Domain analysis of transcription factors Pu.1 and SpiC during Bcell development.

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PU.1 and Spi-C are both Ets transcription factors active during B cell development. PU.1 and Spi-C have homologous DNA binding domains, however their activation domains are divergent. PU.1 is critical for B cell and macrophage development from stem cells, and is expressed throughout B cell development. Spi-C is expressed selectively during B cell development and in mature macrophages, but its functions are still unclear. PU.1 and Spi-C can bind to identical DNA recognition sites in target genes, but have opposing biological activities. For the IgH gene, PU.1 acts as a repressor while Spi-C acts as an activator. For the Fc R IIb gene, PU.1 acts as an activator while Spi-C acts as a repressor. *We hypothesize* that differences in transcriptional regulatory activity between PU.1 and Spi-C are due to different N-terminal activation domains, with no difference arising from the conserved C-terminal domains. To test this hypothesis we constructed chimeras, swapping the N-terminal domain of PU.1 with that of Spi-C and vice versa. *We expect* that when expressed in pro-B cells, a chimeric protein with a Spi-C DNA-binding domain and a PU.1 activation domain will behave identically to PU.1 (increase Fc R IIb, decrease IgH). Conversely, we expect that a chimeric protein with a PU.1 DNA binding domain and a Spi-C activation domain will behave identically to Spi-C (decrease Fc R IIb, increase IgH). The results of these experiments are pending; these proteins will be expressed in pro B-cell 38B9 cell lines, along with luciferase reporters linked to transcription of the IgH intronic enhancer or Fc R IIb promoter.