REGIONAL CENTRE FOR BIOTECHNOLOGY

Seminar series

Visualizing Transient Structures in A-site RNA of Ribosome

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Abstract

Dynamic changes in RNA structure drive many essential processes in living cells. Studies of RNA dynamics have focused on fluctuations about the dominant ground state at sub-microsecond timescales or large-scale transformations in secondary structure occurring at timescales slower than seconds. By using NMR relaxation dispersion and mutagenesis, we show that non-canonical regions of A-site Ribosomal RNA undergo transient excursions away from the ground state towards short-lived (μs lifetimes) and low populated (2%) excited states that feature local rearrangements in secondary structure and base-pair alignment in regions rich in non-canonical residues. A-site ribosomal RNA contains two highly conserved internal loop adenines A1492 and A1493, which serve to decode the mRNA message by looping out and stabilizing a codon-anticodon mini-helix when it is formed between mRNA and its cognate aa-tRNA. A-site is also known to bind to many antibiotics where drug binds the internal loop, flips the two adenines out and the adenines are forced to bind the codon-anticodon minihelix irrespective of correctness of tRNA. The excited state conformation we proposed is highly conserved and defines a new type of RNA switching that can be integrated into biological circuits. The A-site ES sequesters the A92 and A93 into base-pairs, such that they are no longer available for interacting with incoming tRNAs. Indeed, the C1407U mutation, which stabilizes the A-site ES has previously been shown to significantly increase the stop-codon readthrough and frame shifting, suggesting that the mutation weakens codon-anticodon interactions in the A-site and decreases the fidelity of elongating ribosomes.