Developing a Novel Inhibitor for Cdc14 in the Fungus Aspergillus niger

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Fungal pathogens are a major cause of crop damage. In these fungi, Cdc14 could be a critical phosphatase for regulating cell division by ending the mitotic process, as demonstrated by studies in Saccharomyces cerevisiae. Due to Cdc14's absence in higher plants and noncritical role in animals, an inhibitor which can reduce its activity could function as a potential fungicide. In this project, I developed an inhibitor for Cdc14 in the fungal pathogen Aspergillus niger (AnCdc14), a pathogen that causes black mold on crops. After characterizing the catalytic specificity of AnCdc14, I designed multiple inhibitors that modeled the specificity. A combination of bioinformatic and biochemical approaches was used to determine the most effective inhibitor: one that contained four benzene rings and functioned through irreversible inhibition. Through computer modeling, I optimized this inhibitor to improve its affinity for AnCdc14. This modified inhibitor can be tested in vitro and in vivo for its efficiency in preventing A. niger growth and eliminating its pathogenicity. Due to high conservation of Cdc14 among fungi species, the inhibitor I created could be tested in multiple fungi, such as F. graminearum. Eventually, these results could be developed into a new antifungal compound that broadly prevents plant fungal infections.

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