Researchers gain insights into the growth of liver cancer tumors and their genetic diversity

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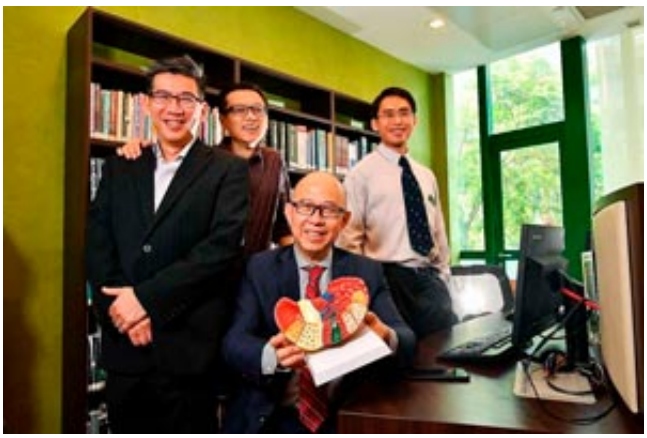

(Left to right): Roger Foo and Zhai Weiwei from the Genome Institute of Singapore, with Pierce Chow (seated), from the National Cancer Centre Singapore, and Wan Wei Keat from Singapore General Hospital. Credit: A*STAR Genome Institute of Singapore

Liver cancer tumors are genetically diverse and therefore difficult to treat, a Singaporean research team reports. The genetic differences found in each patient may one day enable personal, targeted therapies to treat the disease.

Hepatocellular carcinoma (HCC), the most common type of liver cancer, remains the second most common cause of cancer-related death

worldwide. This is partly because HCC tumors are often not discovered until they reach an advanced stage, and treatments for the disease are limited because scientists do not fully understand how the cancer evolves.

"One problem with developing effective cancer treatments is that tumors change and spread very rapidly and resistance to treatment evolves quickly; this is certainly the case for liver cancer," says Weiwei Zhai of the A*STAR Genome Institute of Singapore who led the research with Roger Foo, also of A*STAR, and Pierce Chow of the National Cancer Centre. "Determining the level of heterogeneity—or genetic diversity—within each tumor is key to understanding tumor evolution, disease progression and treatment response."

Zhai's team and colleagues used next-generation DNA sequencing technology to analyze 66 tumor samples from nine HCC patients whose cancers stemmed from different causes. The samples were taken from multiple sites within each tumor, and from different tumors within each liver—this differs from current HCC-diagnosis biopsies, which only take a single sample from one part of one tumor.

"We discovered that there is considerable genetic diversity both within and between tumors in a single individual," says Zhai. "The spatial growth pattern of the tumors was rather like the growth rings inside a tree trunk, suggesting HCC tumors grow by expanding outwards in a sequence. This is very different from what researchers have found in colorectal cancers, for instance. The next challenge is to consider how to target this spatial pattern in future treatments."

The high tumor heterogeneity helps explain why targeting HCC tumors with a single drug has had limited success. The team's next challenge is to unravel the natural history of tumor evolution and build a full picture of disease progression, from primary tumor surgery to patient relapse.

"We have received a NMRC Translation and Clinical Research grant to conduct the most comprehensive and methodical study of HCC to date," says Zhai. "Led by Pierre Chow, the project will be multidisciplinary with researchers from A*STAR, the National Cancer Center of Singapore, SingHealth Translational Immunology and Inflammation Centre, and the Cancer Science Institute of Singapore."

More information: Weiwei Zhai et al. The spatial organization of intra-tumour heterogeneity and evolutionary trajectories of metastases in hepatocellular carcinoma, *Nature Communications* (2017). DOI: 10.1038/ncomms14565

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