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.