

## Ingenuity<sup>®</sup> Science Spotlight:

Articles featured in the Ingenuity Science Spotlight represent some of the best and most diverse examples of how IPA<sup>®</sup> has contributed to research across multiple platforms, research areas, and research goals.



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### Identification of Transcriptional Networks during Liver Regeneration.

Peter White, John E. Brestelli, Klaus H. Kaestnert, and Linda E. Greenbaum. J Biological Chemistry. 2005. 280(5):3715-3722.

<http://www.ncbi.nlm.nih.gov/pubmed/15546871?dopt=Abstract>

The regenerative ability of the liver in humans and animals is well known, however little is known about the mechanisms that regulate the proliferation of hepatocytes. The partial hepatectomy model in rodents is an extensively used experimental model of hepatic growth in which partial removal of the liver induces normally quiescent hepatocytes and non-parenchymal liver cells to reenter the cell cycle and restore the liver in about two weeks. Using this model, researchers at the University of Pennsylvania Medical School identified differentially expressed genes from mouse liver cDNA samples taken at 0, 2, 16, and 40 hr post-hepatectomy (time points that correspond to the priming phase, hepatocyte mid-G1 phase, and peak of the hepatocyte S phase in the partial hepatectomy model).

To help understand their role in regulatory and signaling networks that control hepatic proliferation in vivo, the differentially expressed genes were uploaded to the IPA. Although Fos, JunB, JunD, and Myc were not detected by microarray analysis due to sensitivity limitations, IPA included these genes as likely members in a network that regulates early growth responses at the 2 hr time point. Subsequent quantitative PCR analysis confirmed that these genes were upregulated. This underscores the power of IPA when microarray analysis is limited by sensitivity or a gene of interest is not represented on an array. The network analysis also revealed an association between Myc and DUSP6 (MPK3), an inhibitor of extracellular signal-regulated kinase/mitogen-activated protein kinase signaling activity- a new finding for the partial hepatectomy model.

At the 16 hr time point, network analysis showed that the proteins encoded by the differentially expressed Myc targets are involved in cytokine signaling, matrix remodeling, and cell cycle progression. At the 40 hr time point, differentially expressed genes participate in regulatory networks involved in DNA replication, mitotic spindle assembly, and mitotic checkpoint control.