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Structural and functional characterization of the *Aspergillus fumigatus* transacylase SidF.

Iron acquisition via chelation by siderophores plays a crucial role in the virulence of numerous bacterial and fungal pathogens. Therefore, the biosynthetic pathway for siderophores has great potential for improving the diagnosis and treatment of fungal infections. In this study, we characterized SidF, an essential enzyme of extracellular siderophore biosynthesis from *Aspergillus fumigatus*, the causative agent of deathly aspergillosis in immunocompromised patients, employing X-ray crystallography, SAXS, and enzymatic assays. We discovered that the structure of the N-terminal domain largely resembles that of the C-terminal domain of SidF. However, the GCN5-related N-acetyltransferase (GNAT) domain is found only in the C-terminal domain. SidF is a tetramer in crystal structure and in solution, as confirmed by SAXS analysis. Previous studies indicated that the transacylase function of SidF uses anhydromevalonyl-CoA as a donor and N5-hydroxy-L-ornithine as an acceptor to produce N5-anhydromevalonyl-N5-hydroxy-L-ornithine. We found that SidF can also accept acetyl-CoA as a donor and that the specificity for N5-hydroxy-L-ornithine may involve its hydroxylamine group. Our results provide insights into the SidF structure and suggest another potential SidF function in the siderophore biosynthesis pathway.

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