

Aneuploidy Shortens Replicative Lifespan in *Saccharomyces cerevisiae*

Aneuploidy and aging are correlated; however, a causal link between these two phenomena has remained elusive. Here, we show that yeast disomic for a single native yeast chromosome generally have a decreased replicative lifespan. In addition, the extent of this lifespan deficit correlates with the size of the extra chromosome. We identified a mutation in *BUL1* that rescues both the lifespan deficit and a protein trafficking defect in yeast disomic for chromosome 5. Bul1 is an E4 ubiquitin ligase adaptor involved in a protein quality control pathway that targets membrane proteins for endocytosis and destruction in the lysosomal vacuole, thereby maintaining protein homeostasis. Concurrent suppression of the aging and trafficking phenotypes suggests that disrupted membrane protein homeostasis in aneuploid yeast may contribute to their accelerated aging. The data reported here demonstrate that aneuploidy can impair protein homeostasis, shorten lifespan and may contribute to age-associated phenotypes.