Bioinformatics and quantum mechanics analysis of tRNA tertiary interactions

ID - 126

Oliva Romina[1], Cavallo Luigi[2], Tramontano Anna[3]
[1]Dipartimento di Scienze Applicate, Università di Napoli "Parthenope", Napoli
[2]Dipartimento di Chimica, Università di Salerno, Fisciano (SA)
[3]Dipartimento di Scienze Biochimiche 'A. Rossi Fanelli", Università di Roma La Sapienza, Roma

Motivation

Tertiary interactions are crucial in maintaining the tRNA structure and functionality [1,2]. Recently, structural elements resembling tRNAs tertiary motifs have been identified in RNase P, in the ribosome and in RNA viruses genome, suggesting that larger RNAs may use conformation-stabilizing strategies analogous to those found in the small tRNA molecule. Unfortunately a systematic investigation of the stability of tRNA tertiary interactions is still missing.

Methods

We used a combined approach, based on sequence and structure analysis and quantum mechanics calculations, to investigate the stability of the most frequent tRNA tertiary base pairing interactions.

Results

Tertiary base pairing interactions are estimated to contribute roughly 25% of the overall tRNA base pairing interaction energy. Six analyzed posttranslational chemical modifications are shown to have minor effect on the geometry of the tertiary interactions. Modifications that introduce a positive charge strongly stabilize the corresponding tertiary interactions [3]. Our analysis indicates that most of the classical tertiary interactions are held in place mainly by H-bonds between the bases. The G15-C48 Levitt base pair, located at a crucial position in the core of canonical tRNAs, seems to represent an exception to this rule. It assumes indeed a reverse Watson-Crick (RWC) geometry in experimental structures while reaches a stable bifurcated geometry in gas phase simulations. Our bioinformatics analyses revealed that one of the few strong metal binding sites of cytosolic tRNAs is localized on G15 and that half of the available archaeal tRNA sequences have a complex posttranscriptional chemical modification, named archaeosine, at position 15. By further quantum mechanics calculations, the G-C RWC geometry is shown to take advantage of the additional stabilizing effects from metal binding and posttranscriptional chemical modification. The predicted G-C bifurcated geometry, never reported before, was searched for in the PDB and several occurrences in real RNA structures at high/medium resolution, including that of 23S rRNA from Thermus thermophilus, were matched. References:

[1] O'Mahony, D.J., Mims, B.H., Thompson, S., Murgola, E.J. and Atkins, J.F. (1989) Glycine tRNA mutants with normal anticodon loop size cause-1 frameshifting. Proc. Natl Acad. Sci. USA, 86, 7979v7983.
[2] Francisci, S., De Luca, C., Oliva, R., Morea, V., Tramontano, A. and Frontali, L. (2005) Aminoacylation and conformational properties of yeast mitochondrial tRNA mutants with respiratory deficiency. Rna, 11, 914-927.
[3] Oliva, R., Cavallo, L. and Tramontano, A. (2006) Accurate energies of Hydrogen bonded nucleic acid base pairs and triplets in tRNA tertiary interactions. Nucleic Acids Res, 34, 865-879.

Email: romina.oliva@uniparthenope.it