

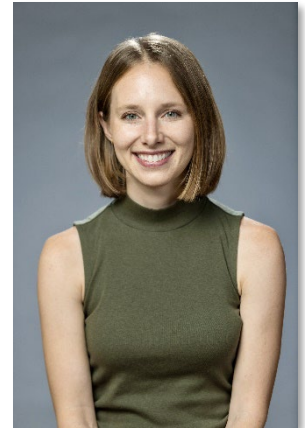
## The Department of Nutritional Sciences Spring 2025 Seminar Series

### "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.