Spring 2018

The Role of the Ribsomal RNA in Translation Quality Control in Saccharomyces cerevisiae

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In all domains of life, the ribosome is the machine responsible for translating mRNA transcripts into polypeptide chains. Often, the ribosome encounters a block (for example, a damaged mRNA), which causes the ribosome to stall and stop protein synthesis. To alleviate this, eukaryotic cells evolved a pathway called no-go decay (NGD) to rapidly degrade these defective mRNAs by cleaving the transcript upstream of the stalled ribosome. However, the endonuclease responsible for this cleavage activity is yet to be identified. Previous studies from our lab suggest that the ribosome might be responsible for the cleavage reaction. In particular, I hypothesize that the ribosomal RNA of the small subunit catalyzes the cleavage reaction at stalled ribosomes. To test this hypothesis, I carried out a screen by introducing a mutagenized library of 35S pre-rRNA-containing plasmids into yeast strains harboring an integrated reporter gene subject to NGD. These reporter plasmids contain inhibitory (arginine) codons upstream of the *ade2* gene that stall the ribosome as a proxy for damage. Upon transformation of the library, we selected for white colonies that indicate translation of the *ade2* gene and thus, cleavage inhibition. I am currently attempting to confirm that six of my isolates contain rRNA mutations, that are causative and do not contain secondary mutations. In addition to the screen, 18S rRNA mutants were rationally designed based on their location near the mRNA. One mutant (T1430D) resulted in white colonies, indicating that this region of the ribosome is likely to be important for endonuclease activity. Moreover, western-blotting analysis indicated increased synthesis of the NGD reporter. These preliminary findings provide insight into how quality control mechanisms evolved to integrate into fundamental biological machines. Further delineation of the details of this mechanism will contribute to the understanding of how cells identify and degrade defective biological molecules.