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LIVER STEM CELL GENERATION FOR THERAPEUTIC APPLICATIONS

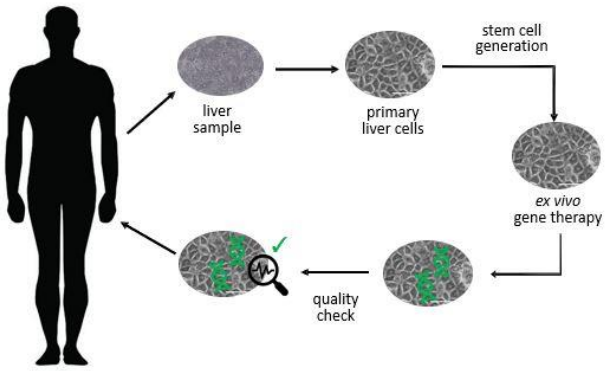
Keywords: liver stem cells, EGFL6, autologous, gene therapy, rare diseases

INVENTION NOVELTY

Researchers of Hannover Medical School (MHH) have developed a novel process for generating liver stem cells capable to differentiate into various liver cell types (hepatocytes, cholangiocytes, liver sinusoidal endothelial cells (LSEC)) *in vitro* and *in vivo*. Protocols based on the newly identified factor EGFL6 allow controlled dedifferentiation and cultivation of cells derived from patient liver samples for subsequent manipulation and therapeutic application.

VALUE PROPOSITION

The proprietary technology facilitates the generation of patient specific liver stem cells that can be kept in culture for a long period of time without the need for further immortalization. This allows safe and efficient *ex vivo* gene transfer for autologous therapy for hereditary liver diseases. Expression of therapeutic genes as well as potential tumorigenicity of manipulated cells can be thoroughly evaluated prior to transplantation of gene-corrected cells into the patient.



Liver stem cell generation and autologous gene therapy

TECHNOLOGY DESCRIPTION

Primary liver cells are isolated by collagenase treatment and mechanical shearing of liver tissue sample e.g., a patient biopsy. Primary liver cells subsequently are incubated in cell culture medium containing EGFL6, which results in the generation of liver stem cells. In the presence of EGFL6, liver stem cells can be passaged at least 30 times while proliferating and maintaining their stem cell characteristics. Liver stem cells generated by this process have been found to differentiate *in vivo* into hepatocytes, cholangiocytes, and LSEC in mouse models. After genetic manipulation and thorough evaluation of resulting cell clones, gene-corrected autologous liver cells can be reimplanted into patients for *in vivo* differentiation and restoration of patient liver function.

COMMERCIAL OPPORTUNITY

Licensing or developmental cooperation are possible.

DEVELOPMENT STATUS

Proof of concept has been demonstrated in mice.

PATENT SITUATION

European and US patent applications based on WO2021259814A1 with priority of 2020 are pending.

FURTHER READING

WO2021259814A1: Process for producing liver cells.

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