

Promoter analysis of genes involved in T-helper cell fate decisions and lineage maintenance

Yü-Hien Lee¹, Ria Baumgrass², Manuely Benary¹, Hanspeter Herzel¹

¹Institute for Theoretical Biology, Humboldt University of Berlin, Invalidenstr. 43, 10115 Berlin, Germany

²German Rheumatism Research Centre, Chariteplatz 1, 10117 Berlin, Germany

Naive T-helper (Th) cells differentiate into distinct lineages including Th1, Th2, Th17 and regulatory T (Treg) cells. Each of these Th-lineages has specific functions in immune defense and T cell homeostasis. Th cell fate decisions and commitment is dependent on the kind and strength of T cell stimulation and the subsequent gene expression profiles.

Our analysis targeted the identification of new regulatory transcription factor binding sites (TFBSs) and complexes of TFBSs in the promoter regions of up- and down-regulated genes in Treg cell differentiation and lineage maintenance. For this approach we compared different composed gene groups from microarray analysis data with a background model of randomly selected genes to identify significantly overrepresented TFBSs and complexes of TFBSs. Results of our analysis contain AML1-NFAT and GATA3-Foxp3 as overrepresented complexes in Treg specific genes and Foxp3 dependent genes, respectively. Furthermore our data suggest that PU.1 has an inhibitory effect on genes essential for Treg cell induction.