The TFIID subunit TAF4 directs promoter occupancy of HNF4A to induce post-natal hepatocyte gene expression

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Recognition of the core promoter element by the general transcription factor TFIID is the inaugural event in the transcription initiation. It binds multiple promoter elements and allows formation of pre-initiation complex and recruitment of RNAPII. TFIID comprises the TATA-box binding protein (TBP) and 13-14 TBP-associated factors (TAFs). Despite the extensive studies the functions of the TAF subunits of mammalian TFIID, particularly in complex physiological processes, remain poorly characterised.

Using liver-specific inactivation in mice, we show that the TAF4 subunit of TFIID is essential for post-natal hepatocyte gene expression leading to death of the knockout animals by P15. We show that TAF4 is not only required for pre-initiation complex (PIC) assembly and activation of post-natal expressed hepatocyte genes, but it also regulates embryonic expressed genes by modulating RNA polymerase II pausing/elongation. Our data indicate that TAF4 interacts directly with HNF4A, the key liver enriched transcription factor, and is necessary to maintain HNF4A-directed embryonic gene expression at post-natal stages. Moreover, TAF4 promotes HNF4A occupancy of functional cis-regulatory modules located adjacent to the transcription start sites of post-natal expressed genes. Local promoter-proximal HNF4A-TFIID interactions therefore act as instructive signals for post-natal hepatocyte differentiation.