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Project Title: Enzymatic Detoxification of Deoxynivalenol.

PROJECT 2 ABSTRACT

(1 Page Limit)

The most important mycotoxin in the U.S. is deoxynivalenol (DON), and it is estimated that the economic losses associated with DON alone exceed $650 million per year in the U.S. The overall goal of our project is to discover and employ enzymes to detoxify DON. The epoxide group on DON is responsible for its toxicity; it is required for the inhibition of protein synthesis. Though a number of enzymes may modify DON and reduce its toxicity (e.g., Tri101, UDP-glycosyltransferases, etc.), targeting the epoxide group is generally regarded as the most reasonable (feasible) strategy. We hypothesized that: (1) newly identified epoxide hydrolases and clycloisomerases can detoxify DON, (2) the phenomenon of enzyme promiscuity can be used and engineered to design new *de novo* biosynthetic pathways to remediate DON, and (3) yeast expressing DON detoxification enzymes can reduce DON in wheat and barley samples. The specific objectives of the proposed project are to (1) identify and engineer functional enzymes (epoxide hydrolases and cycloisomerases) to reduce the toxicity of DON and (2) engineer yeast to express DON-detoxification enzymes in wheat and barley samples. We propose to test enzymes from known sources for their ability to detoxify DON and identify novel enzymes to destroy DON using a new de novo pathway design algorithm. The proposed work directly addresses (1) the FY14-15 PBG priority (from the FY14 PD-RP) to 'develop new strategies for reducing impact of FHB disease and mycotoxin contamination in barley and wheat' and (2) the FY14-15 PBG research need (from the action plan) to 'identify enzymes to detoxify DON'. Recent work by PI Schmale and colleagues highlighted the potential of transgenic yeast to detoxify DON. Co-PI Senger has developed a de novo biosynthetic pathway development program (called "SyPath") to identify new enzyme candidates for the biodegradation of DON. The SyPath approach is coupled to molecular modeling techniques (including molecular docking and dynamics simulations), and will be used to identify and engineer new enzymes to degrade DON based on the structural characteristics and functional groups present in the DON molecule. This technique will not only provide a new strategy for minimizing DON toxicity, but it can be applied universally, giving scientists and engineers a unique platform to design enzymes capable of degrading any biocontaminant. This proposal represents a new (currently unfunded) collaboration, and Co-PI Senger has not received previous support from the USWBSI.