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Research Proposal Reflection

In Qin’s research proposal he brings up the question of aging and tests the various hypothesis of cellular aging in *Saccharomyces cerevisiae.* In his proposal he hypothesized that cellular aging is an emerged property of gene/protein networks at the cellular level. This hypothesis makes the prediction that the rate of cellular aging should be proportional to the robustness of the gene/ protein network. Qin proposed both computational and experimental tests of his hypothesis.

In Thomas B.L. Kirkwood’s “Systems biology of aging and longevity” he describes the effects on the ageing process are mediated via coordinate influences on a very large number of proximate mechanisms, most of which control components of the organism's network of maintenance and reproductive functions. In Qin’s proposal he measured both the replicative and chronological life span of yeast. Other aging research involves the study of telomeres, whose reduction in length with age and cell division may underlie cellular senescence.

Some well-known genes that can influence the life span of yeasts are SIR2, TOR1, and SCH9. SIR2 is argued to have a toxic effect on life span because of an accumulation of extrachromosomal rDNA circles. TOR1 affects replicative life span by either decreasing ribosome function and translation or the hyper-activation of cellular functions. Both SIR2 and TOR promote genomic stability during aging. Qin also predicted new genes that can be associated with aging such as AKR1, ARP1, EFT1, PAC10, SAC6, EFT1 and TIF1. Some of these genes are discussed in Sean P. Curran’s paper, “Lifespan Regulation by Evolutionarily Conserved Genes Essential for Viability.

Robustness can be defined as insensitivity to stochastic fluctuations, mutations, and environmental changes. In Qin’s proposal he defines robustness as the ability of cells to maintain homeostasis despite stochastic fluctuations, environmental changes, or polymorphic and mutation changes. He finds that small phenotypic variances in deletion mutants suggest robustness plays a large role for duplicated genes. Robustness can be estimated using robust statistics.

In Qin’s proposal he quantifies the aging process based on a two-parameter Gompertz model. The Gompertz function is a mathematical model for a time series, where growth is slowest at the start and end of a time period. Using two equations, he was able to calculate the average life span in *Saccharomyces cerevisiae.* He defined the rates of aging as the Gompertz coefficients (G). He expects that the Gompertz coefficients will have an association to Hsp90, a phenotypic capacitor that can buffer mutations in its substrate proteins, or TOR inhibitors, or oxidative stress. It is also expected that smaller G values and a slower dying-off phase will occur when the cells age in the presence of Hsp90 inhibitors.

He expects that his research will lead to new experiments that tests new finding from computational analysis as well as new computational analysis and modeling based on experimental findings.