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Mechanisms of Quality and Quantity Control during mRNA Translation

A major goal of my group’s research efforts is to understand how cells identify failures during protein maturation and dispose of aberrant products to maintain cellular homeostasis. Failures can occur at any step on the pathway to a functional protein, including translation, folding, localization, modifications, and assembly. This talk will focus on the mechanisms cells use to monitor the translation of mRNAs by ribosomes and make crucial decisions about whether to degrade the mRNA and nascent protein. During quality control, cells have mechanisms to selectively detect when mRNAs are damaged or incorrectly processed. This is accomplished by recognizing stalled ribosomes, an indicator of a defective mRNA, and recruiting factors that recycle some components and degrade others. During quantity control, cells respond to an excess of particularly critical proteins such as tubulins and histones by selectively targeting their respective mRNAs for degradation. This is accomplished by poorly understood mechanisms by which excess proteins communicate privately to the ribosomes synthesizing more copies of that protein and degrade the associated mRNA. I will discuss our ongoing efforts to delineate the molecular machinery and mechanisms underlying quality and quantity control occurring on translating ribosomes.

Biography

Ramanujan Hegde earned his MD and PhD from UCSF, then established his laboratory at the US National Institutes of Health. After eleven years at the NIH, he moved to the MRC Laboratory of Molecular Biology in Cambridge, where he is currently a Programme Leader. The Hegde lab investigates the mechanistic basis of protein biosynthesis and how cells deal with inevitable inefficiencies and errors in these protein maturation pathways. Hegde’s research has been recognized by several prizes and by his election as a member of EMBO and as a Fellow of the Royal Society.

https://www2.mrc-lmb.cam.ac.uk/groups/hegde/