Researchers prove protein synthesis and mRNA degradation are structurally linked

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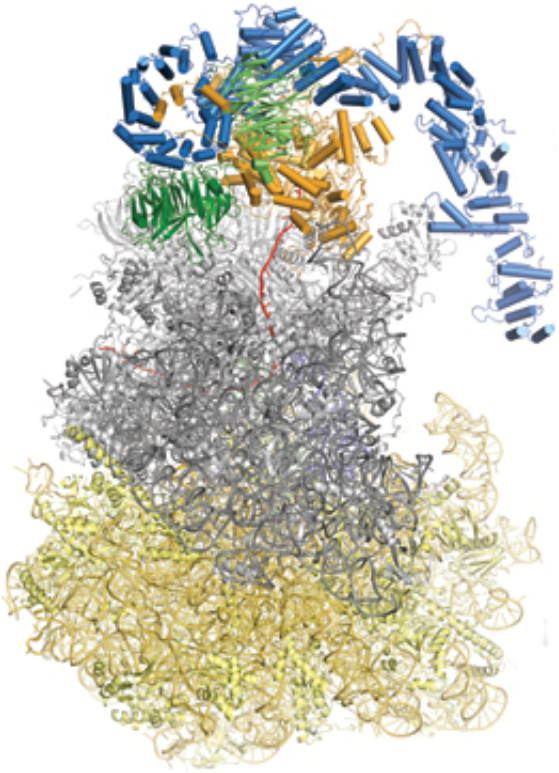

Ribosome-Ski complex. Credit: LMU

Protein synthesis is programmed by messenger RNAs, and when enough of a given protein has been made, the mRNAs that encode it are destroyed. LMU researchers have now shown that protein synthesis and mRNA degradation are structurally linked.

In all cells, the genetic information stored in DNA molecules encodes the instructions for the synthesis of proteins. The information is first "transcribed" into messenger RNAs, which program molecular machines called ribosomes that "translate" the instructions into defined sequences of amino acids, i.e. proteins with specific functions. When an mRNA molecule is no longer needed or is recognized as being defective, it is delivered to a protein complex known as an exosome. This organelle serves as a molecular shredder, and slices mRNAs into their component subunits, starting from the trailing (3') end of the molecule. LMU structural biologist Roland Beckmann, in collaboration with researchers at the Max Planck Institute for Biochemistry and the Institut Pasteur (Paris), has now shown that there is a direct molecular link between the ribosome and the exosome that degrades mRNAs. Their findings were published recently in the leading journal *Science*.

A set of proteins known as the Ski complex plays a crucial role in the disposal of mRNA. It essentially feeds the molecules into the exosome, and in doing so it unfolds their intricate spatial conformation, which makes it possible for them to be enzymatically destroyed. "With the aid of cryo-electron microscopic imaging, we have now shown, for the first time, that the ribosome interacts structurally with the Ski complex," Beckmann says, "largely because we succeeded in isolating and visualizing the critical intermediate in the interaction."

Ribosome profiling allows one to identify and quantify the mRNAs that are undergoing translation, and to determine the distribution of the translating ribosomes on them. Using an innovative, targeted variant of ribosome profiling, Beckmann and his colleagues went on to verify that the ribosome-Ski complex is actually engaged in degrading RNA in cells. By targeting the method to ribosomes bound to Ski, they showed that sequences located at the 3' ends of mRNAs associated with the complex were notably underrepresented. This is compatible with the mode of action of the exosome, which is known to degrade mRNAs from the 3'

end. Further work carried out by the French group demonstrated that defective mRNAs, which must be extracted from the ribosomes, are also degraded in this fashion.

More information: Christian Schmidt et al. The cryo-EM structure of a ribosome–Ski2-Ski3-Ski8 helicase complex, *Science* (2016). DOI: 10.1126/science.aaf7520

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