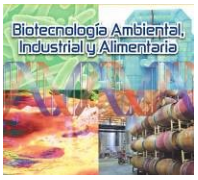
*Talk*




# Generation of new tools to fight/counteract protein aggregation.

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*Keywords:* aggregation; neurodegenerative; proteotoxic

## ABSTRACT

**Cells need to eliminate unfolded, damaged, or aged protein in order to maintain protein homeostasis, a mechanism known as proteostasis. Whereas molecular chaperones contribute to proteostasis by promoting correct protein folding, the proteasome, and autophagy are the main proteolytic machinery for the selective elimination of these proteins.[1] Mutation in components of these systems or stress situations that overwhelm these proteostasis mechanisms results in the accumulation of damaging protein aggregates that in humans cause neurodegenerative diseases. Furthermore, during aging, there is an overall decrease in the activity of these proteins' clearance machinery which generates a state of chronic proteostasis stress that eventually leads to cell death.[2]**

**In this project, we aim to build different genetic tools to assay proteolytic activities in S. pombe cells and determine the relative level of protein aggregation. These tools will allow us to characterize in more detail both, the stress-induced protein aggregations and the activity and relative level of aggregation in different proteasome mutants. In addition, using different molecular biology techniques, we will develop genetic tools to induce proteotoxicity through the expression of human proteins prone to aggregation, and hallmarks of neurodegenerative diseases.**

**Finally, it is known that molecular chaperones prevent protein aggregation by interacting and blocking aggregation-prone domains. In this context, using both, a mutant of the proteasome which accumulates protein aggregates and mimics an aged cell, and some of the tools generated.., we will screen compounds that function as chemical chaperones and decrease proteotoxicity. These chemical chaperones might help to develop new treatments for neurodegenerative diseases and aging.[3]**

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