Keynote Lectures

[KN14] Structure of bacterial and yeast ribosome

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Ribosomes from bacteria consist of a large and a small subunit, which together compose the 2.5 megadalton (MDa) 70S ribosome. Their eukaryotic counterpart is the 80S ribosome (from 3.5 MDa in lower eukaryotes to 4.5 MDa in higher). Many ribosomal key components are conserved across the three kingdoms of life: bacteria, archaea, and eukarya and constitutes a common core undertaking the fundamental processes of protein biosynthesis. The mechanism for decoding based on X-ray structures of bacterial 70S ribosome determined at 3.1-3.4 Å resolution and modeling cognate or near-cognate states of the decoding center has been investigated. We show that the 30S subunit undergoes an identical domain closure upon binding of either cognate or near-cognate tRNA. This conformational change of the 30S subunit forms a decoding center that constrains the mRNA in such a way that the first two nucleotides of the A codon are limited to form Watson-Crick base pairs. When a U•G or G•U mismatch, generally considered to form a Wobble base pair, is at the first or second codon-anticodon position, the decoding center forces this pair to adopt the geometry close to that of a canonical C•G pair. This by itself or together with distortions in the codon¬anticodon mini-helix and the anticodon loop causes the near-cognate tRNA to dissociate from the ribosome. Our study provides structural insights into a universal principle of decoding on the ribosome.

The complete structure of the full 80S ribosome from Saccharomyces cerevisiae at a resolution of 3Å have been determined. The model includes nearly all the rRNA sequences as well as all ribosomal proteins, with the single exception of protein L1. The eukaryotic 80S and bacterial 70S ribosome shares 34 common proteins and eukaryotic ribosome has additional 45 unique proteins and bacterial ribosome has 22 additional unique proteins. The majority of eukaryotic specific elements are located on the periphery of the conserved core thus broadening the surface of interactions between the two subunits through additional eukaryotic bridges. The molecular interactions creating these bridges together with their eukaryotic-specific components can now be described in details. Our crystals capture the ribosome in two different conformations which are believed to reflect intermediate states in course of mRNA and tRNA translocation. The structural comparison of these states, which differ by the degree of rotation of the small subunit and the swiveling of its head with respect to the large subunit, provides a detailed description of conformational rearrangements as well as coordinated movements of intersubunit bridges.