Modeling and Molecular Dynamics of the CD20 Receptor, Molecular Target of the Monoclonal Antibody Rituximab

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Introduction: The CD20 receptor has 297 amino acids arranged in four transmembrane helices and five linear domains. Its biological function remains uncertain, but some evidences indicate that it acts as a calcium ion channel. The molecular modeling and the Molecular Dynamics (MD) simulation are methods to provide structural and energy information of antigen-antibody interaction and to propose modifications to the antibody, to improve its affinity and specificity for the antigen. **Objective:** Obtain a stable CD20 receptor model in dimyristoilphosphatidylcholine (DMPC) membrane. **Material and Methods:** The helices of CD20 were drawn with Swiss-PdbViewer software, then connected to the five linear domains and immersed in interface of n-hexane/water, in order to simulate the internal environment of the biological membrane, hydrophobic, and the external environment, hydrophilic. CD20 in n-hexane/water was submitted to MD simulation. Then, CD20 in DMPC membrane was submitted to 100 ns of MD simulation using GROMOS53a6 force field. Structural stability and inter- and intramolecular interactions of the loop of CD20 that binds to Rituximab and the epitope were evaluated. **Results and Discussion:** The structure of the loop stabilizes after 27 ns of simulation, with Root mean square deviation (RMSD) of 0,09 nm, in reference to its first structure of simulation; and the structure of epitope stabilizes after 25 ns of simulation, with RMSD of 0,02 nm. The potential curve of inter- and intramolecular interactions corroborates the RMSD results, confirming that the loop of CD20 that binds to Rituximab and the epitope have the structure well conserved during the MD simulation. **Conclusions:** The low values of RMSD imply that a stable model of CD20 in DMPC membrane was obtained, corroborating the function of CD20 and enabling the study of antigen-antibody interaction with Rituximab. Therefore, future prospects are to obtain, from a Rituximab miniantibody, variants with higher affinity and specificity.

Keywords: CD20; Molecular Modeling; Molecular Dynamics; Structural stability

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