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Structure Watch

RE-EVALUATING THE DECODING PRINCIPLE

Following delivery of tRNA to the aminoacyl-tRNA binding site (A site) of the ribosome, a proofreading step ensures that the selected tRNA matches the mRNA codon of the A site. Previous studies suggested that the universally conserved nucleotides G530, A1492 and A1493 of 16S ribosomal RNA (rRNA) promote a conformational change (domain closure) on the 30S ribosomal subunit only when they detect the formation of Watson–Crick base pairs at the first two positions of the codon–anticodon helix. Here, Demeshkina *et al.* challenge this view showing that 30S domain closure also occurs in the presence of nucleotide mismatches at the codon–anticodon helix. Moreover, G530, A1492 and A1493 nucleotides of the 16S rRNA interact in a similar manner with mismatched base-pairs as with Watson–Crick base pairs. Thus, it seems that it is the formation of a tight decoding centre following 30S domain closure that destabilizes the incorrect base pairs, leading to the release of near-cognate tRNAs.

ORIGINAL RESEARCH PAPER Demeshkina, N. *et al.* A new understanding of the decoding principle on the ribosome. *Nature* 21 Mar 2012 (doi:10.1038/nature10913)

FREEING STALLED RIBOSOMES

Two recent studies shed light onto the mechanism of stalled ribosome rescue and reveal how proteins can regulate translation by mimicking RNA. Translation of mRNAs that lack a stop codon results in ribosome stalling. Transfer-messenger RNA (tmRNA) — which contains a tRNA-like domain (TLD) that can be aminoacetylated with Ala and an mRNA-resembling open reading frame — acts in concert with SmpB and elongation factor Tu (EF-Tu) to release stalled ribosomes in bacteria. Neubauer *et al.* resolved the crystal structure of bacterial ribosomes bound to a fragment of tmRNA (Ala-tmRNA$^{\Delta m}$), SmpB and EF-Tu. Interestingly, the carboxyl terminus of SmpB interacts with ribosomes downstream of the aminoacyl-tRNA binding site (A site). As this ribosomal region is occupied by mRNA in translating ribosomes, the C terminus of SmpB contributes to the specific recognition of stalled ribosomes. Moreover, the interaction of SmpB with the decoding centre of the ribosome induces domain closure of the 30S subunit, which presumably leads to the EF-Tu-mediated positioning of the TLD into the peptidyl transferase centre (PTC). This, in turn, promotes ribosome release.

YaeJ, a protein that shares similarities with the catalytic domain of polypeptide chain release factors, can rescue stalled ribosomes in a tmRNA-independent manner. Gagnon *et al.* resolved the crystal structure of YaeJ bound to bacterial ribosomes. The C-terminal tail of YaeJ was shown to detect stalled ribosomes also by binding to the ribosome downstream of the A site. This binding facilitates positioning of the YaeJ GGQ motif into the PTC, which can then mediate peptide release.

ORIGINAL RESEARCH PAPERS Neubauer, C. *et al.* Decoding in the absence of a codon by tmRNA and SmpB in the ribosome. *Science* **335**, 1366–1369 (2012) | Gagnon, M. G. *et al.* Structural basis for the rescue of stalled ribosomes: structure of YaeJ bound to the ribosome. *Science* **335**, 1370–1372 (2012)