Modeling of a Single-Chain Variable Fragment and Analysis of ScFv-Epitope Interaction: a Molecular Dynamics Simulation Study

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Introduction: Rituximab is a chimerical monoclonal antibody that targets a cellular surface protein CD20. CD20 can be found in lymphomas that affects lymphocytes B. Thus, it suggests the importance of studies with this immunizer, which is already used against diseases, such as lymphomas and leukemia. Antibody single-chain variable fragments (scFvs) are fragments of a monoclonal antibody containing its variable regions of light and heavy chains (VL, VH), and a short linker peptide linking these chains. They maintain affinity and specificity for antigens as the complementarity-determining regions (CDRs) are preserved. **Objective:** To model a scFv and analyze its interaction with CD20 loop containing the antibody recognition site, the epitope. **Materials and Methods:** Crystallographic data of Rituximab's Fab portion (code PDB: 2OSL) were utilized for the scFv assemble. VH and VL were connected by the residues sequence GGGGSGGGGSGGGGS (linker). Gromacs 5.0.2 software was utilized to perform molecular dynamics simulations and study the scFv-CD20 loop interaction in water, temperature 37ºC. **Results and Discussion:** Analysis of the root mean square deviation (RMSD) of scFv configurations, during simulation in water, shows that the equilibrium structure is achieved at 40ns (RMSD ~0.2nm). VH domain and linker also become stable around 40ns and both RMSD were ~0.3nm. VL domain achieves stability after 60ns (RMSD ~0.2nm). In scFv-CD20 loop interaction studies, the scFv become stable at 40ns (RMSD ~0.3nm) and the epitope interacts stably directly with the CDR H3 of the VH (RMSD ~0.6nm). The interaction takes place both by carbonyl and amine groups of the main chain as by side chains. Attractive interactions are also observed between the CD20 loop, and CDRs H1 and H2. **Conclusion:** Evaluation of the scFv-CD20 loop interaction indicated some scFv residues interact more attractively than others, and some interact repulsively, making it possible to suggest point mutation enhancing affinity and specificity.

Keywords: scFv, Rituximab, Molecular Dynamics
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