OTR11 - Understanding the interaction effects between a monoclonal antibody and HBsAg by molecular dynamics aiming the affinity mAb improvement

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Introduction:

Currently, hepatitis B virus (HBV) infection is one of the major health problems worldwide and the most serious type of viral hepatitis. The diagnosis of the infection is made by detecting the hepatitis B surface antigen (HBsAg) by the use of monoclonal antibodies (mAbs). In this work, we report the investigation of the dynamical features of a complex formed between an Fv fragment developed by the use of hybridoma technology and HBsAg. After evaluation of the binding mode, the molecular dynamics (MD) of the complex was performed, in order to analyze the maintenance of polar contacts, hydrogen bonds, salt bridges and other structural alterations in the region close to the contact interface. The *Homology Modeling* methodology was used to build the 3D model of Fv, followed by Docking with HbsAg and MD of the formed complex.

Objetcive:

Computational structural and molecular characterization of mAb and HBsAg complex aiming at the understanding of the dynamical behavior in order to establish a structure-activity correlation and to improve the affinity of the mAb.

Methodology:

In order to build the structure of the mAb, the Modeller v.9.14 software was used. The structure of HBsAg was obtained using the Robetta server. The docking with HBsAg was performed with Haddock software. MD simulations was made with GROMACS software.

Results:

In order to understand how the conformational and electrostatic changes in the binding site can interfere in the formation of this complex, a molecular dynamics of 25 ns was performed. The RMSD, ranging from 0.3 to 0.7 A, showed

that both proteins are stable along the simulation. Interestingly, a loop from HBsAg contact directly the CDR3 from both light and heavy chains, as well as the CDR2 from light chain stabilize the region close to this same loop. An average number of 7 hydrogen bonds was found in the interface between mAb and HBsAg. The total surface area of the complex is 11742 Å2 , while only 843 Å2 encompass the area of the interface. The region between the CDR3 from heavy and light chains is predominantly negative, while the loop from HBsAg is almost completely positive.

Conclusion:

The analysis of molecular dynamics showed the structural features responsible for the interaction in the complex mAb-HBsAg. Particularly, the electrostatic profile seems to have an important role in the recognition between both, mainly due to the recognition loop found in HBsAg. It is also remarkable the evidence of a strong stability of CDR3 from both light and heavy chains when bound to the antigen. Based on these results, site direct mutagenesis will be performed in order to improve the affinity between the mAb and HBsAg surface antigen.

Keywords: Monoclonal antibody, HBsAg, molecular dynamics