A Novel Complementarity at the Heart of Biology

Initiative: "Leben?" - Ein neuer Blick der Naturwissenschaften auf die grundlegenden Prinzipien des Lebens

(beendet)

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The origin of the universal genetic code - one of the most important foundational problems in molecular biology - is still open. The stereochemical hypothesis proposes that the code evolved from nucleobase/amino-acid binding preferences, but direct evidence has been lacking. Recently, the research team has demonstrated that the nucleobase density profiles of mRNA coding sequences match the respective nucleobase affinity profiles of protein sequences they encode. This finding generalizes the stereochemical hypothesis to complete biopolymers and suggests that mRNAs and their cognate proteins may be physicochemically complementary and bind in a co-aligned fashion, especially if both are unstructured. The present project employs a battery of experimental and computational approaches to test this hypothesis at systems level and explores its implications in a particular case of paramount biological significance. Specifically, the team will assess the potential of human mRNAs to bind their cognate proteins under different conditions. Moreover, it will be addressed how non-cognate RNAs modulate phase separation of the C-terminal domain of RNA polymerase II. Finally, the team will analyze the relationship between the sequence specificity behind such effects and the structure of the genetic code. If successful, the project will transform the understanding of RNA-protein interactions, while forging a powerful link between the distant past and the present of biological systems.

Projektbeteiligte

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Open Access-Publikationen

Structure and phase separation of the C-terminal domain of RNA polymerase II
Conformational Dynamics of Intrinsically Disordered Proteins Regulate Biomolecular Condensate Chemistry.
Widespread autogenous mRNA protein interactions detected by CLIP-seq
Interaction preferences between protein side chains and key epigenetic modifications 5 methylcytosine, 5 hydroxymethycytosine and N6 methyladenine
Coding From Binding? Molecular Interactions at the Heart of Translation.