Interaction between a CD52 Antigen's Mimotope and Campath-1H Antibody's scFv: a Study by Molecular Dynamics Simulation

Frota, N.F.[1,2]; Guimarães, A.V.F.[1,2]; Rebouças, A.S.[1,2]; Lourenzoni, M.R.[1]

[1]Departamento de Modelagem, Simulação e Evolução, in silico, de Biomoléculas, Fundação Oswaldo Cruz Ceará, Ceará, Brazil; [2]Departamento de Bioquímica e Biologia Molecular, Universidade Federal do Ceará, Ceará, Brazil

Introduction: Antibodies are glycoproteins that bind specifically to antigens. A strategy to better understand how this binding works is the antibody engineering, obtaining fragments of antibodies containing their variable domains (VH and VL) responsible for recognize antigens and proposing mutations to obtain molecules with higher specificity and affinity to antigens. The regions of the variable domains responsible for binding to the antigens are called by complementarity determining regions (CDRs). **Objectives:** To model the single chain variable fragment (scFv) of the Campath-1H, submit it to Molecular Dynamics (MD) simulation and analyze its structural stability in water and interaction with a synthetic fragment (mimotope). **Materials and Methods:** The Campath-1H`s scFv was modeled. Crystallographic data (code PDB: 1CE1) containing its VH and VL sequences was utilized and the linker that connects these two domains was drawn (GGGGSGGGGSGGGGS). Using the Gromacs 5.0.2 package, this model was submitted to MD in two systems: one with water and ions and other containing also a mimotope (GTSSPSAD). **Results and Discussion:** The root mean square deviation (RMSD) shows that the scFv achieves stability in water after 50 ns, the VH after 15 ns and the VL after 20 ns (RMSDs 0,55, 0,22 and 0,25 nm, respectively). Interacting with the mimotope, the scFv and VH stabilize after 100 ns, RMSDs around 0,30 and 0,25 nm, respectively. The VL structure stabilizes (RMSD 0,22 nm) after 50 ns. The linker moves less when the scFv is bound to the mimotope, due to the large amount of glycine. The mimotope profile oscillates around 0,34 nm after 150 ns. Its binding site is in the VH, between the CDR1 and CDR2. **Conclusions:** The simulation time was enough to the scFv achieves stability and the binding site to the mimotope was identified, which allows to perform site-directed mutations to enhance Campath-1H's affinity and specificity.

Key words: scFv, Campath-1H, Molecular Dynamics
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