MICROARRAY ANALYSIS OF YEAST AGING TO 12 GENERATIONS

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Introduction

The replicative aging of yeast mother cells is a process that could be driven by a genetic program, or alternatively could be a response of the cells to damaging events (1,2). As a first step in analysis of which model is a better descriptor of yeast aging, we have studied gene expression at 1, 4, 8, and 12 generations.

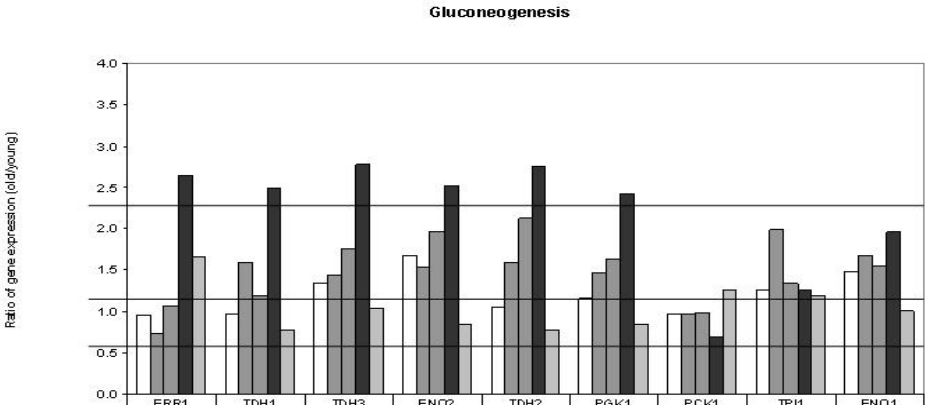
Materials and Methods.

Aging cells were obtained via magnetic bead sorting (3). For the 12 generation cells, chloramphenicol was included in the medium to prevent bacterial contamination, so young control microarrays with chloramphenicol were included for comparison with 12 generation data. Gene expression was assessed via 70-mer oligonucleotide microarrays printed at the Institute for Systems Biology for the Genome Consortium for Active Teaching. Four microarrays per age were hybridized with 50 ug total RNA samples and scanned on GenePix2000. Genetree clustering in GeneSpring showed that there are groups of genes change in a monotonic fashion during aging. Our preliminary analysis is based on a 2 fold change criterion, but statistical analysis via ANOVA and Tukey tests is underway.

Results

The genes encoding gluconeogenesis enzymes are generally increased in aging (Figure 1), as are those that encode ribosomal/nucleolar components. Most of the glucose transport proteins are high at 4 generations but become very low following that time, most likely because of a metabolic shift away from glycolysis during aging up to 8 generations (4) that appears to continue up to 12 generations. Interestingly, the heat shock response genes either decrease in expression or do not change appreciably in this interval. These findings agree with enzymatic changes and nucleolar fragmentation found by others at 8 generations.

Figure 1: Gluconeogenesis gene expression changes in yeast aging.



	ERR1	TDH1	TDH3	ENO2	TDH2	PGK1	PCK1	TPI1	ENO1
Young	0.952	0.979	1.345	1.682	1.062	1.158	0.967	1.253	1.483
4G	0.734	1.596	1.445	1.531	1.593	1.47	0.976	1.987	1.68
8G	1.07	1.192	1.75	1.968	2.125	1.63	0.988	1.332	1.551
12G	2.643	2.484	2.779	2.52	2.748	2.422	0.692	1.26	1.956
Chlor. Control	1.66	0.779	1.036	0.844	0.778	0.835	1.264	1.187	1.002

We have found that many of the Ty retroposon genes decrease in transcription during this interval. Interestingly, the Tye7 transcription factor also decreases from an average of 1.088 in young to an average of 0.207 fold at 12 generations. The Tye7 regulon is under investigation as a possible program of aging in yeast.

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