Abstract

Cellular aging in Saccharomyces cerevisiae can lead to genomic instability and impaired mitotic asymmetry. Here, we focus on the role of oxidative stress on genomic instability and mitotic asymmetry. We treated yeast cells from a collection of natural isolates with hydrogen peroxide, and monitored the frequencies of loss of heterozygosity (LOH) in response to hydrogen peroxide concentration. We found that the increase of hydrogen peroxide-dependent genomic instability occurs before a drop in viability. This leadoff is negatively correlated with chronological lifespan, with an R-squared of 0.54 and a p-value of 0.024, and positively correlated with a measure of endogenous mitotic asymmetry with an R-squared of 0.43 and a p value of 0.054. This indicated that better resistance to exogenous hydrogen peroxide is associated with a longer chronological lifespan and better mitotic asymmetry. Moreover, we previously observed that elevation of genomic instability generally lags behind the drop in viability during chronological aging. Hence, hydrogen peroxide treatment and chronological aging lead to opposite timing of genomic instability with regards to viability. This contrast argues that the effect of oxidative stress on genome integrity is well prevented up to the dying-off phase during chronological aging. Overall, our results demonstrate strong associations between oxidative stress, genomic instability, and mitotic asymmetry within the context of aging.