

Evolution of *Aspergillus fumigatus* in Cystic Fibrosis Lungs to Higher Virulence in a Hyperosmotic Environment

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Cystic fibrosis (CF) patients experience inhibited clearance of airways leading to a higher rate of colonization by opportunistic microbes. Approximately 60% of CF patients are infected by *Aspergillus fumigatus*, which leads to an increased rate of lung decline. The growing resistance of *A. fumigatus* to common azole antifungals establishes a need for new, targeted anti-fungal immunotherapies. This project aims to examine virulence in CF clinical isolates of *A. fumigatus* in order to provide insights to improve treatment for CF patients. *A. fumigatus* isolated from a single CF patient over four years was tested in vitro using a germination assay in either lung homogenate medium or a nutrient-rich medium supplemented 2M sorbitol to simulate the hyperosmotic environment of CF airways. The germination rates of CF isolates of *A. fumigatus* were significantly increased and, in some strains, rescued in hyperosmotic conditions. The CF lung environment encouraged adaptation that increased fungal germination to a level higher than non-CF *A. fumigatus* clinical isolates, indicating greater virulence. SSK1, a response regulator for the two-component HOG1 MAPK pathway, was not responsible for the heightened growth of *A. fumigatus* in high osmotic conditions despite its role in other clinical isolates. The aggression demonstrated by CF-adapted *A. fumigatus* supports a need for adjusting antifungal response in CF patients. Although SSK1 is not a viable option for targeted therapeutics against *A. fumigatus* infections, these results signify a unique and unknown adaptive response occurring within CF isolates that is imperative to decipher.