Poster J-9

In silico motif search along with in vivo confirmation of NF-kB regulated gene sets in NPC microarray data.

Authors:
Yuching Lai (*Life Science Department, Chang Gung University*)
Greg Tyrelle (*Life Science Department, Chang Gung University*)
Kuang-Den Chen (*Life Science Department, Chang Gung University*)

Short Abstract: NF-kB has been implicated as a link between chronic inflammation and cancer. We use in silico promoter analysis of genes up-regulated in a NPC microarray study to determine NF-kB activated gene clusters. Results show significant clusters of up-regulated cytokines in NPC are activated by NF-kB.

Long Abstract:

A mechanistic understanding of disease requires the de-convolution of complex gene regulatory networks. In silico determination of transcription factor binding motifs in the upstream regions of genes with similar expression patterns may provide insight into these networks.

The pro-inflammatory transcription factor nuclear factor-kappaB (NF-kB) has been reported as a key factor in regulating the expression of cytokines and immune related genes. Furthermore, NF-kB has been implicated as a possible link between chronic inflammation and cancer.

Here we use in silico promoter analysis of genes up-regulated in an NPC microarray study to determine NF-kB activated gene clusters. Results show that statistically significant clusters of up-regulated cytokine genes in NPC cancer are activated by NF-kB.

To facilitate this work we have developed a pipeline for analyzing the regulatory motifs of functional gene clusters up-regulated in microarray experiments. The pipeline utilizes publicly available bioinformatics tools and databases such as ENSEMBL, JASPAR and the TAMO motif searching tool kit to determine whether a given transcription factor is significantly over-represented in a functional gene cluster.

Putative motif targets are further validated in genome-wide screening experiments by using immuno precipitation arrays. Multiple sequence alignment is then performed on binding sequences from positive signals to reconstruct an NPC specific NF-kB motif matrix.