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**Education**

Ph.D., Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Tainan.
M.D., School of Medicine, National Cheng Kung University, Tainan.
Residency program: Resident, Department of Pathology, National Cheng Kung University Hospital, Tainan.
Visiting researcher: Department of Pathology, Mount Sinai Medical Center, New York, NY, USA.

**Research**

As a pathologist, I want to study pathogenesis and biomarkers for cancers, especially hepatocellular carcinoma (HCC). Ground glass hepatocytes (GGHs) harboring pre-S mutant have been shown to be associated with tumorigenesis of HCC. In my research, we found that GGHs in the background liver significantly correlated with de novo HCC recurrence, and type II GGH was one of the important predictors of the overall survival (A clustered ground-glass hepatocyte pattern represents a new prognostic marker for the recurrence of hepatocellular carcinoma after surgery. Cancer 117(13):2951-60). HBx was usually expressed in more scattered pattern and could co-localize with HBsAg. HBx and pre-S2 mutant coexpression showed an enhanced expression of vascular endothelial growth factor-A (VEGF-A), phosphorylated (p)-AKT1/2/3, p-extracellular signal-regulated kinase 1/2 (ERK1/2) and p-mammalian target of rapamycin (mTOR) signals, indicating a synergistic effect by HBx and pre-S2 mutant (Ground glass hepatocytes co-expressing hepatitis B virus X protein and surface antigens exhibit enhanced oncogenic effects and tumorigenesis. Human Pathology, 45(6):1294-301). We also tried to clarify the impacts of anti-HBV therapy on the liver pathology and the response of GGHs in the liver tissue. We found that although oral nucleos(t)ide analogues could effectively reduce viral replication, the GGHs were resistant to nucleos(t)ide analogue treatment (Resistance of Ground Glass Hepatocytes to Oral Antivirals in Chronic Hepatitis B Patients and Implication for the Development of Hepatocellular Carcinoma. Oncotarget 7(19): 27724-34). These findings could explain why there is residual risk of HCC incidence and de novo HCC recurrence in patients already receiving anti-viral treatment. Additional therapeutic agent is recommended to be combined in patients with high levels of serum pre-S mutants or intrahepatic GGHs. As for tumor biomarkers and pathology, I characterized the clinicopathologic and prognostic significance of combined hepatocellular-cholangiocarcinoma using the updated WHO classification (Histopathology. 2021 Oct;79(4):556-572). I evaluated the significance of serum hepatitis B virus large surface protein as high-risk recurrence biomarker for HCC after curative surgery (Int J Mol Sci. 2022). We also characterized integrated hepatitis B virus DNA harboring pre-S mutations in hepatocellular carcinoma patients with ground glass hepatocytes (Journal of medical virology 2024).