Molecular Dynamics of Superoxide Dismutase 3

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Introduction: Superoxide Dismutase 3 (SOD3) is the representative of its enzyme family, which is involved in the response to extracellular oxidative stress. Three natural variants of SOD3 have been described: A58T, A91T and R231G, which are related to the following diseases: Glioma, Myocardial Infarction, Coronary Artery Disease and Chronic Obstructive Pulmonary Disease. **Objectives:** This work aims to analyze the implications of amino acid variation on protein structural and functional behavior. **Materials and methods:** In this study, a complete SOD3 protein model was generated using the Rosetta algorithm and was evaluated using the following validation servers: Qmean, Procheck, ProSa and Verify 3D. Based on the validated model, the mutants were generated with the Visual Molecular Dynamics (VMD) mutagenesis tool. The wild type and mutants were submitted to a GROMACS 5.0.7 dynamics simulation developed using the Amber99SB-ILDN force field and TIP3P water cubic box with dimensions of 52 angstroms. The dynamics preparation consisted of the addition of water, followed by neutralization and minimization of the system. The NVT ensemble and the NPT ensemble were realized during 100 picoseconds, using a temperature of 300K and pressure of 1 atm. The molecular dynamics simulation lasted 100 nanoseconds, and the results were graphically plotted and analyzed. **Results and discussion:** The model was considered reliable based on the validation servers cited. The dynamics study highlighted significant differences between the wild type and mutants in the following aspects: Root Mean Square Deviation (RMSD), Root Mean Square Fluctuation (RMSF), Radius of Gyration, Solvent Accessible Surface Area and Hydrogen Bonds, pointing to functional and structural alterations. **Conclusions:** These behavior fluctuations in the dynamics may explain the involvement of the SOD3 mutants in disease.

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