The changes of the mitotic activity and the rate of polyploidization due to the inhibition of MEK/ERK signaling pathway in cholestatic liver

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Diversity of regulatory factors and signaling pathways of regeneration create significant obstacle in the study of refined molecular mechanisms of restoration in the various pathologies. It is known that percentages of cells with different ploidy are changed in liver parenchyma during cholestasis. Early we have showed, that the suppression of HGF signaling pathway by inhibition of c-MET-receptor, results the reduction of proliferative activity of parenchymal cells, but does not influence on polyploidization of cholestatic liver. Due to the fact, that the signaling pathway that triggered by HGF can be activated by MEKK1 (TNF and IL1) on the level of MEK, it can be thought that after the inhibition of c-Met receptor the activation of MEK by MEKK1 and the formation of polyploidy cells take place.

The aim of the work is to determine mitotic activity and changes of polyploidization rate of hepatocytes due to the inhibition of MEK/ERK signaling pathway in cholestatic liver.

Experimental animals: white rats (130-150g). Model of cholestatic liver: common bile duct ligation. MEK inhibitor (PD98059) was used for blocking HGF signaling pathway. Proliferative activity: colchicine mitotic index. Nuclear DNA content of hepatocytes, stained by Schiff reagent (Feulgen staining), was detected by using of computer software ImageJ 1.36b.

It was established that the inhibition of MEK signaling pathway causes alternation of hepatocytes ploidy. Cells with ploidy 4CX2, 8C is not revealed in liver parenchyma of experimental group. At the same time the mitotic activity of cells is increased.

From obtained results we can conclude that the origin of polyploid cells in cholestatic liver, is achieved by the activation of MER/ERK from various signaling pathways triggered by HGF.