MEDIA RELEASE
FOR IMMEDIATE RELEASE

16 MARCH 2017

DOCTORS A STEP CLOSER TO GIVING LIVER CANCER PATIENTS A MORE PRECISE TREATMENT

- *Outcome of a recently published study using a novel comprehensive approach offers doctors a better understanding of genomic diversity within liver cancers of individual patients and the possibility of precision therapy using currently available drugs*
- *Researchers leveraged on multi-region sampling and next-generation DNA sequencing technology to sequence large amounts of DNA*

SINGAPORE – Researchers have successfully characterised the genetic diversity of individual liver cancers in the first comprehensive study on intra-tumour heterogeneity in Hepatocellular carcinoma (HCC), the most common type of liver cancer. Few efficacious drugs are available to treat HCC, and the findings have provided doctors with fresh insights into potentially adopting more targeted and effective treatments and the promise of Precision Medicine.

Liver cancer is the second most common cause of cancer deaths worldwide[1], and HCC has one of the poorest survival rates among cancers. In addition, this disease type is most commonly found in Asia, where 80% of the world's cases occur.

This latest finding is from a collaborative study between A*STAR's Genome Institute of Singapore (GIS) and National Cancer Centre Singapore (NCCS), supported by the National Medical Research Council (NMRC) Translational and Clinical Research (TCR) flagship programme **P**recision Medicine in **L**iver Cancer across **A**sia-Pacific **Net**work, (PLANET). It was recently published in *Nature Communications*.

In a novel approach, researchers used next-generation DNA sequencing technology to study 66 liver tumour samples surgically resected from 9 patients, with multiple samples obtained from different parts of each tumour. They found a wide range of intra-tumoural genetic diversity in the samples across patients, which demonstrated how the cancer evolved from the original cancer cell into cancer cells with diverse genomic makeup. This explains why drug therapy for HCC is challenging. Comparing cancer that has recurred at another part of the liver after surgery, to that of the original tumour, they further found that the cancer cells giving rise to the recurrent cancer can arise from before or after genetic diversification of the original tumour. These recurrent tumours

[1] World Health Organization (2015) http://www.who.int/mediacentre/factsheets/fs297/en/

diversified more quickly than expected in the distant sites, into many different clones, suggesting that each patient with HCC needs to be treated differently.

“This work sheds light on the genomic profile and evolutionary trajectories of HCC. The deeper understanding of HCC gained from our study provides a solid foundation for future therapeutic strategies,” said co-lead author Dr Zhai Weiwei, Senior Research Scientist of Human Genetics at GIS.

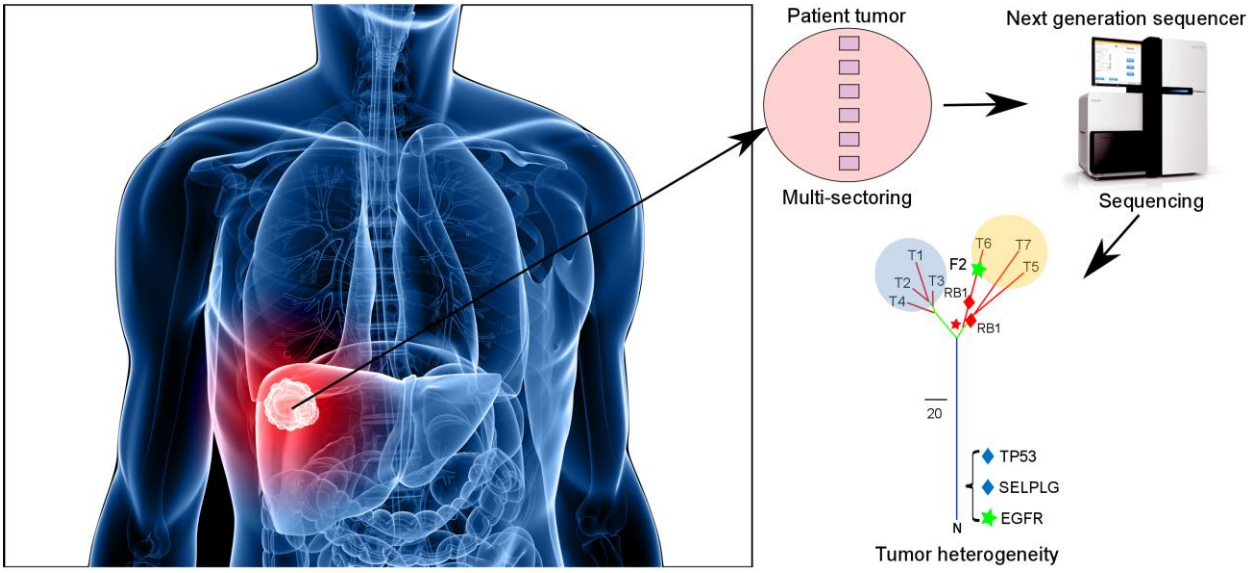
While there are scattered teams studying intra-tumour heterogeneity in HCC worldwide, they work on a smaller scale (often using single patients) and focus on only subsets of the HCC cohorts (e.g. HBV positive HCC). This Singapore study is the most comprehensive and detailed one to date. Following these significant results, the team has commenced a definitive prospective multi-centre study across diverse ethnic and etiological backgrounds across the Asia-Pacific, which will correlate both genomic and immunological heterogeneity with the clinical trajectory (behaviour) of the HCC.

Joint-lead author and GIS Human Genetics Group Leader Associate Prof Roger Foo added, “Our approach reveals that liver cancer may contain many more genetic mutations, targetable by drugs that are already available. Re-positioning of drugs offers the hope of immediate treatment, on top of ongoing strategies for new drug discovery. We hope to build on our study to devise ever more means of precision therapy for liver cancer.”

Prof Pierce Chow, the liver surgeon leading the NCCS team in this collaboration said, “Although early stage HCC can be well treated by surgical resection and transplantation, no subsequent adjuvant systemic therapy is currently available. Thus long-term outcomes even in early HCC are significantly poorer compared with other common cancers where good adjuvant systemic therapy is available after surgical resection. The data from this study and our prospective multi-centre study will potentially enable treatment to be individualised to the genomic and immunological make-up of each patient. This will help both early and late stage patients with HCC.” Prof Chow is also the lead PI for the NMRC TCR Flagship program in Liver Cancer and protocol chair of the PLANET study which has commenced and wil eventually involve 4 countries.

GIS Executive Director Prof Ng Huck Hui said, “Such collaborations are imperative in our quest to improve patient stratification and therapy. The greater synergy harnessed from our combined expertise and technologies will accelerate the development of targeted therapies for liver cancer, translating into benefits for the patients.”

IMAGE



*(Image source: National Cancer Centre Singapore and A*STAR's Genome Institute of Singapore)*

By sequencing cancer cells from different parts of the tumour, researchers can profile and understand the level of tumour heterogeneity across liver cancer patients.

Notes to Editor:

The research findings described in this media release can be found in the scientific journal *Nature Communications,* under the title, *"The spatial organization of intra-tumour heterogeneity and evolutionary trajectories of metastases in hepatocellular carcinoma"* by Weiwei Zhai[1,*,**], Tony Kiat-Hon Lim[2,*], Tong Zhang[1,*], Su-Ting Phang[3], Zenia Tiang[1], Peiyong Guan[1], Ming-Hwee Ng[1,4], Jia Qi Lim[1,4], Fei Yao[1], Zheng Li[1], Poh Yong Ng[1], Jie Yan[1], Brian K. Goh[5], Alexander Yaw-Fui Chung[5], Su-Pin Choo[6], Chiea Chuen Khor[1], Wendy Wei-Jia Soon[1], Ken Wing-Kin Sung[1,7], Roger Sik-Yin Foo[1,8,**] & Pierce Kah-Hoe Chow[3,5,9,**]

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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 will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

The key research areas at the GIS include Human Genetics, Infectious Diseases, Cancer Therapeutics and Stratified Oncology, Stem Cell and Regenerative Biology, Cancer Stem Cell Biology, Computational and Systems Biology, and Translational Research.

The genomics infrastructure at the GIS is 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.gis.a-star.edu.sg

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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 contributing to societal benefits such as improving outcomes in healthcare, urban living, and sustainability.

We play a key role in nurturing and developing a diversity of talent and leaders in our Agency and Research Institutes, the wider research community and industry. A*STAR oversees 18 biomedical sciences and physical sciences and engineering research entities primarily located in Biopolis and Fusionopolis.

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About National Cancer Centre Singapore
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