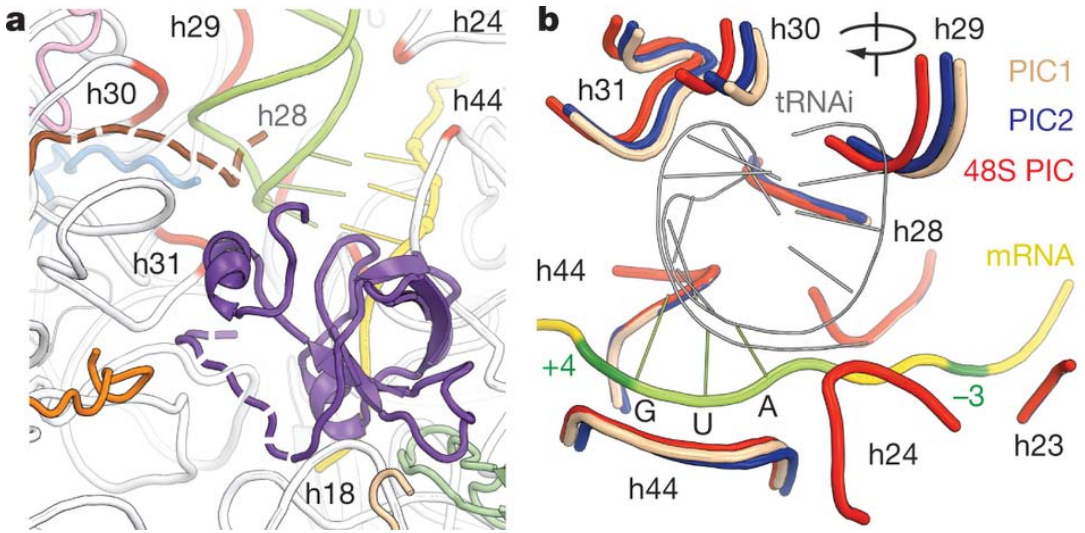
Understanding the Initiation of Protein Synthesis in Mammals

Scientific Achievement

Determined the first crystal structure of mammalian small ribosomal subunits with mRNA and initiator tRNA inside.

Significance and Impact

Capturing the details of the initiation of protein synthesis is critical for understanding how abnormalities in the process can lead to diseases like cancer or Alzheimer's Disease.



Interactions of tRNA and initiation factor eIF1A with the ribosomal subunit are shown. In a) eIF1A (violet) binds to a helix (h44) and ribosomal proteins rpS30e (wheat) and rpS23 (green). Possible positions of the amino-terminal tail of eIF1A and the C terminus of rpS15 (brown) are shown in dotted lines. The tRNA binding pocket regions are in red and rpS16 (blue), rpS18 (pink) and rpS31 (orange) are shown. In b) see the superposition of the pre-initiation complexes. Only regions of rRNA that are important for the interaction with tRNA are shown. Clockwise rotation of the head domain – which holds the start codon – is indicated.

Research Details

- Used X-ray crystallography to define the positions and roles of cellular machinery involved in protein synthesis, the most important cellular function.
- Discovered that initiator tRNA compete with initiation factor 1 (eIF1) for access to the P site, at which point eIF1 binds to the top of helices 44, 24, and 45 and senses for non-optimal coding from mRNA.

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Work was performed at Brookhaven National Laboratory and Yale University

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