End-of-life Cell Cycle Arrest Contributes to Stochasticity of Yeast Replicative Aging

There is growing evidence that stochastic events play an important role in determining individual longevity. Studies in model organisms have demonstrated that genetically identical populations maintained under apparently equivalent environmental conditions display individual variation in life span that can be modeled by the Gompertz-Makeham law of mortality. Here, we report that within genetically identical haploid and diploid wild-type populations, shorter-lived cells tend to arrest in a budded state, while cells that arrest in an unbudded state are significantly longer-lived. This relationship is particularly notable in diploid BY4743 cells, where mother cells that arrest in a budded state have a shorter mean life span (25.6 vs 35.6) and larger coefficient of variance with respect to individual life span (0.42 vs 0.32) than cells that arrest in an unbudded state. Mutations that cause genomic instability tend to shorten life span and increase the proportion of the population that arrest in a budded state. These observations suggest that randomly occurring damage may contribute to stochasticity during replicative aging by causing a subset of the population to terminally arrest prematurely in the S or G2 phase of the cell cycle.