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Structure watch

TEAMWORK IN TRANSCRIPTION

The transmembrane receptor Notch mediates intercellular communication. Following ligand binding, Notch is cleaved and its intracellular domain (ICD) translocates to the nucleus. There, the ICD forms a transcription-activation complex with the DNA-bound transcription factor CSL and the coactivator protein Mastermind (MAM). In *Cell*, two groups have now furthered our understanding of this complex through structural studies. Blacklow and colleagues present the structure of a human complex that contains the ankyrin domain (ANK) of Notch1, CSL, DNA and Mastermind-like-1 (MAML1). Wilson and Kovall describe the structure of a *Caenorhabditis elegans* complex that contains the Notch ICD, CSL, DNA and MAM.

Both studies found that CSL and ANK together create a binding groove for MAM/MAML1, which explains why CSL and this region of Notch are both needed for MAM/MAML1 binding. The structure derived by Wilson and Kovall also contains the RAM domain of Notch, and the papers together provide insights into the assembly of the transcription-activation complex. The Notch RAM domain seems to interact with CSL first. ANK then binds to another region of CSL to create the composite surface for MAM/MAML1 binding. The binding of RAM, or the synergistic interaction of RAM and ANK with CSL, seems to induce a conformational change in CSL that might convert it from a repressor to an activator of Notch target genes.

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MODIFICATION REMOVAL

Specific Ser and Thr residues in nucleocytoplasmic proteins can be modified by *O*-linked *N*-acetylglucosamine (*O*-GlcNAc), and this modification can regulate processes such as the cell cycle and transcription. Two papers now give insights into how this modification is removed by describing crystal structures of close homologues of the human glycoside hydrolase *O*-GlcNAcase.

In *The EMBO Journal*, van Aalten and colleagues describe structures of an *O*-GlcNAcase from *Clostridium perfringens*, whereas, in *Nature Structural & Molecular Biology*, Vocadlo, Davies and co-workers present structures of an *O*-GlcNAcase from *Bacteroides thetaiotaomicron*. Both groups determined the structures of the native protein and of these proteins in complex with mimics of reaction intermediates. They found that *O*-GlcNAcase uses a variant of the substrate-assisted catalytic mechanism (the key catalytic residues are a tandem Asp–Asp pair), and showed that these proteins are suitable models for further studies of the function of human *O*-GlcNAcase.

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