An atomic model of INF-β enhanceosome structure

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Interferon is required for the immediate early response against most human pathogens. The virus-dependent assembly of the interferon-β enhanceosome has served as a paradigm for understanding signal integration at higher eukaryotic enhancers. Transcriptional activation of the interferon-β gene requires assembly of an "enhanceosome" – a tightly regulated set of 8 polypeptide chains that associate on a ~60 bp enhancer. We have determined several protein:DNA co-crystal structures that together give a complete atomic view of the enhanceosome. The structure shows that association of the eight proteins on DNA creates a continuous surface for the recognition of the enhancer sequence. The transcription factor binding sites form one composite binding element and cooperativity arises mainly through nucleotide sequence dependent structural changes in the DNA that allow formation of complementary DNA conformations. Because the binding sites overlap on the enhancer, the unit of recognition is the entire nucleotide sequence, not the individual subsites. The absence of strong protein-protein interfaces indicates that there are little inherent constraints for combinatorial assembly and evolvability of this system. Overall, our structural analysis gives us for the first time detailed insights into the structure of an enhanceosome and yields important insight into design and architecture of such higher order signaling assemblies.