MOLECULAR MODELING AND DYNAMICS SIMULATIONS OF ANG PROTEIN SIGNAL PEPTIDE IN AMYOTROPHIC LATERAL SCLEROSIS

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**Introduction and Objectives:** The role of the protein angiogenin (ANG) in angiogenesis is well-established in the literature. Recent studies have found an association between mutations in the signal peptide of ANG and the development of familial amyotrophic lateral sclerosis (ALS). ALS is a progressive, lethal, neurodegenerative disorder, characterized by the degeneration of motor neurons. This research aims to investigate, using molecular modeling and dynamics simulation (MD) approach, the conformational changes in the ANG mutant protein structure (M1I, F12S, F12L, G15D, P20S, P21Q, and P21S). **Material and Methods.** Structural theoretical models were created for the wild type protein through ab initio (I-Tasser, QUARK and Rosetta) modeling. The structure of the ANG protein was obtained from I-Tasser modeling. To build the mutant structures, we performed in silico mutagenesis. These structures were energetically optimized by GROMACS package 4.5.5 using an AMBER 99S force field. During energy minimization, both native and mutant structures were solvated in an octahedral box with simple point charge (SPC) water molecules. Initially, the solvent molecules were relaxed, and all of the solute atoms were harmonically restrained to their original positions. Then, the whole molecular system was subjected to energy minimization. **Results and conclusions:** The theoretical structures were created, and the I-Tasser model was used for the molecular dynamics simulation, which showed conformational alterations in the mutants of the signal peptide ANG protein. Due to the mutations, ANG protein might alter the structure, subcellular location, and functional behavior of protein and play a major role in inducing ALS. **Acknowledgments:** CAPES-DAAD, CNPq, FAPERJ, UNIRIO. **Key Words:** ANG, Database, Molecular Dynamics.