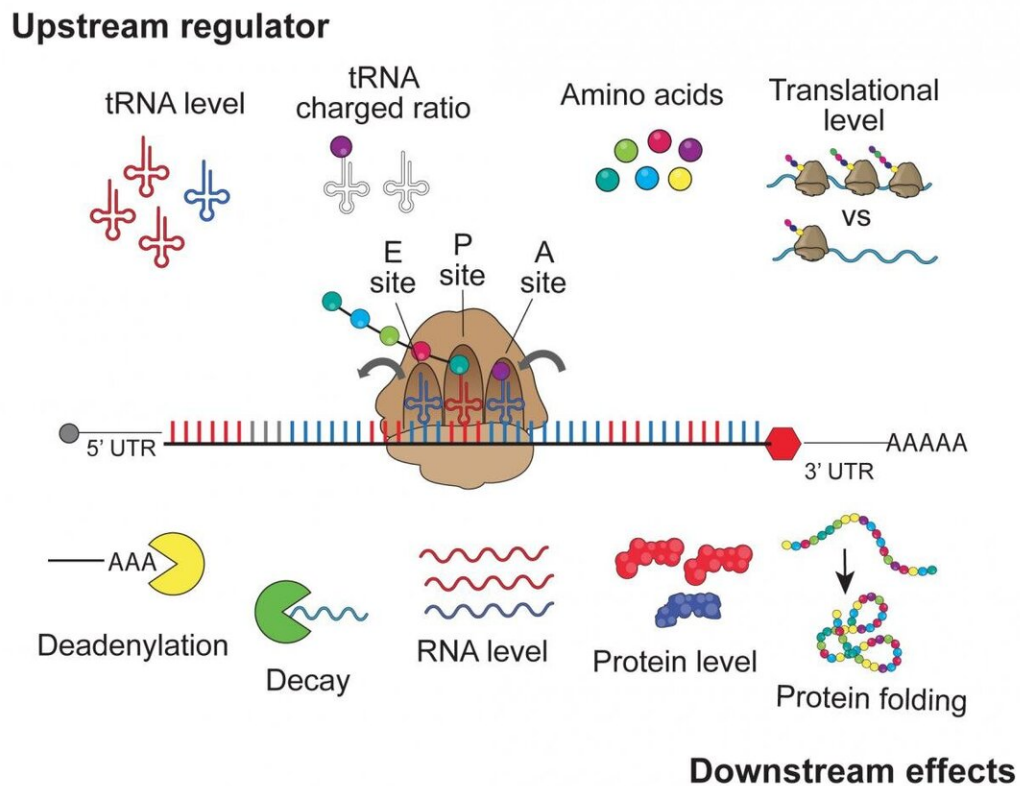


More than a protein factory: A role for ribosomes in regulating human gene expression

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A new study using human cell lines provides insight on how instructions embedded within mRNA messages can affect mRNA levels, mRNA stability, and protein production in a translation-dependent manner. Credit: Bazzini Lab

Researchers from the Stowers Institute for Medical Research have discovered a new function of ribosomes in human cells that may show the protein-making particle's role in destroying healthy mRNAs, the messages that decode DNA into protein.

"For a long time, many people have viewed ribosomes as a passive player in the cell—a molecular machine that's just producing proteins," says Stowers Assistant Investigator Ariel Bazzini, Ph.D. "Now there's growing evidence that ribosomes regulate [gene expression](#), including in [human cells](#)."

These findings, which were recently published online in *eLife*, could lead to further understanding mRNA's role and the causes of gene misregulation in human diseases.

In the process of translation, ribosomes make proteins by serving as the site for the biological synthesis of them. Specifically, a [ribosome](#) reads codons—sets of three consecutive nucleotides—in an mRNA message to determine which [amino acids](#) to add to the growing protein chain. As part of this process, ribosomes also act as quality control, triggering the destruction of improperly made mRNA.

A growing body of evidence has shown ribosomes also play a role in affecting the stability (life) of properly processed mRNAs, thereby acting as a key factor in modulating mRNA stability, level of mRNA, and protein production. This had been shown in organisms such as yeast, *E. coli*, and zebrafish. In this study, researchers showed that ribosomes affect mRNA stability in human cell lines as well.

"We're seeing that the amount of gene expression is a combination of mRNA production (transcription) and stability," Bazzini says. "Think of a glass of water. To get an idea of how much water the glass holds at any particular time, it's important to know how much water you initially pour

into the glass but also important to know how much water you drink. The same is true with mRNAs. You can measure how many mRNAs are properly made, but if you don't know how many of them are being broken down, how do you really know how many there are?"

These findings open the door to two exciting research avenues, says Bazzini. The first is better understanding how ribosomes trigger mRNA destruction, the molecular mechanism of which is still unknown. Ribosomes may not be the passive player researchers have long thought them to be.

"Similar to ribosomes, molecules called tRNAs, or transfer RNAs, are also fundamentally involved in protein synthesis," says first author on the report and Stowers Predoctoral Researcher Qiushuang Wu. "We think that tRNAs, which recognize codons in mRNA and provide corresponding amino acids to ribosomes, might have a strong regulatory role in development and in human diseases."

The second research avenue is looking at how this newly discovered regulatory [molecular mechanism](#) may be related to genes associated with human diseases. Sequencing of human genomes has shown that individuals sometimes have a "silent mutation," which is a change in DNA sequence and codon that does not change the amino acid makeup of the resulting [protein](#), as many amino acids are coded by multiple codons. However, the silent mutation might still have an effect if it leads to ribosomes destroying healthy mRNA.

"One of the most basic concepts of biology is how genes are regulated and how those regulations drive cells to become specialized. We're interested in studying how post-transcription mechanisms work and, in particular, how ribosomes trigger mRNA destruction—how they trigger or recruit factors to carry out this process," Bazzini says. "Understanding how translation affects mRNA expression at a molecular level allows us

to start thinking about how mRNA translation might shape gene expression in cancer, aging, or viral infection."

Provided by Stowers Institute for Medical Research

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