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Homework 4

The purpose of this study was to identify the genes that regulate the aging process. *Saccharomyces cerevisiae* was chosen to study because they are orthologus to humans, have short and simple life spans, have a known genome, have easy genetic material to manipulate, and has established methods of study. The main findings of the study were that long lived (LL) and short lived (SL) genes have similar dynamic expression (?), LL and SL genes display different time course gene expression, LL and SL genes have a common set of transcription factors mediating them, LL genes have higher epigenetic modifications, and that the time course expression of methylase, demethylases and Sir complex. Long lived and short lived genes were determined to have similar dynamic expression. This was shown by using the Kaeberlein dataset for replicative lifespan analysis of 564 genes. The dataset shows the 564 gene deletion strains compared to the wild type. The data was broken down into three groups; long lived (lifespan greater than 36 generations), short lived (lifespan less than 20 generations), and middle lived (there was no difference in their lifespan or the average lifespan was 26 generations). The strains from the three groups were then put through high throughput studies to analyze and compare them with each other. The parameters were; mRNA abundance, mRNA half life, Ribosome occupancy, Protein Abundance, Protein half life, and Noise. The data showed that LL and SL genes occur in the same concentrations at the protein level based on the similar mRNA abundance and ribosome occupancy, LL and SL genes do not have any differences in stability, that LL and SL genes are equally expressed on the protein and transcript levels. The data from the Kaeberlin dataset was also compared with an extended data set that measured unique protein-protein interactions based on Krogan data. The Krogan data and Kaeberlin did not show any differences. LL and SL genes showed differences in time course gene expression. Since the LL and SL genes do not have any expression at the mid log phase, it was necessary to measure the amount of gene expression when the cell transitions from the log to stationary phase. The data was analyzed using data from Gasch *et al.* The expressions of the LL and SL genes were plotted at 2, 10 and 24 hours respectively. The gene expression of LL genes greatly decreased with time. The expression of SL genes decreased slightly over time. LL and SL genes have a common set of transcription factors mediating them. This was determined by looking at all of the Transcription Factors (TFs) for SL and LL genes, and determining if there was any overlap between the two groups. This was done by looking at the yeast transcriptional regulatory network. It was found that 88 TFs were common, which showed that the LL and SL genes were regulated by the same TFs.

LL genes have higher epigenetic modifications. This was shown by comparing the affects of histone modification (acetylation and methylation) on LL and SL genes. The differences between the two groups as a result of the modifications were analyzed by using Wilcoxon statistical method and calculating the P-value. When the LL and SL genes underwent acetylation there was not a significant difference between the two sets. But when the sets underwent methylation the LL genes had higher methylation patterns. Time course expression of methylase, demethylases and Sir complex. The time course was used to show the expression of histone modifications when the cell transitions from the log to stationary phase. This was done by using data from Gasch *et al.* The expression of methylases decrease over time, while demethylases increase with time. The low expression of methylase causes methylation to decrease, which brings about the silencing of chromatin by the formation of the Sir complex.

Transcription is mediated by epigenetic modifications and/or transcription factors. The data have shown that LL and SL genes are modulated by the same transcription factors, so the differences between them must lie in the epigenetic modifications. The epigenetic modifications that were analyzed in this study were acetylation and methylation. The results concluded that there weren’t any significant differences between LL and SL genes involved in histone acetylation, but that there were differences as a result of methylation. Long lived genes were affected by methylation, and caused a series of events to occur. I think that a new research direction should be to study all of the histone modifications that there are in order to see what other ways LL genes differ from SL genes. If methylation causes a chain of events, then I suspect that there other histone modifications which also cause chains of events that are important in gene expression and regulation of replicative aging.