Fragment molecular orbital and MD calculation study: Interaction analysis of HIV-1 antibody 2G12 and glycan Ligand

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I. Introduction

In HIV-1 infection, human antibody 2G12 is capable of recognizing the high-mannose glycans on the HIV-1 surface glycoprotein, gp120 [1]. To investigate the ligand binding mechanisms of antibody 2G12 with glycans aiming for the contribution to the medications, we carried out classical molecular dynamics (MD) simulations and ab initio fragment molecular orbital (FMO) calculations [2] on the antibody 2G12 complex with its high-mannose ligand ($Man_9GlcNAc_2$).

II. Method

The X-ray crystal structure of the Fab region of the antibody 2G12 with the ligand $Man_9GlcNAc_2$ was utilized as the calculation model (Fig. 1, PDB ID 1OP5 [1]). The 2G12-ligand complex extracted from classical MD simulations at several time steps and evaluated the glycan-antibody affinities with MP2/6-31G level of FMO calculations.

III. Results and discussion

Our calculation results showed that monosaccharide Man D1 in the high-mannose ligand was the most important moiety of the ligand binding to the antibody 2G12, which supported the experimental results. In addition to Man D1, significant roles of Man D4 and D4' in the ligand binding was theoretically indicated (Fig.2). We concluded that the high binding affinity of oligosaccharide $Man_9GlcNAc_2$ was dominated by terminal monosaccharide Man D1. Branched structure of Man 4 and Man 4' could provide more flexibility to the ligand binding to the Fab 2G12 [3].

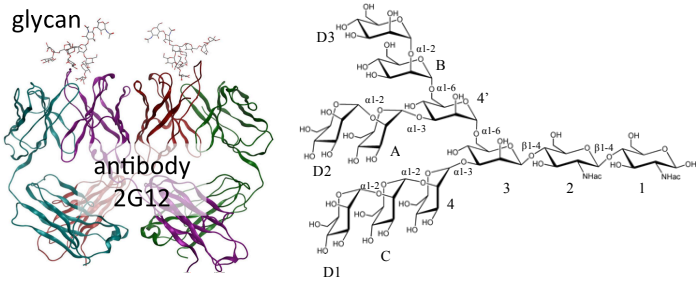

Fig.1 The crystal structure of antibody 2G12 and the ligand ($Man_9GlcNAc_2$) (PDB ID :1OP5 [1])

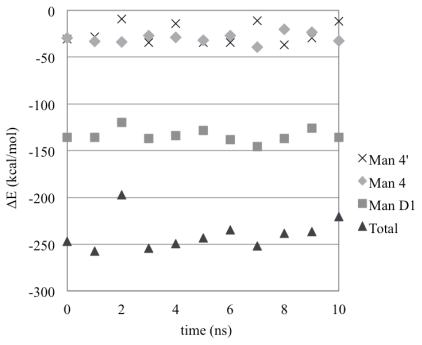

Fig.2 Total interaction energy of the antibody with $Man_9GlcNAc_2$ and the ligand moieties (Man D1, Man 4, and Man4') (kcal/mol) (MP2/6-31G*)

[1] D. A. Calarese *et al*. *Science* 2003, **300**, 2065.
[2] D. G. Fedorov, K. Kitaura, *J. Phys. Chem. A*, 2007, **111**, 6904.
[3] Y. Koyama et al. Chem. Phys. Lett. 2013, **578**, 144.