# PMT1 Deficiency Enhances Basal UPR Activity and Extends Replicative Lifespan of Saccharomyces cerevisiae

Pmt1p is an important member of the protein O-mannosyltransferase (PMT) family of enzymes, which participates in the endoplasmic reticulum (ER) unfolded protein response (UPR), an important pathway for alleviating ER stress. ER stress and the UPR have been implicated in aging and age-related diseases in several organisms; however, a possible role for PMT1 in determining lifespan has not been previously described. In this study, we report that deletion of PMT1 increases replicative lifespan (RLS) in the budding yeast Saccharomyces cerevisiae, while overexpression of PMT1 (PMT1-OX) reduces RLS. Relative to wild-type and PMT1-OX strains, the pmt1Δ strain had enhanced HAC1 mRNA splicing and elevated expression levels of UPR target genes. Furthermore, the increase RLS of the pmt1Δ strain could be completely abolished by deletion of either IRE1 or HAC1, two upstream modulators of the UPR. The double deletion strains pmt1Δhac1Δ and pmt1Δire1Δ also displayed generally reduced transcription of UPR target genes. Collectively, our results suggest that PMT1 deficiency enhances basal activity of the ER UPR and extends the RLS of yeast mother cells through a mechanism that requires IRE1 and HAC1.