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Genome wide analysis of factors regulating gene expression in liver

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Short Abstract: We performed a genome-wide screen to identify genetic factors regulating gene expression in liver. We conclude that the existence of central factors in liver gene expression is unlikely and expression of individual genes in liver is more likely to be dependent on individual combinations of regulating factors for each gene.

Long Abstract:
In recent decades, multiple individual genes have been studied with respect to their level of expression in liver tissue and in many cases substantial progress has been made in identifying individual factors promoting gene expression in liver. However, the overall picture is still undefined and general rules or factors regulating gene expression in liver have not yet been established. Thus, a genome-wide screen for factors regulating gene expression in liver is of high interest, as it may reveal common regulatory mechanisms for most genes highly expressed in liver. These factors represent potential new targets in liver disease associated with differential gene expression. Using a novel bioinformatics approach, we have performed a genome-wide, bioinformatic screen to identify genetic factors regulating gene expression in liver. As the expression of an individual gene is generally driven by its promoter activity, we compared the level of expression to individual promoter sequences. Expression data of 15704 individual genes in 12 tissues were obtained from a normal tissue microarray dataset. The genes were subsequently divided into two groups, according to whether or not their highest expression level was found in liver tissue. Scanning 1000 bp upstream of the transcription start of each individual gene and using the PromoterScan algorithm, we were able to identify a total of 7042 promoters containing a total of 241,984 transcription factors. To eliminate the possibility that currently unknown transcription factors may be crucial to liver expression regulation, we investigated all possible nucleotide combinations of 8 bp and 10 bp which we reasoned may serve as novel binding sites for transcription factors. In both screens we did not detect any significant, biologically relevant differences in numbers of transcription factors and binding sites between the two groups. Furthermore, we excluded possible differences in distribution of TATA-boxes or CpG-islands as well as differences in nucleotide composition of RNA sequences or amino acid composition of transcribed protein sequences.
We conclude that the existence of central, superordinated regulatory factors in liver gene expression is unlikely and that expression of individual genes in liver is more likely to be dependent on individual combinations of regulating factors for each gene.