MEDIA RELEASE

Six clinician scientists receive funding support for translational and clinical research

S$5.3 million awarded to support research to study heart failures in Asian populations, translational research in cancer and infectious diseases and conducting clinical trials

1. Six clinician scientists have been awarded a total of S$5.3 million under the Clinician Scientist Awards (CSAs) to conduct cutting-edge translational and clinical research in the areas of cardiology, oncology and infectious disease. The CSAs are an important part of Singapore’s Biomedical Sciences initiative to train and build up internationally competitive research talent to take scientific discoveries at the bench and translate them into meaningful healthcare outcomes.

2. Associate Professor Pierce Chow from the Singapore General Hospital (SGH) and Dr Goh Boon Cher, from the National University Hospital (NUH) were the awardees under the CSA-Senior Investigators (CSA-SI) category. The CSA-SI category funds senior clinician researchers for up to S$350,000 per year for 5 years.

   - A/Prof Chow, Senior Consultant at the Department of General Surgery, NUH will be conducting a multi-center Phase III clinical trial to compare the outcomes of two known therapies for primary liver cancer and the clinical data obtained from the study would be used to determine which therapy is more beneficial to primary liver cancer patients.

   - Dr Goh, who is a Senior Consultant at NUH’s Department of Haematology-Oncology will be conducting several early phase clinical trials which seek to test the efficacy of a class of drugs that show promise in restoring the body’s anti-tumor capabilities previously turned off by rogue cancer cells.

3. Dr Carolyn Lam and Dr Lawrence Lee from NUH, Dr Mei Wang from Duke-NUS Graduate Medical School and Dr Charles Chuah from SGH were the
awardees under the Four CSA–Investigator (CSI-INV) category. The CSA-INV category funds junior clinician scientists for S$225,000 per year for 3 years.

- Dr Carolyn Lam, Associate Consultant NUH’s Department of Cardiology, will be returning to Singapore from the Mayo Clinic in the USA to conduct studies relating to heart failure in Asian populations – an area not studied widely by the scientific community. Her research will generate much needed scientific information so as to enable a better understanding of the disease which would lead to better management and treatment in primarily Asian, multi-ethnic countries such as Singapore.

- Dr Lawrence Lee, Associate Consultant at the Clinical Trials Unit, NUH will be looking into the use of drug combination therapies to treat cancer and HIV. He will be studying how drugs react inside the body and hopes through his findings to optimize dosages in order to work towards personalizing medicine for individual patients.

- Dr Mei Wang, Assistant Professor at Duke-NUS Graduate Medical School will be studying the actions of a class of experimental molecules which help block the effects of cancer-causing proteins produced by oncogenes. A particular focus of her study will be on an oncogene called Ras, which is found to be active in over half of human cancers.

- Dr Charles Chuah, Senior Consultant at SGH’s Department of Haematology, will be looking into methods to eliminate leukemia stem cells, which have been shown to lead to disease recurrence as they are notoriously difficult to eradicate as they are resistant to drug therapy. Dr Chuah will be looking at ways to eliminate such cells by investigating the use of combination drug therapies.

4. Said Mr Lim Chuan Poh, Co-Chair of Singapore’s Biomedical Sciences Executive Committee (BMS-EXCO) and Chairman of the Agency for Science, Technology and Research (A*STAR), “The BMS EXCO would like to congratulate all the six clinician scientists on the Clinician Scientist Awards and wish them the very best in their endeavours. Indeed, the research of this year’s awardees demonstrates the deepening TCR capabilities here in Singapore.” Singling out the research of the two CSA Senior Investigators for special comment, Mr Lim added, “Dr Goh Boon Cher and A/Prof Pierce Chow’s work in conducting early phase and Phase III clinical trials respectively are particularly promising. They not only bear testimony to the progress that Singapore has been making in cancer research, but also hold promises of delivering outcomes that will contribute to our economy and make an impact on our society. All CSA recipients serve as role models for budding clinician scientists to come forward and participate in the very important work of creating knowledge and improving healthcare solutions to benefit Singapore and the world.”
5. Added Ms Yong Ying-I, Co-Chair of the BMS-EXCO and Permanent Secretary, Ministry of Health, “I am very encouraged by the results from the CSA year on year – they are internationally competitive and of solid scientific merit. I am also pleased to see that one of the CSA awardees, Dr Carolyn Lam will be returning to Singapore to continue her research career. Singapore has made its mark as a credible research hub and I hope to see more Singaporeans who are based overseas consider returning to Singapore to develop their careers and contribute in bridging clinical research with healthcare delivery.”

About the Clinical Scientist Awards

6. Funded by the National Research Foundation and administered by the National Medical Research Council of MOH, the CSA is a part of the overall talent development programme under phase II of Singapore’s Biomedical Sciences (BMS) Initiative. Coupled with good research infrastructure and institutional support, this programme aims to provide the clinician scientists with a conducive environment for medically relevant research that will one day translate into better healthcare delivery for Singapore patients. A total of 21 CSAs have been awarded to date. More details can be found at the following link: https://www.nmrc.gov.sg/corp/fellowship.aspx?id=308.

Ministry of Health & A*STAR
22 June 2010

For media queries, please contact:
Joshua Woo
Corporate Communications
Ministry of Health
Tel: +65 9642 4567
Email: joshua_woo@moh.gov.sg

Wang Yunshi
Corporate Communications
Agency for Science, Technology and Research
Tel: +65 6826 6443
Email: wang_yunshi@a-star.edu.sg

Encl:

Annex A – List of CSA recipients
Annex B – Profiles of CSA recipients
About the Agency for Science, Technology and Research (A*STAR)

The Agency for Science, Technology and Research (A*STAR) is the lead agency for fostering world-class scientific research and talent for a vibrant knowledge-based and innovation-driven Singapore. A*STAR oversees 14 biomedical sciences, and physical sciences and engineering research institutes, and seven consortia & centres, which are located in Biopolis and Fusionopolis, as well as their immediate vicinity.

A*STAR supports Singapore's key economic clusters by providing intellectual, human and industrial capital to its partners in industry. It also supports extramural research in the universities, hospitals, research centres, and with other local and international partners.

For more information about A*STAR, please visit www.a-star.edu.sg.
### 2010 Clinician Scientist Awards recipients

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Area of Research</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Senior Investigators</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A/Prof Pierce Chow Kah Hoe</td>
<td>Singapore General Hospital</td>
<td>Liver Cancer</td>
</tr>
<tr>
<td>Dr Goh Boon Cher</td>
<td>National University Hospital</td>
<td>Oncology</td>
</tr>
<tr>
<td><strong>Investigators</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dr Carolyn Lam Su Ping</td>
<td>National University Hospital</td>
<td>Heart Failure</td>
</tr>
<tr>
<td>Dr Charles Chuah</td>
<td>Singapore General Hospital</td>
<td>Leukaemia Stem Cells</td>
</tr>
<tr>
<td>Dr Lawrence Lee Soon-U</td>
<td>National University Hospital</td>
<td>Infectious Diseases</td>
</tr>
<tr>
<td>Dr Mei Wang</td>
<td>Duke-NUS Graduate Medical School</td>
<td>Oncology</td>
</tr>
</tbody>
</table>
PROFILE OF WINNERS OF CLINICIAN SCIENTISTS AWARDS (CSA) 2010

Associate Professor Pierce Chow Kah Hoe (CSA-SI)

Senior Consultant
Department of General Surgery, Singapore General Hospital

Associate Professor
Duke-NUS Graduate Medical School

Area of Research: Liver Cancer

Project Title: Phase III Multi-Centre Open-Label Randomized Controlled Trial of Selective Internal Radiation Therapy versus Sorafenib in Locally Advanced Hepatocellular Carcinoma (AHCC protocol 06)

Primary liver cancer, also known as hepatocellular carcinoma (HCC) is an important cancer worldwide and this is especially so in the Asia Pacific region as 70 to 80% of all HCC are found here. It affects approximately 500 patients a year in Singapore. While surgery offers potential cure for HCC, at the time the disease is diagnosed, most patients have the cancer at a stage where surgery is not possible (inoperable).

There is currently only one systemic drug, sorafenib which has been proven to give inoperable patients better survival over no treatment. This drug is especially important when the patient has HCC that has already spread outside of the liver. However when the inoperable cancer is confined to the liver (locally advanced), another type of therapy called Selective Internal Radiation Therapy (SIRT) is also reported to confer good survival. Such patients with HCC confined to the liver form the majority of patients with advanced HCC. Although both sorafenib and SIRT are good therapies for HCC, it is currently unclear which is more beneficial to patients with locally advanced HCC.

A/Prof Chow and his team will embark on a phase III clinical trial to compare the outcomes of sorafenib with SIRT in patients with locally advanced disease (with no spread outside of the liver). This large clinical trial will involve 360 patients randomly divided into 2 equal groups to be treated with either SIRT or sorafenib, and will involve about 20 hospitals in the Asia-Pacific region. The team will be able to obtain definitive clinical data at the end of the trial to determine which of these 2 therapies is more beneficial to patients in terms of giving them better survival, tumour shrinkage and quality of life. The results of this clinical trial will potentially impact on the clinical management of HCC worldwide.

In conducting this multi-center trial, A/Prof Chow and his team will be leveraging on the experience and previous trials of the Asia-Pacific Hepatocellular Carcinoma (AHCC) Trials Group which was first established in Singapore in 1997. This trial will be the 6th and largest multi-center clinical trial conducted by the AHCC Trials Group.
**Dr Goh Boon Cher (CSA-SI)**

**Adjunct Associate Professor**
Department of Haematology-Oncology,
National University Cancer Institute, Singapore (NCIS)
National University Health System

**Area of research: Oncology**

**Project Title:** Translational pipeline - Developing novel therapeutics for cancer treatment, including the role of histone deacetylase inhibitors

Cancer is a top cause of mortality in Singapore. Despite significant advances in surgical and radiation technique, and implementation of chemotherapy regimens, a significant proportion of patients with cancer still develop metastatic disease and die of cancer. Currently the understanding of biochemical and biological events at the cell level leading to cancer is gathering at unprecedented pace, and there is a multitude of drugs that are in the developmental stage that can block crucial pathways and thus lead to cancer killing. Dr Goh’s research program is divided into two parts:

1. To conduct clinical trials to determine the action and effect of these novel drugs in cancers, with in-depth analysis of the effects on the molecular circuity of the cancer cell. Dr Goh and his team will be doing a study of a new drug called regorafenib, in patients with colorectal cancer.

2. To focus on development of a new class of cancer drugs (histone deacetylase inhibitors) that can act by uncoiling cellular DNA and allowing expression of genes that may kill the cancer cell, through detailed analysis of their effects on cancer causing pathways. The team will be looking at developing combinations of these agents with standard anticancer drugs, to enhance cell killing potency.

This research would have impact on the understanding of drug effects on cancer, and has obvious benefits to patients.

**Dr Carolyn Lam Su Ping (CSA-INV)**

**Assistant Professor**
Department of Medicine
NUS Yong Loo Lin School of Medicine

**Associate Consultant**
National University Heart Centre, Singapore
National University Health System

**Area of Research: Heart Failure**

**Project Title:** Singapore Heart Failure Outcomes and Phenotypes

Heart failure (HF) is a major global public health problem and is associated with poor quality of life, significant morbidity and high mortality despite contemporary treatment. In Singapore, age-adjusted HF hospitalization rates rose by almost 40% from 1991-98 and
accounted for more than 5300 admissions in 2000 alone, constituting the most common cardiac cause of hospitalization in Singapore. More than half of patients are dead within 5 years. Further, racial disparity in outcomes has been reported in Singapore, with Indians and Malays incurring a worse prognosis than ethnic Chinese. The reasons for these differences are unclear, underscoring the need for further research in this area.

Previous research efforts have focused on HF with reduced ejection fraction (HFREF or systolic HF), where the heart fails to ‘pump’ properly. Increasingly, doctors are realizing that HF can also occur when the heart still pumps adequately but fails to ‘relax’ properly – the syndrome called HF with preserved ejection fraction (HFPEF or diastolic HF). In fact, it is now recognized that HFPEF may be just as common, disabling and deadly as HFREF. This is particularly worrying since HFPEF predominantly affects the elderly and may therefore reach epidemic proportions in aging societies such as in Singapore. Also, unlike HFREF where proven therapies exist, doctors still have not found an effective therapy that improves outcomes for HFPEF. Intense research is on-going to better understand this disease syndrome before effective ways can be developed to prevent or cure it. Dr Lam has been actively engaged in these research efforts in the US and now hopes to address these important issues in Southeast Asian populations, in whom virtually no data currently exist.

As part of a research program coordinated by the National University Heart Center Singapore and involving 5 centers in Singapore (AH, CGH, SGH, TTSH and NUH) as well as 3-5 centers in New Zealand, Dr Lam and her team, hopes to address the following questions:

1) How common is HFPEF versus HFREF among Singaporeans and are there differences between ethnicities?
2) What are outcomes like for patients with HFPEF versus HFREF in Singapore?
3) What are the underlying mechanisms that may cause or worsen HF in Singaporeans?

In this large, prospective "Singapore Heart Failure Outcomes and Phenotypes" Study ("SHOP Study"), patients with HF will undergo clinical assessment, comprehensive bio-imaging, neurohormonal profiling and follow-up for all-cause mortality and rehospitalization at 2 years. A pilot clinical trial is also proposed to evaluate the safety and efficacy of a novel drug (ABC-NP) that was synthesized from naturally occurring cardiac hormones (natriuretic peptides) in the body and has shown promise as a potential treatment for HF in animal studies.

This research will provide important information regarding the epidemiology, pathophysiology and outcomes of HF in multiethnic Singapore, leading to greater understanding of the HF burden in Southeast Asians and identification of potential therapeutic targets.
Dr Charles Chuah (CSA-INV)

Senior Consultant
Department of Haematology, Singapore General Hospital
Assistant Professor
Program in Cancer and Stem Cell Biology, Duke-NUS Graduate Medical School

Area of Research: Leukaemia stem cells and chronic myeloid leukaemia

Project Title: Eliminating chronic myeloid leukaemia stem cells by targeting protein post-translational modification

The treatment of many leukaemias, such as chronic myeloid leukaemia (CML), has improved tremendously over the past few years since the introduction of targeted drug therapy. However these ‘magic bullets’ are not effective in eliminating leukaemia stem cells (LSC), which are known to be highly resistant to drug therapy. The failure to completely eradicate these LSC may lead to disease recurrence once treatment is discontinued.

There are many ongoing research efforts to discover methods to eradicate these LSC. One strategy is to combine drugs that are effective against different targets or pathways required for the survival of the LSC and this is the premise of our research. Dr Chuah and his team will investigate if the combination of both novel and existing targeted drug therapies is effective in killing LSC. This work will be done in collaboration with researchers from Duke-NUS Graduate Medical School and the Cancer Science Institute of Singapore.

The team hopes to translate the research findings into new treatment strategies for CML that can be moved to the clinics and that the knowledge gained can also be applied to other forms of leukaemias.

Dr Lawrence Lee Soon-U (CSA-INV)

Assistant Professor
Department of Medicine
NUS Yong Loo Lin School of Medicine
Academic Consultant
Department of Infectious Disease
National Healthcare Group

Area of Research: Infectious Diseases and Oncology

Project Title: Individualizing doses and predicting drug-drug interactions for anti-cancer and anti-HIV medications metabolized by UDP-glucuronosyltransferases

Correct selection of drug doses is critical for successful therapy. This is especially so when using toxic drugs which are used to treat cancer and human immunodeficiency virus (HIV) infection. Overdosage of such drugs can cause lethal toxicities, while underdosaging these drugs could cause failure or resistance to therapy and thus early demise.
The so-called phase 2 drug metabolism enzymes clear a number of key drugs such as irinotecan, a leading cancer chemotherapy drug used to treat colorectal and other cancers, and some anti-HIV drugs. More and more drugs will be cleared by these enzymes instead of (or in addition to) the more well-studied phase 1 enzymes. The activity of these phase 2 enzymes varies greatly between individuals. The same dose of these drugs may be too high and toxic for someone, yet be too low and ineffective in someone else. Differences in phase 2 enzyme activity transcend ethnicity, gender, weight and even genetics, making it difficult to predict using standard approaches. Therefore it is necessary to directly measure the activity of these enzymes in order to individualize therapy for patients on these drugs.

Dr Lee’s research programme focuses on comparing different methods to measure the activity of these phase 2 enzymes. He will concentrate on using the probe approach, which is giving non-toxic drugs which are cleared by phase 2 enzymes to patients, then measuring the levels of these “probe” drugs. The data produced will be used to predict the doses needed for the toxic chemotherapy and anti-HIV drugs. His team will also compare this approach with the more well-known genetics approach, whereby mutations which reduce or increase the activity of these enzymes will be detected and the genetic data will be used to adjust doses accordingly. In using such approaches, the team hopes to reduce toxicities due to overdoses of these drugs while maintaining optimal efficacy.

It is hoped that the knowledge generated from this work will optimize treatment for cancers, infectious diseases and other diseases treated by an increasing number of phase 2 enzyme-cleared drugs. Dr Lee’s vision is to personalize medicine in order to achieve the best outcomes for patients who are using such drugs.

Dr Mei Wang (CSA-INV)
Assistant Professor
Program in Cancer and Stem Cell Biology
Duke-NUS Graduate Medical School

Area of Research: Oncology

Project Title: Elucidation of the Roles of CAAX Proteins That Mediate the Antitumor Efficacy of Cysmethynil, a Novel Icmt Inhibitor

The most common way in which cancer develops is because cells have developed faults in particular genes that control normal cell growth. These faulty genes are called oncogenes, and the abnormalities result in their being activated at all times, instead of only when they are needed. One example of these oncogenes is known as Ras, and it is found activated in over half of all human cancers.

Scientists have been searching for many years for ways by which the functions of these oncogenes can be shut off, as doing this can stop the growth or induce death of these cancer cells. A route to do just this came from the discovery that the many cancer-causing proteins, including Ras proteins, are modified by attachment of a lipid chain termed a prenyl group, and that the cancer-causing effects of proteins could be eliminated by blocking this prenyl modification.
Dr Wang's team have recently discovered a new class of drugs that can block a specific step of the prenyl modification pathway, and are testing these experimental drugs on cancer cells in the laboratory. They found that blocking the prenylation process can cause cells to have tremendous increase in a self-digestive process called autophagy, which leads to cell death in cancer cells not only grown in the laboratory, but also in human tumours grown in mouse. Since many cancer cells are resistant to cell death, finding a new way to promote cancer cell death will be very meaningful in treating this challenging disease.

In this project, Dr Wang and her team are going to find out exactly how this new class of drugs regulates this important aspect of cell physiology. By doing so, they would be able to advance the understanding of autophagy and cancer cell death. Such crucial information is needed before clinical trials of experimental drugs can be initiated and the knowledge obtained will help in the development of this particular class of anti-cancer drugs.