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A New Sterol Regulatory Element Binding Protein, SrbB Is Critical for Hypoxia Adaptation and Virulence in the Human Fungal Pathogen *Aspergillus fumigatus*

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Aspergillus fumigatus is a major cause of invasive aspergillosis (IA), a significant health issue worldwide with high mortality rates up to 95%. Our lab is interested in how *A. fumigatus* adapts to low oxygen conditions 'hypoxia', which is one of the important host microenvironments. *A. fumigatus* SrbA is a basic helix-loop-helix (bHLH) transcriptional regulator and belongs to sterol regulatory element binding protein (SREBP) family members. Loss of SrbA completely blocks growth in hypoxia and results in avirulence in murine models of IA suggesting an essential role of SrbA in hypoxia adaptation and virulence in *A. fumigatus*. We conducted chromatin immunoprecipitation sequencing (ChIP-seq) with *A. fumigatus* wild type using a SrbA specific antibody, and 97 genes were revealed as SrbA direct targets. One of the 'SrbA regulons' (AFUB_099590) was a putative bHLH transcriptional regulator whose sequence contained a characteristic tyrosine substitution in the basic portion of the bHLH domain of SREBPs. Therefore, we designated AFUB_099590 SrbB. Further characterization of SrbB demonstrated that SrbB is important for radial growth, biomass production, and biosynthesis of heme intermediates in hypoxia and virulence in *A. fumigatus*. A series of quantitative real time PCR showed that transcription of several SrbA regulons is coordinately regulated by two SREBPs, SrbA and SrbB in hypoxia. This suggests that SrbA and SrbB have both dependent and independent functions in regulation of genes responsible for hypoxia adaptation in *A. fumigatus*. Together, our data provide new insights into complicated roles of SREBPs in adaptation of host environments and virulence in pathogenic fungi.