HGF/R-spondin1 rescues liver dysfunction through the induction of Lgr5+ liver stem cells

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The induction of endogenous adult stem cells by administering soluble molecules provides an advantageous approach for tissue damage repair, which could be a clinically applicable and cost-effective alternative to transplantation of embryonic or pluripotent stem cell-derived tissues for the treatment of acute organ failures. Here we show that HGF/Rspo1 induce liver stem cells to rescue liver dysfunction. Carbon tetrachloride treatment causes both fibrosis and Lgr5+ liver stem cell proliferation, whereas Lgr5 knockdown worsens fibrosis. The Injection of HGF in combination with Rspo1 increases the number Lgr5+ liver stem cells and improves liver function by attenuating fibrosis. We observed Lgr5+ liver stem cells in human liver fibrosis tissues, and once isolated these cells were able to form organoids, treatment with HGF/Rspo1 promoted their expansion. We suggest that Lgr5+ liver stem cells represent a valuable target for liver damage treatment and that HGF/Rspo1 can be used to promote liver stem cell expansion.