

RNA Innovation Seminars

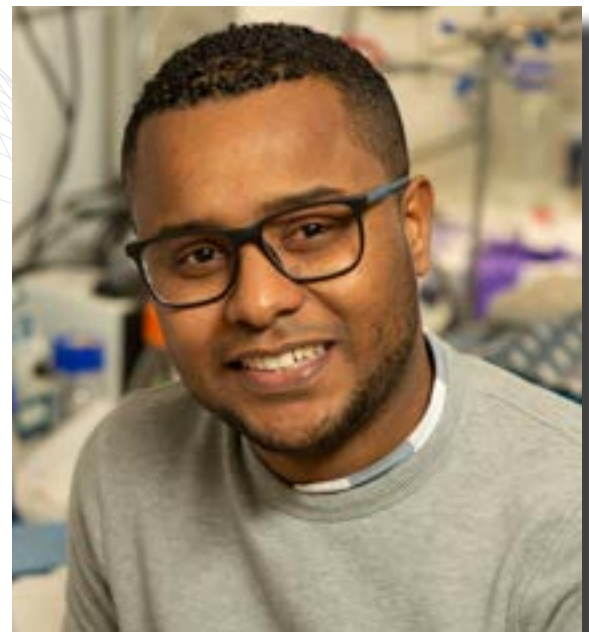


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Zoom Registration

Structural insights into mRNA translation initiation in humans

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Abstract

A key step in translational initiation is the recruitment of the 43S pre-initiation complex (43S PIC) by the cap-binding complex (eIF4F) at the 5' end of mRNA. Eukaryotic initiation factors eIF1, eIF1A, eIF3, eIF5, and the ternary complex (TC) of eIF2-GTP-tRNA^{iMet} bind to the 40S ribosomal subunit to form the 43S PIC. Once assembled, the 43S PIC is recruited to the cap-binding complex eIF4F at the 5' end of mRNA to form a 48S initiation complex (48S). The 48S then scans along the mRNA to locate a start codon. To understand the mechanisms involved, we determined the structure of a reconstituted human 48S using cryo-electron microscopy. The structure reveals insights into early events of translation initiation complex assembly. It reveals how eIF4F interacts with subunits of the eIF3 structural core near the mRNA exit channel in the 43S. The location of eIF4F is consistent with a slotting model of mRNA recruitment and suggests a "blind-region" that would preclude recognition of start sites upstream of the location of the P site at the point of recruitment.