The fungal CCAAT-binding complex and HapX display highly variable but evolutionary conserved synergetic promoter-specific DNA recognition.

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Abstract

To sustain iron homeostasis, microorganisms have evolved fine-tuned mechanisms for uptake, storage and detoxification of the essential metal iron. In the human pathogen *Aspergillus fumigatus*, the fungal-specific bZIP-type transcription factor HapX coordinates adaption to both iron starvation and iron excess and is thereby crucial for virulence. Previous studies indicated that a HapX homodimer interacts with the CCAAT-binding complex (CBC) to cooperatively bind bipartite DNA motifs; however, the mode of HapX-DNA recognition had not been resolved. Here, combination of in vivo (genetics and ChIP-seq), in vitro (surface plasmon resonance) and phylogenetic analyses identified an astonishing plasticity of CBC:HapX:DNA interaction. DNA

motifs recognized by the CBC:HapX protein complex comprise a bipartite DNA binding site 5'-CSAATN12RWT-3' and an additional 5'-TKAN-3' motif positioned 11-23 bp downstream of the CCAAT motif, i.e. occasionally overlapping the 3'-end of the bipartite binding site. Phylogenetic comparison taking advantage of 20 resolved Aspergillus species genomes revealed that DNA recognition by the CBC:HapX complex shows promoter-specific cross-species conservation rather than regulon-specific conservation. Moreover, we show that CBC:HapX interaction is absolutely required for all known functions of HapX. The plasticity of the CBC:HapX:DNA interaction permits fine tuning of CBC:HapX binding specificities that could support adaptation of pathogens to their host niches.

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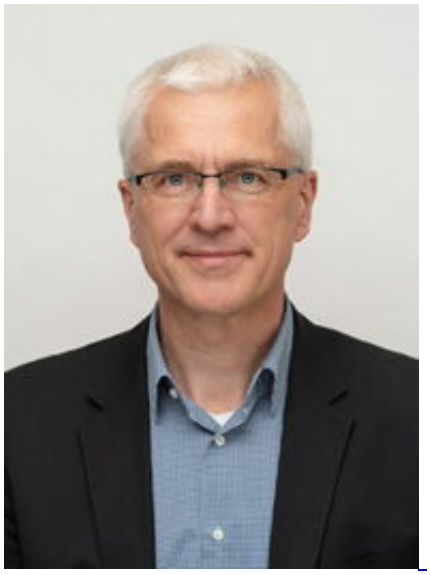

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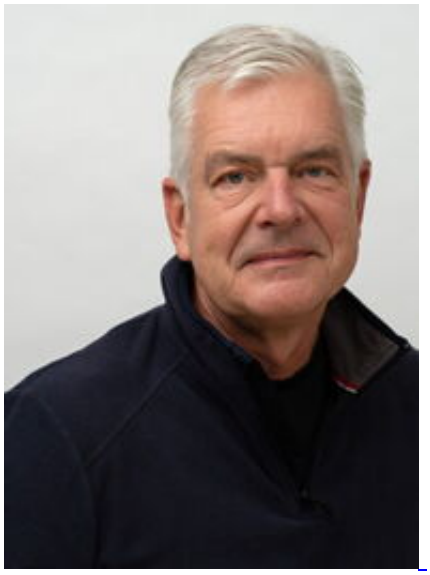

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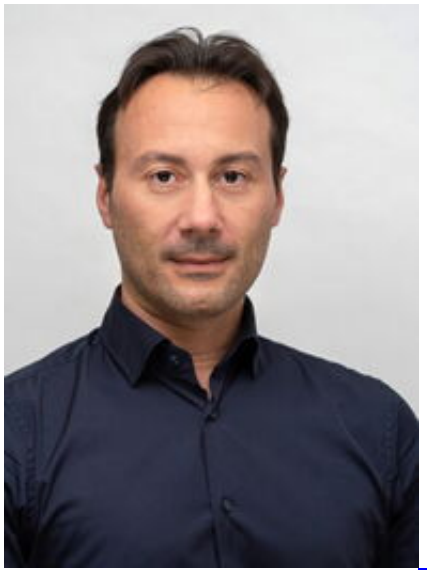

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