

**MS05-2-2 Role of aIF5B in archaeal translation initiation**

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**Abstract**

Translation initiation (TI) allows accurate selection of the initiation codon on a messenger RNA (mRNA) and defines the reading frame. In all domains of life, translation initiation generally occurs within a macromolecular complex made up of the small ribosomal subunit, the mRNA, a specialized methionylated initiator tRNA and translation initiation factors (IFs). Once the start codon is selected at the P site of the ribosome and the large subunit is associated, the IFs are released and a ribosome competent for elongation is formed. However, even if the general principles are the same in the three domains of life, the molecular mechanisms are different in bacteria, eukaryotes, and archaea.

In eukaryotes and in archaea late steps of translation initiation involve the two initiation factors e/aIF5B and e/aIF1A. In eukaryotes, the role of eIF5B in ribosomal subunit joining is established and structural data showing eIF5B bound to the full ribosome were obtained. To achieve its function, eIF5B collaborates with eIF1A. However, structural data illustrating how these two factors interact on the small ribosomal subunit have long been awaited. The role of the archaeal counterparts, aIF5B and aIF1A, remains to be extensively addressed. We studied the late steps of *Pyrococcus abyssi* translation initiation. Using in vitro reconstituted initiation complexes and light scattering, we show that aIF5B bound to GTP accelerates subunit joining without the need for GTP hydrolysis. We report the crystallographic structures of aIF5B bound to GDP and GTP and analyze domain movements associated to these two nucleotide states. Finally, we present the cryo-EM structure of an initiation complex containing 30S bound to mRNA, Met-tRNA<sup>Met</sup>, aIF5B and aIF1A at 2.7 Å resolution. Structural data shows how archaeal 5B and 1A factors cooperate to induce a conformation of the initiator tRNA favorable to subunit joining. Archaeal and eukaryotic features of late steps of translation initiation are discussed.