Transplanted genetically-modified adipose cells offer potential therapy for liver diseases

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Using mesenchymal stromal cells derived from adipose (fat) tissues, genetically modified to express a bioluminescent marker, researchers in Italy have tracked cells after transplantation. The cells were followed from their injection into the spleen of mice modeling liver disease, to their characterization as "hepatic precursors," and to their subsequent migration through the spleen before engrafting at regenerating sites in the liver by bioluminescent imaging.

Their study is described in a recent issue of Cell Transplantation. It adds to the developments in cell transplantation that have the potential to offer an alternative to liver transplantation for patients with liver disease. It also increases the validation of the therapeutic potential for cell transplantation with cells other than hepatic cells,

"Liver transplantation is the major therapeutic option for patients affected by liver disease," said study co-author Dr. Gabriele Toietta of the Ospedale Pediatrico Bambino Gesu in Rome, Italy. "However, scarcity of organs, high costs and lifelong immunosuppressive treatment make the potential for transplanting hepatic precursor cells an attractive alternative. In addition, hepatocytes obtained from organs are generally not suitable for transplantation."

Historically, the isolation and preservation of hepatic cells from non-living liver donors has been a limiting factor impacting on organ transplantation. The advantage of using adipose tissue derived stromal cells (AT-SCs) comes from the great availability of fat cells and the ease

of obtaining them. Also, the possibility of manipulating and transplanting autologous (self-donated) cells eliminates the need for lifelong immunosuppression treatments. However, in cases of genetically-caused liver disease, cells would have to be obtained from other donors than the patient (allogenic), and so would still require immunosuppressive therapy.

In this study, the researchers demonstrated that modified and transplanted AT-SCs were capable of migrating through the spleen, engrafting in the liver into regenerating sites, and persisting in the hepatic parenchyma for up to two months. In addition, the researchers were able to track the AT-SCs transplanted in their study.

"To our knowledge, this is the first use of bioluminescence imaging - which involves the detection of photons from cells expressing luciferase enzymes - to monitor an experimental approach of cell therapy using AT-SCs for liver disorders," said the researchers.

The researchers also discovered the activation of a "promoter" that suggested that the transplanted cells had a "commitment towards hepatogenic differentiation in vivo."

"Our data suggests engraftment and repopulation of injured livers by transplanted AT-SCs and we confirmed that AT-SCs differentiate towards hepatogenic-like characteristics both in vitro and in vivo," concluded the researchers. "In addition, we detected the activation of a promoter - normally silent in adult tissues - but can be re-activated during liver regeneration."

More information: Di Rocco, G.; Gentile, A.; Antonini, A.; Truffa, S.; Piaggio, G.; Capogrossi, M. C.; Toietta, G. Analysis of Biodistribution and Engraftment Into the Liver of Genetically Modified Mesenchymal Stromal Cells Derived From Adipose Tissue. Cell

Transplant. 21(9):1997-2008; 2012.