ABSTRACT FOR THE GENERAL PUBLIC (*Specify the objective of the project, describe the research to be carried out in the project and give reasons for attempting this particular research topic.)*

Aging is the main risk factor for prevalent diseases in developed countries. With progressing aging of human societies, diseases including cancer, cardiovascular and neurodegenerative diseases will become an increasing burden for society. In many cases, lack of basic understanding of cellular processes that lead to the development of the disease impedes the progress of identifying novel and necessary treatments to sustain health during aging. The negative impact of damaged proteins on the progression of neurodegenerative diseases is widely discussed in the field of aging. The cell constantly produces new proteins that need to gain a certain shape in order to fulfil its biological function. Maturation of proteins often requires specialized machinery, called chaperones that assist this process. However, erroneous proteins or cellular stress that results into damaged proteins challenges the chaperone machinery and in extreme cases, such as during the process of aging, exceeds its capacity to assist protein maturation. In such circumstances, proteins tend to gain an inaccurate shape and subsequently aggregate. Protein aggregates inhibit normal cellular processes, thus are toxic for the cell, and sequentially compromise the health of the entire organism.

Cells developed sophisticated mechanisms to prevent progressive wrong folding of proteins. Many stressors, both extracellular and intracellular, which cells encounter, result in the decrease of bulk protein production. This has the advantage of decreasing the load of newly produced proteins that need to be taken care of by the chaperone machinery and at the same time can make these chaperones available to attend to the increasing amount of misfolded proteins in the cell. However, little is known what chaperones can switch their function during cellular stress, what kind of cellular proteins they attend too and what mechanism these chaperones utilize to help removing damaged proteins from the cell. Our research suggests that the prefoldin chaperone is a candidate to accomplish additional function upon cellular stress conditions. It moderates aggregation of proteins that are implicated in Parkinson’s and Huntington disease in cellular models and in model organisms. On the other hand, increased amounts of prefoldin chaperone were found in cancer indicating its important role in cellular stress conditions. We found that loss of prefoldin decreases normal lifespan of yeast, which complements very recent observation that prefoldin in the small soil nematode *C. elegans*, is necessary for lifespan extending mechanisms. The proposed project will identify the function of prefoldin upon cellular stress conditions, what kind of cellular proteins the prefoldin chaperone engages with and helps to detoxify in order to maintain a balanced environment in the cell that leads to restoring of cellular function and organismal health. Investigating fundamental processes activated to manage cellular stress will ultimately result in the development of new interventions to sustain health in humans in the future.