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Influence of adenoviral transduction with Adv5-optHGF-RFP on phenotype of hepatic stellate cells

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Hepatic stellate cells (HSC) play an important role in liver development and differentiation of progenitor cells into hepatocytes. This becomes possible due to creation of specific microenvironment, they produce extracellular matrix components and an amount of growth factors: fibroblast growth factor 4 (FGF4), stem cell growth factor (SCF) and the key factor - hepatocytes growth factor (HGF), responsible for cells migration, proliferation and differentiation into hepatocytes. There are various ways to deliver these factors into the cells and adenovirusis a promising gene delivery vector that has a high efficiency and relative ease of construction. These advantages make this system attractive for diverse research applications. In this project we performed transduction of hepatics stellate cells (HSC) with adenoviral vector containing hepatocytes growth factor (HGF) and red fluorescent protein (RFP) as a reporter (Adv5-optHGF-RFP), which let us to visualize the transduced cells. Further changes of phenotype were studied by real-time PCR and immunocytochemical staining 3, 7, 10, 14 and 21 days of cultivation. According to our results transduction of HSC with adenovirus is the simple and effective method of growth factor gene delivery, that was confirmed by stable RFP fluorescence and high expression of HGF (1200 times higher than in control HSC culture). Transduction of HSC with Adv5-optHGF-RFP lead to their activation and increase of desmin, α-SMA expression, didn`t change the morphology and proliferation of the cells (Ki-67 staining) and induced hepatogenic differentiation (appearance of α-FP). Interestingly, expression of HGF and α-SMA, expressions of desmin and α-FP had the similar dynamics, probably, they are interrelated. On the 21st day of the experiment all expression levels gradual return to normal meanings. Adenoviral transduction of HSC is applicable for short time stimulation of genes expression and probably can be used for the study of liver regeneration by transplantation of gene-modified cells.