BioISI Research Seminar

How mRNA translation can modulate nonsense-mediated decay

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About one third of the gene mutations found in human genetic disorders, including cancer, result in premature translation-termination codons (PTCs) and the rapid degradation of the corresponding mRNAs by nonsense-mediated decay (NMD). However, we have found that human mRNAs with a PTC in close proximity to the translation initiation codon (AUG-proximal PTC) can substantially escape NMD, which contradicts the current models for this mechanism. In fact, our data support a model in which cytoplasmic poly(A)-binding protein 1 (PABPC1) is brought into close proximity with an AUG-proximal PTC via interactions with the translation initiation complexes. This proximity of PABPC1 to the AUG-proximal PTC allows PABPC1 to interact with eukaryotic release factor 3 (eRF3) with a consequent enhancement of the termination reaction and repression of the NMD response. Here, I will provide strong evidence that the eukaryotic initiation factor 3 (eIF3) is involved in delivering eIF4G-associated PABPC1 into the vicinity of the AUG-proximal PTC, and I will dissect the biochemical interactions of the eIF3 subunits in bridging PABPC1/eIF4G complex to the 40S ribosomal subunit.

Host: Margarida Gama-Carvalho (GER-BioISI)

When: March 8 🕐 12h00
Where: Building C1, Room 1.3.33 A
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