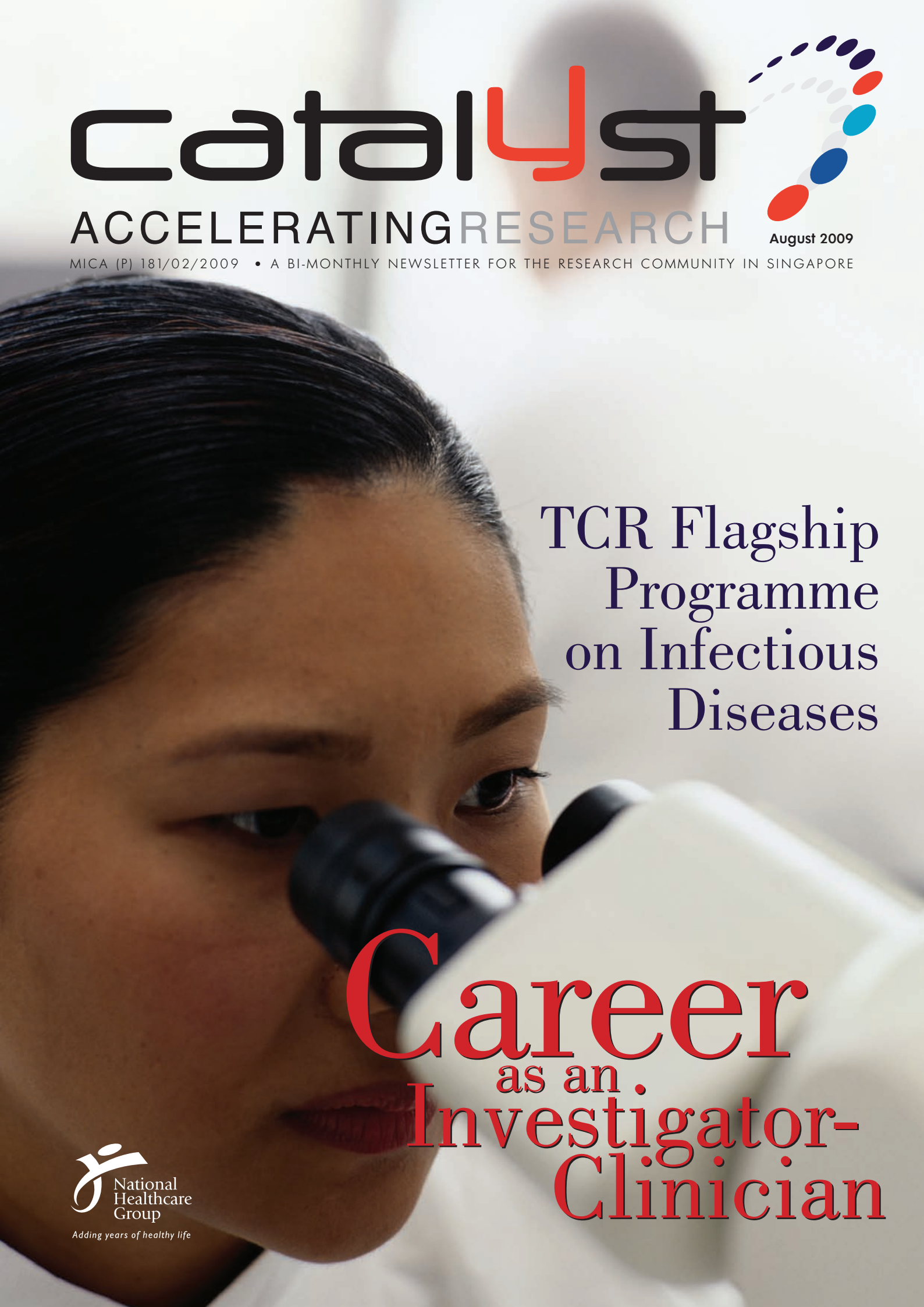
catalYst
ACCELERATING RESEARCH
August 2009
MICA (P) 181/02/2009 • A BI-MONTHLY NEWSLETTER FOR THE RESEARCH COMMUNITY IN SINGAPORE



TCR Flagship Programme on Infectious Diseases

Career as an Investigator-Clinician

National Healthcare Group
Adding years of healthy life

Contents

Research & Development Office

National Healthcare Group
Adding years of healthy life

Editorial team
Zawiyah, Wenald, Renuka, Norsalleha, Malini, Kin Poo, Karabee, Hwee Hian, Farah, Alvin and Adeline

From The Editor-in-Chief

From the Editor-in-Chief
Welcome to the 2nd edition of Catalyst, the NHG Research newsletter that aims to bring you the latest information on research activities happening around us, and in depth exploration of some of the top notch research that are happening in our institutions.

In this issue, we bring you the nuts and bolts of the latest Translational & Clinical Research (TCR) Flagship Program award on Infectious Disease. You can understand in greater depth, the aim of this massive study, how it will be carried out, and what benefits it will bring to our patient.

We then switch to a softer angle to look at how clinicians who are passionate in research strive to excel in their field, and share their in-depth thoughts on the life of being an Investigator-Clinician.

As you can see, we aim to balance content by bringing you the science of some greatest study happening in Singapore, as well as detailed biography of how clinicians strive to engage in research, in the midst of their busy clinicial schedule. Some of this information would not be revealed in normal life, if not for this platform.

As we all know, human capital is the only resource in Singapore, as we do not have oils to dig, or coal to mine. This is especially true in the research field, whereby the success of biomedical science research in Singapore will depend greatly on the availability of capable and committed Investigator-Clinician who will strive to challenge the status-quo and explore the edge of science to discover better treatment for diseases and adding years of healthy life to Singaporean.

Happy Reading,
Editor

Your Newsletter, Your Comments

Do you have any of these:

- Research articles to share?
- Research topics that you want covered?
- Comments/Feedbacks on published contents of this newsletter?
- Comic strips/cartoon illustrations that is science/research-related that can bring smiles to your colleagues?

If you have answered "YES" to any of the above, we invite you to write in and share with us your thoughts, feedback on published articles or cartoon clips (original materials, jpeg format please).

And if your contribution is accepted for print, we will send you a token of appreciation, with compliments from the Editorial team!

Own this newsletter, send us your contributions and add your personal touch today!

Modes of contribution:
By Mail
Editorial Team – Catalyst Newsletter
Research & Development Office
National Healthcare Group Pte Ltd
6 Commonwealth Lane
#04-01/02 GMTI Building
Singapore 149547
By Email
rdo-rtdu@nhg.com.sg

Do remember to add in your contact details, where applicable, for our future communications with you:

- Name
- Department & Institution
- Mailing address
- Contact numbers (telephone & mobile); and
- Email address

The Editorial Team

Translational & Clinical Research (TCR)

Flagship Programme on Infectious Diseases

Scientific Exploration, Translational Research, Operational Evaluation of Disease Prevention and Preventive Measures Through New Treatment Strategies Against Dengue (STOP Dengue)

Mr Alvin Chong
Research Training & Development Unit (RTDU), RDO

Programme Leader
A/Prof Leo Yee Sin
Clinical Director, Communicable Diseases Centre & Head, Department of Infectious Diseases, Tan Tock Seng Hospital

Dengue fever and dengue hemorrhagic fever (DF/DHF) are the most common mosquito-borne viral diseases in the world. Transmitted by the Aedes aegypti mosquito, the dengue diseases caused a high mortality in the 1960s in Singapore, especially on the younger population – the children. Despite the efforts put in to control the breeding opportunities of the mosquitoes, Singapore continued to witness the lingering presence of the dengue diseases with a surge in numbers in the 1990s, this time affecting the young adults.

There is no specific anti-viral treatment for patients afflicted with the dengue diseases or vaccinations as a form of preventive treatment. Affected persons usually present an onset of fever, body aches, nausea, vomiting and skin rashes, with severe cases with complications of low platelet counts and bleeding. There are four strains of viruses that can cause the dengue diseases (Serotypes 1 to 4). The current mode of care is mainly supportive care with intravenous fluids and frequent blood test monitoring to reduce the complications of the disease. In severe cases, blood transfusions may be required[1].

Following the dengue outbreak in Singapore in 2005, the Singapore Dengue Consortium, formed in 2003, conducted studies to better understand the disease characteristics of dengue and the clinical outcomes of the infection. The studies demonstrated the possibility of differentiating dengue from other fever-causing infections at the early stage. Protocols for diagnosis and serotyping were developed, facilitating the close monitoring of the viral strain circulating in the country[2].

In 2008, A/Prof Leo Yee Sin, Clinical Director of the Communicable Disease Centre and Head of Department, Infectious Diseases, Tan Tock Seng was awarded the Translational & Clinical Research (TCR) Flagship Programme for Infectious Disease to look into the development of evidence-based case management and disease prevention for dengue (STOP Dengue).


A/Prof Leo Yee Sin

The research team comprises of members from the public medical institutions and primary healthcare centres from Singapore Health Service and National Healthcare Group, Changi General Hospital and the National University Health System, with research centres from the Duke-NUS Graduate Medical School, Genome Institute of Singapore (A*STAR), Novartis Institute for Tropical Diseases, DSO National Laboratories, Singapore MIT Alliance for Research and Technology (SMART) and the Environmental Health Institute of the National Environmental Agency.

The main objectives[2] of this TCR Flagship Programme are (i) Create a global centre of excellence for clinical study and management of dengue diseases; (ii) Establish a centre for clinical trials of new therapeutics and therapeutic antibodies to all four serotypes of the dengue virus; (iii) Elucidate causal effects from the infection of adult dengue disease and identify markers for early diagnosis and early prognostication of dengue diseases; and (iv) Develop new strategies for disease control using state-of-the-art epidemiology and full-length genome analysis.

To meet its set of objectives, the research team aims to harness the existing strengths of its members and affiliated institutions to unravel a detailed and comprehensive clinical description of the varied presentations of dengue diseases; to understand the host-viral interactions that affects the disease outcome; to establish biomarkers for early diagnosis and prognosis of the disease for better clinical management; to capitalize on the collaborative efforts of the healthcare institutions for a comprehensive conduct of clinical trials on new therapeutics; and to improve the efficacy and sustainability of disease prevention through a better understanding of the spread of the disease, and the dynamic of virus-mosquito-human-environment interactions.

With a strong cohort of investigators, the benefits from the completion of this programme will not only bring to light the nature of the dengue diseases, it will also provide the medical community with the knowledge to effectively treat patients afflicted with the dengue diseases and to develop vaccines against the four serotypes.

1 Source from Health Promotion Board, Singapore
2 Source from TCR Factsheet for Infectious Diseases, National Medical Research Council, Singapore

Career in Childhood Obesity Research

A/Prof Lee Yung Seng, MBBS, MMed(paeds), PhD, MRCP(UK), MRCPCH, FAMS
Clinical Investigator, Singapore Institute for Clinical Sciences (SICS), A*STAR
Associate Professor and Senior Consultant, University Children's Medical Institute, NUHS


A/Prof Lee Yung Seng

I recalled my interest in the childhood obesity research began in my clinics when I was a registrar training in paediatric endocrinology, where severely obese children were regularly referred for assessment. I began to question how it was possible for young children to become so overweight in a relatively short period of time. I also wondered why some children gained much more weight compared to their lean siblings despite living in a similar environment. At that time, the epidemic of childhood obesity and its attendant risks was a relatively recent phenomenon, and there was limited experience in the management of childhood onset obesity-related complications, with a paucity of evidence based data and management guidelines. I was left hungry for answers.

At around that time, scientific papers began to emerge which reported rare cases of leptin deficiency and leptin receptor defect causing severe early onset obesity, and also reports of melanocortin-4 receptor gene mutations as single gene defects causing early onset obesity almost 6% of obese populations in United Kingdom and France. I can still recall vividly a conference in Sydney in year 2000 where I was inspired by a symposium on this subject by Professor Steve O'Rahilly and his Dr Sadaf Farooqi from Cambridge (who later became by mentors). I decided to study the genetic mutations and variations that cause or predispose children to obesity and its complications. I believed a single gene defect can be the dominant factor that causes obesity in some obese children. I also relished the challenge to uncover genetic variants which collectively predisposes an individual to obesity when exposed to the obesogenic environment (assuming that common obesity is a multifactorial trait).

I received the support of the International Fellowship from the Agency of Science, Technology and Research (A*STAR) in 2003 to pursue a research stint at the University of Cambridge. I had a further opportunity and privilege to join the renowned Genetics of Obesity Study (GOOS), and I was tasked to examine the proopiomelanocortin (POMC) gene of more than 900 DNA samples from the obese cohort, using a combination of direct sequencing and denaturing high performance liquid chromatography (dHPLC).

Upon my return from Cambridge in 2005, I had to juggle my duties as a clinician, educator, and researcher. I applied and was fortunate to be presented the NMRC-BMRC Clinical Scientist Investigator (CSI) Award, which allowed me to spend sufficient time pursuing my research. The CSI award has given clinician-researchers due recognition for their role in our healthcare setup. With the presence of this award, both the clinical departments and hospitals are now more aware and conscious to make time for us to do research. This award has helped me to further realize my research goals.

Biomedical research in Singapore has developed exponentially in the last decade, and research funding and opportunities are increasingly available to clinicians who aspire to embark on this journey. The Singapore Institute for Clinical Sciences (SICS) is the newest biomedical research institute set-up by A*STAR, and its research laboratories are housed in the Brenner Centre for Molecular Medicine, located adjacent to the School of Medicine (NUS) and NUH, underpinning its efforts to bridge bedside and laboratory research. SICS has several disease-oriented intramural research programmes, and recently I was privileged to have the opportunity to join the Growth, Development and Metabolism programme as a part-time clinical investigator. The draw for me was the opportunity to immerse in a research environment of like-minded researchers with common interests, facilitating exchange of ideas and collaborations. I felt it is the next step in the right direction to expand my boundaries and bring my research work up another level. It is also an exciting opportunity to be able to shape the local research landscape in the field of metabolism and growth. Importantly, SICS will encourage and mentor young doctors who aspire to take up research. Indeed, the support from senior investigators and research directors, as well as their expert knowledge and guidance, are crucial to nurture the development of the next generation of clinician scientists.

Life as a clinician-scientist is hectic but exciting, as there are more opportunities to explore new research ideas and hopefully apply them back to patient care. The ongoing emphasis by our Government to develop our expertise in biomedical science has created multiple training opportunities and financial support. Over the last decade, I have witnessed increasing number of schemes and programmes which train and help young doctors start their research career, and a multitude of research funding opportunities. For the clinician who is contemplating a career in research, these changes auger well for the future.

Childhood Obesity:
The genes or not the genes?

A/Prof Lee Yung Seng, MBBS, MMed(paeds), PhD, MRCP(UK), MRCPCH, FAMS

Obesity has escalated into a global pandemic and become one of the top healthcare issues of the decade. It is a major health concern because of the consequent morbidity and premature mortality, as obesity predisposes to serious morbidities such as type 2 diabetes, hypertension, and coronary heart disease. The increasing obesity prevalence all over the world is due to rapid industrialization, creating an "obesogenic" environment with caloric abundance and ubiquitous automation which encouraged sedentary lifestyle, resulting in energy intake and expenditure imbalance. The current obesity epidemic is a relatively recent global event, and thus it is inconceivable that genetic mutations or major genetic shifts are responsible for this surge in this short period of time. The role of the obesity related genetic variants in this current epidemic is passive, but its impact is highly significant, because individuals with these genetic variants may be predisposed to severe or even morbid obesity when exposed to the modern "obesogenic" environment. The proportion of overweight people has risen steadily over the years, and in particular, there is a pronounced increase in morbid obesity which cannot be explained by a mere shift in population mean. The hypothesis is that the "obesogenic" environment has caused a subgroup of the population, who is genetically susceptible to severe weight gain, to become excessively obese.

Obesity is also increasingly prevalent amongst our children, and the global escalation of childhood obesity is worrying, because obesity related co-morbidities can surface in our obese children, and paediatricians now have to handle chronic illnesses such as type 2 diabetes and hypertension which were once regarded as adult diseases.

Our paediatric endocrine research group at the Children's Medical Institute, NUH/NUS, recruited over 250 children with severe early onset obesity over 3-4 years for this endeavor. We are grateful for the assistance of the staff of the Youth Health Division, Health Promotion Board to recruit the subjects. We recruited young children who develop severe early onset obesity in an attempt to increase the likelihood of identifying children who are genetically predisposed to obesity, as we hypothesized that genetic factors rather than the environment play a predominant pathogenic role in these individuals. As melanocortin 4 receptor (MC4R) deficiency is the commonest monogenic form of obesity described to date, and the significance of MC4R mutations in Asian obese populations has not been adequately examined, we first determined the role of MC4R mutations in our severely obese local cohort, using polymerase chain reaction (PCR) and direct sequencing. We identified three mutations in three subjects: 4 bp deletion from nucleotides 631-634 (c.631-634delCTCT), Tyr157Ser (c.470A>C), and 1 bp deletion at nucleotide 976 (c.976delT) (1.32% of study subjects). In vitro transient transfection studies supported the pathogenic role of the mutations, where the signalling activities of the mutant receptors were impaired. Heterozygous MC4R mutations were associated with early onset severe obesity, and homozygosity of the MC4R mutation Tyr157Ser resulted in morbid obesity. MC4R mutations result in an autosomal codominant form of obesity with variable expressivity. MC4R deficiency is not as common among the obese children in this study compared to UK and French obese populations. Our family studies revealed that adults heterozygous for the mutations were less obese compared to the children. We postulate that this may be due to amelioration of phenotype severity with age, or difference in exposure to modifying factors at critical stages of childhood such as the environment.

Melanocortin 3 receptor (MC3R) plays a critical role in weight regulation of rodents, but its role in humans remains unclear. To identify genetic variants of the MC3R gene and determine its association with childhood obesity, we screened our obese children for MC3R gene mutations, We identified three novel heterozygous missense mutations (Ile183Asn, Ala70Thr, and Met134Ile), and two common polymorphisms Thr6Lys and Val81Ile (single nucleotide polymorphisms). In-vitro functional studies of the mutant receptors revealed impaired signaling activity but normal ligand binding and cell surface expression. The heterozygotes demonstrated higher leptin levels and adiposity, and less hunger, compared to obese controls, reminiscent of the MC3R knockout mice. Family studies showed that these mutations may be

continue on page 5

The Singapore Institute for Clinical Sciences (SICS) is the Agency for Science, Technology and Research's (A*STAR's) key initiative to develop world-class clinical sciences programs. Its mission is to improve the health and economic well-being of Singaporeans by better understanding Asian-relevant diseases and by developing new diagnostics and therapeutics.

SICS is located in the Brenner Centre for Molecular Medicine within the NUS campus. It's in-house research programs, which are led by clinician scientists, are organized around human diseases and involve close collaboration with other scientists and clinicians in Singapore and overseas. For more information about SICS log on to their corporate website at www.sics.a-star.edu.sg

*Dr Melvin Leow was awarded the NHG Investigator-Clinician Career Development Scheme in 2008. Dr Leow conducts his research at the Singapore Institute for Clinical Sciences (SICS), A*STAR. His focus is on the role of developmental origins in the pathways to metabolic diseases. This stems from the discovery of the role of epigenetic mechanisms operating during in-utero and early phases of growth in the phenotypic expression and risks of various forms of metabolic disorders later on in life. To communicate directly with Dr Leow on his research and collaborative work, please email him at melvin_leow@sics.a-star.edu.sg*

Career as an Investigator-Clinician

Dr Melvin Leow, MBBS, MMed (Int Med), FACP, FACE (USA), FAMS
Academic Consultant
Consultant, Department of Endocrinology, Tan Tock Seng Hospital
Clinical Investigator, Singapore Institute for Clinical Sciences (SICS), A*STAR

How would a clinician respond when confronted with the question, "Would you take up medical research for a career?" After all, most medical students and doctors alike have their fair share of reasons for believing that research is a crucial aspect for the advancement of our fields. Many health institutions have also placed research strategically in their mission statements. Perhaps, a great majority of this audience has considered about being involved in research very early on, at the time when they were contemplating applying for entry into medical school.

Having been a fulltime clinician sub-specialized in endocrinology, I too, recognized the value of doing research. While I suspect none among this audience would disagree about the importance of research, when it comes to the crux of it – committing one's life with nearly full dedication to research and sidelining clinical practice, most would start to wonder if they are prepared to make such a 'life-changing transition', or indeed such a "sacrifice". In the United States where I had the opportunity to train, perhaps the fact that many physician-scientists there undergo rigorous research early in their training, this unique breed of doctors might never have any trouble integrating substantial research time to their clinical commitments.

Being a relatively mature clinician, it is natural to consider very carefully the pragmatic aspects, risks and implications to my family, financial and promotional prospects if I were to proceed along this "inverse path", even though I have honestly been extremely passionate about research for as long as I remember. For a while, I had been promulgating that research-oriented clinicians be allowed more opportunities for research. That opportunity finally came in the form of the Investigator-Clinician track. It was very new when I was introduced. But it offered interesting and challenging prospects of medical research that I could only dream about previously. It's requirement for 80% fulltime-equivalent in research and 20% in clinical work seemed daunting initially, but sank in quickly as a necessity for any clinician-scientist to excel in a research-based career. I jumped at the chance with no hesitation. To this end, I had transferred my employment to NHG and also become affiliated academically to the Singapore Institute for Clinical Sciences under A*STAR. Frankly, I could not have accomplished such as career move at my age without the wise counsel, support and advice of my research mentors and even my family.

Thus far, I already gained a considerable amount of basic science exposure. All the numerous sophisticated molecular "wet-bench" techniques I acquired will undoubtedly help propel me in medical research. My experience has been an extremely positive one at the Brenner Center for Molecular Medicine. I count myself very blessed to be among a highly internationally renowned multidisciplinary group of research scientists particularly adept at nurturing research creativity, and am incredibly impressed by the potential for novel research in this group. That our group has just been awarded the Translational and Clinical Research (TCR) Flagship grant fuelled extra incentives for engaging in high quality and impactful research. The clinician scientist career may be an arduous one riddled with risks and pitfalls. However, to any clinician who is seriously interested in devoting his life to research and bold enough to leave his comfort zone and already-established successful life, this track should represent a pursuit of a lifetime they might otherwise never imagined possible. As much as clinicians can benefit his patients, clinician scientists have great potentials for making meaningful contributions towards society and to the science of their fields.

The NHG Investigator-Clinician Career Development Scheme is in support of NHG clinicians who wish to pursue research as their primary career. The scheme provides a career backbone for investigator-clinicians, bridging grants for 100% salary support, evaluates research performance for career advancement, and allow for joint appointments across the NHG Cluster, Research Institutes, Academia and Industries. This scheme aims to foster competitiveness and collaboration in one's research.

To find out more about this scheme, please send your enquiries to rdo-rtdu@nhg.com.sg.

Facts about B2BResearch Online

you've always wanted to know but were just too busy to ask (Part 2 of 2)

6 Do I need to submit any more hardcopy signatures?

No, for the online DSRB Applications, no hardcopy signatures are required.

For the Principal Investigator By clicking on the submit button in the Application Form, the PI has "signed" the online application.

For the Study Team members The DSRB assumes that the PI has done his due diligence to inform study team members of their involvement in the Study and that all Study team members have agreed to be in the Study.

For the PI's Department & Institution Representatives Endorsements by the Department Representative and Institution Representative are made online through the B2BResearch Online portal. Hence, the Principal Investigator is to ensure that his Department Representative has been registered with the B2BResearch Online portal.

From page 3

Childhood Obesity: The genes of not the genes

associated with childhood or early onset obesity. The common variants Thr6Lys and Val81Ile were in complete linkage disequilibrium, and in-vitro studies revealed reduced signaling activity compared to wildtype MC3R. Obese subjects with the 6Lys/81Ile haplotype had significantly higher leptin levels, percentage body fat, and insulin sensitivity, and the causative role of the 6Lys/81Ile variants is supported by the presence of an additive effect, where heterozygotes had an intermediate phenotype compared to homozygotes. MC3R mutations may not result in autosomal dominant forms of obesity, but may contribute as a predisposing factor to childhood obesity, and exert an effect on the human phenotype. Our study supports the role of MC3R in human weight regulation.

From the study conducted at the University of Cambridge, under the renowned Genetics of Obesity Study (GOOS), I examined the proopiomelanocortin (POMC) gene of more than 900 DNA samples from the obese cohort, using a combination of direct sequencing and denaturing high performance liquid chromatography (dHPLC). Five probands were heterozygous for a rare missense variant in the region encoding β-MSH, Tyr221Cys. This frequency was significantly increased compared to the general UK Caucasian population, and the variant co-segregated with the obesity/overweight phenotype in affected family members. Obese children carrying the Tyr221Cys variant of β-MSH were hyperphagic and showed increased linear growth, reminiscent of MC4R deficiency. We also found a heterozygous POMC mutation His143Gln in one obese subject, which affected the core binding motif of α-MSH. However, the transmitting parent was not obese. Both mutant peptides demonstrated impaired binding and activation of the MC4R in-vitro. The results supported the role of β-MSH in human energy homeostasis. Compared to α-MSH, β-MSH may even be the more critical mediator of melanocortin signaling pathway in humans. POMC screening of the GOOS cohort also revealed two heterozygous missense mutations, Cys28Phe and Leu37Phe, which resulted in substitution of highly conserved residues of the sorting signal motif of POMC. Cys28Phe and Leu37Phe co-segregated with obesity/overweight in the families. In-vitro studies revealed less efficient sorting and processing of the two mutant POMC peptides, with less α-MSH production.

Such genetic research help us better understand the pathogenesis of common obesity, which will help us better plan preventive and treatment strategies. By identifying single gene defects which lead to human obesity, we can then identify and validate molecules as critical mediators of the human weight regulation mechanism, and these in turn can be targets development of new drugs in the future.

Dr Karabee Murkherjee
Domain Specific Review Board (DSRB), RDO

NHG Research Ethics Committee (REC)

Farewell to Outgoing Chairperson –

Associate Professor Wong Kim Eng

Clinical Director, National Medical Health Programmes
Institute of Mental Health
Service Period: 1 December 2003 to 31 March 2009

The Research Ethics Committee (REC) and the Domain Specific Review Boards (DSRB) play a key role in protecting human subjects while encouraging cutting edge research to be conducted in the National Healthcare Group (NHG). The REC formulates the ethics policies and oversees the functions of the DSRB in NHG.

A/Prof Wong Kim Eng made valuable contributions and showed exceptional leadership as the Chairperson of the NHG Research Ethics Committee. During her term of office from 1 December 2003 to 31 March 2009, A/Prof Wong saw the establishment of the NHG DSRB in 2004 and guided its growth and maturity to attain international recognition in 2007, when the DSRB was accredited by the Association for the Association for the Accreditation of Human Research Protection Program (AAHRPP), USA. This was a landmark achievement for the National Healthcare Group, National University Health System (NUHS), Alexandra Hospital (AH) and also for Singapore, as we were the first public healthcare institution outside of North America to be awarded full accreditation by AAHRPP.


A/Prof Wong Kim Eng

And it is therefore with great gratitude that the NHG bids farewell to our pioneer REC Chairperson, A/Prof Wong Kim Eng for the contributions and leadership rendered.

Welcome New Chairperson –

Associate Professor Chin Jing Jih

Senior Consultant, Department of Continuing & Community Care
Tan Tock Seng Hospital
Service Period: 1 April 2009 to current

A Senior Consultant in the Department of Continuing & Community Care, Tan Tock Seng Hospital, A/Prof Chin is also the Head of the hospital's Cognition and Memory-related Disorders Service.

A/Prof Chin joined the Research Ethics Committee as a pioneering member in December 2003. In 2004, he was appointed Chairman of the NHG Domain Specific Review Board, to oversee the management of the ethics review of research activities conducted under the purview of the National Healthcare Group. A/Prof Chin was later appointed as the Programme Director for the NHG Research Quality Assurance Program, the program that helps to assess the quality of the NHG Human Subject Protection Program (HSPP) and to continually work towards promoting a research culture with high ethical standards in NHG, NUHS and AH. Through his involvement, A/Prof Chin has contributed extensively to the success of NHG's achievement of the AAHRPP accreditation in 2007. A/Prof Chin was appointed Deputy Chairperson of the NHG Research Ethics Committee between 1 April 2008 to 31 March 2009 and later appointed Chairperson on 1 April 2009.


A/Prof Chin Jing Jih

In addition to his contributions and involvement at our Cluster, A/Prof Chin is also a member of the National Medical Ethics Committee (NMEC) and Director for the Advanced Specialty Training (AST) Course on medical ethics, professionalism and health law. At the Singapore Medical Association (SMA), he serves as Executive Director of the Centre for Medical Ethics and Professionalism, and as Chairperson of the SMA Ethics Committee. He is also appointed Adjunct Associate Professor at the NUS Centre for Biomedical Ethics. A/Prof Chin was awarded the Healthcare Humanity Award in recognition for his contributions in promoting awareness and practice of clinical ethics among healthcare professionals in 2007.

A/Prof Chin is passionate about and has an in depth understanding of ethical issues concerning participants in clinical studies. He has delivered numerous presentations on ethical issues including at the NHG-NUS Clinician Leadership in Research Training Programme, NHG Annual Research Ethics Forum, as well as conducts training of new DSRB members.

NHG welcomes its new REC Chairperson, A/Prof Chin Jing Jih, and looks forward to his leadership in bringing the NHG REC to attain greater heights in the governance of research ethics for NHG, NUHS and AH.

Code of Ethical Practice in Human Biomedical Research

The Ministry of Health has recently in April 2009, published a code that puts in place the ethical principles upheld and adopted by our community of clinicians and researchers. The principles of ethical practice in this Code aim to protect human research subjects; and the adherence to the Code would allow the uphold of scientific integrity. This Code is intended to be a national reference document on ethical principles, standards and guidance for researchers.

The Code

1 The credibility of human biomedical research with society is dependent upon the maintenance of the highest ethical standards in its conduct. Research is ethically justifiable only if it is scientifically sound and does not expose research subjects to unwarranted discomfort or risks without likely benefit to the advancement of biomedical science. Research should also abide by accepted moral standards within the community and be carried out responsibly, in ways that respect and protect the research subjects, and maintain scientific integrity to promote trust and accountability.

2 Researchers have a personal and non-delegable responsibility to ensure the ethical conduct of their research. This Code lays down principles and standards for ethical practice in human biomedical research in Singapore. Researchers should use this Code as a yardstick for their conduct and behaviour. In addition, researchers should have an understanding of research ethics, develop the knowledge, skills and attitude needed to manage ethical conflicts, and to consult with colleagues, ethics committees and other experts when ethical issues arise.

3 Researchers are to uphold the principles[1] fundamental to the protection of human subjects. In general, researchers are expected to:

i. Respect persons as individuals:
   (a) obtain fully informed consent from subjects who are autonomous;
   (b) accord due protection to persons with diminished autonomy and who are vulnerable;
   (c) protect subject privacy and maintain data confidentiality at all times;
ii. Strive to promote the well-being and safety of human research subjects, protecting them from unnecessary risks, and never let the goals of research undermine this priority;
iii. Abide by local laws, regulations, guidelines and commonly agreed standards of good practice[2] on the conduct of human biomedical research;
iv. Embody professionalism by upholding integrity, openness, and a commitment to intellectual honesty in the conduct of research, and avoid any actual, potential or apparent conflict of interest;
v. Exercise responsible custodianship of resources under their charge and be a responsible steward in the use and management of those resources;
vi. Treat all fellow researchers with dignity and respect, and managing researchers under their supervision with care;
vii. Observe the Code in all respects of their professional lives.

Source from Ministry of Health, Singapore

Facts about B2BResearch Online

you've always wanted to know but were just too busy to ask (Part 2 of 2)

7 I submitted my Application just before the submission deadline. Why doesn't the DSRB accept it for the month's Full Board Review?

The submission deadline for the month's Full Board Review is the first working day of that same month.

When the online DSRB Application Form is submitted, it is automatically forwarded to the appropriate Department and Institution Representatives for their review and endorsement.

The DSRB will only accept the online Application when all the appropriate Department and Institution Representatives have given their endorsements via the B2BResearch Online portal.

The submission Deadline does not take into account the time needed for the Department and Institution Representatives to review and endorse the Application.

Hence, Principal Investigators are strongly advised to prepare and submit their Applications at least one week before the Deadline.

8 I haven't received my DSRB Approval Letter. Where can I get a copy?

The Principal Investigator (as well as the entire Study team and Protocol Administrators) can download and print a copy of the DSRB Approval letter from the "DSRB Approval Letters" section of the virtual study folder.

[1] The principles as presented in the Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research are Respect for persons, Beneficence and Justice.
[2] The primary emphasis for the conduct of research should be to ensure due process for validity and reproducibility, rather than to focus on the results of the research.

The Code of Ethical Practice in Human Biomedical Research is available online at the MOH website (http://www.moh.gov.sg), under "Publications/ Guidelines for Healthcare Professionals/ Human Biomedical Research" section

SoCRA Improving Clinical Research Quality through Education, Training and Certification

Dr Joanne Goldberg

Ms Ng Hwee Hian
Research Quality Assurance (RQA), RDO

SoCRA - The Society of Clinical Research Associates – is one of the global leaders supporting the professional development of clinical research associates internationally and conducts and issues the Certification in Clinical Research Professional (CCRP) for research coordinators who are able to demonstrate levels of high competency and knowledge to support and enable proper research administration.

This June, NHG Research & Development Office (RDO) is privileged to host the first Singapore CCRP examination at Spring Singapore. This examination was proctored by Dr Joanne Goldberg, President, SoCRA from Quebec, Canada. A total of 27 National Healthcare Group (NHG), SingHealth (SHS) and private candidates registered and took part in this certification examination. It is encouraging to have such a group of candidates pursuing this professional certification and we wish them all the best as we await the release of results in August 2009.

In addition to proctoring the CCRP examination, Dr Goldberg also met up with our Deputy Director, Mr Choo Kin Poo as well as representatives from Alexandra Hospital, Changi General Hospital, National Skin Centre, National University Hospital, Singapore General Hospital, Tan Tock Seng Hospital and Singapore Clinical Research Institute to discuss and explore further options on improving clinical research quality while enhancing and supporting continuing education for CRCs.

The finale for Dr Goldberg's trip to Singapore ended with a presentation at the 3rd NHG-SHS Clinical Research Coordinator Society Forum at Tan Tock Seng Hospital on 23rd June 2009. Dr Goldberg's presentation topic was on "Quality in Clinical Research: Implementation of Site Quality Assurance Standards & Processes". The Forum was well attended by more than 120 participants. Presentation slides have since been uploaded onto the b2bresearch website. For more information on this and past Forums, please refer to: http://www.b2bresearch.nhg.com.sg

Facts about B2BResearch Online

you've always wanted to know but were just too busy to ask (Part 2 of 2)

9 Why can't I update my minimum training status in my account profile?

The minimum training status can only be updated by DSRB Staff. If you have completed the training requirements but your status has not been updated, please contact your Domain coordinator. You can also fax us a copy of your CITI Certificate (or equivalent) together with the waiver form if applicable to 6496 6257 (Attn: Nor –DSRB).

10 Do I need to update the CV section of my B2BResearch Online account?

Yes, all NHG users are strongly encouraged to complete the CV section.

If you are submitting an online DSRB application for review as the Principal Investigator, please note that you are required to complete the CV section as the qualification of the PI is an integral part of the review process.

NHG Small Innovative Grant (SIG) I/II

Ms Malini Krupa Shankar Sintre
Research Support Services (RSS), RDO

The NHG Small Innovative Grant I (SIG I) is a short-term grant designed to support clinical research that answer specific, targeted research questions or to perform pilot or feasibility studies. It is designed to support smaller exploratory studies that may provide preliminary findings for larger research proposals. Creative and novel concepts or innovative technologies that increase knowledge of human disease or improve the quality of healthcare are encouraged. SIG I funds up to S$50,000 per year for a maximum term of 2 years.

The NHG Small Innovative Grant II (SIG II) is a follow-on grant offered to successfully completed SIG I projects to encourage continuing translation of research into patient care. SIG II aims to fund follow-on research questions for the same project or an extension of the same research interest as the completed SIG I project. This grant is an added incentive, especially for projects that have demonstrated potential in translating basic discoveries into the prevention, diagnosis, treatment and cure of disease, or in building clinical research capabilities. SIG II funds up to S$200,000 per year for a maximum term of 3 years.

In the FY2009 Grant Call, 16 SIG I and 3 SIG II projects will be funded.

The FY2010 grant call will be announced soon. For more information on the SIG I Grant application, please visit our website at http://www.b2bresearch.nhg.com.sg

Congratulations to the following successful SIG I / II applicants!

The lists of funded proposals are as below
(in alphabetical order by Institutions name)

FY09 SIG I Awardees

No.	Principal Investigator	Institution	Project Title
1	Dr Anton Cheng	AH	Site specific adipocyst adiponectin gene expression (a substudy among diabetic individuals)
2	Ms Toy Wan Ching	AH	Functional genetic and pharmaco-genetic of adiponectin gene in human visceral pre-adipocytes
3	Dr Sun Yan	NHG HQ	Healthcare utilization and clinical outcomes of stroke patients with diabetes mellitus (DM) vs without DM
4	Dr Aung Le Le	NUH	Singapore Childhood Cancer Survivor Study (Singapore-CCSS):a multi-institutional collaborative study on long-term survivors of childhood cancer
5	Dr Tan Poh Lin	NUH	Improving specificity and efficacy of cancer immunotherapy through use of adjuvant cancer antigens specific monoclonal antibodies and FCGR3A activated NK cellular therapy
6	Dr Lee Le Ye	NUH	Incidence of immunoprophylaxis failure and hepatitis B surface antibody escape mutants in infants born to hepatitis B carrier mothers in Singapore
7	Dr Hsu Li Yang	NUH	Clinical impact of low ceftriaxone MIC ampC- and ESBL-positive enterobacteriaceae
8	Dr Shaik Ahmad Buhari	NUH	Use of CK19 mRNA expression as a single biological marker for intra-operative detection of lymph node metastasis in breast cancer
9	Dr Neo Jong Jong	TTSH	Is Vitamin D deficiency a problem? A prospective study of the vitamin D status of patients admitted to a rehabilitation centre
10	Miss Chan Ee Yuee	TTSH	Pain and Functional Recovery Post Total Knee Replacement - Effectiveness of Continuous Femoral Nerve Block versus Single-Injection Femoral Nerve Block and Intraveneous Patient Controlled Analgesia
11	Dr Emily Felicia Shen	TTSH	The effect of low or high FODMAPs diet in patients with Functional Gut Disorders
12	A/Prof Ding Yew Yoong	TTSH	Very old patients Hospitalized for Acute Medical Illnesses: Are their outcomes better when under the care of Geriatricians?
13	A/Prof Leo Yee Sin	TTSH	Clinical characteristics of patients with human influenza A/B PCR test on respiratory speciments within 48 hours of admission to Tan Tock Seng Hospital
14	Dr Leong Yi Onn Ian	TTSH	Transitional care for patients in the post-acute period
15	Dr Gregory Cham	TTSH	To determine the efficacy of an abbreviated, patient-tailored course of intraveneous N-acetylcysteine in preventing hepatotoxity from paracetamol overdose
16	Dr Ong Kiat Hoe	TTSH	Flow cytometric detection of phosphorylated signaling molecules as a diagnostic and prognostic tool in the management of myeloproliferative neoplasms

FY09 SIG II Awardees

No.	Principal Investigator	Institution	Project Title
1	Dr Tavintharan S	AH	Can co-enzyme Q10 co-administration with simvastatin reduce the risk of hepatotoxicity in hypercholesterolemic patients?
2	A/Prof Fisher, Dale Andrew	NUH	Costing MRSA and its control in a large hospital with highly prevalent disease
3	Dr Kevin Lee Boon Leng	NUH	A Multi-center randomised controlled trial evaluating a novel minimally-invasive technique of cartilage repair in the human knee using autologous Mesenchymal Stem Cells and Hyaluronic Acid

Researcher-Investigator-Scientist Enabler (RISE) Grant Scheme

Ms Adeline Lu
Research Training & Development Unit (RTDU), RDO

The RISE Grant Scheme is a time protect grant designed to complement current institutional and departmental efforts in providing researchers funded time in research. The RISE Grant Scheme allows for 20% to 40% Full Time Equivalent funded time (FTE) (i.e 1 to 2 days per week) in research per award.

In the FY2009 Grant Call, 4 applicants were awarded the RISE Grant Scheme.

The FY2010 RISE Grant Scheme will be announced soon. For more information on the RISE Grant Scheme, please visit our website at http://www.b2bresearch.nhg.com.sg

Congratulations to the successful RISE applicants!

The lists of funded proposals are as below
(in alphabetical order by Institutions name)

No.	Principal Investigator	Institution	Department
1	Dr Raymond Seet Chee Seong	NUH	Medicine
2	Dr Aung Le Le	NUH	Paediatrics
3	Dr Tan Poh Lin	NUH	Paediatrics
4	A/Prof Shek Pei-Chi Lynette	NUS	Paediatrics