A Novel Link Between the Nonstop Decay of mRNA and Autophagy

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Since its discovery in 2002, little has been revealed about the mechanisms of the Nonstop Decay (NSD) mRNA degradation pathway. To date, only 10 yeast genes have been found to be directly involved in NSD. To discover new genes involved in NSD, we performed a genome wide investigation in *Saccharomyces cerevisiae*. We first obtained a NSD construct and transformed it into the commercially available yeast deletion set. We then performed a selection screen in triplicate, yielding 477 gene candidates. Next, we performed growth curves on a large subset of the gene candidates to confirm the results from our screen. After analysis, we found several gene families that seem to occur, which contain multiple hits from our screen. In particular, our screen seems to produce several gene~~s~~ candidates involved in autophagy. We therefore chose to investigate the potential relationship between NSD and autophagy. First, we used an autophagy inhibiting drug verteporfin to confirm autophagy does not occur in our mutants. The results confirm our prediction that autophagy is inhibited in these two candidates, as the addition of verteporfin resulted in no additional influence over the growth the mutants. Next, we assessed the abundance of nonstop mRNA using qPCR analysis. This resulted in lower than expected nonstop mRNA abundance relative to the WT, which has led us to investigate nonstop protein abundance. Interestingly, we see a dramatic increase in the abundance of nonstop protein abundance relative to the WT. Together, our results echo a previous study which suggests that NSD occurs at both the transcriptional and the translational level. Specifically, our results suggest that NSD occurs through autophagy on the translational level. Further, having several hits in the autophagy pathway from a genomic screen supports the hypothesis that the NSD machinery requires the autophagy pathway.