Molecular dynamics study of the structural stability of CDR-H3 of anti-HIV neutralizing antibody PG16

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PG16 is a broadly neutralizing antibody to HIV. A crystal structure of the antigen-binding fragment (Fab) of PG16 shows that the long 28-residue complementarity determining region (CDR) H3, which is involved in antigen recognition, forms a unique subdomain referred to as “hammerhead” [1]. Although the structural diversity of CDR-H3s is well known [2], a large conformational difference is not observed in the crystal structures of the CDR-H3 of PG16 in the antigen-bound and unbound states (Cα-RMSD: 0.44Å) [1].

In this study, to elucidate the structural stability of the CDR-H3 of antibody PG16 the structural fluctuation was examined by using the molecular dynamics simulations. We used the crystal structure of antigen bound and unbound states (PDB ID:4DQO and 3MUG) as initial structure.

Our simulations showed that the structural stability of the CDR-H3 of PG16 was attributed to many hydrogen bonds inside and outside of the CDR-H3. Among them, we revealed that the hydrogen bond between Pro99 and Tyr100Q plays an important role in supporting the structure.

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