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MOLECULAR DYNAMICS OF HUMAN TYROSYL-tRNA SYNTHETASE ACTIVE CENTER IN THE COMPLEX WITH TYROSYL-ADENYLATE

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Tyrosyl-tRNA synthetase (TyrRS) is a key enzyme of protein biosynthesis, which catalyzes the aminoacylation of $tRNA^{Tyr}$ via tyrosyl-adenylate intermediate formation. Once formed, the aminoacyl-adenylate is stabilized by specific interactions at the enzyme active site.

In this work we have studied the conformational changes in human tyrosyl-tRNA synthetase induced by tyrosyl-adenylate formation using computational MD simulations.

Three-dimensional structure of the complex of full-length HsTyrRS with tyrosyl-adenylate and K^+ ion was constructed in Modeller 9.7 using structure templates from RCSB PDB. The 100 ns MD simulations were performed in grid environment using the services of MolDynGrid virtual laboratory (http://moldyngrid.org/) and computed using NAMD 2.10 software in Charmm27 force field. The Distributed Analyzer Script was used for analytical tools automation (Savytskyi et al, 2011).

Root mean square deviation (RMSD) analysis revealed relaxation period after 20 ns of MD simulation time. It was found that tyrosyl-adenylate bound at the active site via hydrogen bonds interactions with more than 10% of time: Thr42 – 76.08%, Asp173 – 76.08%, Tyr39 – 71.24%, Trp40 – 46.14%, Gln170 – 42.46%, Ala43 – 16.85%, Asn212 – 16.33% and Val215 – 13.49%. The lowest values (~ 0.06 nm) of root mean square fluctuation (RMSF) in active site were observed for the catalytic KMSSS loop in monomer A in the complex with substrate, while in monomer B in the absence of substrate they were much higher (~ 0.2 nm). The α-helix and β-turn formations in Asp343 – Asp369 region were revealed for 5-90 ns time interval at the interdomain linker.

The conformational changes both at the active site and at the interdomain linker of human tyrosyl-tRNA synthetase in the complex with tyrosyl-adenylate were observed during MD simulations. The active site of monomer A in the complex revealed more compact conformation with lower values of RMSF in comparison with free monomer B. Some local conformational changes, i.e. antiparallel β-sheet and β-turn formations have been observed at the linker.

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