Invited Lecture

tRNAslational control of eukaryotic gene expression

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My Max Planck Research Group studies different translation control mechanisms, which regulate the production of specific sets of proteins by chemical modifications of tRNA molecules. Every protein in the cell is produced by the ribosome, which uses transfer RNA (tRNA) molecules to translate the sequence information coded in mRNAs into correctly assembled poly-peptide chains. The lab is focusing on understanding the molecular mechanisms that lead to the specific base modifications in anticodons of tRNAs. These modifications have a strong influence on the efficiency and accuracy of the codon-anticodon pairing and therefore regulate the translational rates and folding dynamics of protein synthesis. Recent findings have shown that alterations of these modification pathways play important roles in the onset of certain neurodegenerative diseases and cancer. We mainly use X-ray crystallography (MX) and cryogenic electron microscopy (cryo-EM) to obtain snapshots of the involved macromolecular machines and analyse their reaction intermediates at atomic resolution. Subsequently, we employ different complementary in vitro and in vivo approaches to validate and challenge our structural observations. Furthermore, we have started working on other (t)RNA modification pathways and elucidate the structure of folded RNA molecules directly by cryo-EM. Furthermore, we aim to understand how these post-transcriptional modifications affect ribosomal decoding and translation elongation by directly imaging translating ribosomes at atomic resolution. Last but not least, we develop novel structural, biochemical and biophysical approaches to study structured RNA domains. In summary, our work contributes to the fundamental understanding of eukaryotic gene expression and its complex regulatory mechanisms.

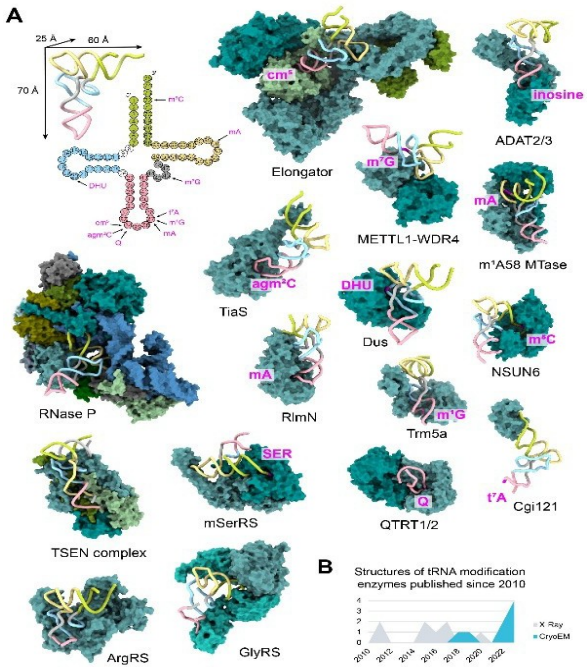

Figure 1. tRNA modification enzymes bind and recognize tRNAs using diverse strategies [5].

[1] Abbassi N et al.; Cryo-EM structures of the human Elongator complex at work *(2024). Nature Communications (in press)*

[2] Jain S et al.; Modulation of translational decoding by m6A modification of mRNA *(2023). Nature Communications Aug 8*

[3] Jaciuk M et al.; Cryo-EM structure of the fully assembled Elongator complex *(2023). Nucleic Acids Res. Mar 21*

[4] Dauden MI et al.; Molecular basis of tRNA recognition by the Elongator complex *(20219). Science Advances Jul;5(7)*

[5] Biela A et al.; The diverse structural modes of tRNA binding and recognition *(2023). JBC J Biol Chem. Jun 26*

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