Eukaryotic Transcription Factors
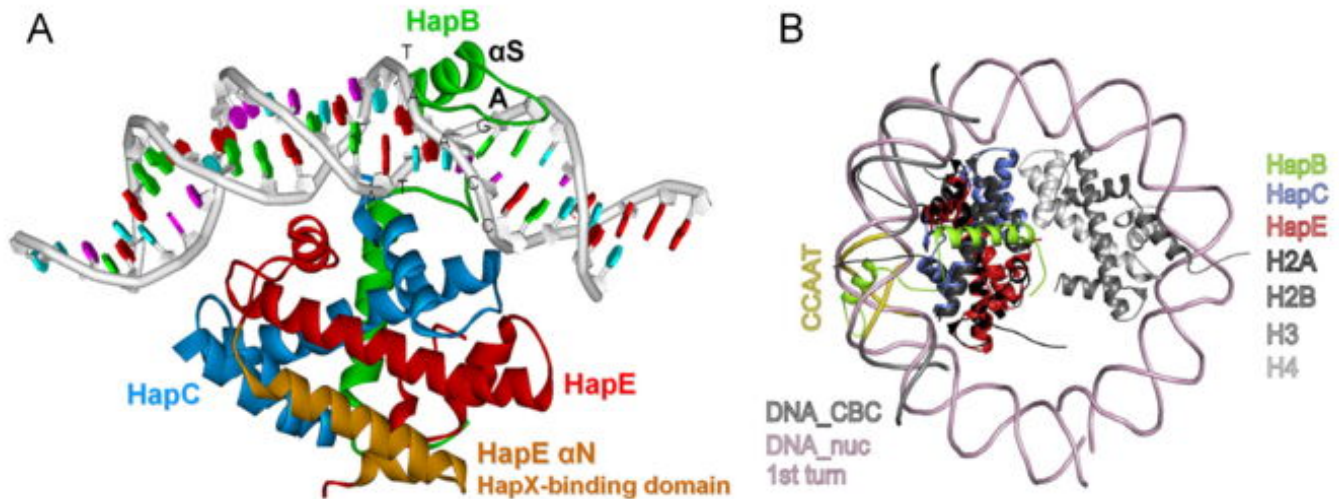

Structure of the CBC:DNA complex. (A) Ribbon plot of the CBC bound to the CCAAT box in the cycA promoter. (B) Structural superposition of the CBC and the first turn of the nucleosome.

Transcription factors play an important role in both infection biology and the regulation of natural product biosynthesis. Our aim is to elucidate molecular mechanisms of gene regulation in filamentous fungi by sequence-specific transcription factor complexes. To this end, we use protein biochemical methods, biosensor techniques and, in cooperation, structural analyses to investigate the assembly of transcription factor complexes and to learn to understand their structure-function relationship. Our work focuses on the CCAAT-binding complex (CBC). In *Aspergillus nidulans* and *A. fumigatus*, the CBC consists of the subunits HapB, HapC and HapE. A large number of genes are positively or negatively regulated by the CBC, including genes involved in the synthesis of natural products, the regulation of iron homeostasis and essential for the virulence of *A. fumigatus*. In collaboration with Michael Groll (TU Munich), the crystal structure of the CBC:DNA complex was solved.
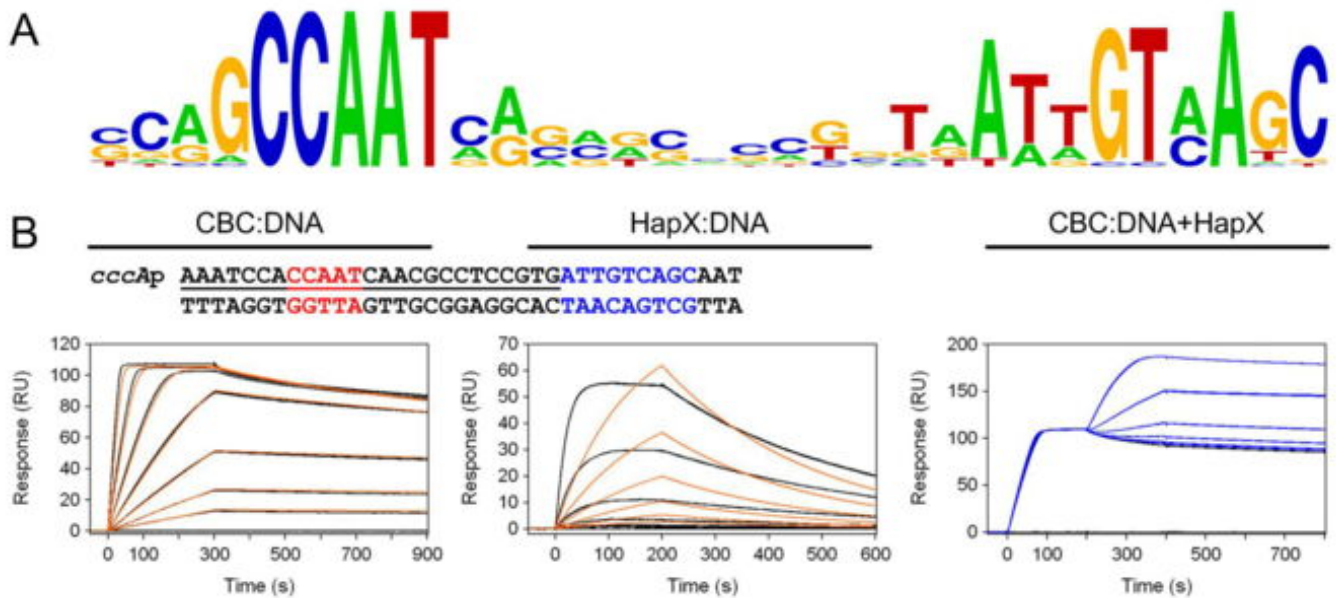
A) Bipartite DNA motif present in cccA promoters. (B) Surface Plasmon Resonance analysis of the CBC/DNA-HapX ternary complex.

The bZIP transcription factor HapX plays a central role in adaptation to iron deficiency and thus also for the virulence of *A. fumigatus*. HapX binds to CBC. In collaboration with Hubertus Haas (Medical University of Innsbruck), we were able to show that HapX is furthermore essential for the detoxification of iron by activating vacuolar iron storage. CBC and HapX bind cooperatively to an evolutionarily conserved DNA motif. HapX, as a Janus-type transcription factor, functions as both an activator and a repressor depending on the availability of iron.

In addition, possible protein chemical methods for the therapy of SARS-CoV2 infections are also being developed.