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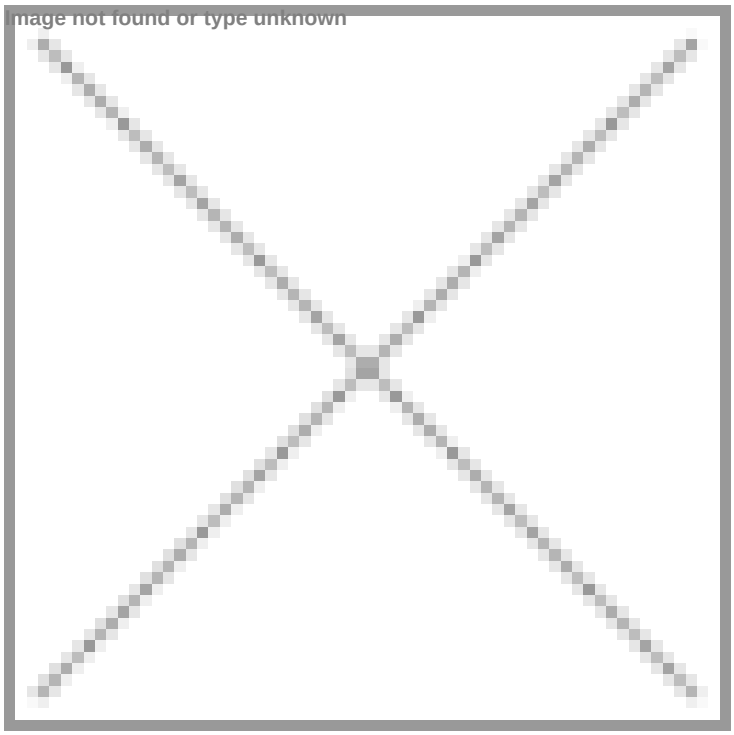

Singapore: Researchers at the Institute of Cellular and Organismic Biology (ICOB) in Taiwan, working with collaborators from Chang Gung Memorial Hospital, have developed a transgenic zebrafish model suitable for studying fibrosis and intrahepatic cholangiocarcinoma (ICC) associated with hepatitis B (HBV) and C (HCV) infection. The research was reported online in the journal Hepatology on June 23.

Intrahepatic cholangiocarcinoma (ICC) is the second most common liver cancer worldwide. It is an aggressive malignancy with poor prognosis. Liver cirrhosis, HBV and HCV infection are among the risk factors for the disease, but the mechanisms that mediate the initiation and development ICC and its association with HBV and HCV infection are largely unknown.

Recently, a research team, lead by Dr Jen-Leih Wu, distinguished research fellow at ICOB, developed a zebrafish model of ICC by dual expression of hepatitis B virus X and hepatitis C virus core protein in the liver. Animal models are routinely developed and used by scientists to gain a better understanding of human diseases and zebrafish make ideal models because their ability to produce pathological phenotypes comparable to those in humans. This is the first animal model developed to study the relationship between ICC, HCV and HBV, and it provided the first evidence that ICC can be induced by the co-expression of HBx and HCP. The biomarker networks of the model zebrafish ICC were found to be frequently involved in the development of the human cancer, and potential biomarker genes of zebrafish ICC were similar to those in the human bile duct cancer. Using the model, the researchers revealed that the cytokine TGF-beta1 plays an important role in

hepatitis B virus X and hepatitis C virus core protein-induced ICC development.

Dr Wu said, "Hepatocytes are the major site of HBV and HCV replication. However, the mechanism by which hepatitis B and C virus induces ICC is still unknown. HBV and HCV are causative agents of liver fibrosis, which is a predominant feature of bile duct disorder in the liver. In this study, we found that conditional dual expression of HBx and HCP in zebrafish liver leads to fibrosis and ICC formation, which demonstrate the potential of this zebrafish model to study HBV and HCV induced fibrosis and bile duct cancer. We hope that the model can be used in the future to enable more detailed study of ICC initiation, progression and to develop new therapies."