Macrophage-based cell therapy to treat acute liver injury

A novel cell-based therapeutic intervention to treat patients suffering from acute episodes of liver injury. When injected into patients showing acute or drug-induced liver injury, alternatively-activated macrophages could promote liver repair, by reducing cell death, stimulating hepatocyte proliferation and suppressing systemic inflammation.

Features

Targets the inflammatory stage of drug-induced liver injury
Induces liver repair
In vitro and in vivo stability in biological fluids
Quick delivery to the site of injury-within 4 hours of injection

Benefits

Benefits late-presenting patients
Potential to be beneficial to a range of inflammatory liver diseases
Flexibility in achieving the desirable phenotype
Wide therapeutic applications, including when the patient is progressively deteriorating

The Challenge

Drug-induced liver injury is the main cause of acute liver failure in western countries. Most cases of drug-induced liver injury are caused by acetaminophen (APAP) poisoning. The existing treatment is only effective if taken within 8-10 hours of APAP ingestion, and effectiveness is substantially diminished in late-presenting patients, resulting in acute liver failure and a need for liver transplantation. Due to the shortages of compatible organ donors and associated life-long immunosuppression required, there is a pressing need to develop novel therapies.

Technology

Naïve, bone-marrow derived macrophages can be polarised to an alternatively activated macrophage (AAM) phenotype in vitro and subsequent in vivo injection of these cells can promote liver regeneration in acute or drug-induced liver injury. These AAMs exhibit pro-reparative characteristics in vivo, including: promoting hepatocyte proliferation; clearing up necrotic debris; and reducing the systemic inflammation brought about by APAP poisoning. Researchers at the University of Edinburgh have shown improved functionality in the liver after AAM injections, which predicts this therapy could treat the later stages of acute liver injury and prevent acute liver failure, thereby negating the need for liver transplantation.

Exemplification Data

In vitro data showing naïve macrophages can be polarised to different phenotypes depending on the stimuli provided. Moreover, using a mouse model of APAP poisoning, it was shown polarised macrophages (but not naïve macrophages) rapidly engraft the liver and spleen in injured animals and significantly reduce necrosis (within 36 hours) and generate an 8-fold increase in hepatocyte proliferation.

Applications

- Cell therapy for acute episodes of inflammatory liver diseases