Biologists uncover a novel cellular proofreading mechanism

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(PhysOrg.com) -- To make proteins, cells assemble long chains of amino acids, based on genetic instructions from DNA. That construction takes place in a tiny cellular structure called a ribosome, to which amino acids are delivered by transfer RNA (tRNA).

Each of the 20 amino acids encoded by the genetic code is carried by a specific type of tRNA. The matching between amino acid and tRNA must be precise, or else the wrong amino acid will be added to the protein.

A team of MIT researchers has now discovered that cells have a proofreading mechanism that destroys any malformed tRNA molecules. This ensures that only the correct amino acids are used, preventing proteins from being misassembled.

The finding is reported in the Nov. 10 issue of the journal *Science*. Lead author of the paper is Jeremy Wilusz, a postdoc in the David H. Koch Institute for Integrative Cancer Research at MIT. Senior author of the paper is Phillip Sharp, Institute Professor at MIT.

It was already known that all tRNAs, which are made of nucleotides, just like DNA, have a CCA sequence at one end, which is where an amino acid can latch onto the tRNA. This CCA is added to the tRNA after it is transcribed from DNA, by an enzyme called the CCA-adding enzyme. Without CCA, the tRNA would be nonfunctional.

The new study shows that the CCA-adding enzyme can also add a CCACCA sequence. This sequence is added to abnormal tRNAs – those with a mutation or a structural flaw. The CCACCA tag marks the tRNA for destruction by other enzymes called exonucleases.

“It’s a way to prevent these mistakes, by taking the tRNA out of service and not giving it the chance to add the wrong amino acid,” says Wilusz. “If it can’t quite fold right, the structure falls apart a little bit and everything’s a bit more flimsy, so you’re able to add this second CCA.”

The researchers observed this mechanism in species from all kingdoms of life.

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