by hydrogen sulphide: A novel approach to prevent arrhythmias

Principal Investigator: Dr Bian Jinsong

DEPARTMENT OF PHARMACOLOGY

Rescue from liver failure by novel mitochondria-targeting drugs

Principal Investigator: Assoc Prof U A Boelsterli

Signaling mechanism for the vasorelaxant effect of hydrogen sulphide

Principal Investigator: Dr Bian Jinsong

Studies to identify the bioactive fraction from crude ethanolic extract of *Solanum nigrum* and evaluate its effects in nude mice implanted with MDA-MB-231 human breast cancer

Principal Investigator: Assoc Prof Benny Tan K H

The role of hydrogen sulphide in hyperhomocysteinaemia: Implications for cardiovascular disease

Principal Investigator: Prof Philip Moore

Therapeutic effects of glycogen synthase kinase - 3 β inhibitor in mouse models of allergic airway inflammation

Principal Investigator: Assoc Prof Fred Wong

Therapeutic effects of respirable antisense oligonucleotides in a mouse asthma model of allergic airway inflammation

Principal Investigator: Assoc Prof Fred Wong

Co-Principal Investigator: Dr Leung Pui Lam Bernard

On-going Projects

Acute pancreatitis and associated lung injury: The role of nitric oxide as a potential therapeutic target

Principal Investigator: Assoc Prof Madhav Bhatia

Alpha_{1A}-adrenergic receptor stimulation regulates hERG potassium channel function

Principal Investigator: Dr Bian Jinsong

An investigation of the cardiovascular significance of hydrogen sulphide: Role in the vascular complications of diabetes mellitus

Principal Investigator: Prof Philip Moore

Androgen regulates hERG/IKr expression and function: why women are at higher risk than men for development arrhythmias

Principal Investigator: Dr Bian Jinsong

Antiplatelet and anticoagulant activities in plants commonly found in Singapore

Co-Principal Investigator: Assoc Prof Tan Chay Hoon

Apoptosis of pancreatic acinar cells and acute pancreatitis

Principal Investigator: Assoc Prof Madhav Bhatia

Blood-derived proteases and brain damage

Principal Investigator: Assoc Prof Peter Wong

Co-Principal Investigator: Dr Low Chian Ming

Breakdown of acetylcholine-induced potentiation of nMDA receptor function as a putative mechanism of glutamatergic hypofunction and cognitive decline in

Principal Investigator: Assoc Prof Peter Wong

Can traditional yin tonic Chinese herbs improve oxidant status in diabetic animals treated with Western drugs?

Principal Investigator: Assoc Prof Benny Tan KH



Studying in vitro pharmacology using cultured cells

Contribution of drug transporters and cyp450 pharmacogenetics to statin myotoxicity

Principal Investigator: Prof Edmund Lee.

Cross talk between two neuromodulators: the anxiogenic action of cck requires crf1 receptor

Principal Investigator: Dr Zhu Yi Zhun

Functional and genetic diversity in the concentrative nucleoside transporter in Singapore population and herbal interaction

Principal Investigator: Prof Edmund Lee

Functional characterization of ion channel and calcium-handling protein genetic variants in sudden death syndrome

Principal Investigator: Prof Edmund Lee

Harnessing the potential of rodents as biosensors for the detection of explosives and chemical agents (dirp 2004)

Principal Investigator: Dr Gavin Dawe

Hydrogen sulfide (H₂S) regulation of calcium homeostasis in the brain cells - direct evidence of h₂s as a new neuromodulator

Principal Investigator: Dr Bian Jinsong

Hydrogen sulphide: A novel mediator of inflammation

Principal Investigator: Assoc Prof M Bhatia

Identifying genetic abnormalities in mitochondria as determinants of susceptibility to drug-induced idiosyncratic liver injury

Principal Investigator: Assoc Prof U Boelsterli

Investigating the neurotoxicity of cysteine in ischemia using in vivo animal models of stroke and in vitro primary cell cultures

Principal Investigator: Assoc Prof Peter Wong

Investigation into the mechanism of pancreatoprotective and hypoglycaemic effects of *Andrographis paniculata* and its diterpenoids in diabetic animals

Principal Investigator: Assoc Prof Benny Tan KH

DEPARTMENT OF PHARMACOLOGY



Classical Pharmacological experimental technique using isolated tissues/ organs

Is hydrogen sulfide cardioprotective or destructive in ischemic heart disease?

Principal Investigator: Dr Zhu Yi Zhun

Molecular mechanisms of the CCK₂ receptor in the regulation of fear and anxiety: Generation & analysis of an inducible cck₂ gene deletion in mouse

Principal Investigator: Assoc Prof P Wong

Nitric oxide is an endogenous inhibitor of proteasome - significance for inflammatory and neurodegenerative disease

Principal Investigator: Prof Philip Moore

Pathogenesis of acute pancreatitis and associated lung injury: the role of neurogenic inflammation

Principal Investigator: Assoc Prof Madhav Bhatia

Protein structure, autoantibodies and stroke

Principal Investigator: Dr Low Chian Ming

Proteomics of airway inflammation: Identification of pathogenetic molecules and therapeutic targets

Principal Investigator: Assoc Prof Fred Wong

Regulation of dopamine- dependant intracellular trafficking of N-methyl-D-aspartate receptor subunits and their co-localization with D₁ receptor

Principal Investigator: Dr Low Chian Ming

Research of East Asia Psychotropic Drug Prescription (REAP)

Principal Investigator: Assoc Prof Tan Chay Hoon

Serotonin receptor subtypes expressed by neural progenitor cells and the molecular pharmacology of anti- depressant-induced call

Principal Investigator: Dr Gavin Dawe

Structural & pharmacological studies on NMDA receptor ligand binding domains

Principal Investigator: Dr Low Chian Ming

Substance P as a mediator of inflammation in sepsis

Principal Investigator: Assoc Prof Madhav Bhatia

The effects of ethnicity and pept2 transporter genetics on single oral dose pharmacokinetics of cephalexin and ceftriaxone

Principal Investigator: Prof Edmund Lee

The role of hydrogen sulphide in inflammation

Principal Investigator: Prof Philip Moore

Enhancing professionalism, skills & competency of examiners

Principal Investigator: Assoc Prof Tan Chay Hoon
Co-Principal Investigators: Assoc Prof Koh Dow Rhoon,
Prof Matthew Gwee

For student academic factors correlating with performance as an intern and doctor

Principal Investigator: Assoc Prof Tan Chay Hoon
Co-Principal Investigators: Dr Jeremy Lim,
Assoc Prof Koh Dow Rhoon

Gerontology Research Programme: Biological, clinical, psychosocial and behavioural predictors of health status in prospectively followed-up cohorts of elderly persons

Principal Investigators: Assoc Prof Ng Tze Pin,
Prof Kua Ee Heok
Co-Principal Investigator: Assoc Prof Tan Chay Hoon

Research of East Asia Psychotropic Drug Prescription (REAP)

Principal Investigator: Assoc Prof Tan Chay Hoon

INTERNATIONAL PUBLICATIONS

Ang ET, Dawe GS, Wong PTH, Moomhala S, Ng YK

Alterations in spatial learning and memory after forced exercise. Brain Res 1113(1):186-93.

Anuar F, Whiteman M, Bhatia M, Moore PK

Flurbiprofen and its nitric oxide-releasing derivative protect against septic shock in rats. Inflammation Research 55:498-503.

Anuar F, Whiteman M, Siau JL, Kwong SE, Bhatia M, Moore PK

Nitric oxide releasing flurbiprofen reduces formation of pro-inflammatory hydrogen sulphide in lipopolysaccharide-treated rat. Br J Pharmacol 147:966-974.

Bhatia M, Li L, Moore PK

The role of hydrogen sulfide in lung inflammation. Drug Discov Today: Dis Mech 3:71-75.

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Cao Y, Adhikari S, Ang AD, Moore PK, Bhatia M

Mechanism of induction of pancreatic acinar cell apoptosis by hydrogen sulfide. Am J Physiol Cell Physiol 291:C503-C510.

Cao Y, Adhikari S, Ang AD, Wallig M, Clément MV, Bhatia M

Crambene induces pancreatic acinar cell apoptosis via the activation of mitochondrial pathway. Am J Physiol Gastrointest Liver Physiol 291:G95-G101.

DEPARTMENT OF
PHARMACOLOGY**Watt F, Reshmi R, Ren MQ, Tan BKH, Halliwell B**A Nuclear Microscopy Study of Trace elements Ca, Fe, Zn and Cu in atherosclerosis. *Nuclear Instruments and Methods* 646:249-252.**Lai MKP, Tsang SWY, Garcia-Alloza M, Minger SL, Nicoll JAR, Esiri MM, Wong PTH, Chen CPLH, Ramirez MJ, Francis PT**Selective effects of the APOE e4 allele on presynaptic cholinergic markers in the neocortex of Alzheimer's disease. *Neurobiology of disease* 22(3):555-561.**Lau HY, Bhatia M**Effect of CP96, 345 on the expression of tachykinins and neurokinin receptors in acute pancreatitis. *J Pathol* 208:364-371.**Lee SW, Hu YS, Lu Q, Dawe GS, Moore PK, Wong PTH, Bian JS**Hydrogen sulphide regulates calcium homeostasis in microglial cells. *Glia* 54(2):116-124.**Li L, Bhatia M, Moore PK**Hydrogen sulfide - a novel mediator of inflammation. *Curr Opin Pharmacol* 6:125-129.**Liu X, Lee TL, Wong PTH**Cyclooxygenase-1 inhibition shortens the duration of diazepam-induced loss of righting reflex in mice. *Anesthesia and Analgesia* 102(1):135-40.**Manoharan KP, Fan JS, Tan BKH, Yang D**Triterpenoids from *Eugenia grandis*: Structure elucidation by NMR spectroscopy. *Magnetic Resonance in Chemistry*:MRC 45:279-281. (United Kingdom).**Pawlak J, Mackessy SP, Fry BG, Bhatia M, Mourier G, Fruchart-Gaillard C, Servent D, Ménez R, Stura E, Ménez A, Kini RM**Denmotoxin: A three-finger toxin from colubrid snake *Boiga dendrophila* (Mangrove Catsnake) with bird-specific activity. *J Biol Chem* 281:29030-29041.**Puneet P, Hegde A, Ng SW, Lau HY, Lu J, Mochhala S, Bhatia M**Preprotachykinin-A gene products are key mediators of lung injury in polymicrobial sepsis. *J Immunol* 176:3813-3820.**Qu K, Chen CPLH, Halliwell B, Moore PK, Wong PTH**Hydrogen sulfide is a mediator of cerebral ischemic damage. *Stroke* 37:889-893.**Ramnath RD, Bhatia M**Substance P treatment stimulates chemokine synthesis in pancreatic acinar cells via the activation of NF- κ B. *Am J Physiol Gastrointest Liver Physiol* 291:G1113-9.**Ramnath RD, Ng SW, He M, Sun J, Zhang H, Bawa MS, Bhatia M**Inflammatory mediators in sepsis: cytokines, chemokines, adhesion molecules, and gases. *J Org Dysfunc* 2:80-92.**Ren M, Reshmi M, Pan N, Tan BKH, Ong CN, Watt F, Jenner AM, Halliwell B**Zinc supplementation decreases the development of atherosclerosis in rabbits. *Free Radical Biology And Medicine* 41(2):222-225.**Reshmi R, Pan N, Ren M, Tan BKH, Halliwell B, Watt F**Promotion of atherogenesis by copper or iron Which is more likely? *Biochemical and Biophysical Research Communications* 353:6-10.**Rufaihah AJ, Hadier HK, Sim MK, Ding PZ, Ramos LB, Jian S, Sim EKW**Cardioprotective effect of des-aspartate-angiotensin-I (DAA-I) on cytokine gene expression profile in ligation model of myocardial infarction. *Life Sci* 78:1341-1351.**Sim MK, Chen WS**Effects of losartan on angiotensin receptors in the hypertrophic rat heart. *Regul Pept* 137(3):140-146.**Tsang SWY, Lai MKP, Kirvell S, Francis PT, Esiri MM, Hope T, Chen CPLH, Wong PTH**Impaired muscarinic M1 receptor coupling to G-proteins in the neocortex is associated with the severity of dementia in Alzheimer's disease. *Neurobiology of Aging* 27:1216-1223.**Wang Q, Tang XN, Wang L, Yenari MA, Ying W, Goh BC, Lee HS, Wilder-Smith EP, Wong PTH**Effects of high dose of simvastatin on levels of dopamine and its reuptake in prefrontal cortex and striatum among SD rats. *Neurosci Lett* 408(3):189-193.**Whiteman M, Li L, Kostetski I, Chu SH, Siau JH, Bhatia M, Moore PK**Evidence for the formation of a novel nitrosothiol from the gaseous mediators nitric oxide and hydrogen sulfide. *Biochem Biophys Res Commun* 343:303-310.**Wong PTH, Qu K, Chimon GN, Seah ABH, Chang HM, Wong MC, Ng YK, Rumpel H, Halliwell B, Chen CPLH**High plasma Cyst(e)ine level may indicate poor clinical outcome in acute stroke patients. *J Neuropath Exp Neurol* 65(2):109-115.**Yusuf M, Cheong YP, Mok YYP, Li L, Whiteman M, Bhatia M, Moore PK**Regulation of vascular nitric oxide in vitro and in vivo; a new role for endogenous hydrogen sulphide? *Br J Pharmacol* 149:625-634.**Zhang H, Zhi L, Moore PK, Bhatia M**The role of hydrogen sulfide in cecal ligation and puncture induced sepsis in the mouse. *Am J Physiol Lung Cell Mol Physiol* 290:L1193-L1201.

STAFF PROFILE

Professor & Head:

Professors:

Associate Professors:

Assistant Professors:

Senior Research Fellow:

Philip K Moore

Edmund Lee Jon Deoon

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DEPARTMENT OF PHARMACOLOGY

Research Fellows:

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Drug Studies using molecular biology techniques



DEPARTMENT OF PHYSIOLOGY

INTRODUCTION

The Department of Physiology has 4 focused research programs to facilitate more collaborative and programmatic research within our department. The focus of these programs is to provide an environment that stimulates excellence in scientific thoughts and reasoning while simultaneously providing exposure to the major fields of study relevant to the particular program.

The Cancer Biology Programme is designed to provide a broad understanding of cell growth regulatory machinery and the mechanism(s) involved in oncogenesis. Research is broadly focused on signal transduction, reactive oxygen species, regulation of the death signal, cell cycle control, gene regulation, oncogene and tumor suppressor action, metastasis and invasion, drug resistance and antitumor pharmacology.

The Cell and Tissue Engineering Programme is involved in the study of cellular processes and manipulation of the structural-function relationship of cells and tissue to enable tissue repair and regeneration. Research is focused primarily on liver regeneration, bioartificial livers, the role of extracellular matrices and novel membrane structures.

The Immunology and Inflammation Programme serves to provide a platform for the study of the genetic control and mechanisms of

immune function and development. An understanding on how the inflammatory process can be regulated and harnessed will aid in the treatment and management of many immune-mediated diseases like autoimmune diseases, allergies and tissue rejection. Research in the program is focused on T-cell biology, tumor immunology, inflammation and cancer, autoimmunity and allergy.

The Neurobiology Programme brings together scientists interested in molecular, cellular and system neurophysiology, particularly in Parkinson's disease, motor coordination, learning and memory, and pain. The various labs in the program are skilled in vitro and in vivo electrophysiology, and the study of behavioural responses, ion channelopathies, axon guidance and synaptic plasticity.

The team's research output is widely supported by competitive national and institutional grant funding. In 2006, the Department secured 48 competitive grants and published 50 international peer-reviewed publications, many in top-tier, high impact journals such as Current Biology, Cancer Research, Human Molecular Genetics, FASEB Journal, Journal of Hepatology, Journal of Immunology, Journal of Neuroscience and Pain. Faculty members have extensive project collaborations with researchers from DMERI, Genome Institute of Singapore, IBN, IMCB, NCC, NNI, SGH and TTSH. Moreover, they are successful in initiating and continuing international collaborations with institutes in the USA, Canada, Japan, Hong Kong, Germany and UK.

DEPARTMENT OF
PHYSIOLOGY

Holistic Approach: Associate Professor Hanry Yu (standing) and team looks at the entire process of liver fibrosis to find solutions to the disease.

The department is proud to have its excellent researchers recognised. In particular, Assoc Prof Soong Tuck Wah was awarded the Faculty Research Excellence Award 2005/6 as well as the UK-Singapore Partners in Science Collaboration Award – Neuroscience, June 2006. Asst Prof Celestial Yap was awarded the UK-Singapore Collaboration Development Award in 2006.

Our laboratories are equipped with high end research facilities and have been recognised for their good safety standards. The Department received the Merit Award with commendation for Safety Improvement Project for ASHPA 2006 and the “Outstanding Achievement” (Noise Control) for Occupational Safety & Health Best Practices Award 2006 from the Ministry of Manpower.

The Department continues to place significant emphasis on its teaching efforts and in 2006 we had 79 graduate students. 3 graduate students were recipients of the President’s Graduate Fellowship. We are also pleased to mention that Prof Shazib Pervaiz received the Faculty of Science Excellent Teaching Award 2006.

Also in 2006, 5 staff members shifted their labs into the brand new Centre For Life Sciences building, and are an integral part of the Office of Life Sciences Neurobiology & Aging, and Immunology Programs.

PROJECT DESCRIPTION

Grants Awarded in 2006

Investigating the anti-oncogenic and oncogenic roles of gelsolin in the development of tumours

Principal Investigator: Dr Yap Celestial Therese
Collaborators: Dr Sutherland K Maciver,
Dr Goh Yaw Chong,
Dr So Bok Yan

Molecular and functional characterization of the preligand assembly domain in the cytokine receptor CD137

Principal Investigator: Assoc Prof Herbert Schwarz

Investigating the roles of actin-associated proteins in the epithelial-mesenchyme progression of colorectal tumour cells

Principal Investigator: Dr Yap Celestial Therese
Collaborators: Assoc Prof Hooi Shing Chuan,
Dr Tay Puei Nam

Interaction of the anti-apoptotic protein Bcl-2 with the small GTPase Rac1: A possible mechanism for Bcl-2-mediated increase in intracellular superoxide

Principal Investigator: Prof Shazib Pervaiz
Collaborator: Dr David Hsu

Expansion and engraftment of hematopoietic stem and progenitor cells by CD137, stromal derived factor-1 and 3-dimensional scaffolds

Principal Investigators: Assoc Prof Herbert Schwarz,
Assoc Prof Victor Nurcombe
Collaborators: Dr Tan Lip Kun,
Dr Law Ping,
Dr William Hwang Ying Khee

Functional and molecular analysis of C/EBPalpha gene knock-in hepatocytes to characterize altered and improved attributes that may be beneficial in bioartificial livers

Principal Investigator: Assoc Prof Hooi Shing Chuan

Regulation of T cell activation and apoptosis by the cytokine receptor CD137

Principal Investigator: Assoc Prof Herbert Schwarz
Co-Principal Investigators: Prof Shazib Pervaiz,
Dr Paul Macary

Dissecting the role of phingosine kinase 1 in acute inflammation

Principal Investigator: Assoc Prof Alirio Jose Melendez Romero
Co-Principal Investigator: Dr Leung Pui Lam Bernard

Alternative splicing diversifies CA_v1.3 channels and acts as molecular switch to regulate hippocampus-dependent learning and memory

Principal Investigator: Assoc Prof Soong Tuck Wah
Collaborator: Prof Susumu Tonegawa

Evaluation of biopolymer-based depot system of RhoA inhibitor in promoting neuronal regeneration

Principal Investigator: Dr Alan Lee Yiu Wah
Co-Principal Investigator: Assoc Prof Wang Chi-Hwa

The role of leukotriene B₄ in malignant lymphoma growth and survival

Principal Investigator: Dr Lim Yaw Chyn
Collaborators : Assoc Prof Chong Siew Meng
(Faculty of Medicine & Health Sciences, UAE University, UAE),
Asst Prof Tan Kong Bing

Role of lipid mediators, leukotriene B₄ and lipoxin A₄, as inflammatory and immune modulators in Hodgkin Lymphoma

Principal Investigator: Dr Lim Yaw Chyn
Collaborators : Assoc Prof Chong Siew Meng
(Faculty of Medicine & Health Sciences, UAE University, UAE),
Assoc Prof Luke Tan

Characterizing the carbohydrate composition on apolipoprotein E using inbred and transgenic animal models as potential biomarkers for atherosclerosis

Principal Investigator: Dr Wong Boon Seng
Collaborators: Prof Barry Halliwell,
Dr Roland Stocker
(Sydney University, Australia)

DEPARTMENT OF PHYSIOLOGY

Investigating the effect of caloric restriction on neuronal glucose metabolism in an AD animal model

Principal Investigator: Dr Wong Boon Seng
Collaborators: Prof Barry Halliwell,
Assoc Prof Sanjay Swarup
(Biological Sciences, NUS),
Dr Christopher Chen (NNI)

Identifying the glycan profile on apolipoprotein E polymorphism as clinical tool for Alzheimer's disease

Principal Investigator: Dr Wong Boon Seng
Collaborator: Dr Christopher Chen (NNI)

Comparative glycomics of neuronal ageing and degeneration

Principal Investigator: Dr Wong Boon Seng

Regulation of cell division and DNA repair by BRCA2 tumor suppressor gene product.

Principal Investigator: Srividya Swaminathan
Collaborator: Manoor Prakash Hande

On-going Projects

Investigations into the neural circuitry underlying hippocampal nociceptive responses and its influence on formalin nociception, an animal model of persistent pain

Principal Investigator: Assoc Prof Sanjay Khanna

Biochemical characterization of cubic membrane transition in amoeba chaos and alternative model systems

Principal Investigator: Dr Deng Yuru

The implication of plexin-b3/rhogtpases interaction in axon guidance

Principal Investigator: Dr Lee Yiu Wah

Functional characterization of a novel axon guidance molecule plexin-b3

Principal Investigator: Dr Lee Yiu Wah

Cubic membranes: a novel 3d nano-periodic biological structure - implications for cellular response to starvation and ischemia

Principal Investigator: Dr Deng Yuru

Immunogenetics of systemic lupus erythematosus

Principal Investigator: Assoc Prof Koh Dow Rhoon

Interplay between intracellular redox status and pro-apoptotic protein bax during drug-induced tumor cell death: potential implications for cancer chemotherapy

Principal Investigator: Prof Shazib Pervaiz

Study to assess the role of cellular redox status on intracellular pH regulation and its effect on drug-induced apoptosis in tumor cells to develop

Principal Investigator: Prof Shazib Pervaiz

Inhibition of telomerase in human brain tumour cells

Principal Investigator: Assoc Prof Manoor Prakash Hande

Biomarkers that regulate metastatic potential in colorectal cancer cells: The role and regulation of cxcr4 and beta1 integrins

Principal Investigator: Assoc Prof Hooi Shing Chuan
Co-Principal Investigator: Dr Lim Yaw Chyn
Dr Lim Hsiu Kim Lina

Regulation of subfamily v nuclear receptors by sumo-modification and dead-box helicases

Principal Investigator: Dr Martin Lee Beng Huat

Investigations into the neurobiological consequences of overloading iron into neurons via an iron transporter: implications in Parkinson's disease

Principal Investigator: Assoc Prof Soong Tuck Wah
Collaborators: Prof Ted Dawson,
Dr Lim Kah Leong

Analysis of growth and selection advantages which tumor cells gain by expressing cd137 as a neoantigen evaluation of a novel therapeutic approach

Principal Investigator: Assoc Prof Herbert Schwarz

Implications of alternative splicing of voltage-gated calcium channel alpha1.2 subunit in cardiovascular physiology and disease

Principal Investigator: Assoc Prof Soong Tuck Wah
Co-Principal Investigators: Dr Chua Yeow Leng,
Dr Tan Seck Guan
Collaborators: Prof David Yue,
Assoc Prof George Wellman,
Assoc Prof Sathievel

Characterization of the gene expression profile and the activation stage induced by cd137 in hematopoietic stem cells

Principal Investigator: Assoc Prof Herbert Schwarz

Characterization of a novel candidate tumor suppressor gene

Principal Investigator: Assoc Prof Hooi Shing Chuan

Regulation of hepatocyte functions in co-culture with non-parenchymal cells

Principal Investigator: Assoc Prof Henry Yu

Investigation of neurological consequences of specific ablation of alternative spliced exons of voltagegated calcium channels: Generation of knock-out mice and assessment of altered behavioural traits

Principal Investigator: Assoc Prof Soong Tuck Wah
Collaborators: Prof David Yue,
Assoc Prof Sathievel,
Prof David Linden

Molecular mechanisms underlying SUMO-mediated repression of SF-1 by DP103 and PIAS proteins

Principal Investigator: Dr Martin Lee Beng Huat

Investigation into the role of septo-hippocampal region in pain

Principal Investigator: Assoc Prof Sanjay Khanna

The effectiveness of a naturally occurring compound on leukocyte activation in allergy: Role of annexin-1

Principal Investigator: Dr Lim Hsiu Kim Lina

Mechanism of defective drug-induced apoptotic signaling in B cell lymphomas

Principal Investigator: Prof Shazib Pervaiz

Generation of novel inhibitors for sphingosine kinase: Validation in physiological responses triggered by immune-cells

Principal Investigator: Assoc Prof Alirio Jose Melendez Romero

DEPARTMENT OF
PHYSIOLOGY

The isolation and characterization of putative colon cancer stem cells: Correlation with tumorigenicity and metastasis

Principal Investigator: Assoc Prof Hooi Shing Chuan

Investigations of the tumor suppressor activity and the adhesion/migration properties of hepacam, a novel cell adhesion molecule of the immunoglobulin superfamily, which is abrogated

Principal Investigator: Dr Shen Shali

A novel E-SIGE technology to bioimage alternative splicing activity in neuron and muscle

Principal Investigator: Assoc Prof Soong Tuck Wah

Genetic analysis of a lipoapoptosis pathway in yeast

Principal Investigator: Dr Yang Hongyuan Robert

Co-Principal Investigator: Prof Shazib Pervaiz

Characterization of a novel candidate tumor suppressor gene

Principal Investigator: Assoc Prof Hooi Shing Chuan

Modulation of hippocampus field CA1 synaptic excitability by hypothalamic supramammillary region

Principal Investigator: Assoc Prof Sanjay Khanna

Characterization of soluble CD137 and its ability to enhance the efficacy of cancer chemotherapy

Principal Investigator: Assoc Prof Herbert Schwarz

Reactive oxygen species-dependent inhibition of map kinase phosphatase for sensitization of tumor cells to trail-induced apoptosis

Principal Investigator: Prof Shazib Pervaiz

Novel receptor-ligand interactions that mediate tumour cell adhesion to endothelial cell from different organ sites (PI)

Principal Investigator: Dr Lim Yaw Chyn

Co-Principal Investigator: Assoc Prof Teh Ming

Collaborators :
Dr John Tam,
Dr Jerry Chan,
Dr Arijit Biswas

Uncovering the neuropathological role of SOD1 and mitochondrial dysfunction in Down syndrome

Principal Investigator: Dr Wong Boon Seng

Co-Principal Investigator: Prof Barry Halliwell

Collaborators:
Dr Jeffrey Armstrong,
Assoc Prof Goh Li Meng Denise

Functional analysis of Ataxia Telangiectasia Mutated (ATM) in BRCA and non-BRCA tumors.

Principal Investigator: Dr Srividya Swaminathan

Co-Principal Investigator: Manoor Prakash Hande

Qiu G, Xie H, Wheelhouse N, Harrison D, Chen GG, Salto-tellez M, Lai P, Ross JA, Hooi SC

Differential expression of hDAB21PA and hDAB21PB in normal tissues and promoter methylation of hDAB21PA in hepatocellular carcinoma. *Journal of Hepatology* (2006) 46(4):655-663. (United States).

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Expression of Urocortin 2 and its Inhibitory Effects on Intracellular Ca(2+). *Neuropsychopharmacology* (2006) 31(12):2600-2609. (United Kingdom).

Pan TT, Feng Z, Lee SW, Moore PK, Bian J

Endogenous hydrogen sulfide contributes to the cardioprotection by metabolic inhibition preconditioning in the rat ventricular myocytes. *Journal of Molecular and Cellular Cardiology* (2006) 40:119-130. (United States).

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pH dependent high transfection efficiency of mouse neuroblastomas using TransFectin. *Journal of Neuroscience Methods* (2006) 158(1):56-63. (United States).

Soo R, Wu J, Aggarwal A, Tao Q, Hsieh W, Putti T C, Tan K B, Soon WL, Lai YF, Mow B, Hsu SI, Loh KS, Tan KSL, Tan BOP, Goh BC

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3D hepatocyte monolayer on hybrid RGD/galactose substratum. *Biomaterials* (2006) 27(33):5669-5680. (United Kingdom).

Soong TW, Venkatesh B

Adaptive evolution of tetrodotoxin resistance in animals. *Trends in Genetics* (2006) 22(11):621-626. (Netherlands).

Pervaiz S, Lee SC

Apoptosis in the pathophysiology of diabetes mellitus. *International Journal of Biochemistry & Cell Biology* (2006) 39(3):497-504. (United States).

Md MK, Pervaiz S, Ng APP, Howe FJ, Dawn NS, Hirpara JL, Huan JH, Chen C

Cleavage of misfolded nuclear receptor corepressor confers resistance to unfolded protein response-induced apoptosis. *Cancer Research* (2006) 66(20):9903-9912. (United States).

Shen Y, Yu D, Hiel H, Liao P, Yue DT, Fuchs PA, Soong TW

Alternative splicing of the CaV1.3 channel IQ domain, a molecular switch for Ca2+-dependent inactivation within auditory hair cells. *Journal of Neuroscience* (2006) 26(42):10690-10699. (United States).

Pan X, Wohland T, Aw C, Du Y, Yu H

Characterization of poly(acrylic acid) diffusion dynamics on the grafted surface of poly(ethylene terephthalate) films by fluorescence correlation spectroscopy. *Biophysical Reviews and Letters* (2006) 1(4):1-9. (Singapore).

INTERNATIONAL PUBLICATIONS

Pervaiz S

Pro-oxidant milieu blunts scissors: insight into tumor progression, drug resistance, and novel druggable targets. *Curr Pharm Des* (2006) 12(34):4469-4477. (United States).

DEPARTMENT OF
PHYSIOLOGY**Jiang F, Khanna S**

Microinjection of carbachol in the supramammillary region suppresses CA1 pyramidal cell synaptic excitability. *Hippocampus* (2006) 16:891-905. (United States).

Toh YC, Ng SS, Khong YM, Zhang X, Zhu Y, Lin PC, Ten CM, Sun W, Yu H

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Jayapal M, Tay HK, Renji R, Zhi L, Chow KK, Rauff M, Melendez A

Genome-wide gene expression profiling of human mast cells stimulated by IgE or Fc(epsilon)RI-aggregation reveals a complex network of genes involved in inflammatory responses. *BMC Genomics* (2006) 7:210. (United Kingdom).

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Francia S, Weiss RS, Hande MP, Freire R, d'Adda di Fagagna F

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Sphingosine kinase 1 regulates pro-inflammatory responses triggered by TNFalpha. *Journal of Cellular Physiology* (2006) 208(1):109-115. (United States).

Ng S, Han R, Chang S, Ni J, Hunziker W, Goryachev AB, Ong SH, Yu H

Improved Hepatocyte Excretory Function by Immediate Presentation of Polarity Cues. *Tissue Engineering* (2006) 12(8):2181-2191. (United States).

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Sphingosine kinase 1 regulates pro-inflammatory responses triggered by TNFalpha in primary human monocytes. *Journal of Cellular Physiology* (2006) 208(1):109-115. (United States).

Heng BC, KJ Vinoth, Liu H, Hande MP, Cao T

Low temperature tolerance of human embryonic stem cells. *International Journal of Medical Sciences* (2006) 3:124-129. (United States).

Zakaria AMA, Kohlwein SD, Deng Y

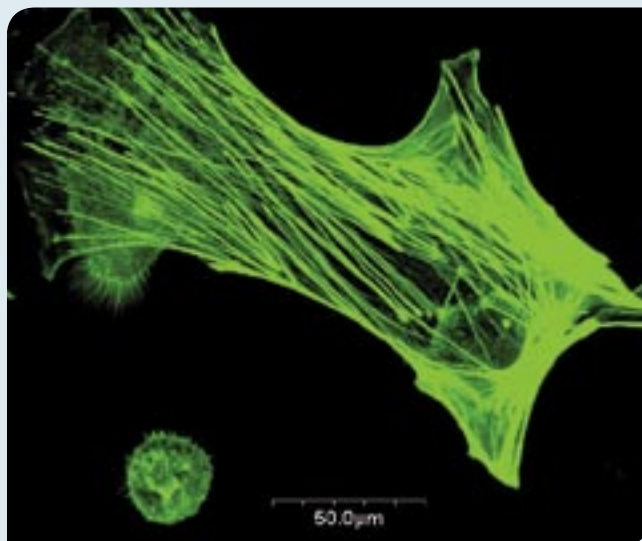
Cubic membranes: a legend beyond the Flatland* of cell membrane organization. *Journal of Cell Biology* (2006) 173(6):839-844. (United States).

Pushparaj PN, Melendez A

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Pervaiz S, Olivio M

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Jayapal M, Melendez A

DNA Microarray technology for target identification and validation. *Clinical and Experimental Pharmacology And Physiology* (2006) 33(5/6):504-10. (Australia). (Invited Review Article).

Liu H, Leung PLB

CD4+CD25+ regulatory T cells in health and disease. *Clinical and Experimental Pharmacology And Physiology* (2006) 33(5-6):519-524. (Australia).

Lim LHK, Burdick MM, Fatimah BM, Hudson S, Konstantopoulos K, Bochner BS

Stimulation of human endothelium with interleukin-3 (IL-3) induces selective basophil accumulation in vitro. *Journal of Immunology* (2006) 176:5346-5353. (United States).

Wong S, Yu H, So JB

Detection of telomerase activity in gastric lavage fluid: a novel method to detect gastric cancer. *Journal of Surgical Research* (2006) 131(2):252-255. (United States).

Lee SC, Clement MV, Pervaiz S

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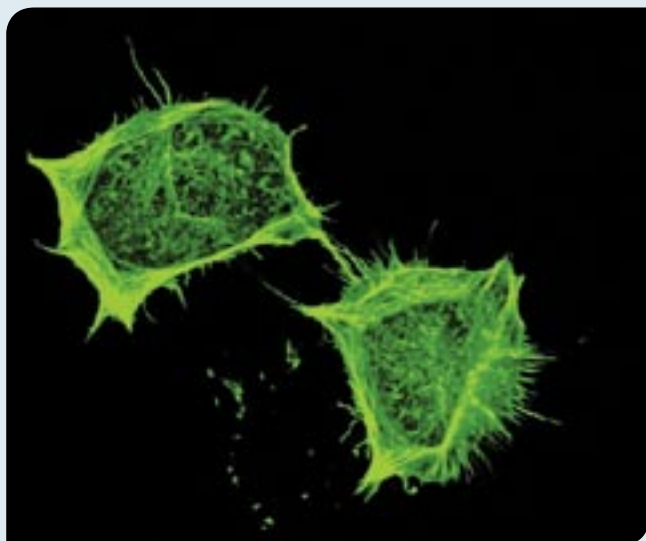
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DEPARTMENT OF
PHYSIOLOGY

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Chaw KC, Manimaran M, Tay FEH, Swaminathan S

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Pervaiz S

Cancer Cell Redox Status: Novel Target for Designing Strategies to Overcome Apoptosis Resistance. *Current Pharmaceutical Design* (2006) 12(34):4409-4410.

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DEPARTMENT OF PHYSIOLOGY

Senatorov V, Malyukova I, Fariss R, Wawrousek E, Swaminathan S, Sharan SK, Tomarev S

Expression of mutated mouse myocilin induces open-angle glaucoma in transgenic mice. *Journal of Neuroscience* (2006) 26(46):11903-11914. (Times Cited: 1)

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A quantitative observation and imaging of single tumor cell migration and deformation using a multi-gap microfluidic device representing the blood vessel. *Microvascular Research* (2006) 72(3):153-160.

Chaw KC, Manimaran M, Tay FEH and Swaminathan S

Three-dimensional (3D) extra-cellular matrix coating of a microfluidic device. *Journal of Physics* (2006) 34: 747-751.



Hematopoietic progenitor cells differentiated to myeloid cells by the cytokine receptor CD137.

STAFF PROFILE

Associate Professor & Head:	Hooi Shing Chuan
Professor:	Shazib Pervaiz
Associate Professors:	Koh Dow Rhoon
	Sanjay Khanna
	Soong Tuck Wah
	Herbert Schwarz
	Henry Yu
	Ho Ting Fei
	Lee Chee Wee
	Manoor Prakash Hande
Professorial Fellow:	Peter Hwang Lam Hum
Associate Professorial Fellow:	Wong Chong Thim
Assistant Professors:	Alirio J Melendez
	Deng Yuru
	Leung Pui Lam, Bernard
	Lee Beng Huat, Martin
	Lee Yiu Wah
	Lim Hsiu Kim, Lina
	Lim Yaw Chyn
	Shen Shali
	Wang Nai-dy
	Srividya Swaminathan
	Yap Suen Mei, Celestial Therese
	Wong Boon Seng
Adjunct Associate Professors:	Graeme Guy
	Walter Hunziker
	Lee Kim Hock, Lionel
	Li Fuk Loi, Benjamin
	Sohail Ahmed
Adjunct Assistant Professors:	Tan Boon Ooi, Patrick
	Ong Siew Hwa
	Lam Yeng Po, Paula
	Ng Chun Yeen, Aylwin
	Carol Tang
	Craig McLachlan
Research Fellows:	Chang Siao Yun
	Chia Ser Mien
	Dipanjan Gosh
	Gong Yue
	Jayapal Manikandan
	Jiang Fengli
	Kishore Ramaji Sakharkar
	Koo Mei Keng
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Liu Jian-Jun
Padnam Puneet
Peter Natesan Pushparaj
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Tang Yanxia
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DEPARTMENT OF PSYCHOLOGICAL MEDICINE



INTRODUCTION

The strategic research initiatives of the Department include research on:

- Psychiatric Epidemiology and Gerontological Research
- Early identification and treatment of psychiatric disorders, particularly schizophrenia and related psychoses
- Psychological aspects of general medical and surgical conditions

Our aim is to engage in collaborative research with local and overseas partners in both clinical and basic sciences, leveraging on platform technologies like functional neuron-imaging and molecular/genetic research.

Research

Research in psychosis by the First Episode Schizophrenia (FES) Study Group has produced interesting new results of dorsal lateral precortex activation in schizophrenia patients using fMRI.

The Gerontology Research Programme (GRP) is a flagship research initiative of the Department and provides a systematic, coordinated programme of research activities on the health of the elderly Singaporeans that provide the scientific information needed for formulating strategies of disease prevention and health promotion. The research has produced the first nationally representative

estimates of the prevalence of depression and dementia in the elderly for policy information and planning. It has also published the first human evidence of the link between curry consumption and better cognitive functioning in the elderly.

PROJECT DESCRIPTION

Grants Awarded in 2006

Singapore Study of Successful Aging (SSOCA): A collaborative project between National University of Singapore and University of California, San Diego, USA

Principal Investigator:	Dr Rajeev Kumar
Co-Principal Investigator:	Assoc Prof Ng Tze Pin
Collaborator:	Prof Kua Ee Heok

Response shift in quality of life in Chinese breast cancer patients

Principal Investigator:	Assoc Prof Ng Tze Pin
Co-Principal Investigators:	Cynthia Goh, Ng Gim Yew
Collaborators:	Grace Pang, Gao Fei, See Hui Ti, Ho Gay Hui

DEPARTMENT OF PSYCHOLOGICAL MEDICINE

A 1-year prospective neuroimaging study of genetic variation in cortical dopamine influencing working memory prefrontal dynamics in first-episode schizophrenia

Principal Investigator: Dr Tan Hao Yang
Collaborator: Michael Chee Wei Liang

Functional neurophysiology of working memory processes using genetic imaging

Principal Investigator: Dr Tan Hao Yang

Gambling behaviour in Singapore University students

Principal Investigator: Prof David Arthur
Co-Principal Investigators: Prof Kua Ee Heok,
Assoc Prof Hing Ai Yun,
Dr Miharu Sagara-Rosemeyer

On-going Projects

Gerontology Research Programme: Biological, clinical, psychosocial & behavioural predictors of health status in prospectively followed-up cohorts

Principal Investigator: Assoc Prof Ng Tze Pin

Randomised controlled trial of a community-based early psychiatric intervention strategy (cepis) to screen and manage depression in the elderly

Principal Investigator: Assoc Prof Ng Tze Pin

INTERNATIONAL PUBLICATIONS

Ng TP, Chiam PC, Kua EH

Depression and asthma in the elderly: a population-based study. *International Journal of Geriatric Psychiatry* (2006) Epub. (United Kingdom).

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Tan EC

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Ng TP, Niti MM, Chiam PC, Kua EH

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Ng TP, Chiam PC, Lee T, Chua HC, Kua EH

Curry consumption and cognitive function in the elderly. *American Journal of Epidemiology* (2006) 164(9):898-906. (United States).

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Congenital long QT syndromes: clinical features, molecular genetics and genetic testing. *Expert Reviews of Molecular Diagnostics* (2006) 6(3):365-374. (United Kingdom).

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Prevalence and Correlates of Functional Disability in Multiethnic Elderly Singaporeans. *Journal of the American Geriatrics Society* (2006) 54:21-29. (United States).

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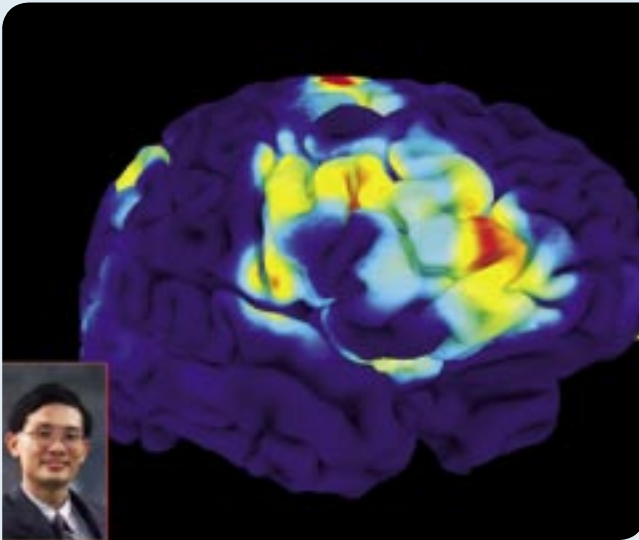
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Hormone replacement therapy, brain volumes and white matter in postmenopausal women aged 60-64. *Neuroreport* (2006) 17:101-104. (United Kingdom).

Sachdev PS, Anstey KJ, Parslow R, Wen W, Maller J, Rajeev K, Christensen H, Jorm AF

Pulmonary function, cognitive impairment and brain atrophy in a middle-aged community sample. *Dementia and Geriatric Cognitive Disorders* (2006) 21:300-308. (United States).

DEPARTMENT OF PSYCHOLOGICAL MEDICINE



Neuroimaging Research on Schizophrenia.

Rajeev K, Parslow RA, Jorm AF, Roseman S, dePlater G, Maller J, Meslin C, Anstey KJ, Christensen H, Sachdev PS

Clinical and neuroimaging correlates of mild cognitive impairment in a middle-aged community sample: The PATH through life 60+ study. *Dementia and Geriatric Cognitive Disorders* (2006) 21:44-50. (United States).

Tan EC

The Singapore human polymorphism/mutation database: a country-specific database for mutations and polymorphisms in inherited disorders and candidate gene association studies. *Human Mutation* (2006) 27(3):232-235. (United States).

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What makes a good medical doctor. *Medical Teacher* (2006). (UK).



Research Mentoring.

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STAFF PROFILE

Professor & Head:	Kua Ee Heok
Associate Professor:	Ng Tze Pin
Assistant Professors:	Rajeev Kumar Tan Hao Yang
Adjunct Professors:	Calvin Fones Ko Soo Meng Peh Lai Huat Wong Sze Tai Tan Ene Choo
Teaching Assistant:	Ng Mei Yi
Research Fellow:	Mathew Niti
Research Assistant:	Ma Shwe Zin Nyunt

DEPARTMENT OF SURGERY



INTRODUCTION

The Department comprises of eight clinical divisions, namely, General Surgery, Urology, Plastic and Reconstructive Surgery, Cardiac, Thoracic & Vascular Surgery, Neurosurgery, Paediatric Surgery, Colorectal Surgery and Hepatobiliary and Pancreatic Surgery. In addition, the Department also co-ordinates the interdepartmental and multidisciplinary clinical services associated with minimally invasive and transplantation surgery. The Department carries out clinical, as well as undergraduate and postgraduate teaching activities and both clinical and basic research.

The research carried out in the department is primarily focused on cancer biology, wound healing, bone regeneration/grafting, cardiology and stem cells. Funding for these projects comes from the Biomedical Research Council, National Medical Research Centre, NUS, The National Health Group and The Singapore Cancer Syndicate. There are active collaborative research projects with other departments in the Faculties of Medicine, Science and Engineering in NUS and with the Institute of Molecular and Cell Biology, National University Medical Institute, Genome Institute of Singapore, the Defence Military Research Institute as well as local Hospitals.

The research highlights for this year include the recruitment of several Cardiothoracic surgeons Prof Uwe Klima and Asst Prof Theodoros Kofidis. Together with Dr Eliana C Martinez they will further develop

Cardiothoracic research in the Department. Throughout the year, meetings and visits were conducted with research institutes and departments in NUS and NTU to further encourage the development of interdisciplinary and translational research activities. The Wound Healing and Stem Cell Research Laboratory in the Department of Surgery, headed by Asst Prof Phan Toan Thang hosted several researchers from Vietnam and France for a 3-month laboratory attachment. Asst Prof Edmund Chiong received the inaugural award from the "Pitch for Funds" scheme organised by the Clinician scientist Unit, NUS Leadership in Academic Medicine Program, National University of Singapore.

PROJECT DESCRIPTION

Grants Awarded in 2006

Human gene polymorphisms and response to bacillus calmette-guerin immunotherapy for superficial bladder cancer

Principal Investigator:

Asst Prof Edmund Chiong

Collaborators:

Assoc Prof Kesavan Esuvaranathan,
Asst Prof Tan May Chin,
Dr Ratha Mahendran

DEPARTMENT OF
SURGERY

Dr Shaik Ahmad performing a surgery.

Roles of stem cell factor/C-Kit and therapeutic effects of Glivec/ST1571 in keloid and scar pathogenesis

Principal Investigator: Asst Prof Phan Toan Thang
Collaborator: Dr Cao Xin Min (IMCB)

Transcriptional program differences between keloid and normal skin derived keratinocytes and fibroblasts: a cDNA microarray analysis

Principal Investigator: Asst Prof Phan Toan Thang
Collaborators: Adj Assoc Prof Lim IJ,
Dr Cao Xin Min (IMCB),
Dr Lim Cheh Peng (IMCB)

Investigating the role of novel growth factor HDGF (Hepatoma-derived Growth Factor) in wound repair and regeneration

Principal Investigator: Asst Prof Phan Toan Thang
Co-Principal Investigators: Adj Assoc Prof Ivor Lim (NUS),
Dr Lim Cheh Peng (IMCB),
Dr Cao Xin Min (IMCB),
Dr Alvin Chua (SGH)

Prevention of the loss of alveolar margins with a bioresorbable scaffold of poly-D-caprolactone

Principal Investigator: Assoc Prof Lim Thiam Chye
Co-Principal Investigator: Dr Ang Chee Wan
Collaborators: Dr Chung K W,
Dr Teoh S H,
Dr DW Huttmacher

Novel therapeutic effects of plant-derived coumarins on skin cell culture system

Principal Investigator: Dr Sanjay Swarup
Co-Principal Investigator: Asst Prof Phan Toan Thang
Collaborator: Adj Assoc Prof Lim IJ

On-going Projects

Characterization of the migratory potential of mesenchymal precursor cells

Principal Investigator: Asst Prof Jan Thorsten Schantz
Co-Principal Investigator: Dr Dietmar Werner Huttmacher

Risk factors for vascular disease in patients with systemic lupus erythematosus in Singapore

Principal Investigator: Assoc Prof Peter Robless
Co-Principal Investigator: Dr Ling Lieng Hsi

Screening for complex genomic rearrangements in the BRCA2 gene of Singaporean patients presenting with early-onset breast cancer with or without family history

Principal Investigator: Dr Sng Jen-Hwei
Co-Principal Investigator: Dr Philip Lau Tsau Choong

Prospective, randomized controlled study of the effects of N-acetylcysteine in patients with preoperative renal impairment undergoing coronary revascularization surgery with cardiopulmonary

Principal Investigator: Prof Lee Chuen Neng
Co-Principal Investigator: Dr Atasha Asmat

Isolation, cultivation, characterisation and utilization of umbilical cord membrane-derived epithelial and mesenchymal stem/progenitor cells: A novel source of stem cells for regenerative medicine, cell-based therapy and tissue engineering

Principal Investigator: Asst Prof Phan Toan Thang
Co-Principal Investigator: Adj Assoc Prof Ivor Lim

End-to-side anastomoses for stretch expanded polytetrafluorethylene in a rabbit epigastric free flap model

Principal Investigator: Dr Marcus Wong
Collaborator: Assoc Prof Lim Thiam Chye

Use of a long length, small diameter ePTFE graft to create a low flow venous system in an animal model

Principal Investigator: Dr Shenthilkumar s/o Sritharan N
Collaborator: Assoc Prof Lim Thiam Chye

In vivo characterization of human adipose-derived adult progenitor (hADAP) cells - adipogenic potential and potential applications for soft tissue repair

Principal Investigator: Adj Assoc Prof Susan Lim

Breaking tolerance to tumour antigens using anti-IL-10, PGE2 or TGF- β in conjunction with BCG or cytokine gene immunotherapy in murine models of bladder cancer

Principal Investigator: Dr Ratha Mahendran
Co-Principal Investigator: Assoc Prof Kesavan Esuvaranathan

Producing animal models for the pre-clinical evaluation of therapies for bladder cancer

Principal Investigator: Dr Ratha Mahendran
Co-Principal Investigator: Assoc Prof Kesavan Esuvaranathan

Modified Lactobacilli as delivery vehicles for antigens for the induction of local and systemic immunity

Principal Investigator: Dr Ratha Mahendran
Co-Principal Investigator: Dr Shabbir Mochhala
Collaborators: Assoc Prof Bay Boon Huat,
Assoc Prof Lee Yuan Kun

Examining the transfection efficiency/stability of DOTAP/DNA/methyl- β -cyclodextrin solubilized cholesterol

Principal Investigator: Dr Ratha Mahendran
Co-Principal Investigator: Assoc Prof Lim Lee Yong

DEPARTMENT OF SURGERY

Cell therapy replacement and diabetes

Principal Investigator: Assoc Prof Li Guang Dong (NUMI)
Co-Principal Investigators: Asst Prof Phan Toan Thang,
Adj Assoc Prof Ivor Lim

Co-culture of human embryonic stem cells with foetal lung tissue

Principal Investigator: Dr Elaine Lim (Medicine)
Co-Principal Investigators: Assoc Prof Wong Poo Sing,
Assoc Prof Wong Peng Cheang,
Dr Lim Bing
Collaborator: Dr Anne Bishop

Reconstruction of the orbit with a poly-caprolactone Implant

Principal Investigator: Assoc Prof Lim Thiam Chye
Collaborators: Asst Prof Jan Thorsten Schantz,
Dr DW Hutmacher,
Assoc Prof Shabbir Moomhala (DMRI)

The role of Vascular Endothelial Growth Factor (VEGF) in epithelial-mesenchymal interactions in keloid

Principal Investigator: Asst Prof Phan Toan Thang
Collaborator: Adj Assoc Prof Ivor Lim

National Fibrovascular Disorder Research Program

Principal Investigator: Dr M Ragunath (Bioengineering)
Co-Principal Investigator: Asst Prof Phan Toan Thang
Collaborators: Assoc Prof Koh Dow Roon,
Prof Donald Tan
(SERI and, Ophthalmology),
Asst Prof Wilson Wang

Molecular profiles of periodontal tissue after tooth re-plantation

Principal Investigator: Assoc Prof Sae-Lim Varawan (Dentistry)
Co-Principal Investigators: Asst Prof Phan Toan Thang,
Asst Prof George Yip Wai Cheong

A comparison of the immunotherapeutic potential of Lactobacillus spp. and Mycobacterium bovis, Bacillus Calmette Guérin

Principal Investigator: Dr Ratha Mahendran
Co-Principal Investigator: Assoc Prof Lee Yuan Kun
Collaborator: Assoc Prof Bay Boon Huat

Evaluation of intravesical gene transfer using a novel liposome-based preparation in a porcine model

Principal Investigator: Assoc Prof Kesavan Esuvaranathan
Collaborators: Dr Ratha Mahendran,
Dr Wu Qinghui

Non-viral gene therapy for human bladder cancer

Principal Investigator: Asst Prof Edmund Chiong
Collaborators: Assoc Prof Kesavan Esuvaranathan,
Dr Ratha Mahendran

Evaluation of the anti-tumor efficacy of the ESAT-6 antigen in gene therapy for bladder cancer

Principal Investigator: Asst Prof Edmund Chiong
Collaborators: Assoc Prof Kesavan Esuvaranathan,
Dr Ratha Mahendran

Intravesical interferon alpha and BCG immunotherapy for patients with recurrent bladder cancer after previous BCG therapy

Principal Investigator: Assoc Prof Kesavan Esuvaranathan

The role of connective tissue growth factor (CTFG) in the biology of epithelial-mesenchymal interactions of scar pathogenesis and skin aging

Principal Investigator: Asst Prof Phan Toan Thang

Adipose-derived mesenchymal cells for bone reconstruction: A Preliminary study in a mouse model

Principal Investigator: Assoc Prof Lim Thiam Chye
Collaborators: Assoc Prof Shabbir Moomhala (DMRI),
Asst Prof Jan Thorsten Schantz

Intramyocardial engraftment of skeletal myoblast for cardiac repair: optimization of transplantation conditions

Principal Investigator: Adj Assoc Prof Eugene Sim
Collaborators: Dr KH Haider (NUMI),
Ms Jiang Shujia (NHC),
Assoc Prof Teh Ming

Prevalence of the founder BRCA1 mutation c.2845insA in Singapore Malay breast and ovarian patients unselected for family history

Principal Investigator: Dr Sng Jen-Hwei
Co-Principal Investigator: Dr Philip Iau Tsau Choong
Collaborators: Dr Lee Soo Chin
(Haematology Oncology, NUH),
Prof John Wong Eu-Li,
Assoc Prof Ilandcheran A,
Asst Prof Mahesh Choolani,
Dr Khalil Raziv,
Asst Prof Putti Thomas Choudary

Does BRCA1 promotor hypermethylation play a significant role in Singapore women with breast cancer? A population based study

Principal Investigator: Dr Sng Jen-Hwei
Co-Principal Investigators: Dr Philip Iau Tsau Choong,
Dr Putti Thomas Choudary

Are medullary breast cancers an indication for BRCA1 mutation screening? A mutation analysis of 42 cases of medullary breast cancer

Principal Investigator: Dr Sng Jen-Hwei
Co-Principal Investigator: Dr Philip Iau Tsau Choong
Collaborators: Dr IO Ellis,
Dr S Pinder (Dept of Pathology,
Nottingham City Hospital, UK),
Dr E Denley (Dept of Pathology,
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Dr G Cross (Dept of Molecular Genetics,
Nottingham City Hospital, UK),
Prof RW Blamey (City Hospital,
Nottingham, UK)

Islet transplantation for type 1 diabetes using the edmonton protocol

Principal Investigator: Sir Roy Calne
Co-Principal Investigators: Prof Lee Kok Onn,
Assoc Prof Thai Ah Chuan
Collaborators: Dr Sum Chee Fang (AH),
Dr Lim Su Chi (AH),
Dr Cheah Wei Keat,
Dr Pary Sivaraman,
Assoc Prof Wang Shih Chang

DEPARTMENT OF
SURGERY**Continuing investigations into the role of epidermal-mesenchymal interactions in keloid pathogenesis and aberrant skin fibroproliferation**

Principal Investigators: Adj Assoc Prof Ivor Lim,
Asst Prof Phan Toan Thang

Collaborators: Dr Robert Qi
(HKUST, SAR, China formerly IMCB),
Assoc Prof Boon Huat Bay
(Anatomy),
Dr Sabine Werner
(ETH, Zurich, Switzerland),
Dr Michael T Longaker
(Stanford, USA)

Engineered bone graft in the reconstruction of the craniofacial skeleton

Principal Investigator: Assoc Prof Lim Thiam Chye

Collaborators: Dr Chou Ning,
Assoc Prof Shabbir Moomchala
(DMRI/CCPL),
Dr Dietmar Hutmacher

Intramyocardial engraftment of skeletal myoblast for cardiac repair, optimization of transplantation conditions

Principal Investigator: Adj Assoc Prof Eugene Sim

Co-Principal Investigator: Dr Kh Haider

Collaborators: Dr Ye Lei,
Ms Jiang Shujia,
Assoc Prof Teh Ming

Lipofection of angiogenesis genes in skeletal myoblasts for hind limb ischemia

Principal Investigator: Dr Kh Haider

Co-Principal Investigator: Adj Assoc Prof Eugene Sim

Collaborators: Assoc Prof Teh Ming,
Dr Terrance Chua (NHC),
Dr Philip Wong (NHC),
Dr Ye Lei

Non-viral delivery system for angiogenic gene transduction with human skeletal myoblasts for angiomyogenesis: making it safe for the ailing heart

Principal Investigator: Adj Assoc Prof Eugene Sim

Co-Principal Investigator: Assoc Prof Yean Teng Lim

In vivo assessment of human skeletal myoblasts for treatment of insulin resistance type II diabetes using KK.Cg-Ay/J transgenic mice

Principal Investigator: Adj Assoc Prof Eugene Sim

Auto transplantation of mesenchymal stem cell into chronically failing heart porcine model

Principal Investigator: Adj Assoc Prof Eugene Sim

Collaborators: Adj Assoc Prof Reida El Oakley,
Dr Sunil Rangappa,
Prof Lee Eng Hin,
Assoc Prof Teh Ming

VEGF mediated blood vessel formation in myocardial infarction model using human embryonic stem cell derived embryoid bodies

Principal Investigator: Adj Assoc Prof Eugene Sim

Co-Principal Investigator: Assoc Prof Yean Teng Lim

5-azacytidine induced cardiomyocyte transformation of bone marrow derived mesenchymal stem cells and their therapeutic potential for the treatment of chronic myocardial infarction

Principal Investigators: Adj Assoc Prof Eugene Sim,
Dr K H Haider (NUMI)

Collaborators: Prof Lim Yean Leng,
Dr Ye Lei,
Assoc Prof Liu Teh Chih,
Dr Phillip Wong

Transplantation of tissue stem cells from adult bone marrow for tissue replacement and genetic therapy: an in vivo cellular alternative to bioengineering and vector mediated gene therapy

Principal Investigator: Adj Assoc Prof Reida Oakley

Collaborators: Dr Lim Sai Kiang (GIS),
Dr Lee Eng Hin,
Dr Ng Soon Chye,
Assoc Prof Teh Ming,
Dr Lim Yean Teng,
Dr Lee Szu Hee,
Dr Manuel Salto-Tellez

INTERNATIONAL PUBLICATIONS

Beilner J, Schantz JT, Lim J, Lim TC

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Cranioplasty after trephination using a novel biodegradable burr hole cover: technical case report. *Neurosurgery* (2006) 58(1 Suppl):ONS-E176.**Chim H, Schantz JT**

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DEPARTMENT OF SURGERY

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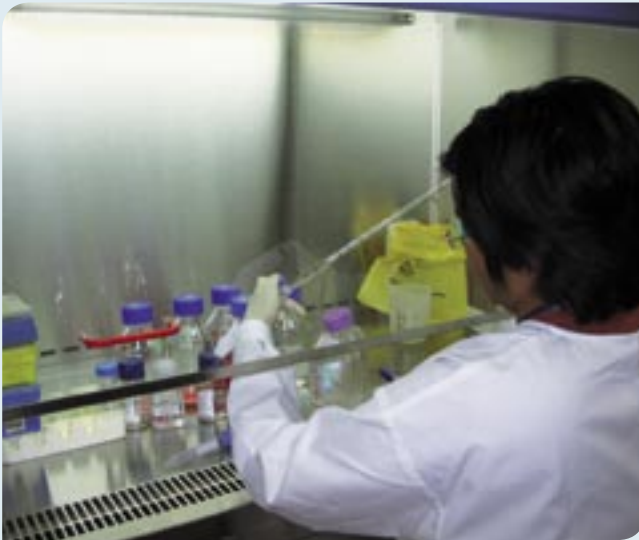
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DEPARTMENT OF
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Ms Juwita Rahmat preparing media.

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STAFF PROFILE

Professor & Head:
Associate Professor &
Deputy Head:
Professors:

Professorial Fellow:
Adjunct Professors:

Visiting Professors:

Associate Professors:

Adjunct Associate Professors:

Visiting Associate Professor:

Lee Chuen Neng

Leong Peng Kheong, Adrian
Soo Khee Chee
Uwe Klima

Ti Thiow Kong
Abu Rauff
Alan Porter
Walter Tan

Bernat Soria Escoms
Liu Chi Leung
Sydney Chung Sheung Chee
Tan Hock Lim
Sir Roy Calne

K. Prabhakaran
Kesavan Esuvaranathan
Lim Thiam Chye
Peter Ashley Robless
Wong Poo Sing

Chin Chong Min
Eugene Sim
Foo Chee Liam
Fong Poh Him
Ivor Lim
Reida Menshawe El Oakley
Susan Lim

Ngoi Sing Shang

DEPARTMENT OF SURGERY

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Visiting Senior Fellow:	
Assistant Professor & Research Staff:	Phan Toan Thang Ratha Mahendran
Senior Research Fellow:	Eliana C Martinez Valencia
Research Fellows:	Gan Shu Uin Kerrie Tang Lian Qizhou Pook Sim Hwee Sng Jen Hwei Wu Qinghui Winston Shim (Adjunct Fellow)
Research Assistants:	Jayavani d/o Karuppasamy Khoo Ying Ting, Audrey Lim Yew Koon, Eugene Que Qian Wen Tan Ai Lin, Diane Tay Yuh Ling, Amy Tham Sin Mun, Rachel
Laboratory Officers:	Deng Wei Elias Lye Ivy Seah James Boon Juwita Rahmat Ngo Kae Siang Revathi Kamaraj

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NATIONAL UNIVERSITY MEDICAL INSTITUTES (NUMI)

INTRODUCTION

The cardiovascular research programme investigates cell therapy and therapeutic angiogenic gene therapy in cardiac repair and regeneration. The programme explores the efficacy and mechanism of skeletal myoblast and embryonic stem cell transplantation in cardiac repair and regeneration. The project aims to develop non-viral vector (such as liposome and nanoparticle) mediated angiogenic gene transfer in cardiac neovascularisation. A total of 13 papers or abstracts were published. Fifteen abstracts had been presented in local and international congresses. Three awards had been won.

Islet beta-cell biology; differentiation of stem cells into insulin-producing cells for type 1 diabetes therapy; diabetic dysfunctional endothelial cells.

Major achievement: Having generated functional insulin-producing cells from mouse embryonic stem and progenitor cells.

The focus of research in the Oncology Research Institute has been on four main cancers:

A. Gastric cancer – Gastric cancer carries a poor prognosis with 79% of tumors diagnosed at stage IV and five year survival less than 5%. Diagnosed at an early stage, it is a curable disease. Two main studies are being conducted; first, examining the role of RUNX3 in human gastric cancer, and second, a study of a cohort of 4,000 high risk patients by examining their biopsy specimens.

Achievements: (i) discovered RUNX3 is involved in 40% of stage 1 gastric cancer and in over 90% of stage 4 gastric cancer (ii) succeeded in isolating monoclonal antibodies which detect only RUNX3 in human tissue sections (iii) the pilot gastric cancer screening programme GCEP, has been successful in diagnosing screen-detected cancers (iv) performed the world's first validation of confocal endomicroscopy technique in human stomach (v) optical detection of gastric cancer by RAMAN spectroscopic imaging (vi) proof of principle economic modeling of life-saving potential of screening endoscopy (vii) published the first report of detection of telomerase in gastric juice.

B. Breast cancer – Projects currently being pursued - Phosphoproteomics of breast cancer progression, regulation of cell division and DNA repair by BRCA2 tumor suppressor gene product & Alkylator-induced, BRCA2 Dependant Repair by AGT: Implications for Cancer Therapy.

Achievements: (i) Established two modern isotope- and liquid chromatography-based mass spectrometry methods for quantitative measurement and identification of phosphorylated proteins (ii) identified EGFR as a potential biomarker for early detection and prognosis of breast cancer (iii) identified 3 phosphoproteins in human epidermoid cancer cells as novel targets of oncogenic EGF signaling (iv) the studies in BRCA2 will clarify (a) cellular involvements of tumor suppressor protein BRCA2, (b) implications of BRCA2 loss on cell cycle and cell division, (c) DNA repair capabilities of BRCA2 KD models, in the absence of other genetic alterations and provide clarification of

NATIONAL UNIVERSITY MEDICAL INSTITUTES (NUMI)

various aspects of AGT function contributing to efficacy of alkylating chemotherapeutics viz. its regulation, transport and degradation.

C. Colorectal cancer – focus is on the role of RUNX3 in colorectal cancer and carcinogenesis with focus on TGF-beta & Wnt/beta-catenin signalling; new prognostic insights in Gastrointestinal Stromal Tumours (GIST); determinants of fluoropyrimidine sensitivity, ethnicity and chemoresponse, and methylation and chemosensitivity.

Achievements: (i) Molecular Information Arrays (MIA) allow detection of *VEGF protein overexpression signature*, as a statistically significant discriminator of prognosis in GIST (ii) validated that the levels of three enzymes critical to 5-FU metabolism can be useful markers of likely benefit from 5-FU, providing further conviction in clinical practice; characterized a number of novel variants in the TYMS gene, known to be a major target of 5-FU activity (iii) characterized significant difference in distribution of chemoresponse genotypes between Asians & Caucasians; developed this further by showing a number of response phenotypes predicted by genotype distribution as evident in clinical trial data by meta-analysis (iv) our recent studies show the gene encoding DPYD, a critical protein in 5-FU clearance, is regulated by methylation and have identified improved quality controls for methylation analysis to examine the clinical relevance of methylation in clinical samples.

D. Leukemia – main studies focus on the role of N-CoR in haematopoietic stem cell growth and lineage commitment, targeting ER (endoplasmic reticulum) stress in APL (acute promyelocytic leukemia) for therapeutic intervention and the role of protease in APL pathogenesis.

Achievements: (i) both the mis-folded N-CoR and the activity which cleaves it have the potential to become important bio-markers for AML, and could represent attractive molecular targets for selective anti-leukemia therapy (ii) our in-vitro study demonstrates that genistein is equally effective against retinoic acid (RA) resistant APL cells. Genistein is a natural component of soy protein and is devoid of any adverse effect. Due to its potent effect, its abundance in traditional diet, and its tolerance and lack of systematic toxicity, genistein holds great promise in the treatment of APL, including the RA resistant APL. (iii) identified novel cytoprotective branch of unfolded protein response (UPR) which is activated through induction of protease and regulates tumor cell's response to UPR-induced apoptosis through processing mis-folded proteins.

PROJECT DESCRIPTION

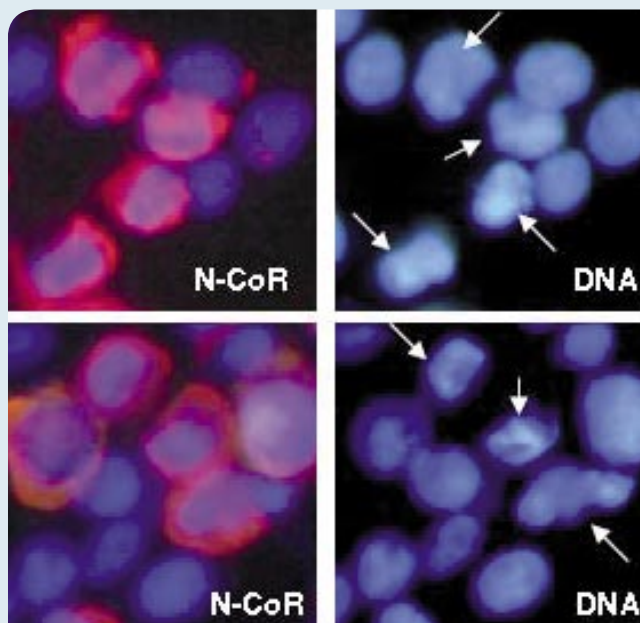
Grants Awarded in 2006

Role of aberrant protease activity in the pathogenesis of acute myeloid leukaemia (AML)

Principal Investigator: Dr Md Matiullah Khan
Co-Principal Investigators: Assoc Prof Chen Chien-Shing,
Dr Motomi Osato

Role of Nuclear Receptor (N-CoR) in the regulation of Haematopoietic Stem Cells (HSCs) growth, lineage commitment and malignant transformation

Principal Investigator: Dr Md Matiullah Khan
Co-Principal Investigators: Prof Shazib Pervaiz,
Assoc Prof Chen Chien Shing
Collaborator: Dr Motomi Osato



Accumulation of mis-folded N-CoR is cytotoxic: Features suggestive of cell death (marked by arrow) in cells containing mis-folded N-CoR protein (Red).

Regulation of cell division and DNA repair by BRCA2 tumor suppressor gene product

Principal Investigator: Dr Srividya Swaminathan
Collaborator: Assoc Prof Manoor Prakash Hande

Molecular changes during breast cancer progression

Principal Investigator: Dr Lim Yoon Pin
Collaborators: Assoc Prof Saraswati Sukumar,
Dr Brian J Druker,
Prof Hew Choy Leong,
Dr Gunaretnam Rajagopal,
Dr Tan Puay Hoon,
Assoc Prof Manuel Salto-Tellez,
Dr Lin Qingsong,
Dr Newman Sze,
Jeffery Hill

Alkylator-induced, BRCA2 dependant repair by AGT: Implications for cancer therapy

Principal Investigator: Dr Srividya Swaminathan
Collaborator: Dr Lim Yoon Pin

To define ES cell-derived progenitors for differentiation of insulin-producing cells for replacement therapy of type I diabetes

Principal Investigator: Assoc Prof Li Guodong
Co-Principal Investigator: Assoc Prof Lim Sai Kiang
Collaborators: Assoc Prof Kon Oi Lian,
Assoc Prof Manuel Salto-Tellez,
Dr Paolo Meda

Cancer therapeutics animal model program for pre-clinical testing in NUS/NUH

Principal Investigator: Assoc Prof Chen Chien-Shing
Co-Principal Investigators: Assoc Prof Hanry Yu,
Prof Yong Eu Leong

NATIONAL UNIVERSITY MEDICAL INSTITUTES (NUMI)

Development of an early phase clinical trials oncology program at The Cancer Institute (National Healthcare Group-NHG), in conjunction with the Cancer Therapeutics Research Group (CTRG)

Principal Investigator: Assoc Prof Chen Chien-Shing
Co-Principal Investigators: Prof Jean-Paul Deslypere,
Prof John Wong

Development of the transplantation material medical research centre at NUS: Therapeutic applications in haematological malignancies and solid with tumors Non-Myeloablative Transplantation (NMT)

Principal Investigator: Assoc Prof Chen Chien-Shing
Co-Principal Investigators: Dr Tan Lip Kun,
Dr Ping Law

Elucidation of the roles of a novel protein MLL5 in cell cycle regulation and tumor suppression

Principal Investigator: Dr Deng Lih Wen
Co-Principal Investigator: Dr Motomi Osato

Multi-center PEPTidomics Initiative (PEPTITE) and biomarkers for predicting response in target-directed cancer therapeutics

Principal Investigator: Dr Lim Yoon Pin
Co-Principal Investigators: Prof Hew Choy Leong,
Dr Tan Puay Hoon,
Assoc Prof Manuel Salto-Tellez,
Dr Ross Soo,
Dr Darren Lim,
Dr Lee Soo Chin,
Dr Philip Iau,
Assoc Prof Goh Boon Cher,
Dr Lin Qingsong,
Dr Nilesh Shah,
Dr Peter Ang,
Dr Wong Chow Yin
Collaborators: Assoc Prof Gunaretnam Rajagopal,
Dr Newman Sze

Platform to link microarrays to nucleic acid-based work in clinical samples and facilitation of molecular diagnosis/technology transfer to the clinical setting

Principal Investigator: Assoc Prof Manuel Salto-Tellez
Co-Principal Investigators: Dr Richie Soong,
Dr Robert Hewitt

Infrastructure for Developing Gastrointestinal Cancer Prognostic and Predictive Markers

Principal Investigator: Dr Richie Soong
Co-Principal Investigators: Prof Alex Cheng,
Assoc Prof Eu Kong Weng,
Dr Liu Yanqun,
Assoc Prof Adrian Leong,
Dr Simon Ong,
Assoc Prof Manuel Salto-Tellez,
Dr Richard Sim,
Dr Ross Soo,
Dr Yap Wai Ming

Expansion of the Gastric Cancer Epidemiology Clinical & Genetics Program (GCEP) for population-based studies to identify clinical, serologic pathological and genetic markers which can be used to define an optimal approach to gastric cancer screening

Principal Investigator: Assoc Prof Yeoh Khay Guan
Co-Principal Investigators: Assoc Prof Ho Khek Yu,
Prof Yoshiaki Ito

The cancer translational pipeline for development of oncologic agent

Principal Investigator: Assoc Prof Goh Boon Cher

To develop reliable and robust biomarkers in breast cancer chemotherapy through high-throughput proteomic profiling

Principal Investigator: Dr Lee Soo Chin

Lung cancer in Singapore: Molecular profiling genotyping & epidemiological assessment

Principal Investigator: Dr Elaine Lim

On-going Projects

Crossing the histocompatibility barriers using transient immunosuppression: implications in cellular cardiomyoplasty using human skeletal myoblasts for cardiac repair

Principal Investigator: Dr Haider Khawaja Husnain

Pathogen recognition and signaling by toll-like receptors, a family of adjuvant receptors for the host immune system to sense different types of pathogens

Principal Investigator: Assoc Prof Lu Jinhua

Targeting the ER stress in APL for therapeutic intervention

Principal Investigator: Dr Md Matiullah Khan
Collaborator: Assoc Prof Manoor Prakash Hande

Human skeletal myoblast transplantation of cardiac repair: Molecular basis of donor cell survival and improvement of myocardial performance

Principal Investigator: Assoc Prof Li Guodong
Co-Principal Investigator: Assoc Prof Eugene KW Sim

Lipofection of human vegf165 in human skeletal myoblasts for angiomyogenesis making it safer for the ailing heart

Principal Investigator: Dr Haider Khawaja Husnain

Molecular mechanism for the activation of rac1 and downstream effectors by glucose stimulation in the regulation of insulin secretion from islet beta-cells

Principal Investigator: Assoc Prof Li Guodong
Co-Principal Investigator: Prof Anjan Kowluru (USA)

The role of runx3 as a tumour suppressor in human colorectal cancer

Principal Investigator: Dr Robert Hewitt
Co-Principal Investigator: Dr Kosei Ito
Collaborators: Dr Masafumi Inoue,
Assoc Prof Teh Ming

Targeting the conformational rearrangement of N-CoR protein for therapeutic intervention in Acute Promyelocytic Leukemia (APL)

Principal Investigator: Dr Md Matiullah Khan
Co-Principal Investigator: Prof Shazib Pervaiz
Collaborator: Dr Shunsuke Ishii

NATIONAL UNIVERSITY MEDICAL INSTITUTES (NUMI)

Generation, isolation and verification of insulin-secreting cells from progenitor cell lines derived from mouse embryos and ES cells

Principal Investigator: Assoc Prof Li Guodong
Co-Principal Investigator: Assoc Prof Lim Sai Kiang (GIS)

Functional analysis of Ataxia Telangiectasia Mutated (ATM) in BRCA and non-BRCA tumor

Principal Investigator: Dr Srividya Swaminathan
Co-Principal Investigator: Assoc Prof Manoor Prakash Hande

Phosphoproteomic fingerprinting and identification of activated tyrosine kinases and substrate in laser-captured microdissection-purified human breast cancer epithelial

Principal Investigator: Dr Lim Yoon Pin
Collaborators: Dr Newman Sze,
Prof Saraswati Sukumar,
Dr Tan Puay Hoon,
Dr Tan Soo Yong,
Dr Brian J Druker,
Assoc Prof Chung Ching Min, Maxey,
Dr Robert Qi,
Dr Wong Chow Yin,
Dr Philip Iau Tsau Choong

Study on vitrification of cells and tissues

Principal Investigator: Dr Lilia Kuleshova

A study to investigate the mechanism involved in H2O2-mediated repression of the Na⁺/H⁺ exchanger 1 (NHE-1) gene expression: possible role in cells' response to apoptotic death

Principal Investigator: Dr Alan Prem Kumar s/o Vasudevan

Gastric cancer epidemiology, clinical and generic programme (GCEP) cohort study of patients at high risk of gastric cancer

Principal Investigator: Assoc Prof Yeoh Khay Guan
Co-Principal Investigators: Prof Yoshiaki Ito,
Assoc Prof Ho Khok Yu,
Dr Andera Rajnakova,
Dr Christoher Jen Lock Khor,
Prof Fock Kwong Ming
Collaborators: Assoc Prof Teh Ming,
Assoc Prof Manuel Salto-Tellez,
Assoc Prof Manoor Prakash Hande,
Assoc Prof Ho Bow,
Dr Kosei Ito,
Dr Richie Soong Chuan Teck,
Assoc Prof Chia Kee Seng,
Dr Robert E Hewitt

General devt of the molecular pathology initiative (devt of pathology SGH: a comprehensive platform to link tissue microarrays to nucleic acid-based work in clinical samples)

Principal Investigator: Assoc Prof Manuel Salto-Tellez

Characterizing the resveratrol-evoked, bax-and p53-independent apoptosis signaling cascades: In relevance to the therapeutic development of resveratrol

Principal Investigator: Dr Lee Shao Chin

Uncovering the neuropathological role of superoxide dismutase 1 and mitochondrial impairment in down syndrome

Principal Investigator: Dr Wong Boon Seng

Oncoproteomics in gastric cancer biomarker discovery

Principal Investigator: Prof Hew Choy Leong
Co-Principal Investigators: Assoc Prof Chung Ching Ming Maxey,
Assoc Prof Yeoh Khay Guan,
Prof Yoshiaki Ito,
Dr Lim Yoon Pin,
Dr Ling Qingson,
Dr Sandra Tan

Characterizing the carbohydrate composition on apolipoprotein e using inbred and knockout animal models as potential biomarkers for atherosclerosis

Principal Investigator: Dr Wong Boon Seng
Collaborators: Prof Barry Halliwell,
Prof Roland Stocker

Establishment of a gastric cancer epidemiology clinical & genetics program (GCEP) for population-based studies to identify clinical, serologi pathological & genetic markers

Principal Investigator: Assoc Prof Yeoh Khay Guan
Co-Principal Investigators: Prof Yoshiaki Ito,
Assoc Prof Ho Khok Yu,
Dr Christoher Jen Lock Khor

Investigating the effect of caloric restriction on neuronal glucose metabolism in an Alzheimer's disease animal model

Principal Investigator: Dr Wong Boon Seng
Collaborators: Prof Barry Halliwell,
Assoc Prof Sanjay Swarup,
Christopher Chen

Identifying the glycan profile on apolipoprotein e polymorphism as clinical tool for Alzheimer's disease

Principal Investigator: Dr Wong Boon Seng
Collaborator: Christopher Chen

A melatonin/quinone oxidoreductase sensitive system that is involved in regulating cell survival

Principal Investigator: Dr Andrea Lisa Holme

Delineation of resveratrol-activated apoptotic signaling cascades through cascades through functional proteomic analysis

Principal Investigator: Dr Lee Shao Chin

INTERNATIONAL PUBLICATIONS

Salto-tellez M, Peh BK, Ito K, Tan SH, Chong PY, Han HC, Tada K, Ong WY, Soong CTR, Voon DC, Ito Y

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Chin TM, Nur DBA, Soo R, Salto-tellez M, Li WQ, Bai BA, Lee SC, Goh BC, Kawakami K, Segal A, Iacopetta B, Soong CTR

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Senatorov V, Malyukova I, Fariss R, Wawrousek E, Swaminathan S, Sharan SK, Tomarev S

Expression of mutated mouse myocilin induces open-angle glaucoma in transgenic mice. *Journal of Neuroscience* (2006) 26(46):11903-11914. (United States).

NATIONAL UNIVERSITY
MEDICAL INSTITUTES (NUMI)**Chaw KC, Manimaran M, Tay EH, Swaminathan S**

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Yan B, Han HC, Peh BK, Lim C, Salto-tellez M

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Pervaiz S, Lee SC

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Kishore KR

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NATIONAL UNIVERSITY MEDICAL INSTITUTES (NUMI)

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STAFF PROFILE

Directors:	Prof Moore Philip Keith (NUMI) Prof Yoshiaki Ito (ORI)
Research Associate Professor:	Li Guodong
Senior Research Scientists:	Wong Boon Seng Koichi Okumura Lim Yoon Pin Md Matiullah Khan Richie Soong Chuan Teck Srividya Swaminathan
Research Scientists:	Alan Prem Kumar Andrea Lisa Holme Lee Shao Chin Lilia Kuleshova

Research Fellows:

Research Assistants:

Lab Officers (Research):

Ko Tun Kiat
Nilesh Manubhai Shah
Gouk Sok Siam
Kishore
Lian Qizhou
Ye Lei
Chong Poh Kuan
Man Pui Sum
Man Xiaohui
Manish
Yang Shu
Zhou Yefang
Chua Ching Ching
Phoo Meng Seng
Quake Ai Li
Wahidah
Anurag Gupta
Emily Chen Yunhao
Chin Sze Yung
Choong Lee Yee
Kah Kong Jie
Lee Huiyin
Lim Simin
Mohd Feroz Bin Mohd Omar
Peh Bee Keow
Wong Hui Sian, Fiona
Lim Mei Li
Luo Ruihua
Teh Song Hooi
Xie Fei
Toh Wee Chi
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ALICE LEE CENTRE FOR NURSING STUDIES



INTRODUCTION

The Alice Lee Centre for Nursing Studies (ALCNS) embraces the need for evidence-based practice for nursing and is working actively and collaboratively with health care agencies, with other departments in the School of Medicine and with other faculties in the university to pursue translational health services research in support of Singapore's aim to be a regional leader in health care research and practice.

Each of the five PhD prepared faculty has been actively seeking funding to pursue their research interests and have taken advantage of the encouraging research atmosphere in Singapore. To date, the ALCNS has attracted funding to the value of \$400,000 in research funding, with a further \$394,000 under consideration.

Topics under investigation include cardiac rehabilitation, adolescent depression, gambling behaviour in university students, parents' experiences of bereavement, post-natal depression, palliative care, cognitive behavioural therapy for depressed adolescents and studies on student performance in the BSc (Nursing). While it is early days, the ALCNS will develop research themes suited to Singapore's health care needs and most likely in the areas of:

- nurse led brief psychosocial interventions;
- nurse led interventions for lifestyle-related disorders (eg. diabetes, heart disease, obesity);

- family health;
- palliative care;
- aged care; and
- virtual technology nursing education

PROJECT DESCRIPTION

Grants Awarded in 2006

Gambling behaviour in Singapore university students

Principal Investigator: Prof David Arthur
Co-Principal Investigators: Assoc Prof Hing Ai Yun,
Dr Miharū Sagara-Rosemeyer,
Prof Kua Ee Heok

Integrative counselling by nurse midwives for women at risk of postnatal depression in Singapore: A pilot study

Principal Investigator: Prof David Arthur
Co-Principal Investigators: Dr Anthony O'Brien,
Dr Helen Chen (KKWCH)

Singapore nurses' perception of postoperative pain management in children

Principal Investigator: Dr He Hong Gu
Co-Principal Investigators: Prof Lee Tat Leang,
Ms Emily Ang (NUH),
Ms Joanne Lian Li Wee (KKWCH)

ALICE LEE CENTRE FOR NURSING STUDIES

Reducing adolescent depression incidence - The effect of Cognitive Behaviour Therapy (CBT) in a psychiatric outpatient setting compared with Computerised CBT (CCBT) web based depression treatment and education

Principal Investigator: Dr Anthony O'Brien
Co-Principal Investigators: Prof David Arthur,
Dr Roger Ho

Singaporean parents' lived experiences of losing a child

Principal Investigator: Dr Miharu Sagara-Rosemeyer

On-going Projects

DREEM (Dundee Ready Education Environment Measure) evaluation of the ALCNS curriculum - A longitudinal project - results will be compared statistically between modules and across departments feeding into the degree program

Principal Investigator: Dr Anthony O'Brien

Audit of the implementation of PBL in a Singapore Bachelor of Science Nursing program

Principal Investigator: Dr Anthony O'Brien
Co-Principal Investigators: Dr Tan Keng Leong (SGH),
Dr Betty Mok,
Dr Fong Yoke Fai,
Prof Peter Hwang,
Prof Hugo Van Bever

Evaluating the clinical buddy (Preceptor System) used as a teaching model with registered nurses ALCNS nursing students' during clinical practicum attachment

Principal Investigator: Dr Jillian Brammer

The Singapore Palliative Care Project

Principal Investigator: Dr Anthony O'Brien
Co-Principal Investigators: Prof David Arthur,
Ms Grace Pang
(Hospice Council of Singapore),
Dr Miharu Sagara-Rosemeyer,
Mr Edward Poon
(Dover Park Hospice),
Ms Angela Lee (TTSH),
Prof Richard Huxtable
(Univ of Bristol, UK),
Prof Alastair Campbell,
Ms Antonia Arnaert
(McGill Univ, Canada),
Ms Colleen Cartwright
(Southern Cross Univ, Australia),
Ms Wendy Hampshire
(Southern Cross Univ, Australia)

East Asian Development Network (EADN): Socioeconomic instability and the availability of health resources: Their effects on infant mortality rates in Singapore and Hong Kong from 1956 - 2005

Principal Investigators: Prof David Arthur,
Dr Tony Chan Moon Fai
(Hong Kong Polytechnic Univ)
Co-Principal Investigator: Ms Tong Wai Leng



Mannequins providing realistic nursing experiences.

INTERNATIONAL PUBLICATIONS

Li Z, Arthur D, Wu XJ, Gao FL, Ma YF, Song SM, Kang XF

The effect of a brief intervention for problem drinkers in general hospital: A randomized controlled trial. Chinese Journal of Nursing 41(7):585-588.

Arthur D

Drinking across China: lessons from a complex culture. Drugs and Alcohol Today 5(4):15-18.

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He HG

Nursing education today and its future trends in mainland China. ICUS and Nursing Web Journal 26 (2006): 1-3

He HG, Polkki T, Pietila AM, Vehvilainen-Julkunen K

Chinese parent's use of nonpharmacological methods in children's postoperative pain relief. Scandinavian Journal of Caring Science (2006) 20(1):2-9.

ALICE LEE CENTRE FOR NURSING STUDIES

STAFF PROFILE

Professor & Head:	David Arthur
Assistant Professors:	Anthony O'Brien He Hong-Gu Miharu Sagara-Rosemeyer
Senior Lecturer:	Gender Kaur
Lecturer:	Liaw Sok Ying
Adjunct Associate Professor:	Ang Beng Choo
Adjunct Assistant Professors:	Emily Ang Edward Poon
Visiting Fellows:	Jillian Brammer Madrean Schober
Research Assistant (EOM):	Tong Wai Leng
Research Assistants (Research Grants):	Chen Chia Pei Ma Aye Aye Cho



Completing a survey/questionnaire.

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Preparing to dress a diabetic ulcer.



Resuscitating a patient.

AWARDS & PRIZES



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STAFF PROFILE

Professor & Head:
Assistant Professors:

David Arthur
Anthony O'Brien
He Hong-Gu
Miharu Sagara-Rosemeyer

Senior Lecturer:

Gender Kaur

Lecturer:

Liaw Sok Ying

Adjunct Associate Professor:

Ang Beng Choo

Adjunct Assistant Professors:

Emily Ang

Edward Poon

Visiting Fellows:

Jillian Brammer

Madrean Schober

Research Assistant (EOM):

Tong Wai Leng

Research Assistants

(Research Grants):

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Ma Aye Aye Cho



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Preparing to dress a diabetic ulcer.

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Resuscitating a patient.

AWARDS & PRIZES



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AWARDS & PRIZES

ANAESTHESIA

Assoc Prof Chen Fun Gee

won the Best Poster award at the 3rd Asia Pacific Medical Education Conference, NUS, in February 2006.

Assoc Prof Eugene Liu Hern Choon

won the Best abstract of equipment - Airway Section Award at the International Anaesthesia Research Society Congress 2006, San Francisco, USA, in March 2006.

BIOCHEMISTRY

Dr Yeong Foong May

won the Young Investigator Award by the Office of Life Sciences, NUS, in March 2006.

Dr Robert Yang

was awarded the Research Excellence Award (Young Scientist, Academic year 04-05) by Yong Loo Lin School of Medicine in February 2006.

Prof Barry Halliwell

was awarded the Tan Chin Tuan Centennial Professorship by the Office of The President, NUS, in July 2006.

Assoc Prof Caroline Lee

won the SingHealth Investigator Excellence Award 2006 by Singhealth Foundation in October 2006.

COMMUNITY, OCCUPATIONAL AND FAMILY MEDICINE

Dr Helena Marieke Verkooijen

won the SIAK / ESSEX prize for her work in the field of breast cancer epidemiology by ESSEX Chemie SA (a subsidiary company of Schering-Plough) in November 2006. This prize is yearly installed by the Swiss Institute for Applied Cancer Research (SIAK).

Assoc Prof Goh Lee Gan

was awarded the Honorary Fellowship of Academy of Family Physicians, Malaysia (FAFP) in April 2006.

Assoc Prof Chia Sin Eng

won the Best Oral Paper Award at the 13th International Conference of the International Society for Respiratory Protection, Toronto, Canada, in September 2006.

Dr Koh Woon Puay

won the Best Oral Paper Award for the category on General Practice at the National Healthcare Group Annual Scientific Congress 2006 in October 2006.

Dr Koh Woon Puay, Andre Tan, Lester Ong, Gowri Doraisamy (NHGP), B Cheah (NHGP)

won Best Poster Award for the category on General Practice at the NHG Annual Scientific Congress 2006 in October 2006.

Dr Koh Woon Puay

won the First Prize in Oral Presentation at the Second Singapore Public Health and Occupational Medicine Conference in July 2006.

Assoc Prof Saw Seang Mei, Prof Chia Kee Seng

won The Garland W. Clay Award by the American Academy of Optometry for the most cited paper in the past five years in Optometry and Vision Science.

Assoc Prof Saw Seang Mei

won the Great Women of Our Time Award 2006 for the Science and Technology Category by Singapore Women's Weekly Magazine in November 2006.

Dr Shen Han-Ming

was awarded the Faculty Research Excellence Award 2005-2006 by Yong Loo Lin School of Medicine in April 2007.

DIAGNOSTIC RADIOLOGY

Dr Sudhakar K Venkatesh, Fiona P Leung, Gabriel Lau, Assoc Prof Wang Shih Chang, Christopher C Au

won the Best Scientific Poster Award for their presentation "Utility of Diffusion Weighted MR Imaging in Differentiation of Focal Hepatic Lesions" by the Singapore Radiological Society in March 2006.

Dr Sudhakar K Venkatesh

was awarded the Magna Cum Laude (Best Educational Exhibit) for his presentation "CT of Blunt Pancreatic Trauma" by European Congress Radiology in March 2006.

Dr Sudhakar K Venkatesh, Gabriel Lau, Fiona P Leung, Christopher C Au, Assoc Prof Wang Shih Chang

won the Young Investigator Award for their presentation "Role of diffusion weighted MR imaging in radio-frequency ablation of liver tumours" by the Asia Oceania Congress of Radiology in August 2006.

MEDICINE

Dr Lam Su Ping, Carolyn

was awarded the Jay N Cohn New Investigator Clinical / Integrative Physiology Award Competition (First prize) by the Heart Failure Society of America in September 2006.

Assoc Prof Ho Khok Yu

won the "NHG Best Poster Award - Medicine & Paediatrics" at the Combined Scientific Meeting 2006, Singapore.

AWARDS & PRIZES

Assoc Prof Yeoh Khay Guan

was given the JGH Emerging Leader Lectureship Award by Journal of Gastroenterology & Hepatology Foundation (JGH) in November 2006. This was awarded by peer-review after national nominations representing respective countries in the Asia-Pacific region.

Dr Raymond CC Wong, Assoc Prof Ling Lieng Hsi

won the Young Investigators' Award, Best Clinical Paper by Singapore Cardiac Society in March 2006.

Assoc Prof Erle Lim Chuen Hian

won the Best Poster Presentation (Merit award) at the 4th Asia Pacific Medical Education Conference.

Assoc Prof Dale Fisher

was awarded the RACP John Sands Medal for Outstanding Contribution to College Affairs in May 2006, Australia.

Dr Annabelle Donaldson, Dr Louis Chai

won the ICAAC Travel Awards for ID Fellows by American Society for Microbiology. This was awarded by the American Society for Microbiology at the ICAAC Annual Meeting.

MICROBIOLOGY

Prof Chan Soh Ha

was given the Excellent Award by the Asia Pacific Society for Medical Virology, New Delhi, India, for his outstanding contribution in medical virology.

Assoc Prof Vincent Chow

was selected as President of Asia Pacific Society for Medical Virology by Asia Pacific Society for Medical Virology. There were more than 500 active members / virologists from the Asia-Pacific region.

Dr S Alonso, Mrs Phoon MC, Mr Ramachandran NP, Assoc Prof V Chow, and Assoc Prof Poh CL

won the Best Poster for Basic Science Award, project title "Identification of neutralizing linear epitopes from VP1 capsid protein of enterovirus 71 using synthetic peptides" at the National Healthcare Group Annual Scientific Congress.

Dr Kevin Tan

was awarded the SMJ 2005 Recognition Award by the Singapore Medical Association in recognition of his outstanding services as a reviewer of scientific manuscripts submitted for publication in SMJ.

Prof Mary Ng's, Assoc Prof Sim Tiow Suan's, and Assoc Prof Ho Bow's postgraduate students: Cheong Yuen Kuen Adrian, Ling Shi Min Samantha, Lye Yu Min and Wee Soon Huat Alvin were awarded the President's Graduate Fellowship.

Wong Kok Loon and Prof Mike Kemeny

won First Prize in the conference organized by the OLS 2007 Organising Committee for their poster presentation "Activated cd8t cells can provide help for th1 development by inducing dendritic cells to produce IL-12p70 via CD40-CD40L interactions".

Assoc Prof Ho Bow, Loke MF

won the Best Poster Award on "Bacterial Pathogenesis" for the paper "Antiadhesive property of microalgal polysaccharide extract on the binding of *Helicobacter pylori* to gastric mucin", presented at the 7th International Workshop on Pathogenesis and Host Response in *Helicobacter Infections*, 1-4 Jul 2006, LO Skolen, Helsingor, Denmark.

OBSTETRICS & GYNAECOLOGY

Dr Kothandaraman Narasimhan, Prof Vladamir B Bajic, Assoc Prof Pang Nghee Kheem Brendan, Ms Peh Bee Keow, Assoc Prof Manuel Salto-Tellez, Dr Khalil Razvi, Assoc Prof Arunachalam Ilancheran, Dr Mahesh Choolani won the Oral Award at the 7th International Conference on Ovarian Cancer, 29 November to 2 December 2006.

Mr HM Zhang, Dr AP Mayuddin, Dr S Ponnusamy, Mr CQ Zhao, Assoc Prof B Arijit, Assoc Prof M Rauff, Dr M Choolani won the Best Oral Presentation Award by the National Healthcare Group, 30 September to 1 October 2006.

Mr CQ Zhao, Dr L Annamalai, Mr CF Guo, Dr N Kothandaraman, Mr HM Zhang, Ms SE Chua, Dr M Choolani won the Best Oral Presentation Award (Surgical Discipline) by the National Healthcare Group, 30 September to 1 October 2006.

Ms Ho Sze Yee Sherry, Assoc Prof Samuel S Chong, Assoc Prof Evelyn SC Koay, Dr Ponnusamy S, Ms Lily Chiu, Mr Wang Wen, Assoc Prof Ashim Roy, Assoc Prof Mary Rauff, Dr Lin Lin Su, Assoc Prof Arijit Biswas, Dr Mahesh Choolani have been awarded the Young Scientist Award by the International Society for Prenatal Diagnosis on 28 to 1 May 2006.

Mr Xu GL, Dr Chan-Park MB, Dr Yang C, Mr Chiew D, Dr Choolani M, Prof Ying JY won the Prize for the Best Poster Presentation at the UK-Singapore Bioelectronics Workshop, 23 to 26 January 2006.

Ms NH Bte Ismail, Ms Tan HQ, Dr Narasimhan K, Dr Lim GB, Dr Choolani M won the Prize for the Best Poster Presentation by Ngee Ann Polytechnic in January 2006.

Prof P Ganesan Adaikan, Dr Srilatha Balasubramanian, Prof Philip Keith Moore, Ms Li Ling won the Emil Tanagho Prize for Best Innovative Research in Sexual Medicine at the 12th World Congress on Sexual Medicine held in Cairo, Egypt from 17 to 21 September 2006. It is a joint study from the Departments of Obstetrics and Gynaecology and Pharmacology submitted to the International Society for Sexual Medicine (ISSM) titled "Hydrogen sulphide, a novel endogenous gasotransmitter facilitates erectile function and opens new window for ED therapy". This prestigious international competitive prize (US\$1000) which is open to 2700 members of the society - is awarded once in 2 years at the world meetings of ISSM.

AWARDS & PRIZES

Dr B Srilatha

was awarded the APSSM-JSM Research Grant Award by the Asia Pacific Society for Sexual Medicine & Journal of Sexual Medicine in November 2006. US\$10,000 was awarded for his proposal titled "Is there role for the novel gasotransmitter hydrogen sulphide in female sexual function / dysfunction". This is a first time award in Asia given to an applied scientific researcher in the area of sexual medicine whose achievement may contribute to the advancement of sexual medicine and the promotion of the Journal of Sexual Medicine (JSM, USA), the official Journal of ISSM. This competitive award is open to members of Asia Pacific Society for Sexual Medicine (APSSM).

Ms Lau Lang Chu

was awarded the APSSM Research Grant Award by the Asia Pacific Society for Sexual Medicine (APSSM) on 12 September 2006. Her research proposal titled "Evaluation of chloride channel blockers in diabetes induced erectile dysfunction in rabbits" has won the prize of US\$5000 for original research in the area of sexual medicine. It is open to all APSSM members residing in the Asia Pacific continent.

OPHTHALMOLOGY

Assoc Prof Aung Tin, Dr Eranga Nishanthie Vithana, Prof Tan Tiang Hwee Donald, Assoc Prof Manuel Salto-Tellez (Pathology)

won the Singhealth Outstanding Publication Award for papers on Gene discovery for Congenital Hereditary Endothelial Dystrophy in July 2006.

Dr Ang Pek Kiang, Leonard

won the Best Oral Presentation (Merit) by the Asia Pacific Academy of Ophthalmology in June 2006.

Dr Ang Pek Kiang, Leonard

was awarded the Young Researcher Award at the University Awards 2006 by the Office of Research (NUS) in April 2006. The award consists of \$2,000 prize money and \$10,000 research grant.

Assoc Prof Wong Tien Yin

was awarded The Commonwealth Minister of Health Award for Excellence in Medical Research by The National Health and Medical Research Council, Australia, in June 2006. It was made in recognition of his outstanding individual achievement in health and medical research in Australia.

Assoc Prof Wong Tien Yin

won the Alcon Award by Alcon Research Institute, USA, in May 2006. This award is given annually for the outstanding contributions to ophthalmology and vision science.

Assoc Prof Wong Tien Yin

won The Novartis Prize in Diabetes (Young Investigator) by Novartis, USA, in September 2006. This is in recognition of innovative patient-oriented research in the fields of physiology, pathophysiology or epidemiology of diabetes mellitus and its complications.

Prof Tan Tiang Hwee, Donald

was awarded the Distinguished Achievement Award by the American Academy of Ophthalmology in October 2006. This is in recognition of his many years of distinguished service to the Academy, and its scientific and continuing education programs.

Prof Tan Tiang Hwee Donald, Assoc Prof Aung Tin, Assoc Prof Wong Tien Yin, Prof Roger W Beuerman, Assoc Prof Saw Seang Mei, Assoc Prof Paul Anantharajah Tambyah (Medicine), and other clinical investigators from all major government eye departments (SNEC, NUH, TTSH, CGH)

were awarded the Minister for Health Award for outstanding performance in Public Health - Outbreak of Fusarium Keratitis by the Ministry of Health in July 2006.

ORTHOPAEDIC SURGERY

Dr Wang Ee Jen Wilson, Shi Zhilong and Prof Neoh Koon Gee (Department of Chemical & Biomolecular Engineering)

were awarded the Singapore Orthopaedic Association-Bioengineering Society (SOA-BES) Prize for Best Bioengineering Paper by the Singapore Orthopaedic Association and Bioengineering Society, for their paper 'Chemical conjugation of norfloxacin antibiotic to bone cement to enhance antimicrobial activity - a new approach' at the 29th Singapore Orthopaedic Association Annual Scientific Meeting, Singapore, 8-11 November 2006.

Dr Saminathan Suresh Nathan

was awarded the Health Service Development Programme by the Ministry of Health in November 2006.

Dr Saminathan Suresh Nathan

was awarded Mentorship Assessment Programme by the National Healthcare Group in April 2006.

Dr Saminathan Suresh Nathan

won the Researcher Investigator Scientist Enabler Award by the National Healthcare Group in April 2006.

Prof Lee Eng Hin

was awarded the Faculty Outstanding Researcher Award 2006 by the Yong Loo Lin School of Medicine in April 2006.

Prof Lee Eng Hin

won the NUS Outstanding Researcher Award by the Office of Research in May 2006.

Prof Wong Hee Kit, Dr Hee Hwan Tak, Naresh Babu, Peng Yian, Tai Hui Ren

were awarded the Young Orthopaedic Investigator Award by the Singapore Orthopaedic Association, for their paper 'Behaviour of proximal thoracic curve after thoracoscopic selective anterior fusion for adolescent idiopathic scoliosis - a longitudinal study with minimum 2 years follow-up' at the 29th Singapore Orthopaedic Association Annual Scientific Meeting, Singapore, 8-11 November 2006.

AWARDS & PRIZES

Assoc Prof Hui Hoi Po

was awarded the BMRC-NMRC Clinician Scientist Investigator Award 2006 by the Agency for Science, Technology and Research in April 2006.

Low Siew Leng, Prof Das De Shamal, Dr Wang Ee Jen Wilson, Prof Satku K

won the Asian Travel Award for their paper 'BMD of the normal knee in pre- and postmenopausal women - A preliminary study' at the 17th International Bone Densitometry Workshop, 5-9 November 2006, Kyoto, Japan.

PAEDIATRICS

Prof Yap Hui Kim, Dr Ng Kar Hui (NUH)

were awarded the 2005 Baxter Healthcare Award for Best Submitted Pediatric Abstract by a Physician at the 26th Year Annual Dialysis Conference, 26-28 Feb 2006, San Francisco.

Dr Lee Yung Seng

won the NMRC-BMRC Clinician Scientist Investigator Award (junior category) in April 2006.

Yeo Wee Song, Soon Gaik Hong, Liang Ai Wei, Tan Li Kiang, Seah Ching Ching, Wei Chang Li, Assoc Prof Ang Siau Gek, Assoc Prof Lai Yee Hing, Prof Yap Hui Kim

won the Best Free Paper Award at the Annual Singapore Paediatric Congress in August 2006.

Soh Jian Yi, PZ Ng, E Morales, S Ma, BW Lee, L Shek

were the runner-up for Best Free Paper Award at the Annual Singapore Paediatric Congress in August 2006.

Assoc Prof Goh Yam Thiam Daniel

was awarded the Fellowship of the College of Chest Physicians (USA) by the American College of Chest Physicians in August 2006.

Dr Ng Kar Hui

was awarded NMRC Medical Research Fellowship in November 2006.

Dr Yi Fong Cheng

won the Travel Award for Korean Academy of Asthma, Allergy, Clinical Immunology (KAAACI) and World Allergy Organization (WAO) Joint Congress 2006 in conjunction with the West Pacific Allergy Symposium (WPAS), Seoul, Korea in November 2006.

Dr Huang Chiung Hui

won the Travel Award for Korean Academy of Asthma, Allergy, Clinical Immunology (KAAACI) and World Allergy Organization (WAO) Joint Congress 2006 in conjunction with the West Pacific Allergy Symposium (WPAS), Seoul, Korea in November 2006.

PATHOLOGY

Prof Wong Lim Soon

was awarded the Singapore Youth Award Medal of Commendation by the National Youth Council, Singapore, in July 2006.

Prof Wong Lim Soon

was awarded the ICAAS Distinguished Service Award by the Imperial College Alumni Association of Singapore in September 2006.

PHARMACOLOGY

Assoc Prof Madhav Bhatia

won the Presidential Paper Award by Asia Pacific Digestive Week in November 2006.

Dr Low Chian Ming

was awarded the Young Investigator Award by Asian-Pacific Society for Neurochemistry in July 2006.

Dr Christopher Chen LH

won the BMRC NMRC Clinician Scientist Award by Biomedical and National Medical Research Councils in April 2006.

Assoc Prof Fred Wong W-S

won the Excellent Presentation Award at the 11th Congress of the Asian Pacific Society of Respiriology by Asian Pacific Society of Respiriology in November 2006.

PHYSIOLOGY

Assoc Prof Soong Tuck Wah

won the following awards:

- UK-Singapore Partners in Science Collaboration Award - Neuroscience in June 2006.
- Faculty Research Excellence Award 2005/6.

Prof Shazib Pervaiz

received the Faculty of Science Excellent Teaching Award 2006.

Dr Yap Suen Mei, Celestial Therese

won the Overseas Travel Grant awarded under the 'UK-Singapore partners in science collaboration awards' (S\$5000).

PSYCHOLOGICAL MEDICINE

Dr Tan Hao Yang

was awarded the US National Institutes of Health Visiting Fellowship from July 2005 to 2007.

AWARDS & PRIZES

SURGERY

Asst Prof Edmund Chiong

won the Best Oral Podium Presentation Award / The Singapore Urological Association Bookprize at the Urology Fair 2006 (The Singapore Urological Association Annual Scientific Meeting, Singapore, 17 to 19 February 2006).

Asst Prof Edmund Chiong

was the first person to receive an award from the Pitch for Funds Round, Clinician Scientist Unit, NUS Leadership In Academic Medicine Program, National University of Singapore (Singapore, 17 April 2006). His research was entitled "Human Gene Polymorphism and Response to Bacillus Calmette-Guerin immunotherapy for Superficial Bladder Cancer".

Dr Catherine Yap-Asedillo

Honorary Fellow in Division of Plastic, Reconstructive and Aesthetic Surgery, won the "Young Investigator's Award" at the Singapore-Malaysia Congress of Medicine in Kuala Lumpur which was held on 26 to 27 August 2006.

NATIONAL UNIVERSITY MEDICAL INSTITUTES (NUMI)

Dr Ye Lei

won the following awards:

- C Walton Lillehei Young Investigator's Award at the 14th Annual Meeting of Asian Society for Cardiovascular Surgery in June 2006.
- Young Investigator Award (First Prize) at the 18th Annual Meeting of Singapore Cardiac Society in March 2006.

PATENTS



NUS

National University
of Singapore

YONG LOO LIN SCHOOL OF MEDICINE

BRINGING RESEARCH STANDARDS
BEYOND THE ORDINARY

DISCOVERING NEW INSIGHTS AND MAKING A DREAM INTO A REALITY

AWARDS & PRIZES

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Dr Catherine Yap-Asedillo

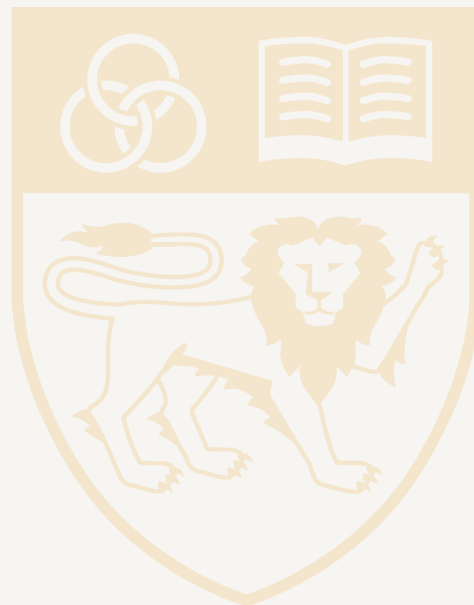
Honorary Fellow in Division of Plastic, Reconstructive and Aesthetic Surgery, won the "Young Investigator's Award" at the Singapore-Malaysia Congress of Medicine in Kuala Lumpur which was held on 26 to 27 August 2006.

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PATENTS



BRINGING RESEARCH STANDARDS
BEYOND THE ORDINARY

DISCOVERING NEW INSIGHTS AND MAKING A DREAM INTO A REALITY

PATENTS

BIOCHEMISTRY

Gopalakrishnakone, P, Twin MM, Jeyaseelan, K, Armugam

Novel therapeutic and prophylactic agents and methods of using same; US Patent Application No. 11/289,494

Jeyaseelan, K, Armugam, A, Chai, SC, Tan KHB, Gopalakrishnakone, P
Cholesterol Biosynthesis Pathway Modulators and Uses Thereof;
Singapore Patent Application No. 200507750-8

MEDICINE

Dr Louis Phee, Assoc Prof Ho Khek Yu, Prof Sydney Chung

A Robotic System to Enhance Therapeutic GI Endoscopic Procedures.
USA Provisional Patent #60-782, 985. Successfully filed in March
2006 (USA).

OBSTETRICS & GYNAECOLOGY

Choolani M, Razvi K, Annalamai L, Biswas A, Zhao CQ

Diagnostic Biomolecules Inventors. Singapore Patent No. 200605961-2.

Choolani M, Ho SSY, Razvi K, Biswas A

FastFish: Improved Technique for Fluorescence In Situ Hybridization
(FISH) on Uncultured Amniotic Fluid Cells that Allows Reporting
within 2 Hours of Amniocentesis. Singapore Patent Application No.
200601942-6.

PAEDIATRICS

Prof Chua Kaw Yan

Recombinant Lactobacillus and use of the same. US Provisional Patent
Application No: BRC/P.04066/00/US. File date: 20 April 2006.

PHARMACOLOGY

Assoc Prof Sim Meng Kwoon

Use of Des-Aspartate-Angiotensin I (Use of des-aspartate-angiotensin
I as an antiviral and anti-diabetic agent). PCT Patent Application No.
PCT/SG2006/000264. File date: 8 September 2006.

Assoc Prof Xiao Zhi Cheng, Ma Quan Hong, Shao Li, Dr Gavin S Dawe
Modulation of neural activity and/or condition. Provisional US Patent
No. 60/841,630. File date: 31 August 2006. Country of registration:
USA.

GRADUATE STUDENTS



NUS

National University
of Singapore

YONG LOO LIN SCHOOL OF MEDICINE

TRAINING EXPERTS TO
**CONTRIBUTE TO
THE COMMUNITY**

THE GRADUATE STUDENTS OF THE
YONG LOO LIN SCHOOL OF MEDICINE
ARE SET TO FURTHER THE BOUNDARIES OF MEDICINE

BIOCHEMISTRY

Novel therapeutic and prophylactic agents and methods of using same; US Patent Application No. 11/289,494

Jeyaseelan, K, Armugam, A, Chai, SC, Tan KHB, Gopalakrishnakone, P
Cholesterol Biosynthesis Pathway Modulators and Uses Thereof;
Singapore Patent Application No. 200507750-8

MEDICINE

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2006 (USA).

OBSTETRICS & GYNAECOLOGY

Choolani M, Razvi K, Annalamai L, Biswas A, Zhao GQ
Diagnostic Biomolecules Inventors, Singapore Patent No. 200605961-2.

FastFish: Improved Technique for Fluorescence In Situ Hybridization (FISH) on Uncultured Amniotic Fluid Cells that Allows Reporting within 2 Hours of Amniocentesis. Singapore Patent Application No. 200601942-6.

PAEDIATRICS

Recombinant Lactobacillus and use of the same. US Provisional Patent Application No: BRC/P.04066/00/US. File date: 20 April 2006.

PHARMACOLOGY

Use of Des-Aspartate-Arginine in Use of Des-aspartate-Arginine as an antiviral and anti-diabetic agent). PCT Patent Application No. PCT/SG2006/000264. File date: 8 September 2006.

GRADUATE STUDENTS



TRAINING EXPERTS TO **CONTRIBUTE TO THE COMMUNITY**

THE GRADUATE STUDENTS OF THE
YONG LOO LIN SCHOOL OF MEDICINE
ARE SET TO FURTHER THE BOUNDARIES OF MEDICINE

GRADUATE STUDENTS

ANAESTHESIA

PhD

Sethuraman Rama

Characterization of new peptides and physiological amino acids present in cerebrospinal fluid of chronic pain patients.

ANATOMY

PhD

Huang En

Misregulation of iron handling proteins in excitotoxic brain injury.

Lin Shuping

Characterization of MP2 cell division and pins function on spindle asymmetry of drosophila central nervous system.

Wang Chaoyang

Development of hybrid promoters and viral vectors for improved gene delivery to the central nervous system.

Wang Huashan

The function of DTRAF1 in drosophila neuroblast asymmetric cell division.

Zheng Zeyi

Functional interactions between the progesterone receptor and estrogen receptor in breast cancer cells.

MSc

Fong Xiao Jun

Pathogenesis of lung inflammation following exposure to toxicants.

Ler Siok Ghee

Stability studies of ricin, staphylococcal enterotoxin B and trichothecene mycotoxins on office matrices.

BIOCHEMISTRY

PhD

Chan Ying Ying

The BpeAB-OprB multidrug efflux pump of Burkholderia pseudomallei.

Cher Dyi Ni, Charmian

Molecular mechanisms underlying the pharmacological activities of Naja Sputatrix venom.

Choy Meng Shyan

The mechanisms of lactacystin-induced apoptosis of mouse primary cortical neurons.

Gopalan Vivek

Analyses of protein domains and genomic elements using bioinformatics approaches.

Gwee Pai Chung

Genetic characterization of nucleoside analogue transporters ABCC4 and ABCC5 gene loci.

Koh Chor Hui, Vivien

Mechanism of U18666A-mediated cell death in cultured neurons.

Lee Teck Kwong, Bernett

Bioinformatics analysis of alternative splice variants.

Lim Kok Seong

Oxidative and nitrosative DNA damage: Occurrence, measurement and mechanism.

Lufei Chengchen

Study of the Associated Proteins of STAT3 and Characterization of their Functions: Roles of GRIM-19 and PIN1 in the Regulation of STAT3 Activity.

Ma Jing

Molecular regulation of STAT3 activation and nuclear translocation stimulated by growth factors & Cytokines.

MD Monowarul Mobin Siddique

Regulation and functional analysis of the tumor suppressor gene product, p53.

Tan Thiam Joo, Paul

Functional prediction of bioactive toxins in scorpion venom through bioinformatics.

Tang Kun

Genetic analysis of SNPs in and around the MDRI gene locus.

Tang Soon Yew

Folk medicine - Cratoxylum cochinchinense: Antioxidant but cytotoxic.

Wang Peng Hua

Molecular Analysis of Oxysterol Binding Proteins in Yeast.

Yang Shu

Cellular changes post hepatectomy in cirrhotic vs normal rats.

Zhang Qian

Triacylglycerol synthesis and stress response in fission yeast schizosaccharomyces pombe.

MSc

Chen Yiliang

Expression studies of the proteolytic p10 fragment of the neuronal Cdk5 activator in mammalian cells.

Hou Qingsong

Sulfatide-Containing Liposome Targeting to the Glioma Cell.

Miao LV

Role of glycosphingolipids in formation and function of lipid rafts.

Mohd Asif Khan Md Shahid Khan

Mapping targets of immune responses in complete dengue viral genomes.

GRADUATE
STUDENTS

Neo Chun Hong, Jason

A proteomic approach to study the apoptotic effects of phenethyl isothiocyanate on the human hepatoma cell line, HepG2.

Yap Yann Wan

Mechanisms of hypochlorous acid-mediated neuronal cell death.

Zhu Yansong

Proteomic analysis of HCC-M and HEPG2 cells after treatment by butyrate.

**COMMUNITY, OCCUPATIONAL AND
FAMILY MEDICINE**
PhD

Huang Qing

Studies of the anti-metastatic potential of emodin on human tumor cells.

Shi Ranxin

Anti-tumor mechanisms of luteolin, a major flavonoid of chrysanthemum.

Won Yen Kim

Studies on the chemopreventive and chemotherapeutic properties of parthenolide, a sesquiterpene lactone.

MSc

Ng Ah Ching, Vivian

Stress and salivary biomarkers among dental undergraduates - a longitudinal study.

Shu Xiaochen

The association of myopia progression with family history of myopia, nearwork, and other risk factors among Singapore school children: A 2 year follow-up study.

Yim Onn Siong

Y chromosome diversity in Singaporean Han Chinese population subgroups.

MSc (Clinical Science)

Song Yushan

Incidence and survival of childhood cancers in Singapore, 1968-1997: A population-based study.

Zhou Huijun

Delta amino levulinic acid dehydratase (ALAD) polymorphism and its effect on human susceptibility to renal toxicity by inorganic lead.

MD

Lee Jen-Mai, Jeannette

Birth Weight: Ethnic differences and health outcomes in childhood.

DIAGNOSTIC RADIOLOGY
M.Eng

Wang Yan

Nanoparticles of Biodegradable Polymers for Medical Imaging

Yu Qianru

Nanoparticles of Biodegradable Polymers for Chemotherapy across the Brain-Blood Barrier (BBB): Effects of Particle Size and Surface Coating

MEDICINE
PhD

Cheng Yan

Hepatitis B virus gene mutations associated with HBeAg seroconversion.

Qiu Diwen

In vitro studies of neutrophil activation by rhinovirus.

Song Guanghui

Exploring the brain-gut axis in irritable bowel syndrome: Specific emphasis on stress and melatonin.

Wang Xueying

Roles for C-ABL and P53 in bone homeostasis and DNA damage response.

Zheng Ling

Pathogenic Mechanisms in the Development of Lupus Nephritis.

Zhu Zhe

Autocrine growth hormone (hGH) and chemotherapeutic drug resistance in mammary carcinoma cells.

MSc

Naslin Rasheed

The role of the ataxia - telangiectasia mutated protein in bone development.

MICROBIOLOGY
PhD

Bai Chen

Identification and characterization of a *Candida albicans* alpha-1,2 mannosyltransferase CaMNN5 that suppresses the iron-dependent growth defect of *Saccharomyces cerevisiae* aft1 delta mutant.

Goh Liuh Ling

Functional and structural analysis of *Plasmodium falciparum* falcipains.

Gong Min

Characterization of *helicobacter pylori* y-glutamyl transpeptidase and its role in pathogenesis.

GRADUATE STUDENTS

Ho Phui San

Feasibility of probiotic lactobacillus and yeast as oral vaccine carrier against coronaviruses.

Lee Sek Yew, Alex

Molecular and functional characterization of the luxS/ autoinducer-2 (AI-2) quorum sensing molecule in clostridium difficile CCUG19126.

Leong Wai Fook, Peter

Characterisation of novel human genes differentially expressed in virus-infected cells.

Sun Yongjiang

Mycobacterium tuberculosis genotypes and their relationships with clinical and immunological phenotypes in Singapore.

Yu Hongxiang

HLA associations with nasopharyngeal carcinoma: Implications in pathogenesis and immunotherapy.

MSc

Lee Hui Cheng

Effect of herbal extract on cell death and immunomodulation of human colonic cells.

Rashmi Tripathi

Analysis of transcription factors in living human cells with the help of split-ubiquitin system.

Tan Yee Sun

Screening for novel protein-protein interactions in living human cells with the help of the split-ubiquitin system.

Wong Hok Sum, Kenneth

Studies on antibiotics action on intracellular bacteria.

Zhang Lin

Immunomodulatory effects of mycobacteria.

OBSTETRICS & GYNAECOLOGY

PhD

Liow Swee Lian

Molecular genetics of Y chromosome in male infertility.

Yap Sook Peng

Estrogenic and anti-proliferative properties of novel prenylflavone from Epimedium brevicornum.

MD

Chong Yap Seng

The use of misoprostol in the active management of the third stage of labour.

ORTHOPAEDIC SURGERY

PhD

Ge Zigang

Tissue engineering approach to anterior cruciate ligament reconstruction.

OPHTHALMOLOGY

PhD

Veluchamy Amutha Barathi

Muscarinic mechanisms in a mouse model of myopia.

MSc

Goh Sui Sin

Generation of mouse graves' ophthalmopathy model with full length TSH receptor plasmid and cytokine evaluation by real-time PCR.

OTOLARYNGOLOGY

PhD

Liang Xiao Hui

Evaluation of the impact of polymorphisms on candidate genes of allergic rhinitis and asthma in Singapore population.

MSc

Ang Hui Chi, Annette

Nasal Polyposi: an immunohistochemical study of cell cycle regulator proteins in epithelial proliferation.

Md Tanveer Raza

Validation of acoustic rhinometry in objective assessment of nasal airway: standardization of measurements and applicability.

MD

Siow Jin Keat

A study of Asian paranasal sinus anatomy using triplanar computed tomography scans.

PAEDIATRICS

PhD

Huang Fu Tao Qi

Development of DNA vaccines for allergic Asthma.

Li Jingguang

Multiplexed genotyping of single nucleotide polymorphisms using microarray technology.

Wong Chee Fung

Enhancing recombinant protein yield and quality using novel CHO GT cells in high density fed-batch cultures.

GRADUATE
STUDENTS**MSc****Aaron Chen Angus**

Cross-comparison of dust mite allergens from several major species.

Liu Xuguo

In vitro drug sensitivity and expression profiling for disease prognostication in childhood acute lymphoblastic leukemia (all): An exploratory model using cell lines.

Soon Gaik Hong

Elucidating the mechanism of the immunosuppressive action of PX3.102, the active molecule from a decoction of Chinese herbs.

PHARMACOLOGY**PhD****Agnes Slater**

Investigations into the effects of traditional Chinese medicinal herbs used in the treatment of human breast cancer.

K Manoharan

Isolation, characterisation and/or evaluation of plant extracts for anticancer potential.

Lu Qing

The roles of angiotensin receptors in cerebral ischemia.

Ong Choon Kiat

Genomic organization and functional study of a novel tumor suppressor gene - OKL38.

Wang Qing

The effects of simvastatin on central dopaminergic systems.

Wang Zhongjing

Roles of angiotensin II receptors on myocardial apoptosis in experimental rat model with ischemia-reperfusion injury.

MSc**Chen Aiqing**

Global analysis of protein expression in focal cerebral ischemia in rats.

Choo Hui Hwa

Characterization of an antisense oligonucleotide targeted at Phospholipase C gamma 1 in the mouse T-cell line EL4.1L-2.

PHYSIOLOGY**PhD****Amit Aggarwal**

Genomic and transcriptomic analysis of gastric cancer: Systematic studies on transcriptional bias in aneuploidy and gene coexpression meta-network.

Low Kwan Leng

Some nutritional aspects influencing lipid metabolism.

Moh Mei Chung, Angela

Molecular cloning and characterization of novel genes HEPN1, hepaCAM and HEPT3 that are altered in human hepatocellular carcinoma.

P Jaya Kausalya

Identification and characterization of proteins that interact with zonula occludens proteins.

Sufyan AkramReactive oxygen species-mediated regulation of the Na⁺/H⁺ exchanger, NHE-1 gene expression: a new mechanism for tumor cells' resistance to apoptotic cell death.**Sun Yu**

Chemoresistance in B cell lymphoma: Role of apoptosome activation.

Tang Zhenzhi

Molecular and functional study of splice variations of the L-type voltage-gated calcium channel CaV1.2 alpha1-subunit.

MSc**Mirtha Laban**

Genes involved in colon cancer development and progression.

SURGERY**PhD****Ng Kee Woei**

Tissue engineering a skin equivalent using a novel combination of poly (lactic-co-glycolic acid) mesh with cell sheets.

MSc**Shridharan Shiva Ranjani**

Nitric oxide mediated transcriptional regulation.

MD**Assoc Prof Kesavan Esuvaranathan**

Local immunopotential of the bladder in response to BCG immunotherapy.

**NATIONAL UNIVERSITY MEDICAL
INSTITUTES (NUMI)****PhD****Ong Lee Lee**

Characterization the role of kinectin in assembly of translation elongation complex to endoplasmic reticulum and its involvement in organelle motility.

Tang Yanxia

Dysfunctional signaling pathway for nitric oxide production in endothelial cells chronically exposed to high glucose or high fatty acids.

PRESS CLIPPINGS

Stem cells: From bench to bedside

Studies on stem cells and their healing qualities are on a ramp, with a renewed focus by the Government and a promise to pump in more funds for research. Cheryl Lee speaks to Professor Lee Kong Hoe of the orthopaedic surgery department at the National University of Singapore and co-chair of the Singapore Stem Cell Consortium.

At what is the state of stem cell research here and what is the future? Singapore is one of the world's top 10 countries for stem cell research. The Singapore Stem Cell Consortium, co-chaired by Professor Lee Kong Hoe, is a pioneer in the use of human stem cells, from the bone marrow to the generation of human embryonic stem cells in the lab.

Since the stem cell was first discovered here, the research has been published in high-impact journals and has been published in high-impact journals. The Singapore Stem Cell Consortium is a pioneer in the use of human stem cells, from the bone marrow to the generation of human embryonic stem cells in the lab.

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New Centre for Biomedical Ethics at NUS

It will help in search for ethical and legal framework for life science research

For a robust ethical and legal framework to guide life science research is a top priority for the Singapore Stem Cell Consortium. The new research centre will be headed by Professor Lee Kong Hoe, who is co-chair of the Singapore Stem Cell Consortium. The new research centre will be headed by Professor Lee Kong Hoe, who is co-chair of the Singapore Stem Cell Consortium.



Areas of focus will include human bio-banks that house patient data for cohort studies, and research on ageing-related problems.

It will include research in biomedical ethics, including multiple disciplines including law, ethics and governance. The new research centre will be headed by Professor Lee Kong Hoe, who is co-chair of the Singapore Stem Cell Consortium.

Dark soya sauce good for health

NUS researchers say it's better than vitamin C and red wine in reducing damage to human cells caused by free radicals

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Pals use nanotech to study malaria

Scientific fusion of nanotechnology and cell biology making big waves in medical world

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SUCCESSFUL TEAM-UP: Dr. Richard L. Neufeld, a nanotechnologist, and Dr. Lee Kong Hoe, a cell biologist, used their "nanobots" to determine the rigidity of malaria-infected cells.

New study on myopia to focus on infants

2,000 youngsters in 2007 study to examine cause of high myopia rates

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Compiled by the Research Division of Yong Loo Lin School of Medicine

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