Transcriptional control of the human collagen IV genes COL4A1 and COL4A2. Characterization of the new transcription factor CTCBF

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The two collagen IV genes COL4A1 and COL4A2 form a special transcription unit in which they are arranged head-to-head in opposite direction, separated by a short common promoter region. Within the promoter, binding of at least three different nuclear proteins could be detected, a CCAAT binding protein, Sp1 and a newly identified factor designated CTCBF. Mutagenesis of binding sites proved that these factors are important for the efficient transcription of both genes, but revealed differential gene-specific effects.

The new transcription factor CTCBF was purified by affinity chromatography on heparan agarose and CTC sepharose. CTCBF contains two subunits, CTC75 and CTC85, with molecular weights of 75 and 85 kDa, respectively. According to sequence analysis, the two subunits are identical, or closely homologous, to the p70 and p80 subunits of the human Ku antigen, originally identified as an autoantigen recognized by sera from patients with various autoimmune diseases. The specific binding of CTCBF represents a tetrameric complex of two CTC75/85 heterodimers. UV crosslink experiments proved that both subunits are involved in sequence specific interaction with the CTC box motif.

Addition of recombinant TATA binding protein (TBP) to the heterodimer CTC75/85 led to the tetrameric complex, whereas dissociation of the tetramer can be induced by depletion of TBP by adding TATA-box containing oligonucleotides. These experiments support the idea that the subunits CTC75 and CTC85 are integral parts of CTCBF and give first indication as to the importance of TBP for the formation of the sequence specific tetrameric complex.