

Regulation of liver regeneration as assessed by means of molecular genetics

Liver regeneration is a noteworthy phenomenon of a vigorous tissue recovery following a wide variety of damaging events. Regenerative ability of the liver is unique among the mammalian visceral organs and plays its role in pathophysiology of heterogeneous hepatic diseases. The recovery process occurs in three phases of which the termination remains the least elucidated. Even the questions of regeneration termination timing and of completeness of organ build-up are still controversial despite decades of studies.

The aim of the present thesis was to analyse gene expression data pertinent to late phase of liver regeneration. We evaluated the course of spontaneous recovery in rats subjected to 2/3 partial hepatectomy. Because of lack of generally agreed parameter of hepatic regeneration completeness we proposed a proprietary indicator denoted as %LReg, based on organ and whole body weight assessments performed throughout the study. Gene expression analysis was first performed using DNA microarrays and consequently by real-time RT-PCR.

Whole genome scale transcriptional analysis yielded vast amount of data covering gene expression dynamics of fourteen post-surgery days after 2/3 partial hepatectomy in adult male rats. This intervention in rats is considered a gold standard of *in vivo* studies in the field of liver regeneration and has a long tradition at our department. Novelty of the present work laid in employing advanced molecular biology methods of analysis and computational bioinformatic approaches in data interpretation. We focused on the termination phase which is rather underrepresented in the literature with the aim to fill this gap. It might be concluded that according to our findings the late phase of regeneration process in the above mentioned model lasts from the fifth day on and that it seems to include active termination mechanisms. For the late days we reached good overall agreement among the DNA microarray and the real-time RT-PCR results.

Besides that our proprietary parameter %LReg indicated incomplete weight recovery even in our longest follow up interval. Final percentage of weight re-gain after fourteen days post-surgery was $83\pm 9\%$. The explanation might be in increased functional capacity of newly proliferated liver cells as compared to those resected in adults during hepatectomy.