

Poster Presentations

[MS5-P32] Structure insight of anti-HIV actinohivin in complex with (1,2)mannotriose

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For invasion of human immunodeficiency virus (HIV) into human cell, high mannose-type glycan (HMTG) which covers the gp120 glycoprotein protruded from HIV surface is required to contact with human CD4 protein at the beginning. A new anti-HIV lectin actinohivin (AH) can bind to HMTG and disturb HIV approaching. Therefore, AH has been expected to be a good candidate for investigation as an effective microbicide to help prevent HIV transmission. In order to obtain structural insight of AH which specifically binds to the target D1 chain of HMTG, we performed X-ray analysis of AH in complex with (1,2)mannotriose (MT) at 1.40 Å resolution. In the AH-MT complex, three MT molecules are separately bound in the three pockets of an AH molecule, which is composed of the three structural modules to exhibit a molecular three-fold symmetry, as shown [1]. In each pocket, the two mannose residues of the triose are definitely

identified. However, the electron density for the remaining residue appear at the both sides (0 and 3rd) of the two residues at 1st and 2nd (see Fig. 1). This suggests that the triose is disordered at 0-1-2 sites and 1-2-3 sites in binding to AH, their occupancies being estimated to be 0.7 and 0.3. In the major sites at 1st and 2nd, the two residues held in a bracket-shape conformation are trapped by four hydrogen bonds. For the principal binding (see Fig. 2), the Asp91 carboxyl group forms a double hydrogen bond with the two hydroxyl groups attached to C³ and C⁴. Furthermore, the O³ and O⁴ hydroxyl atoms accept additional hydrogen bonds from NH₂ group of Asn104 and OH group of Tyr99, respectively. In addition, the Tyr108 side chain wedges between the two mannose residues to contact the C⁵ and C⁶ atoms through hydrophobic interaction. As compared with the previously solved AH-MB (MB:mannobiose) complexes [2,3], the binding geometry of the two mannose residues of MT are quite the same as that of MB. It shows the unique feature of (1,2)linked MB to be bound to AH. To identify the binding sites for the end residue of the D1 branch, it is necessary to obtain crystals with no disorder or new crystals of AH in complex with Man9 (mannanose of HMTG).

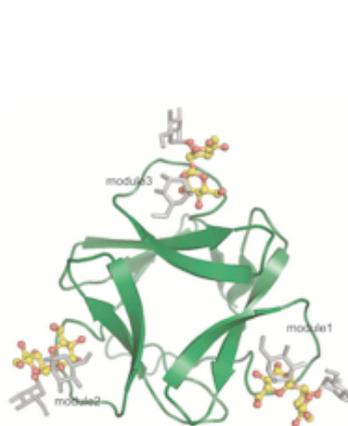


Fig. 1. AH in complex with three MT molecules. The disordered mannose residues are colored in gray.

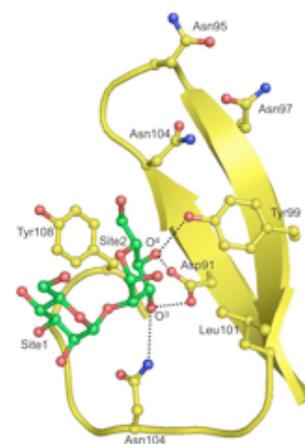


Fig. 2. Two mannose residues of MT accommodated in a binding pocket.

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