**Title: Capturing plasma host-virus chimeric DNA fragments to monitor Hepatitis B virus (HBV) related liver cancer development.**

Scientists from Center for Precision Medicine Research at Marshfield Clinic Research Institute, Beijing Institute of Genomics, Technische Universität München and Janssen China Research & Development Center, have reported tracing the host-virus chimeric DNA fragments in blood could help the individuals with HBV infection to monitor liver disease progression. These findings were published on Feb 25, 2020 in ***Hepatology International***, the official journal of the Asian Pacific Association for the Study of the Liver (APASL).

Over two billion people worldwide have Hepatitis B virus (HBV) infection, and they have significantly increased risk of hepatocellular carcinoma (HCC). HBV DNA can be integrated into the genome of infected human liver cells, which may interrupt functions of cellular genes around the integration sites and become dominant in tumor cell populations after clonal expansion, possibly conferring growth and survival advantages to the cells carrying the integrant. Therefore, a causal impact of HBV integration on tumorigenesis has always been asserted. DNA fragments derived from HBV-Human integration sites will be released to blood when human cells with HBV infection is died and then these specific DNA can be noticed in blood; however, the low abundance of them limit its usage. Direct sequencing the cfDNA without target enrichment required huge sequencing volume to identify these integrants in circulation. Researchers applied DNA capture assay to enrich integration fragments in plasma by and reduced the required sequencing volume. In evaluation of its potential for detection of liver cancer, they showed that the detected plasma integrants exclusively mirrored the counterparts in tumor tissues, but not in non-tumor issues of the same patient. In addition, deep RNA sequencing showed tumor-originated integrants in cfDNA were likely to have transcription activity in tumor cells. Thus, one would expect that less DNA is released from non-HCC liver tissue compared to liver tumor tissue.

Recently, HBV antigens produced by integration sites in liver cancer have attracted pioneering efforts to target these viral proteins as neoantigens in immune therapies for liver cancer. In this study, the researchers also provided a novel strategy to predict the viral integrants and to examine their protein-coding ability from short-reads sequencing data. It aids patient evaluation for this type of novel treatment and the efficacy assessment by monitoring the death of tumor cells carrying viral integrants. Dr. Shicheng Guo, Ph.D from Marshfield Clinic Research Institute and Dr. Dake Zhang, Ph.D., from Beihang University has common interest to translate genomic research to clinical application especially to focus on sequencing approaches in translational medicine aiding the diagnosis and treatment of gastrointestinal diseases.

This study was completed through a collaboration between Marshfield Clinic Research Institute, Chinese Academy of Sciences (CAS), Technische Universität München, Beijing You’an Hospital, Janssen China Research & Development Center Tsinghua University, and Peking Union Medical College.

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