Role of the RNA exosome complex and non-coding RNAs in regulation of the cell wall stress response in yeast S. cerevisiae

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The nuclear RNA exosome is a conserved complex involved in 3'-5' RNA degradation and processing in eukaryotic cells. In yeast, its 9-subunit structural core and catalytic subunit Dis3 are essential for viability, while the absence of the second catalytic subunit Rrp6 is inviable only at high temperature. In this work, we show that RNA exosome mutants undergo osmoremedial cell lysis at high temperature or upon treatment with cell wall stressors (published in Novačić A et al. (2021) Mol. Biol. Cell 32(5), 363-375). The catalytic subunit Dis3 provides exoribonuclease catalytic activity needed for maintenance of cell wall stability in *S. cerevisiae* and is supported by a non-catalytic function of the Rrp6 subunit and the RNA exosome cofactors Rrp47 and the TRAMP complex. Moreover, we identify the mechanism leading to cell wall destabilization, by showing that genes encoding proteins involved in the early steps of protein glycosylation pathway are downregulated in RNA exosome mutants at high temperature, through mechanisms involving increased accumulation of non-coding RNAs transcribed at their gene loci. Consistent with this, overexpression of the essential enzyme Psa1, which catalyzes the synthesis of the mannosylation precursor, suppresses temperature sensitivity and aberrant morphology of these cells. Additionally, we show that the reason why the cell wall instability phenotype of RNA exosome mutants is most pronounced for the commonly used W303 laboratory strain is a mutation that inactivates the *SSD1* gene, which encodes an RNA-binding protein involved in regulating the translation of cell wall-related transcripts.