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Structural basis of bacterial protein translation elongation

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Recently, better understanding of ribosome function has been achieved through structural determination. These results provided a wealth of information on how genetic codes are precisely translated into proteins that control life, as well as established the platform to put ribosome as one of the richest validated targets for antibacterial drug discovery. We discovered a new ribosome crystal form obtained from ribosome lacking subunit L9, which allows crystallization of the ribosome in the presence of elongation factors Tu and G (EF-Tu/EF-G), trapped by antibiotics kirromycin and fusidic acid, respectively. These structures for the first time at atomic level offer insight into the molecular mechanism of protein elongation, which lies at the heart of translation. In each elongation cycle, EF-G facilitates the movement of tRNA-mRNA by one codon, which is coupled to the ratchet-like rotation of the ribosome complex and is triggered by EF-G-mediated GTP hydrolysis. The structure of pre-translocational ribosome bound to EF-G trapped with a GTP analogue, sheds light on how the positioning of the catalytic residue His87 into the active site is coupled to the hydrophobic gate opening which involves the sarcin-ricin loop (SRL) and domain III of EF-G. These results provide the structural basis for the GTPase activation of EF-G. After translocation, a cognate deacylated tRNA can only move together with the codon into the ribosomal E site. We also determined the structure of a cognate tRNA bound to the ribosomal E site, representing an authentic ribosome elongation complex. Quality control in protein translation by bacterial toxin has been associated with ribosome stalling and rescue system that is critical for cell to adapt environmental stress. Finally, I will introduce our structural progress on bacterial toxin bound to ribosome towards understanding of a classical acid-base catalysis mechanism.

[1] *Y.G.Gao, M. Selmer, C.M. Dunham, et al., Science, 2009, 326, 694-699,* ***[2]*** *Y. Chen, S. Feng, V. Kumar, at al., Nat. Struct. Mol. Biol., 2013, 1077-1084,* ***[3]*** *S. Feng, Y. Chen, K. Kamada, et al., Nucleic Acids Res., 2013, 9549-9556*

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