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DRUG A TREATMENT PROLONGS THE LIFESPAN OF HUMAN CHEMICALLY DERIVED HEPATIC PROGENITORS

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Background : In our previous research, we developed human chemically derived hepatic progenitors (hCdHs) as an alternative to address the limitations of liver transplantation. However, hCdHs, which originate from human primary hepatocytes (hPHs), face challenges such as the loss of stem cell characteristics during prolonged culture, with variability among patients. To overcome these challenges, we identified a novel compound that enables the long-term culture of hCdHs while maintaining their stem cell properties.

Methods : hCdHs are generated by culturing hPHs in a reprogramming medium containing HGF, A83-01, and CHIR99021 for 8 to 12 days. Drug A-hCdHs are generated using the same process as hCdHs, with the addition of a medium containing Drug A.

Results : The generation of hCdHs and Drug A-hCdHs was confirmed by assessing the gene and protein expression of hepatic progenitor markers via RT-qPCR and immunofluorescence. It was confirmed that during long-term culture, Drug A-hCdHs exhibited a higher expression level of hepatic progenitor markers compared to hCdHs. We also confirmed the proliferation ability of Drug A-hCdHs through Western blot analysis using the PCNA marker. Additionally, it was confirmed that Drug A-hCdHs have the capability to differentiate into cholangiocytes as hepatic progenitors. Ultimately, we successfully generated organoids through 3D culture using Drug A-hCdHs.

Conclusions : We demonstrated that by treating hCdHs with Drug A, it is possible to culture them for an extended period while maintaining high stem cell potency. This is expected to have a significant impact on the development of personalized cell therapies and artificial tissues and organs.

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