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Monitoring protein synthesis in space and time with ribosome profiling

The translation of mRNA into protein and the folding of the resulting protein into an active form are prerequisites for virtually every cellular process and represent the single largest investment of energy by cells. These are also the most likely steps to fail. We are broadly interested in how cells ensure the integrity of protein production, and cotranslational targeting and folding. We have a particular focus on the following questions: How do cells maximize the efficient production of proteins by ensuring proper trafficking of ribosomes on mRNAs? How do cells dispose of failed translation products? How do cells ensure that the appropriate amount of each protein is produced in the right place and time?

A key tool we developed to address these questions is ribosome profiling which has transformed our ability to globally monitor protein synthesis in vivo. I will discuss our recent applications of ribosome profiling including: the identification of novel protein coding regions, monitoring localized protein translation, and the discovery and characterization of the ER Membrane Complex (EMC).

I will also present our work on the ribosome quality control (RQC) complex which is responsible for degrading nascent chains from failed translation reactions. This will include our discovery of a remarkable mechanism for tagging such nascent chains with carboxy-terminal alanine and threonine extensions (CAT tails) through a noncanonical translation reaction as well as our very recent novel discovery of a novel branch of the RQC that translationally silences faulty mRNAs by blocking ribosome initiation.

Biography

Jonathan Weissman, Ph.D., studies how cells ensure proteins fold properly, as well as the role of protein misfolding in disease and normal physiology. He is also widely recognized for building innovative tools for broadly exploring organizational principles of biological systems. These include ribosome profiling, which globally monitors protein translation, and CRIPSRi/a for controlling the expression of human genes.

Jonathan Weissman is a Howard Hughes Medical Institute Investigator and Professor of Cellular and Molecular Pharmacology at UCSF. He is a member of the National Academy of Sciences and has received numerous awards including the 2015 NAS Award for Scientific Discovery.

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