



**SAMIE JAFFREY, Ph.D**

**Weill Medical College, Cornell University**

**FRIDAY**

**MARCH 20, 2026 @4:00**

**101 BRL**

**LIGHT REFRESHMENTS BRL LOBBY**

**@3:30pm**

## **WRISTON LECTURE**

### *Control of gene expression by chemical modifications of RNA*

The classical model of mRNA as a homogenous polymer composed of the four major nucleotides has been revised by the discovery of site-specific chemical modifications that enable the transcriptome to dynamically respond to diverse signaling states. This lecture describes two newly identified forms of RNA modification that link cellular redox state and nucleotide homeostasis to downstream signaling. First, we characterize a mechanism in which mRNA G-quadruplexes recruit endogenous heme to form catalytic peroxidase centers, directing the site-specific formation of 8-oxoguanosine (8-oxoG). These oxidative lesions act as molecular hurdles, triggering ribosome collisions and activating p38 MAPK inflammatory signaling. Second, we describe the discovery of deoxyribonucleotide incorporation into mammalian poly(A) tails, a previously unrecognized form of mRNA diversification. We find that the DNA nucleotide incorporated into mRNA is predominantly deoxyadenosine (dA), a feature particularly enriched in mitochondrial transcripts. This dA incorporation is sensitive to fluctuating ATP:dATP ratios, allowing these chimeric tails to serve as metabolic sensors. Together, these findings reveal that mRNA chemistry is a dynamic, metabolite-driven feature that dictates the functional life cycle of the transcriptome in health and disease.

Dr. Samie Jaffrey is a Professor of Pharmacology at the Weill Medical College of Cornell University. His research focuses on novel mRNA regulatory pathways that control protein expression in normal and disease states. He helped to launch the field of “epitranscriptomics” with his seminal study which reported transcriptome-wide mapping of N6-methyladenosine (m6A). His work revealed that m6A is a pervasive modification in the transcriptome, enabling critical forms of post-transcriptional regulation. He also developed genetically encoded fluorescent RNAs, known as “RNA mimics of GFP,” including the Spinach aptamer. These imaging approaches are widely used to study diverse aspects of RNA biology.



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