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Nonsense-mediated mRNA decay and how it is regulated by chemotherapeutics to contribute to apoptosis

Abstract:
Staufen1-mediated mRNA decay (SMD), which occurs when translation terminates sufficiently upstream of a STAU-binding site (SBS), is important to many developmental and homeostatic pathways. An SBS can be created by intramolecular base-pairing within an mRNA 3'-untranslated region (3'UTR) or by intermolecular base-pairing between a 3'UTR and one or more long non-coding RNAs (lncRNAs), which we call ½-sbsRNAs. Intermolecular base-pairing in humans involves Alu elements, which are a type of small interspersed repetitive element (SINE), whereas intermolecular base-pairing in rodents involves B and identifier SINEs. Roles of STAU1 dimerization and the STAU1 paralog STAU2 in SMD will be discussed. A new mechanism by which mRNAs crosstalk in a way that involves direct mRNA–mRNA interactions between 3'UTR Alu elements in each mRNA will also be described, uncovering a new role for mammalian-cell mRNAs. This unexpected function, together with our discovery of how STAU1 binding to inverted repeated 3'UTR Alu elements (IR*Alu*s) competes with nuclear retention mediated by p54^{nrb} binding to 3'UTR IR*Alu*s and also the repression of cytoplasmic translation mediated by protein kinase R (PKR) binding to 3'UTR IR*Alu*s, adds new and unanticipated layers of complexity to the intricate network of post-transcriptional interactions that regulate gene expression and involve RNA sequences that do not encode proteins.

About the Speaker:
Lynne E. Maquat, PhD is the J. Lowell Orbison Endowed Chair and Professor in the Department of Biochemistry & Biophysics at the University of Rochester School of Medicine and Dentistry. She is an internationally recognized expert in the field of RNA biology and the molecular basis of human disease. Dr. Maquat is the Founding Director of the University's Center for RNA Biology. She is an elected member of the US American Academy of Arts & Sciences and the US National Academy of Sciences.

Hosted by : Dr Leah Vardy, Principal Investigator, IMB