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Scientists identify rare cancer's genetic pathways

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An international research team, including four Simon Fraser University scientists, has identified the "mutational landscape" of intrahepatic cholangiocarcinoma (ICC), a rare, highly fatal form of liver cancer that disproportionately affects people in Asian countries.

SFU molecular biology and biochemistry professor Jack (Nansheng) Chen and three of his lab members collaborated with Chinese researchers to identify how these mutations affect genes and signalling pathways that might drive the formation of tumours in ICC.

The researchers' findings, published Dec. 15 in the journal *Nature Communications*, could potentially lead to earlier and more accurate diagnosis and increased survival rates for patients with the disease, also known as intrahepatic bile duct cancer.

ICC accounts for approximately 10 per cent of primary liver malignancies worldwide, but its incidence and mortality rates have been increasing rapidly in recent years. It currently strikes about one in 100,000 people annually in North America but 96 per 100,000 in Thailand.

The prognosis for ICC patients is usually poor, as early tumours are undetectable during routine examinations because the bile ducts are deep inside the body, leading to diagnosis only after symptoms develop and the disease has advanced. There are no effective therapies for ICC and the median survival duration is less than six to nine months after

diagnosis, according to a recent study in the *Canadian Journal of Gastroenterology*.

"Our research is by far the most comprehensive sequencing effort to identify mutations associated with ICC and will be an important resource for scientists working to improve understanding and therapy for the disease," says Chen, who specializes in genomics and bioinformatics.

His SFU collaborators included postdoctoral fellow Jiarui Li, doctoral graduate Christian Frech (currently a bioinformatician at the Children's Cancer Research Institute in Vienna, Austria), and M.Sc. student Xinyin Zhao.

The study is also the first and only large-scale effort to target ICC patients in China and the largest of all such projects worldwide. It revealed that Chinese ICC patients show substantial important differences in mutation profile when compared with patients from other countries, which could have important implications for Chinese Canadians with the disease.

Chen says the collaborative nature of this international research project represents a standard for the study of rare cancers in Canada. "Some cancer types, including ICC, are uncommon in Canada, which has a relatively small population but a large diversity of ethnic origins," he says.

"To get insight into the formation of tumors in these rare cancer types, we have to establish international collaborations like ours to gain access to large sample cohorts.

"Results from this study could help us understand the driver mutations in Chinese Canadians with intrahepatic bile duct cancer. And our work illustrates that this is a real opportunity and sets up a model for working

on rare disease conditions."

More information: "Clinical parameters predicting survival duration after hepatectomy for intrahepatic cholangiocarcinoma." *Can J Gastroenterol.* Nov 2011; 25(11): 603–608. www.ncbi.nlm.nih.gov/pmc/articles/PMC3222769/

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