Poster Presentation

MS019.P07

Binding mode of C/EBPbeta and SMAD3 to the p15INK4b promoter

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The basic region:leucine zipper (bZIP) DNA-binding protein, C/EBP β is a key regulator of numerous cellular processes, but can also contribute to tumorigenesis and to viral diseases. It binds to specific DNA sites as homo- or hetero-dimer and interacts with other transcription factors to control the transcription of a number of eukaryotic genes. For example, C/EBP β serves as an essential cofactor for TGF β signaling in the case of Smad2/3/4—FoxO-dependent induction of the cyclin kinase inhibitor p15INK4b. Indeed, in the TGF β -responsive region of the p15INK4b promoter a Smad binding site is flanked by a C/EBP site. We solved the crystal structure of C/EBP β bZIP polypeptide bound to 21-mer p15INK4b promoter fragment containing both sites. Docking Smad3 MH1 domain (PDB ID 1MHD) into this DNA sequence indicates that C/EBP β and Smad3 can bind simultaneously to the p15INK4b promoter and that in this context their DNA-binding domains do not interact with each other. The interactions between C/EBP β and Smad3/4 MH2 domain remain to be determined.

Keywords: C/EBP transcription factors, Smads, DNA recognition