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PRESS RELEASE

SG\$25 MILLION GRANT AWARDED TO MULTI-INSTITUTION RESEARCH TEAM WORKING TO IMPROVE LIVER CANCER OUTCOMES

- Primary liver cancer hepatocellular carcinoma (HCC) is usually diagnosed at a late stage and current therapies have limited efficacy because there are no validated biomarkers to guide individualised treatment.
- Singapore Ministry of Health's National Medical Research Council (NMRC) has awarded a SG\$25 million national grant to a multi-institution Singapore team for research which aims to change clinical practice and improve outcomes for HCC patients.



*From left: **Theme 4 PI A/Prof Edward Chow** (Scientist; Expert in development of complex system analytic to efficiently design drug combinations), **Theme 4 PI A/Prof Tam Wai Leong** (Associate Director of Precision Medicine and Population Genomics, Group Leader of the Lab of Translational Cancer Biology), **Prof Wang Hongjin** (Executive Director of IMCB), **Corresponding/Theme 1 PI Prof Pierce Chow** (NMRC Senior Clinician Scientist, senior consultant and surgical oncologist), **Theme 1 PI Prof Patrick Tan** (NMRC Senior Clinician Scientist and Executive Director of Genome Institute of Singapore and PRECISE), **Asst Prof Mihir Gandhi** (Duke-NUS Medical School), **Theme 3 PI A/Prof Toh Han Chong** (NMRC Clinician Scientist and deputy director of National Cancer Centre Singapore, senior consultant, and medical oncologist). (Image source: National Cancer Centre Singapore)*

Singapore, 13 June 2022 – A multidisciplinary team of clinician-scientists and researchers has been awarded a SG\$25 million grant to conduct clinical and translational studies and

cutting-edge patient-data analysis that will lead to improvements in clinical practice and better health outcomes for patients with the primary liver cancer, hepatocellular carcinoma (HCC). Led by the National Cancer Centre Singapore (NCCS) in collaboration with A*STAR's Genome Institute of Singapore (GIS) and Institute of Molecular and Cell Biology (IMCB), the Cancer Science Institute of Singapore, at the National University of Singapore, and Duke-NUS Medical School, the PLANet 2.0 (**P**recision **M**edicine in **L**iver **C**ancer across an **A**sia-**P**acific **N**etwork) research programme is supported by the National Research Foundation Singapore under its Open Fund-Large Collaborative Grant (OFLCG21JUN-0016) which is administered by the Singapore Ministry of Health's National Medical Research Council (NMRC).

Liver cancer is the sixth most common cancer in the world and fourth most common cause of cancer deaths globally.¹ In Singapore, it is the third most common cause of cancer deaths in males and fifth most common cause in females²; as HCC is usually diagnosed at a late stage, when prognosis is poor. In addition, current standard therapies for HCC, including systemic therapies, have poorer efficacy compared to systemic treatment for other common cancers. This is largely because there are currently no validated biomarkers to guide clinicians in the choice of the best therapy for an individual patient with HCC.

"PLANet 2.0 builds on the success of our earlier programme, PLANet 1.0, bringing together leading clinical and translational research experts across Singapore to address the urgent, unmet clinical need for more targeted and efficient treatment for liver cancer so that patients may have better outcomes," said Professor Pierce Chow, Principal Investigator of the study and Senior Consultant, Department of Hepato-Pancreato-Biliary and Transplant Surgery, Division of Surgery and Surgical Oncology, Singapore General Hospital and NCCS.

Laying the foundation for PLANet 2.0

The PLANet 2.0 research team first came together in 2016 for PLANet 1.0, a five-year multidisciplinary research programme to better understand the tumour biology and mechanisms of HCC. Detailed understanding of the landscape of HCC and robust predictive biomarkers is key to improving clinical outcomes in HCC. Current clinical practice and treatment recommendations for HCC are hindered by the absence of biomarkers that can guide therapy and therefore depend on the individual clinician's judgement, experience and preference.

While immunotherapy is currently the most effective systemic therapy for HCC, only a subset of patients responds to it, with 30% being the best overall response rate. PLANet 1.0 found that HCC's molecular landscape is extremely heterogeneous and shed light on novel mechanisms underpinning the disease, including how it reverts to foetal forms to escape the body's immunological defence, highlighting why HCC is difficult to treat.³

Conducting PLANet 2.0 in Singapore and the region

PLANet 2.0 will conduct two clinical studies that will serve as proof-of-concept for PLANet 1.0's translational findings and allow the team to uncover predictive biomarkers. In the first clinical study, a minimum of 30 patients with HCC who have undergone liver resection or surgery for the tumour will receive immunotherapy after surgery to reduce the chance of the tumour coming back. The second clinical study is a randomised controlled trial for patients with intermediate to advanced HCC ineligible for surgery. These surgically unresectable

¹ Singal, A. G., Lampertico, P. & Nahon, P. Epidemiology and surveillance for hepatocellular carcinoma: New trends. *J. Hepatol.* 72, 250–261 (2020)

² National Registry of Diseases Office. (2022, Jan). Singapore Cancer Registry Annual Report 2019.

³ Zhai, W. et al. Dynamic phenotypic heterogeneity and the evolution of multiple RNA subtypes in Hepatocellular Carcinoma: the PLANET study. *Natl. Sci. Rev.* (2021) doi:10.1093/nsr/nwab192

patients will be treated with Selective Internal Radiation Therapy (SIRT) with yttrium-90 followed by immunotherapy in a novel radiotherapy and immunotherapy combination. This study will enrol 176 patients. The two clinical studies will run concurrently and the recruitment and administration of the clinical studies will be in multiple sites in Singapore (Changi General Hospital, National Cancer Centre Singapore, National University Cancer Institute, Singapore, National University Hospital, Sengkang General Hospital, Singapore General Hospital and Tan Tock Seng Hospital) and 11 other hospitals in the Asia-Pacific region.

These studies leverage their longitudinal study designs to obtain before and after treatment patient samples and clinical data and aim to identify and validate biomarkers that correlate with clinical outcomes including response and resistance to therapy. The research teams will use a wide spectrum of investigations leveraging on their multidisciplinary expertise in the fields of epigenomics, genomics, immunomics, metabolomics, proteomics, data science and clinical care to better understand the landscape of the HCC tumour micro-environment and biomarker co-localisation. This convergence of approaches will enable robust validation of conclusions and inform the change needed in clinical practice to institute more efficacious and personalised treatment for HCC patients in the future.

Dr Tam Wai Leong, Associate Director and Group Leader of the Laboratory of Translational Cancer Biology at GIS, as well as Theme PI, said, “GIS is excited to be part of this multi-disciplinary and multi-institutional study aimed at improving clinical outcomes for liver cancer patients. The project will harness the power of genomic technologies to unlock the secrets of disease genes through deep profiling of consented clinical trial biosamples. The longitudinal tracking of tumours from the same patients will reveal critical genetic insights on why some cancer patients fare better than others, ultimately aiding in tailoring better treatment strategies for patients.”

Professor Vinay Tergaonkar, Research Director at IMCB and Theme PI, said, “Although the composition of various types of cells that constitute a tumour are well-studied in many cancers including HCC, this study would be one of the first ever, wherein changes in the physical co-localisation of various cell populations of the HCC microenvironment will be deciphered during the course of therapy. This information will be beneficial in guiding future therapeutic development.”

The Open Fund-Large Collaborative Grant (OF-LCG) Programme

The annual OF-LCG grant call supports the efforts of the best research teams in Singapore to conduct patient-centric translational research with the goal of advancing human health and wellness and creating economic value. Cancer is one of the seven areas identified as national priorities for research in Singapore.

About the National Cancer Centre of Singapore

The National Cancer Centre Singapore (NCCS) is a leading national and regional tertiary cancer centre with specialists who are experts in treating cancer. NCCS attends to the majority of cancer cases in Singapore’s public healthcare sector. In addition to offering holistic and multidisciplinary oncology care, our clinicians and scientists collaborate with local and international partners to conduct robust, cutting-edge clinical and translational research. To achieve the vision of being a global leading cancer centre, NCCS offers world class care and shares its depth of experience and expertise by training local and overseas medical professionals.

To meet growing needs, the new NCCS building will be completed in 2022 with increased capacity and expanded facilities dedicated to cancer care, rehabilitation, research and education. To give patients the best treatment outcomes, NCCS will offer access to advanced and innovative treatment such as proton therapy at the new Goh Cheng Liang Proton Therapy Centre.

For more information, please visit: www.nccs.com.sg

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

A*STAR is Singapore's lead public sector R&D agency. Through open innovation, we collaborate with our partners in both the public and private sectors to benefit the economy and society. As a Science and Technology Organisation, A*STAR bridges the gap between academia and industry. Our research creates economic growth and jobs for Singapore, and enhances lives by improving societal outcomes in healthcare, urban living, and sustainability. A*STAR plays a key role in nurturing scientific talent and leaders for the wider research community and industry. A*STAR's R&D activities span biomedical sciences to physical sciences and engineering, with research entities primarily located in Biopolis and Fusionopolis. For ongoing news, visit www.a-star.edu.sg.

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About A*STAR's Genome Institute of Singapore (GIS)

The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS pursues the integration of technology, genetics and biology towards academic, economic and societal impact, with a mission to "read, reveal and write DNA for a better Singapore and world".

Key research areas at the GIS include Precision Medicine & Population Genomics, Genome Informatics, Spatial & Single Cell Systems, Epigenetic & Epitranscriptomic Regulation, Genome Architecture & Design, and Sequencing Platforms. The genomics infrastructure at the GIS is also utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

For more information about GIS, please visit www.a-star.edu.sg/gis.

About A*STAR's Institute of Molecular and Cell Biology (IMCB)

The vision of Institute of Molecular and Cell Biology (IMCB) is to be a premier cell and molecular biology institute which addresses the mechanistic basis of human diseases and its mission is to conduct cutting-edge discovery research in disease pathways; to groom early career researchers to be future leaders in research; and to collaborate with the public sector, medical and industry communities for research impact. IMCB plays an important role training and recruiting scientific talents, and has contributed to the development of other research entities in Singapore. Its success in fostering a biomedical research culture in Singapore has

catalysed Singapore's transformation into an international hub for biomedical research, development and innovation.

Funded by A*STAR, IMCB's use-inspired research comprises 4 major programmes: Neurometabolism in Health and Diseases; Cancer Signalling and Therapies; Cell Biology and Therapies; and Innovative Technologies IMCB's technologies and platforms focus on Mouse Models of Diseases, Molecular Histopathology, Cellular Microscopy, and Proteomics & Metabolomics. For more information about IMCB, please visit www.a-star.edu.sg/imcb.

About the Cancer Science Institute of Singapore (CSI Singapore)

The Cancer Science Institute of Singapore (CSI) is one of only six Research Centres of Excellence established by the Government of Singapore with funding from the National Research Foundation and the Ministry of Education. Its mission is to better understand the causes of human cancer across Asia, and thereby improve its detection, treatment and prevention for the benefit of the patients. The CSI's outstanding researchers and excellent scientific facilities create an energetic environment for ground-breaking research and world-class training. The CSI is internationally recognized for its innovative research on the biology of cancers prevalent in Asia, and for taking new methods for cancer treatment from the laboratory to the clinic. Through its local and global partnerships, the CSI works with leading minds from multiple scientific and clinical disciplines in Singapore, the USA and Europe, both in academia and in industry.

For more information on CSI Singapore, visit <https://www.csi.nus.edu.sg/web/>

About Duke-NUS Medical School

Duke-NUS is Singapore's flagship graduate entry medical school, established in 2005 with a strategic, government-led partnership between two world-class institutions: Duke University School of Medicine and the National University of Singapore (NUS). Through an innovative curriculum, students at Duke-NUS are nurtured to become multi-faceted 'Clinicians Plus' poised to steer the healthcare and biomedical ecosystem in Singapore and beyond. A leader in ground-breaking research and translational innovation, Duke-NUS has gained international renown through its five signature research programmes and 10 centres. The enduring impact of its discoveries is amplified by its successful Academic Medicine partnership with Singapore Health Services (SingHealth), Singapore's largest healthcare group. This strategic alliance has spawned 15 Academic Clinical Programmes, which harness multi-disciplinary research and education to transform medicine and improve lives.

For more information, please visit www.duke-nus.edu.sg

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