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Project Title	Exploration of novel carcinogenesis processes by elucidating genomic signatures in Asian cancers
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Report

To leverage and extend current findings for discovering novel causes in Asia-frequent cancers by the international collaboration, we have collected somatic mutations and structural alterations by whole genome sequencing (WGS) of hepatobiliary cancers from different Asian regions and attempt to identify patterns of genetic alterations that are associated with characteristic epidemiological factors.

We have acquired cholangiocarcinoma frozen fresh tissues from Taiwan and identified one with a high signature 22 (AA signature) mutation load. We have analyzed the spatial transcriptomics pathways in the tumor with a high AA signature mutational load using VISIUM and found that 1) the AA signature mutational load of the tumor was heterogeneous and 2) the tumor immune microenvironment was modulated by the presence of cells with AA signature. We obtained 54 cases of four distinct types of oro-gastrointestinal tract cancer (OGITC) from Taiwan. Our analysis revealed that AA signatures in OGITCs are rare and unlikely to be a major contributing factor in the oro-gastrointestinal tract.

This international collaborative project has uncovered diversities of carcinogenesis processes in diverse ethnic populations based on somatic genetic traits. We combined the genetic data with epidemiological factors and identified unique and previously unknown associations of somatic alterations with environmental factors. These data will ultimately be a valuable resource for genome-guided precision cancer prevention in Japan and other Asian countries.