

Liver Regeneration and TGF- β 1. Does Platelet Derived TGF- β 1 Play a Role in Initiating Liver Growth and Could TGF- β 1 Be Introduced as a New Therapeutic Tool?

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Master thesis in Medicine

The liver is the main organ of the abdomen and is involved in numerous vital metabolic and physiological functions. When the liver is injured or suffers a loss of tissue, it has the intriguing and most interesting capability to regenerate to its full size and function. To date, intense research has analyzed the hepatic regeneration process and has clarified several steps, however, factors that trigger the regeneration process are still largely unknown. Research data from rodent models and clinical human data indicate a correlation between platelet counts in the circulating blood and the liver regeneration capacity, suggesting their important role in this process. Studies performed at the Surgical Research Unit of the University of Fribourg suggest that the platelet-derived cytokine TGF- β 1 may trigger the liver regeneration process, through the subsequent induction of IL-6 secretion by liver endothelial cells. Detailed analysis of the role of platelets and their interactions with liver cells is still missing and remains unclear. The aim of my Master thesis was first, to expose the current knowledge of liver regeneration and summarize important studies which lead to the assumption of a potential role of platelets in this process. Furthermore, I will describe in detail the known role of TGF- β 1 in liver regeneration.

The second part of the thesis describes my participation in an ongoing research project of our group that evaluates the effect of TGF- β 1 on liver regeneration by using mice knock-out for TGF- β 1 expression in their platelets. I describe the different technical approaches which have been used to evaluate liver regeneration. The obtained results indicate that the absence of TGF- β 1 expression in platelets delays markedly the liver regeneration process, but does not completely block it. In conclusion, the research project indicates that platelet derived TGF- β 1 is very important as trigger of liver regeneration after injury. The discovery of factors initiating and inducing liver regeneration could bring considerable inputs to develop specific therapies for patients who suffer from acute liver failure as a result of a viral infection, trauma or surgery.

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