Study reveals how ribosomes override their blockades

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Ribosomes are "protein factories" in the cells of all living things. They produce proteins based on existing genetic codes stored on special nucleic acid molecules. These molecules, also called messenger RNA (mRNA) due to the genetic information encoded on them, are read by ribosomes in a stepwise manner. Defined start and stop signals on the mRNA direct this process. If a stop signal is missing, protein formation cannot be completed and the ribosome's mode of operation is blocked.

Until now, it was not understood in all details how a ribosome can overcome such a blockade. At the center of this repair process, called Trans-Translation, is an additional nucleic acid molecule (tmRNA) that unites characteristics of mRNA and another nucleic acid molecule, the transferRNA (tRNA). The tRNA transfers the correct amino acids to the respective gene sequence on the mRNA during protein biosynthesis. The tmRNA molecule is thus able to smuggle in the missing stop signal and lift the blockade. It was never exactly clear how this large tmRNA molecule moves through the ribosome and smuggles its information into the ribosome's mRNA channel.

This process could now be documented for the first time using cryo-electron microscopy. This method offers the opportunity to examine the spatial and chronological interaction between individual components of macromolecules. This is done by flash-freezing ribosomes in liquid ethane at -192° Celsius and several hundred-thousand two-dimensional images are projected back into a three-dimensional reconstruction. "With the help of cryo-electron microscopy a unique glimpse of a

central key step of the interaction between ribosome, tmRNA, a special protein (SmbP) and the elongation factor G could be attained," explained David Ramrath, doctoral candidate at the Institute for Medical Physics and Biophysics at Charité and primary author of the study.

The mRNA channel, in which the tmRNA must smuggle the missing information, goes straight through the ribosome's middle, between the so-called head and body domains of the small ribosomal subunit. Structural analysis showed that cooperation between ribosome and tmRNA in the event of necessary repair is only possible through a change in conformation, that is a short-term and unexpectedly large swivel movement of the ribosome's head domain.

More information: The complex of tmRNA–SmpB and EF-G on translocating ribosomes. David J. F. Ramrath, Hiroshi Yamamoto, Kristian Rother, Daniela Wittek, Markus Pech, Thorsten Mielke, Justus Loerke, Patrick Scheerer, Pavel Ivanov, Yoshika Teraoka, Olga Shpanchenko, Knud H. Nierhaus & Christian M. T. Spahn. *Nature* (2012), DOI:10.1038/nature11006

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