Evaluation of Phosphatase Genes in Aspergillus fumigatus for Viability as Novel Therapeutic Targets, Year Two

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Aspergillus fumigatus is a ubiquitous mold that poses a great risk to many immunocompromised patients and is becoming increasingly resistant to currently used azole-antifungal medications. Phosphatase genes within A. fumigatus are responsible for regulating many important processes, including overall virulence. Prior research concluded with identifying gene PtcB as the most viable phosphatase gene for inhibition and testing two inhibitors in vitro - SKF-86002 and selective inhibitor SB-203580. SKF-86002 completely inhibited growth after 24-hours. Current research focused on learning more about the inhibitors binding to A. fumigatus on a molecular level, through bioinformatic research. Two proteins were chosen based on their similarity to PtcB and key p38 MAPK gene Afu4g10050. Both 2I0O and 6UI4 were chosen after BLASTp comparison for proteins in the RCSB Protein Databank to A. fumigatus, Saccharomyces cerevisiae, and Candida albicans. Proteins and ligands were modeled in PyMol and docked using Autodock Vina for information on their binding affinity and docking positions.The lowest binding energy was between protein 6UI4 and inhibitor SB-203580 at -10.3 kcal/mol. Inhibitor SKF-86002 and 6UI4 had -8.2 kcal/mol. The binding affinity results contradict in vitro observations from last year's research of SKF-86002 outperforming SB-203580, suggesting that inhibitor selectivity might play a larger role in in vitro inhibition than previously assumed. More work - both digitally and through in vitro methods - will have to be done to learn more about the effects selectivity has on the quantitative binding affinity and for the true structures of SKF-86002 and SB-203580 inhibition in A. fumigatus.