

Scientists make breakthrough in study on bile duct cancer with discovery of new gene mutations

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(Medical Xpress) -- A combined team of scientists from Singapore and Thailand has made a significant breakthrough in understanding the cause of bile duct cancer, a deadly type of liver cancer. Using the latest genomic technologies, the researchers identified several new genes frequently mutated in bile duct cancers, paving the way for better understanding on how bile duct cancers develop.

The Singapore-Thailand team was led by Professor Teh Bin Tean, Associate Professor Patrick Tan, Associate Professor Steve Rozen (Duke-NUS Graduate Medical School of Singapore) and Professor Vajjarabhongsa Bhudhisawasdi from Thailand's Khon Kaen University. The breakthrough came after two years of intensive research, which saw scientists from Singapore visiting the villagers in northern Thailand, and Thai researchers coming to Singapore to work in NCCS laboratories. The discovery was published online on 6 May 2012 in *Nature Genetics*.

Bile Duct Cancer, or Cholangiocarcinoma, is a fatal cancer with poor prognosis. Accounting for 10 to 25 per cent of all primary liver cancers worldwide, bile duct cancer is a prevalent disease in Southeast Asia, particularly in the Northeast of Thailand which sees about 20,000 new cases each year. The high incidence in Thailand is attributed to long-term consumption of raw fish that is infected with liver flukes, which are food-borne parasites found in fish. Liver fluke infections are widespread in Northeast Thailand, where they are thought to occur in

over 6 million people. Once eaten, the flukes accumulate in the bile ducts of the human host, causing constant infection and the onset of cancer.

Professor Teh, who was a recipient of the Singapore Translational Research (STaR) Investigator Award in 2009 and the Director and Principal Investigator of the NCCS-VARI Translational Cancer Research Laboratory at the National Cancer Centre Singapore, said the study will pave the way for a better understanding of the roles that newly identified genes play in the development of bile duct cancer. "This discovery adds depth to what we currently know about bile duct cancer. More important is that we are now aware of new genes and their effects on [bile duct cancer](#) and we now need to further examine their biological aspects to determine how they bring about the onset of Cholangiocarcinoma."

Using state of the art DNA sequencing platforms, the researchers analysed eight bile duct cancers and normal tissues from Thai patients, and discovered mutations in 187 genes. The team then selected 15 genes that were frequently mutated for further analysis in an additional 46 cases. Many of these [genes](#), such as MLL3, ROBO2 and GNAS, have not been previously implicated in bile duct cancers.

"With this finding we now know much more about the molecular mechanisms of the disease and we can draw up additional measures that can be taken while we identify the most appropriate treatment protocols. We are talking about the potential to save many lives in Thailand," said Professor Vajjarabhongsa Bhudhisawasdi, Director of the Liver Fluke and Cholangiocarcinoma Research Center, Khon Kaen University of Thailand. "Also, this study shows that we can work closely with our counterparts in other countries and share our expertise and experience to improve the lot for the people."

The researchers also compared the bile duct cancers to other related cancers of the liver and pancreas. Surprisingly, they found that the bile ducts cancers shared certain similarities with pancreatic cancer. "This research provides a strong direction for future studies," said Associate Professor Patrick Tan, faculty member of the Cancer and Stem Cell Biology Programme at Duke-NUS. "Cholangiocarcinoma and Pancreatic Duct Adenocarcinoma appear to share more molecular similarities than earlier studies had indicated, and suggest that there are common biological pathways between the two cancers. By studying these pathways, we can then shed more light on how these tumours develop."

Dr Chutima Subimerb, a Thai scientist involved in the project, said she was pleased with the collaboration and to be able to participate in this health diplomacy project. "We are very privileged to be able to work alongside Prof Teh and the other scientists from [Singapore](#). By pooling our resources we were able to make this discovery which will have very wide impact on the people, especially the poor people who have been eating the fish that they catch from the ponds and rivers in the region. I believe this is only a first step and we will see even more collaborations in time to come between our two countries in the field of scientific research."

Provided by Duke-NUS Graduate Medical School Singapore

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