

Mechanistic insights into the alternative translation termination by ArfA and RF2

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With the support by the National Natural Science Foundation of China, the research team led by Prof. Gao Ning (高宁) at the Ministry of Education Key Laboratory of Protein Sciences, Beijing Advanced Innovation Center for Structural Biology, School of Life Sciences, Tsinghua University, Beijing, recently reported how bacteria make use of a small protein called ArfA to rescue ribosomes stalled on defective messenger RNAs, in *Nature* (2017, 541: 550—553).

The ribosome is a gigantic molecular machine responsible for protein synthesis according to the genetic information carried on messenger RNAs (mRNA). For each mRNA, there is a tri-nucleotide code in its 3'-end called "stop-codon", which signals the ribosome to terminate the translation. When a truncated mRNA lacking a stop codon (non-stop mRNA) is translated, the ribosome would be stalled at the 3' end of mRNA and translation termination could not occur. Accumulation of stalled ribosomes in bacteria is a matter of life or death. As a response, bacteria have evolved multiple systems to rescue stalled ribosomes. ArfA is a newly identified ribosome rescuing factor. With the state-of-art cryo-EM technique, the team has elucidated a high-resolution cryo-EM structure (3 Å) of the *E. coli* 70S ribosome in complex with ArfA, non-stop mRNA and canonical translation termination factor RF2. Their structure reveals two essential roles for ArfA in this rescuing process: (1) the C-terminal loop of ArfA senses the length of mRNA, to ensure that it only works on stalled ribosomes with 3'-end truncated mRNAs; (2) the N-terminus of ArfA interacts with RF2 to compensate the lack of stop-codon and stimulate RF2's function in translation termination. Their results highlight a conserved ribosome rescuing pathway in bacteria, and provide targets for design and screening novel anti-bacterial translation inhibitors.

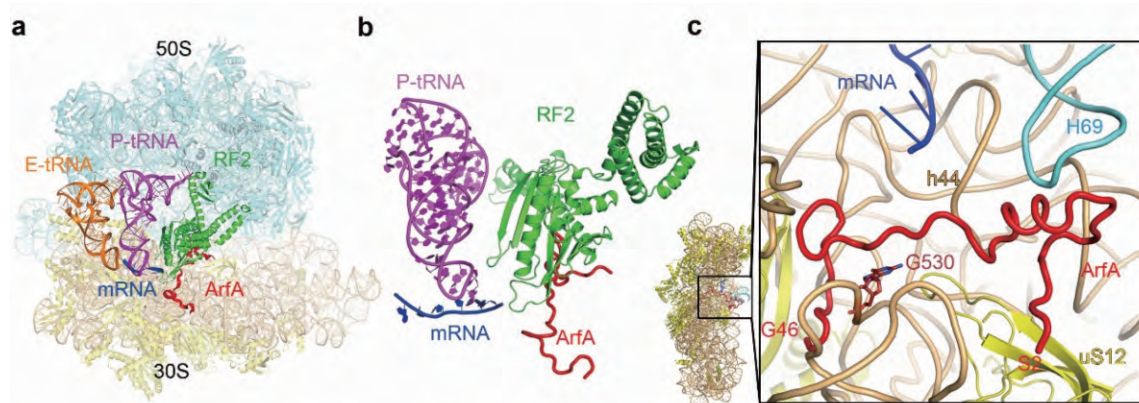


Figure The structure of the non-stop ribosomal complex bound with ArfA and RF2.