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Molecular Genomics and Bioinformatics

Reflection of Qin’s Proposal

The hypothesis of Qins paper is that cellular aging occurs as a product of interacting gene/protein networks. Furthermore this study aims to determine if the complexity or robustness of a gene network is associated with its effects on life span. In essence, this would answer the question of whether the complexity of a gene networks is associated with the lifespan or longevity of a cell or organism. It also aims to determine if there are similarities between lifespan influencing genes and phenotypic capacitors. In addition, the investigator aims to determine if decreased network complexity will slow down the rate of aging.

To accomplish aim one, the investigator will use regression to analyze ~ 500 gene which are known to affect life span and determine the variables affecting aging. Aim two will be accomplished by performing a tolerance test using Hsp90 and TOR inhibitors and oxidative stress in yeast isolates. Tolerance to the Hsp90 and TOR inhibitors and oxidative stress indicate the ability of the cell maintain homeostasis which is a measure of robustness.

This study uses a yeast model which is considered to be well studied and allows ease in measuring replicative and chronological life span. In addition, it contains genes that are important to regulation of aging such as SIR2, TOR1, and SCH9. Although it is speculated that there are no true “aging genes”, it is possible that aging is an emergent property of gene networks and specific aspects of aging cannot be attributed to any given gene. The findings of other studies have suggesting that this is the case.

Studies have shown that aging genes that participate in networks are more enriched. Other studies have shown that the regulation of life span is dependent on interconnected hubs. One scientist even argued that the behavior of proteins associated with aging may help to identify new ones.

According to the reliability model of aging, redundancy of a system correlates with aging and the overlapping of gene roles cause functional compensation which lead to insensitivity to noises, which is essentially robustness. Robustness is proportional to the rate of cellular aging. It can be measured using proxies such as variance of morphological changes, the expression levels of variants, the growth rates of deletion mutants, and competitive growth fitness. It can be achieved by buffering or gene duplication. Furthermore, gene duplication is not the only factor that contributes to robustness.

In order to quantify the aging process, the Gompertz Model was used. This model uses the initial mortality rate, time, and the Gompertz coefficient to determine the average life span. However, the Gompertz model can be modified to include a component that is independent of time. Such factors may include environmental factors, nutrients, radiation, and toxic influences. Other models may also be used to measure aging. However, large numbers are required to distinguish between the various models.

Based on its hypothesis, this study is expected that the variables that serve as measures of robustness are associated with characteristics of cellular aging. In addition, computational strategies will be implemented to find associations between characteristic of cellular aging other factors.