ANALYSIS OF THE MOLECULAR STRUCTURE OF hY4 AND chY4 RNAs FROM HUMAN AND CHINESE HAMSTER BY MOLECULAR DYNAMIC SIMULATIONS.

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The Y-RNAs are a class of non-coding RNAs recognized as important regulators of biological processes such as DNA replication licensing. There are four genes encoding Y-RNAs in humans (hY-RNAs) and Chinese hamster (chY-RNAs). The four hY-RNAs genes are expressed in human cells, but only the chY1 and chY3 RNAs genes are expressed in GMA32 cells. The 2D representations show that chY4-RNA has an unusual structure, with the functional sequence GUG-CAC located in a rod between two loops, very different from that observed in hY4-RNA, which has been functionally characterized. However, in vitro expression experiments show that all four chY-RNAs were able to initiate DNA replication in human late G1 phase nuclei. The aim of this work was to evaluate the stability of the 3D structure of the hY4 and chY4-RNAs through molecular dynamics to seek evidence of their biological function. The 3D structures were generated by RNAComposer, and then, minimized and used in molecular dynamics simulations for 10 ns, 300K, 1atm in a periodic box containing 0.1M NaCl, through Gromacs-4.5.5 using AMBER99SB force field. The analysis of the RMSD from C1’ showed that systems reach equilibrium after 3 ns of dynamic and, the 10ns time was more than sufficient to obtain a picture of the system in balance. The analysis of the \( r_g \) evidences that the structures maintained their original folding, indicating structural stability. The RMSF of all C1’ indicates that functional region GUG-CAC stay completely stable along the simulation exhibiting low fluctuation and a constant number of hydrogen bonds between them. These results from simulations associated with in vitro functional studies, indicate that the Y4-RNAs analyzed here are stable structures and fully functional. So the fact that chY4-RNA not be expressed in vivo, should be related to some physiological condition still unknown or some epigenetic control.

Key Words: Y RNAs, molecular dynamics, DNA replication.

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