

Genome-wide identification and characterization of Notch transcription complex-binding sequence-paired sites in leukemia cells

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Paired regulation in Notch signaling

The formation of Notch transcription complexes on DNA binding sites called sequence-paired sites (SPSs) adjusts transcriptional responses to Notch signals. However, SPSs are not easily identified by genomic sequencing. Severson *et al.* developed a method to identify SPSs throughout the genome. In leukemia cells, which often have Notch-activating mutations, SPSs were found in distal regulatory elements (enhancers) as well as proximal elements (promoters) in the chromatin associated with about one-third of Notch target genes. Some SPSs coordinated Notch-dependent coregulation of protein-coding genes and associated "enhancer" noncoding RNAs. The findings highlight the wide range of Notch response elements that exist and presumably "tune" physiologic responses to Notch in normal tissues and mediate pathophysiologic responses to Notch in disease.

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