Short sequence motifs enriched in 5 upstream and UTR regions of human genes hyper- or hypo-expressed upon statin treatment in familial combined hyperlipidemia patients

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Motivation

Familial combined hyperlipidemia (FCHL) is the most frequent dislipidemic syndrome in our population (0.5 - 1 %), and therefore it has a very important social significance, being strictly associated to the insurgence of coronary artery diseases in affected patients. Statins are the elective drugs for treatment of this syndrome, but in some cases they elicit a strong inflammatory response that prevents any further use of the drugs, greatly increasing the patients risk of cardiovascular disease In a previous project we have carried out genome wide scanning DNA microarrays 'expression profiles', showing that that the expression of approx. 200 genes is significantly alterated (increased or reduced) in FCHL patients as compared to normal control individuals. Furthermore, we have observed that statin treatment restores the expression levels of most of the altered genes to normal values, but the same treatment causes other genes to became hyper or hypo-espressed. In order to understand whether groups of these genes are transcriptionally co-regulated via common cis-acting sequence elements, we decided to undertake the comparison of their transcriptional regulatory regions by searching the 5 upstream region for enriched short sequence motifs.

Methods

We have extracted the -400/-200, -200/+1 and +1/+200 (relative to the transcriptional start site) human genomic sequences corresponding to FHCL patients genes that are either up- or down-regulated by statin treatment, obtaining six dataset.

Each dataset has been searched with the MEME algorithm, setting the program to display up to 10 motifs, and using three different width windows (5-10, 6-15 or 10-20 nucleotides).

Results

We have identified some specifically enriched consensus sequences for each dataset.

By comparison with the Jaspar database, we have been able to identify some of them.For some of the still unidentified consensus sequences EMSA experiments with both lymphocites and liver cells nuclear extracts are in progress.

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