

## **How to increase longevity one cell at a time**

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Grant Application - Lay Summary

Humans are living longer than ever before, but it is often with age-related illnesses. Almost 100 years of research indicates that aging and age-related disease can be delayed, for example through caloric restrictions. While a great deal has been learned about why and how we age at the cellular and whole-body level, much remains unknown. Over time aging impairs the cell's ability to respond to environmental stimuli, and it is this impairment that likely leads to cell death and eventual organ malfunction.

Because the aging process is similar in yeast and humans at the cellular level, we use brewing yeast as a model to discover molecular networks that can be tweaked in order to increase a cell's response to its environment, resulting in enhanced cell health and longevity. We have discovered a protein complex in yeast that links extracellular stimuli with intracellular signaling. When this complex is inactive the cell does not respond appropriately to external stimuli and shows signs of aging, but when it is active, the cell responds appropriately to external stimuli and shows signs of youth, but when it is active, the cell responds appropriately and cell health and lifespan are improved. We will use small peptides that we have identified that activate this complex to glean insight into molecular mechanisms that increase lifespan.

We will also test if aging can be reversed in a novel yeast model of a human premature aging disease called Progeria. Progeria causes children to age normally, but at an 8-fold accelerated rate. We will also use the Progeria model to discover novel conserved pathways that reverse the effects of aging. Our team, composed of researchers with broad expertise in aging at the molecular, cellular and organismal levels, will identify ways to improve health during aging, such that the quality of life humans live will benefit.