

P041 Eukaryotic initiation factors induce structural rearrangements in the small 40S subunit of the eukaryotic ribosome – a cryo-EM study

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Eukaryotic translation initiation is a complex, multistep process culminating in the formation of an 80S complex, in which the AUG start codon is base paired with methyl initiator tRNA in the P site of the ribosome. In the early stages of translation initiation a ternary complex (TC) composed of eIF2, GTP and Met-tRNA_i^{Met} binds to the 40S subunit stabilised by eIF1A and eIF3. Moreover, in budding yeast eIF1, eIF2, eIF3 and eIF5 form a multifactor complex (MFC), which can bind 40S subunits. A considerable body of evidence suggests that the MFC components, together with eIF1A, play key roles in 40S-mRNA recruitment, scanning of the 5' untranslated region, and start codon selection. Here we present a cryo-EM study of the 40S subunit conformationally modified by eukaryotic initiation factors to prepare it for the binding and scanning of mRNA. In particular cryo-EM reconstructions of the 40S subunit complexed with eIF1A and with MFC factors reveal considerable conformational changes in the small subunit. These findings suggest a new model of eukaryotic translation initiation, in which eIF1A binding induces structural rearrangement of the head and platform regions of the small ribosomal subunit, thereby optimising the binding surface for the TC and MFC factors and remodelling the accessibility of the mRNA channel. Altogether, the 40S subunit is thus converted to a recruitment-competent state.