Structural Basis for the Diverse DNA Sequence Recognition by C/EBPβ Homodimer

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The CAAT-enhancer binding proteins (C/EBPs) are the bZIP family transcriptional regulatory factors, which play important roles during cell differentiation through regulating various gene expressions.

There are several kinds of the transcription factors belonging to the bZIP family such as c-Jun, Fos, CREB, etc, which recognize their specific DNA sequence as a homodimer or a heterodimer. In the case of a homodimer, the recognition sequences found in the native promoters are usually symmetric.

On the other hand, C/EBPs recognition sequences in the native promoters are mostly asymmetric even when C/EBPs, also belonging to the bZIP family, work as a homodimer, resulting in their much variety of target sequences.

To elucidate molecular mechanisms of C/EBPs for specific DNA recognition, we performed the structural analyses of several kinds of binary complexes composed of C/EBPβ, which is a member of C/EBPs, and various native promoter sequences or an artificial high affinity symmetric sequence, and the functional analyses such as a measurement of DNA binding affinity of C/EBPβ or its mutants designed from the structure using Surface Plasmon Resonance (SPR).

We could identify several conserved amino acids characteristic for C/EBPβ, which would play critical roles in its recognition of asymmetric DNA sequences.

Keywords: protein-DNA recognition, transcription factor, DNA-gprotein complexes