The interplay between mRNA translation and nonsense-mediated decay in AUG-proximal nonsense-mutated transcripts

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Nonsense-mediated mRNA decay (NMD) is a surveillance pathway that recognizes and rapidly degrades mRNAs containing premature termination codons (PTC). The unified model for NMD, proposes that the decision of NMD triggering is the outcome of the competition between the cytoplasmatic poly(A)-binding protein 1 (PABPC1) and the NMD effector UPF1 for the termination complex. Consequently, PTCs located far, in a linear sense, from the poly(A) tail and associated PABPC1, in mRNAs containing residual downstream exon junction complexes (EJCs), are expected to elicit NMD. Nevertheless, we have reported that human mRNAs containing PTCs in close proximity to the translation initiation codon (AUG-proximal PTCs) can substantially evade NMD through a mechanism independent of translation re-initiation. In this seminar, I will focus on the mechanistic basis for this NMD resistance and how it involves the step of translation initiation.