CENTER FOR RNA BIOMEDICINE

RNA Innovation Seminar

Monday, December 17, 2018 at 3:00pm
ABC Seminar rooms, Biomedical Research Science Building (BSRB), 109 Zina Pitcher

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"Modifications of mRNA can alter translation elongation, fidelity and termination"

Abstract: Chemical modifications of RNAs have long been appreciated as key modulators of non-coding RNA structure and function in cells. However, it has only recently become apparent that such modifications are also found in the coding sequences of mRNAs which direct protein synthesis. It is widely posited that the modification of mRNAs serves as a gene regulatory mechanism because the enzymatic incorporation of mRNA modifications has the potential to modulate mRNA stability, protein-recruitment, and translation in a programmed manner. We tested how two of the most common modifications present in mRNA coding sequences, N6-methyl adenosine (m6A) and pseudouridine (Ψ), impact protein synthesis using a fully-reconstituted E. coli translation system. Our work reveals that replacing a single nucleotide with Ψ or m6A in an mRNA codon impedes amino acid addition, and impedes release-factor catalyzed translation termination. Additionally, we find that the incorporation of Ψ, but not m6A, promotes the synthesis of multiple peptide products from a single mRNA sequence, and blocks translation termination by release factors. Given that the majority of Ψ moieties in mRNAs are found in coding regions where the ribosome is likely to encounter them, our studies provide support for the provocative hypothesis that chemical modifications in mRNA could potentially provide a distinct way for cells to quickly and directly regulate and alter protein production by the ribosome.