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Hepatocellular carcinoma research platform from patient-derived xenograft to organoid toward biobanking for precision medicine

Shin HWANG¹, Kyung Jin LEE², Yun-Gyu KIM², Gi-Won SONG¹, Eunyoung TAK³

Introduction: The basic/translational research platforms for hepatocellular carcinoma (HCC) include 2-dimensional culture, 3-dimensional spheroid, patient-derived xenograft (PDX) and organoid. Every platform has its own merit, but precision medicine should be based on the most appropriate study platform. We have established 50 mouse models of HCC PDX so far, but its maintenance was hurdled by high cost because each animal should be alive. To maintain the tumors cost-effective, we adopted organoid platform replacing PDX models.

Methods: This study includes two parts as interchangeability and preservability between the organoid and PDX and applicability of organoid platform for development of new anti-HCC agents.

Results: For interchangeability test, 5 sets of HCC PDX were harvested and treated to make organoid through the hanging drop and low-binding plate methods. All PDXs were successfully converted to organoid and the efficacy of two processing method was high enough. HCC organoid were cultured and inoculated into the nude mice, by which HCC PDX was formed again. For preservability test, HCC organoid were stored at -150 C in liquid nitrogen tank. After 1-month preservation and melting, all organoid sets were proven to be viable. Glypican antibody-bound crotamine immunotoxin was assessed in the HCC organoid platforms, in which cell viability of each tumor on immunotoxin treatment was very similar in both PDX cell line and organoid platforms.

Conclusions: This study confirmed the interchangeability and preservability of HCC organoid are high enough to be a research platform. Biobanking of HCC organoid will help to establish individualized patient-tailored treatment as an essential component of precision medicine.

Corresponding Author. : **Shin HWANG** (shwang@amc.seoul.kr)

¹Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Korea

²Department of Convergence Medicine, Asan Medical Center, University of Ulsan College of Medicine, Korea

³Asan Institute of Life Sciences, Asan Medical Center, University of Ulsan College of Medicine, Korea