

## Effects of Inflammatory Cytokine Tumor Necrosis Factor- $\alpha$ on Human Mesenchymal Stem Cell Gene Expression: A Mechanism for Liver Regeneration

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### Introduction

Insulin-like growth factor I (IGF-I) which is produced in abundance in the normal adult liver, is deeply involved in hepatocyte survival, growth, and differentiation during liver development. IGF-I plays the roles via the receptor (IGF-IR) signaling pathway. IGF-IR unlike IGF-I is expressed strongly in the developing liver, but much more weakly in adults. Objective: We hypothesized that inflammatory cytokines in liver injury may activate human liver progenitor cells to increase expression of IGF-1R, mediate IGF-1 and its cognate receptor-signaling pathways which contribute to liver regeneration.

### Methods:

To study this, bone marrow-derived mesenchymal stem cells (MSCs) were aspirated from human normal donor after obtaining informed consent. Cells were divided into nine experimental groups and stimulated with inflammatory cytokine tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ). Evaluation of differential expression of IGF-1R in TNF- $\alpha$ -treated human MSCs was done by real time polymerase chain reaction.

### Results:

The MSCs were CD11b (CR3), CD45, CD34, CD31 (PCAM-1), CD40, CD80 (B7-1), and HLA-class II negative because antigen expression was less than 5%, while they showed a high expression of CD90, and CD73. The differentiation of osteoblasts, is determined by deposition of a mineralized extracellular matrix in the culture plates that can be detected with Alizarin Red. Adipocytes are easily identified by their morphology and staining with Oil Red. The real time-PCR data reflected increased expression of IGF-1R in human MSCs upon TNF- $\alpha$  stimulation in a dose response manner.

### Conclusion:

We concluded that ex vivo TNF- $\alpha$  affects IGF-1R expression in human marrow-derived MSCs and might contribute to in vivo-stimulation of liver progenitor cell affected by local inflammatory cytokines due to IGF-1R expression and liver regeneration after injury. It can be a strategy to improve stem cell-effectiveness before in vivo-cell transplantation.

**Keywords:** Adult stem cells, Insulin-like growth factor-I, Gene expression, Liver regeneration.

### Poster Presentation

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