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tmRNA to the rescue

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The molecular processes responsible for protein synthesis are usually very efficient, but the ribosomes can stall if defective or incomplete mRNA molecules dock and initiate translation. To rescue stalled ribosomes, bacteria use tmRNA (also known as 10Sa RNA), an approximately 300-nucleotide-long molecule so-named for its dual tRNA-like and mRNA-like nature. Although the tmRNA structure is well known - an alanyl-tRNA like domain, an open reading frame, and four pseudoknots - its modes of action have been unclear. In the April 4 issue of Science, Mikel Valle and colleagues from the Howard Hughes Medical Institute, Albany, New York, US, present the structure of tmRNA in complex with the ribosome as determined by cryo-electron microscopy (cryo-EM), gathering important new insights into tmRNA function (*Science*, **300:**127-130, April 4, 2003).

Valle *et al.* used purified *Thermus thermophilus* extracts and prepared a stalled ribosome with a docked tmRNA. They added the protein synthesis elongation factor Tu (EF-Tu), SmpB, a small protein required for tmRNA-mediated peptide tagging activity, and kirromycin, an antibiotic that traps ribosome rescue at an early stage. The cryo-EM image of the complex yielded novel details of tmRNA entry into the ribosome, revealing that tmRNA initially binds the ribosome and EF-Tu in a manner similar to canonical tRNAs. SmpB acted by facilitating the contacts between tmRNA and the stalled ribosome, and tmRNA pseudoknots played a role in the presentation of the molecule to the ribosome, helping to orient the alanyl-tRNA like domain and the open reading frame.

"Predictably, the cryo-EM images presented by Valle *et al.* only whet our appetite for higher-resolution structural information about each stage of ribosome rescue", note Sean Moore and colleagues from the Massachusetts Institute of Technology, Cambridge, MA, USA, in an accompanying Perspectives article.

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