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Meeting abstract

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Identification of composite promoter modules in inflammation-regulated genes

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In the context of the collaborative research centre SFB566 entitled "cytokine receptors and cytokine-dependent signalling pathways as therapeutic target structures" we have performed more than 1100 DNA microarray experiments under highly standardized experimental conditions with respect to RNA isolation, cRNA synthesis, cRNA labelling, cRNA hybridization and raw data acquisition. The expression of 90 inflammatory genes including 6 housekeeping genes were assessed in a large variety of human cell systems and stored in our microarray database CytoBASE https://microarray.med.uni-giessen.de/base/index.phtml. A set of 102 experiments comprising 18 human cell types, 59 experimental groups and treatment with 36 different stimuli/inhibitors in 47 different combinations was analyzed by hierarchical clustering using MultiExperiment Viewer (MEV, version 4.1, http://www.tm4.org) and Significance Analysis of Microarrays (SAM, http://www-stat.Stanford.EDU/~tibs/SAM). As a result 20 consistently coregulated inflammatory genes with different biological functions such as cytokines and chemokines (IL-6, CCL2, CXCL3, CXCL8, CXCL10), proteases (MMP-1, MMP-15), metabolic enzymes (COX-2, MnSOD) and intracellular signalling molecules (BIRC2, IkBalpha, IRF1, JUNB) were identified. By genome-wide microarray analysis we also compiled a control set of 48 genes that were not regulated under eight different inflammatory conditions. We searched 1.1 to 2.1 kB of the promoter regions of these genes for enriched transcription factor binding sites using F-Match http://www.biobase.de. We further identified combinations of binding sites of enriched transcription factors that correlate with coregulation of inflammatory but not of control genes by using the composite module analysis tool http://www.biobase.de.

Several promoter modules containing 3 to 10 transcription factor binding sites within a promoter region of 200 bp were identified that distinguished the inducible 20 inflammatory from the 48 control genes. This information can be used in future experiments designed to reveal novel mechanisms of coregulation of different functional classes of inflammatory genes at the level of DNA.