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In silico analysis of miRNA promoters

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MicroRNAs (miRNAs) are an abundant class of eukaryotic non-coding RNAs. They are involved in the negative post-transcriptional regulation of gene expression. Their inhibitory action is exerted by binding to the 3'-UTR region of nascent mRNA transcripts together with several other helper proteins, and in mammals it is observed mainly as an inhibition of protein synthesis. These non-protein coding RNA molecules are master molecular regulators that have been found to be involved in cellular processes ranging from differentiation, cell division, signal transduction and cancer. MicroRNAs expression appears to have a tissue specific signature in which specific miRNAs are expressed preferentially in some tissues or organs. It remains unclear which are the main factors that control this tissue-specificity, however several authors have postulated the existence of a regulatory feedback loops between transcription factors controlling miRNA expression and the regulatory control exerted by miRNA over the transcription factor expression.

Recently, the DNA sequences of 550 human miRNA promoters have been characterized by chromatin-immunoprecipitation. This work had the main objective of performing an *in silico* characterization of all these promoters, studying the possible transcription factors controlling miRNA expression. We looked for transcription factors that could regulate miRNA expression and being simultaneously the target protein-coding gene of that same miRNA.

The first step in the analysis of the transcription factor/microRNA regulation loops it was to predict the transcription factor binding sites (TFBS) for all sequences of miRNA promoters. Given the miRNAs promoters sequences, it was necessary to predict which TFs could bind to those promoters and regulate their transcription. For that we have used seven online available tools. The next step was the detecion of all putative-miRNA targets using six of currently available miRNA targets databases, and

Although cell's machinery is usually adapted to minimize energy consuming and thus being unlikely for a gene to regulate the expression of a miRNA and being simultaneously his target, we found 38773 potential loops, covering 285 distinct transcription factors and 417 distinct miRNAs. Next we computed a score for each predicted loop in order to guide experimental validations of predicted loops. All data was processed and stored in a relational database containing over than 2.5 million records. Furthermore, a web platform was developed in order to enable further investigations. This web interface allows the search for loops using several search criteria and also allows the analysis of all loops details such as predicted TFBS and targets, scores of each prediction, etc.