



PRESS RELEASE

24 Apr 2009

LOCAL RESEARCHERS EXPLORE NEW APPROACHES TO TACKLE AGE-OLD AILMENTS

A*STAR issued research grants for more than 50 biomedical projects on disorders of the immune system, infectious diseases, ageing and cancer

1. A*STAR's Biomedical Research Council (BMRC) and its consortia, namely Singapore Bioimaging Consortium (SBIC), Singapore Immunology Network (SIgN), Singapore Institute for Clinical Sciences (SICS) and Singapore Stem Cell Consortium (SSCC), have issued more than 50 grants amounting to \$36 million to research groups from local universities, research institutes and hospitals this year. The research projects awarded under BMRC's 7th General Grant Call, SBIC-SIgN Joint Grant Call, SSCC Grant Call and SIgN Grant Call, will potentially develop therapeutics for the treatment of ailments of the immune system, infectious diseases, ageing, cancer, etc.

Targeting ailments of the immune system

2. About 20% of the proposals are concerned with the study of what irritates the immune system and causes problems such as allergy, eczema and asthma¹. Championing immune health is Prof Chua Kaw Yan of NUS², who was awarded a record three grants under BMRC's 7th General Grant Call. She will focus on combating the common dust mite, *Blomia tropicalis*, which is responsible for 60-70% of allergy cases here including asthma, allergic rhinitis and eczema. The first grant will investigate the mechanisms of an oral vaccine against the predominant allergen in *B. tropicalis*, Blo t 5 protein. Another will focus on optimising the potency of a genetic vaccine, while the third will

¹ These common bugbears of children and adults alike can have an immense impact on the quality of life, and even be life-threatening when occurring in conjunction with chronic diseases such as cancer.

² Prof Chua is from the Department of Paediatrics, National University of Singapore (NUS) Yong Loo Lin School of Medicine, National University Health System (NUHS).

involve creating a modified or 'recombinant' protein to foster immunity against Blo t 5.

3. Increased prevalence of allergy is a major global problem and a preventive vaccine is currently unavailable. Said Prof Chua, "Immunotherapy remains the only truly disease-modifying treatment for asthma and allergic rhinitis. Traditional forms of immunotherapy use natural sources of allergens and have numerous disadvantages, such as the presence of undefined material, huge variability in sample composition, and contamination of allergens from other sources. We therefore hope to use the major allergen, Blo t 5, to develop a novel and effective therapeutic vaccine for immunotherapy."

Strategic steps to curb infectious disease

4. Grants have also been awarded to research teams that will use various approaches including genomics, proteomics and bioimaging to study various mechanisms of infection³, such as tuberculosis and malaria.

5. The research team led by Dr Ann Lee of the National Cancer Centre of Singapore (NCCS)⁴ is a case in point. Awarded a BMRC grant, the team will confront *Mycobacterium tuberculosis* (MTB)⁵ by sifting through a bank of DNA samples extracted from drug-resistant MTB strains to identify novel mutated genes conferring resistance to Isoniazid, the main drug that combats tuberculosis. Said Dr Lee, "The identification of additional genes associated with Isoniazid resistance is important for the development of comprehensive molecular strategies that are potentially more efficient than current susceptibility testing methods, and could aid in giving more appropriate treatment to patients and decrease the spread of resistant strains. In addition, the discovery of new genes may reveal novel targets suitable for the development of alternative therapeutic options."

6. Another team, led by A/Prof Peter Preiser of Nanyang Technological University (NTU), has been awarded a grant under the SBIC-SIgN Joint Grant Call to conduct basic research on the pathology

³ Infectious diseases such as tuberculosis and malaria retain high mortality rates despite widespread efforts to prevent their transmission; and some of these diseases are even on the rise.

⁴ Dr Lee is also an Adjunct Associate Professor from the National University of Singapore (NUS).

⁵ *Mycobacterium tuberculosis* (MTB) is the agent of the world's leading cause of mortality with an estimated two billion people currently infected worldwide. In Singapore, the incidence rate of tuberculosis has also risen for the first time in ten years, leading to concerns over increased transmission of the MTB bacteria.

of malaria⁶. Prof Preiser said, “A key challenge to successful malaria intervention is our limited understanding of how the malarial parasite evades detection by the spleen – our immune system’s control centre. With this grant, we will use new imaging tools to visualise and measure how many parasites are eliminated in the spleen. This work will give us a better understanding on which factors, both from the host as well as the parasite, contribute to the efficiency of parasite removal and could lead to new intervention strategies against the parasite.”

Tackling problems associated with ageing

7. Also receiving funding are projects that will explore health problems associated with ageing such as neurodegenerative diseases like Alzheimer’s and Parkinson’s. One of them is Dr Gavin Dawe’s group at NUS⁷, which received a grant under the SSCC Grant Call to explore the signaling mechanisms behind Alzheimer’s disease. The grant is a nod to his group’s discovery of an important protein interaction that suppresses neural cell formation in the brains of mice, which might have implications for Alzheimer’s, the most common form of dementia among older people. Said Dr Dawe, “In this project, we will investigate whether this protein interaction also occurs in human stem cells and in the adult mouse brain, as well as how it influences stem cell function. Our findings will increase our understanding of what these proteins do in the brain and in the long term, this knowledge may contribute to the development of treatments for Alzheimer’s disease.”

Exploring ways to deal with cancer pathways

8. At least one-fifth of all the grants have been awarded to projects dealing with cancer pathways or working on cancer cell lines. One of the groups led by Prof Shazib Pervaiz of NUS⁸ has been awarded the BMRC grant to examine how statins – cholesterol-lowering drugs – have the intriguing additional effect of restricting growth and inducing death of cancer cells. This will potentially benefit breast cancer patients. Said Prof Pervaiz, “Current breast cancer therapies include surgery, anti-cancer drugs and radiation, which are invasive or run the risk of relapse. Our team aims to characterise the interactions of statins with other proteins known to promote cell death and survival, and subsequently explore the potential for statins to fill the gap in novel

⁶ Malaria is a disease that infects up to 600 million and kills over 1 million yearly, and that despite extensive efforts still has no vaccine.

⁷ Dr Dawe is from the Department of Pharmacology, NUS Yong Loo Lin School of Medicine, NUHS.

⁸ Prof Pervaiz is from the Department of Physiology, NUS Yong Loo Lin School of Medicine, NUHS as well as the Cancer and Stem Cell Biology Program, Duke-NUS Graduate Medical School.

strategies for more effective and less invasive treatment of breast and other forms of cancer.”

*Continuing A*STAR's efforts in R&D*

9. Said Prof Sir George Radda, Chairman of BMRC, “The grant calls underscore A*STAR’s commitment to foster excellent scientific research and talent in Singapore. The wide range of research areas covered under the grant calls is indicative of the spectrum of biomedical capabilities we have built up in Singapore over the years, as well as the high quality of our researchers. I look forward to the exciting and innovative discoveries that will result from the research the scientists are able to carry out with the funding from A*STAR.”

10. Since its inaugural General Grant Call in 2001, BMRC has awarded a total of 389 grants (amounting to \$285.5 mil) to local research institutes and hospitals including NUS, NUH and NCCS to realise the vision of Singapore becoming a premier centre for biomedical research and development. The 8th BMRC General Grant Call is expected to open for applications on 4 May this year.

AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH

For queries and clarification, please contact:

Ms Adela Foo

Senior Officer, Corporate Communications

AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH (A*STAR)

DID: (+65) 6826 6218 | Fax: (+65) 6478 9593

Email: adela_foo@a-star.edu.sg

National Archives of Singapore

About the Agency for Science, Technology and Research (A*STAR) and the Biomedical Research Council (BMRC)

A*STAR is Singapore's lead agency for fostering world-class scientific research and talent for a vibrant knowledge-based Singapore. A*STAR actively nurtures public sector research and development in Biomedical Sciences, Physical Sciences and Engineering, with a particular focus on fields essential to Singapore's manufacturing industry and new growth industries. It oversees 22 research institutes, consortia and centres, and supports extramural research with the universities, hospital research centres and other local and international partners. At the heart of this knowledge intensive work is human capital. Top local and international scientific talent drive

knowledge creation at A*STAR research institutes. The Agency also sends scholars for undergraduate, graduate and post-doctoral training in the best universities, a reflection of the high priority A*STAR places on nurturing the next generation of scientific talent.

The Biomedical Research Council (BMRC) oversees the development of core research capabilities within A*STAR research units specialising in bioprocessing; chemical synthesis; genomics and proteomics; molecular and cell biology; bioengineering and nanotechnology and computational biology. Through competitive grants, the Council also supports research in the wider scientific community such as public universities and hospitals. As part of its efforts to advance human healthcare, BMRC actively promotes translational medicine and cross-disciplinary research. The Council also engages in human capital development in the biomedical sciences and promotes societal awareness of biomedical research through outreach programmes.

For more information about A*STAR, please visit www.a-star.edu.sg.

National Archives of Singapore

ANNEX

Grant Calls under the Biomedical Research Council (BMRC)

Grants highlighted in the press release are highlighted in blue.

Abbreviations:

CTM – Centre for Transfusion Medicine, Health Sciences Authority
NTU – National Technological University
NUS – National University of Singapore
NCC – National Cancer Centre Singapore
NNI – National Neuroscience Institute
SERI – Singapore Eye Research Institute
SGH – Singapore General Hospital

BMRC General Grant Call

Ongoing since 2001, this annual grant call provides competitive grant support and research resources, in the area of biomedical sciences research, to investigators in the publicly funded institutions such as universities, hospitals and specialty centres in Singapore. Research areas that have been funded includes cell biology, neuroscience, biochemistry, animal models and infectious diseases. The grants provide positions ranging from laboratory technicians to research assistants and research fellows for 1 to 3 years in various local research institutes such as NUS, NTU, NCC and SGH.

Awardees

The 7th General Grant Call awarded 38 out of 140 reviewed proposals. Amounts awarded ranged from \$145,000 to \$1.25 mil, totalling \$27.06 mil (including indirect costs, pegged at 20% of the total project value) and providing for 63 full-time employees. Funding for the 38 projects began on 1 Jan 09, and will last 24-36 months.

S/N	Title	Host Inst	PI
1	Dissecting Molecular Architectures and Roles of Adherens Junctions in Cell Adhesion and Tissue Remodelling with Electron Tomography	NUS	He Wanzhong
2	mTOR as the molecular target for modulation of autophagy, necrosis and tumorigenesis	NUS	Shen Han Ming
3	Developing chemical and enzymatic protein synthesis methods for protein structure-function study - application to histone proteins	NTU	Liu Chuan-Fa

4	Alternative splicing as molecular switch to regulate Cav2.1 channel function in synaptic excitability	NUS	Soong Tuck Wah
5	The role of SARM in infection: mechanisms of action and interaction partners	NUS	Ding Jeak Ling
6	Rational design of a hypoallergenic major dust mite allergen for allergy immunotherapy	NUS	Chua Kaw Yan
7	Understanding the molecular basis of red blood cell selection by malaria merozoites	NTU	Peter Rainer Preiser
8	Establishment of medakafish as a lower vertebrate model for analysis of primordial germ cell development	NUS	Hong Yunhan
9	Defining the structural traits of subunits D and E of the biological energy producer A1AO ATPsynthase	NTU	Gerhard Grüber
10	Spatiotemporal Imaging of Mechano-Sensing by the Src Family Kinase Substrate p130Cas	NUS	Yasuhiro Sawada
11	Resolving fundamental gaps in our knowledge regarding the function of parkin and its role in Parkinson's disease	NNI	Lim Kah Leong
12	Synthesis and evaluation of planar pentavalent ligands targeting dimeric interface of serum amyloid P component for the therapeutic elimination of Alzheimer's disease	NUS	Zeng Huaqiang
13	Characterization of Smad3 function in skeletal muscle growth and atrophy	NTU	Ravi Kambadur
14	Self-Assembly and Ordered Structure of Phospholipid Complexes with Nucleosome and Chromatin	NTU	Lars Nordenskiöld
15	Roles of RanGTP in the nuclear accumulation of Survivin and its impact on apoptosis	NTU	Li Hoi Yeung
16	Lipid metabolism in the survival of dopaminergic neurons - relevance to Parkinson's Disease	NUS	Sashi Kesavapany
17	Is cystathionine b-synthase a viable therapeutic target for the treatment of acute ischemic stroke?	NUS	Peter Wong Tsun-Hon
18	Molecular characterization of the novel tumor suppressor DLEC1: tissue distribution and cellular localization,	NUS	Hooi Shing Chuan

	mechanism of cell cycle arrest and function as a transcription factor		
19	The molecular and structural basis of leukocyte b2 integrins signalling	NTU	Surajit Bhattacharyya
20	Proteome-wide investigation of kinase/substrate interactions using a novel "kinase trapping" probe and its application in drug discovery	NUS	Yao Shao Qin
21	Surviving neurons in sclerotic CA1 area of the hippocampus: their extra- and intra-hippocampal connections and neurophysiological property in the mouse model of human intractable temporal lobe epilepsy	NNI	Tang Feng Ru
22	Rab22B/Rab31, a brain-enriched small GTPase in astrocytic membrane traffic and brain pathophysiology	NUS	Tang Bor Luen
23	Structural and functional characterization of wildtype and three alternatively spliced forms of the Foxp3 protein, the key transcription factor involved in lymphoma	NUS	Kunchithapadam Swaminathan
24	Role of microRNAs in lipid metabolism	NUS	Theresa Tan May Chin
25	Analysis of PTEN's function with its interacting protein ZO-2	NUS	Koichi Okumura
26	Study the Involvement of Reactive Oxygen Species and Rho GTPase in Statin-induced Apoptosis of Breast Cancer Cells	NUS	Shazib Pervaiz
27	Coronavirus ribonucleocapsid assembly and its replicase enzymes: structure and function	NTU	Julien Lescar
28	Singapore Alliance for Antimicrobial Peptides	SERI	Roger Wilmer Beuerman
29	The Immunomodulatory Effects of Probiotics on the Th2 Immune Responses: Role of Gut Dendritic Cells	NUS	Chua Kaw Yan
30	Optimisation and preclinical studies of prophylactic and therapeutic DNA vaccines for dust mite allergy and allergic asthma	NUS	Chua Kaw Yan
31	Validation and Use of the Distributed Parameter Tracer Kinetic Model for Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE MRI) of Hepatocellular Carcinoma	NCC	Thng Choon Hua

32	Gerontology Research Programme: Nutritional, cardiometabolic and vascular factors, ApoE4 gene interactions, and dementia and depression risk	NUS	Ng Tze Pin
33	Identifying novel genes involved in isoniazid resistance in <i>Mycobacterium tuberculosis</i> using new technology	NCC	Ann Lee Siew Gek
34	Molecular Evaluation of Gut Microbiota Signatures in Infants with Eczema	NUS	Lee Bee Wah
35	Systematic study on genetic and epimutational profile of hereditary nonpolyposis colorectal cancer in Singapore	SGH	Liu Yanqun
36	Development and validation of high-density micro-fluidic real-time PCR platform to enable parallel single-cell molecular genomic analysis	NCC	Hui Kam Man
37	Identification of human plaque protein signatures predictive for secondary cardiovascular events using quantitative proteomics	NTU	Newman Sze Siu Kwan
38	Trans-splicing correction of survival motor neuron gene pre-mRNA in patient and mouse model cell lines: A novel therapeutic strategy for Spinal Muscular Atrophy	SGH	Yee Woon Chee

SSCC Grant Call

The SSCC Grant Call was conducted in May 2008 together with the BMRC annual General Grant Call as part of SSCC's effort to better support stem cell research in the wider Extramural community.

Awardees

A total of 3 grants were awarded, at a total amount of \$2.14 mil (including indirect costs, pegged at 20% of the total project value). Funding began on 1 Feb 09, for a period of 3 years.

S/N	Title	Host Inst	PI
1	Interaction of transient axonal glycoprotein 1 (TAX/TAG1) and amyloid precursor protein (APP): an investigation of downstream signaling and functions in adult neural stem cells	NUS	Gavin Dawe
2	Identification and characterization of cancer stem cells from gastric cancer	NUS	Chan Shing Leng
3	Tumor tropism of human bone marrow-derived mesenchymal stem cells is	NCC	Paula Y P Lam

	mediated by matrix metalloproteinase 1		
--	--	--	--

SBIC-SIgN Joint Grant Call

The Singapore Bioimaging Consortium (SBIC) and Singapore Immunology Network (SIgN) jointly announced a Grant Call in August 2008 for collaborative research proposals based on the theme of "Imaging Immune System and Infectious Diseases". Projects under the grant call could include (but were not limited to): *in vivo* imaging of the immune response in models of infection, imaging immunity in physiological and pathological conditions, imaging tumor development *in vivo*, and *in vivo* imaging of immunity in models of inflammation.

Awardees

2 proposals were eventually awarded funding, at a total of \$1.90 mil (including indirect costs, pegged at 20% of the total project value). Funding began on 1 Mar 09 and will last for 3 years.

S/N	Title	Host Inst	PI
1	Assessing trafficking and tissue distribution of live and subunit vaccines against <i>Mycobacterium tuberculosis</i> by dynamic, <i>in vivo</i> fluorescence imaging using ultrafine upconversion fluorescent nanoparticles	NUS	Sylvie Alonso
2	Understanding the mechanism of splenic clearance of malaria infected red blood cells	NTU	Peter Preiser

SIgN Grant Call

The SIgN Grant Call was launched in August 2008 with the theme "*In vivo* immune-regulation during Infection, Inflammation, Autoimmunity and Cancer". Projects under the call could include understanding immunity in the tissues in physiological and pathological conditions; *in vivo* immune-regulation during infection or inflammation; or immune-regulation of perturbations in the tissues during autoimmunity or cancer.

Awardees

9 projects were awarded, totaling \$3.47 mil (including indirect costs, pegged at 20% of the total project value) over 1-3 years. Funding began on 1 Mar 09.

S/N	Title	Host Inst	PI
1	Role of bone-marrow derived cells in tumor-induced lymph node lymphangiogenesis in a	NUS	Angeli Veronique

	mouse model of human melanoma and its significance in human cancer dissemination		
2	Differential regulation of CD14/NFAT and NF-κB pathway in myeloid populations in human gram-negative sepsis and endotoxin “de-sensitization”	NUH/ NUS	Philip Lau
3	HBV-related hepatocarcinoma: molecular and functional characterization of tumour target and effector immune cells	NUH	Krishnakumar Madhavan
4	Structural, functional and immunological characterization of a <i>Plasmodium</i> multigene family associated with the pathogenesis of cerebral malaria	NTU	Julien Lescar
5	Innate immunity against malaria: Studies on the mechanisms of <i>Plasmodium</i> -phagocyte interactions and their consequences	NUS	Kevin Tan S W
6	The role CD39 in the control of inflammatory immune reactions	NUS	Mike Kemeny
7	Genetically engineered IL-2 deficient dendritic cells: the study of <i>in vivo</i> role of IL-2 produced by dendritic cells	NTU	Christiane Ruedl
8	A Genome-wide association study on atopy and allergic diseases in Singaporean Chinese	NUS	Wang De Yun
9	A Phase I/II Single Centre Study to Determine the Safety and Efficacy of a Combination of Regulatory T cells and Rapamycin for the Treatment of Acute Graft Versus Host Disease	SGH, CTM, NCC	Goh Yeow Tee

SICS Grant Call

SICS' first extramural grant call sought collaborators for its programme in Growth, Development, and Metabolism (GDM), which focuses on translational and clinical research relevant to human development. A particular interest of the programme is the role of the fetal environment in inducing developmental plasticity, in determining subsequent susceptibility to diseases such as obesity and type II diabetes, and in influencing cognitive development later in life. Proposed projects could include any of the following: *in vitro* laboratory studies, model systems of development and disease including animal models, human physiological studies, and small epidemiology studies.

Awardees

2 proposals were awarded funding, at a total of \$1.70 mil (including indirect costs, pegged at 20% of the total project value). Funding began on 1 Apr 09 and will last for 3 years.

S/N	Title	Host Inst	PI
1	Influence of Fetal Growth on Cognition and Brain Development in Children	NUS	Qiu Anqi
2	Mechanisms of Epigenetic Control of Leptin-STAT3 Axis in the Body Homeostasis	NUS	Fu Xing Yuan

Details of past grant calls under BMRC can be found at http://www.a-star.edu.sg/biomedical_sciences/179-Past-Calls.

National Archives of Singapore