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THERAPEUTIC POTENTIAL OF EXOSOMES FROM HUMAN CHEMICALLY DERIVED HEPATIC PROGENITOR CELLS (HCDHS) IN LIVER DAMAGE

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Background : Exosomes derived from stem cells are emerging as promising therapeutics for liver diseases. Human chemically derived hepatic progenitors (hCdHs), established in our previous study, differentiate into hepatocytes and cholangiocytes, offering remarkable regenerative potential, demonstrating regenerative capacity. This study evaluated the efficacy of hCdH-derived exosomes(hCdH-exos) compared to bone marrow mesenchymal stem cell-derived exosomes (BMMSC-exos) in mitigating liver damage.

Methods : Efficacy was evaluated through histological and biochemical analyses. Exosomes were isolated from hCdHs and BMMSCs using ultracentrifugation and characterized. In vitro, their ability to suppress hepatic stellate cell (HSC) activation induced by TGF-β1 was assessed. In vivo, exosomes were administered to carbon tetrachloride (CCl_4)-treated C57BL/6 mice, a widely used chemical model of liver damage, and to FRG -/- mice, which lack Fah, Rag2, and Il2rg genes, resulting in immune deficiency and liver damage.

Results : Exosomes from both cell types were successfully isolated using ultracentrifugation. The exosomes were characterized for size, concentration, and marker expression using Flow cytometry, Nano Tracking Analysis (NTA), and western blot. In vitro, hCdH-exo significantly reduced the levels of transcription factors and activation markers in induced HSC (hepatic stellate cells). In vivo, hCdH-exos effectively alleviated liver damage induced by CCl_4 in C57BL/6 mice. Similarly, in FRG -/- mice, hCdH-exos demonstrated comparable therapeutic effects, mitigating liver damage more effectively than BMMSC-exos.

Conclusions : hCdHs-exos demonstrated superior efficacy over BMMSC-exos in mitigating liver damage in both CCl_4 and FRG -/- models. These findings highlight the potential of hCdH-exos as a reliable therapeutic option across diverse liver injury models.

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