Cell transplantation of fetal stem/progenitor cells into the Mdr2 -/- mouse model

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Abstract

Background:
Liver transplantation is the only established therapy for end-stage liver disease. However, due to the limited availability of donor organs, cell transplantation has been suggested as an alternative. Though the majority of patients waiting for liver transplantation has severe fibrosis or cirrhosis, most preclinical settings for the evaluation of cell transplantation are based on non-fibrotic liver injury. In the present study, we analyze the regenerative capacity of fetal stem/progenitor cells by transplantation into a mouse model of progressive liver fibrosis (Mdr2 -/- mice) at early and late stages of liver fibrosis.

Methods:
Fetal liver stem/progenitor cells were isolated from wild-type Balb/c mice. Cells were injected intrasplenically into Mdr2 -/- mice of different ages (sixth weeks vs sixth months) after 1/3 partial hepatectomy. Mice were sacrificed at 2 and 4 months after cell transplantation and liver tissues were taken for total RNA isolation. Engraftment of transplanted fetal liver stem/progenitor cells was investigated by quantitative expression analysis of hepatocyte-specific Mdr2 using RT-PCR.

Results:
Six months old Mdr2 -/- mice reveal only faint (< 0.5%) or rather no Mdr2 expression at any time point after cell transplantation. However, Mdr2 -/- mice of a younger age display considerably higher expression levels of Mdr2 after cell transplantation, rising from maximal 1 % at 2 months after transplantation up to 4 % at 4 months after transplantation.

Conclusion:
Repopulation of Mdr2-/- mice with fetal stem/progenitor cells demonstrated to be successful with mice of a younger age, i.e. less fibrosis. In contrast, Mdr2 -/- mice at a late stage of progressive liver fibrosis seem to be unaffected by fetal liver stem/progenitor cell transplantation. This is possibly due to a lower engraftment efficiency, as the transplanted cells fail to traverse the endothelial barrier in mice with significant matrix.