RUTGERS–NEW BRUNSWICK
School of Environmental and Biological Sciences

The Department of Nutritional Sciences
Spring 2025 Seminar Series

"Metabolic Control of Protein Synthesis by Codon-Specific Ribosome Fall-Off Upon Arginine Limitation"

Alicia Darnell, Ph.D.
Assistant Professor
Pharmacology & Cancer Biology
Duke University School of Medicine

Host: Tracy Anthony, Ph.D.
Professor of Nutritional Sciences, Rutgers

Wednesday, March 19, 2025 @ 2:15 PM

Zoom option: https://go.rutgers.edu/Darnell-Seminar

Amino acids can become directly limiting for protein synthesis through charged tRNA depletion that leads to elongating ribosome stalling and premature fall-off at specific codons, providing a route for metabolism to directly control gene expression. I developed a reporter library to measure ribosome fall-off at all the codons cognate to any amino acid and found that arginine limitation consistently induced synonymous codon-specific ribosome fall-off caused by depletion of a specific charged Arg-tRNA. Ribosome fall-off reduced protein production in a codon-dependent manner upon arginine limitation. Genome-wide FACS-based CRISPRi/a screens implicated the ribosome quality control (RQC) pathway, which resolves irreversible stalling on defective mRNAs, in executing arginine-limited ribosome fall-off. However, RQC initiation during arginine limitation does not require the canonical collision sensor ubiquitin ligase ZNF598, instead proceeding through an alternative ubiquitination signaling pathway. This work outlines a new mechanism for nutrient-responsive control of gene expression by the RQC pathway, and reframes our understanding of the physiological targets of and input signals to this pathway.

For parking permits, please contact Christina Duffy, Department of Nutritional Sciences, cduffy@sebs.rutgers.edu , 848-932-5425