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PMSF and SFN Reduce Alpha-synuclein Aggregation in a Yeast Model of Parkinson’s Disease

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ABSTRACT
Parkinson’s Disease, PD, is the second most common neurodegenerative disease in humans. PD is marked by Lewy body formation in the brain, which disturbs the dopamine transfer system across neurons. Previous studies have shown that the protein, α-Synuclein, is a major contributor in the formation of Lewy bodies. In this study, we modeled α-Synuclein aggregation in the Budding Yeast, Saccharomyces cerevisiae and treated the cells with Phenylmethylsulfonyl fluoride (PMSF) in one trial, and Sulforaphane (SFN) in another. Our goal was to see how PMSF and SFN might affect aggregation, while also monitoring the health of the yeast. Our Preliminary data has suggested that a 4mM concentration of PMSF and 200μg/ml of SFN significantly reduces protein aggregation. Our lab will continue to investigate the role of PMSF and SFN in the prevention and breakdown of α-Synuclein aggregates.

INTRODUCTION
The protein α-Synuclein is found in the neurons of mammalian cells. Although not fully understood, it has been hypothesized that α-Synuclein plays a role in membrane binding and the monitoring of neurotransmitter concentrations. Using yeast as a model organism has shown to be an affective way of observing these human proteins because of its ability to mimic the aggregation and cytotoxicity of α-Synuclein in human pathology. After imaging cells that were overexpressing α-Synuclein, drug therapies were introduced to see how they might affect protein aggregation. Phenylmethylsulfonyl fluoride (PMSF) and Sulforaphane (SFN) have shown the ability to alleviate protein aggregation.

FIGURE 1: Parkinson’s Disease has been linked to alpha-synuclein aggregation in Lewy Bodies

FIGURE 2: Overexpression of Human α-synuclein in Yeast Triggers Aggregation

FIGURE 3: PMSF and Sulforaphane (SFN) Reduce α-synuclein Aggregation in Yeast

CONCLUSIONS
• α-Synuclein aggregates and is toxic in budding yeast.
• PMSF and SFN appear to alleviate protein aggregation.

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