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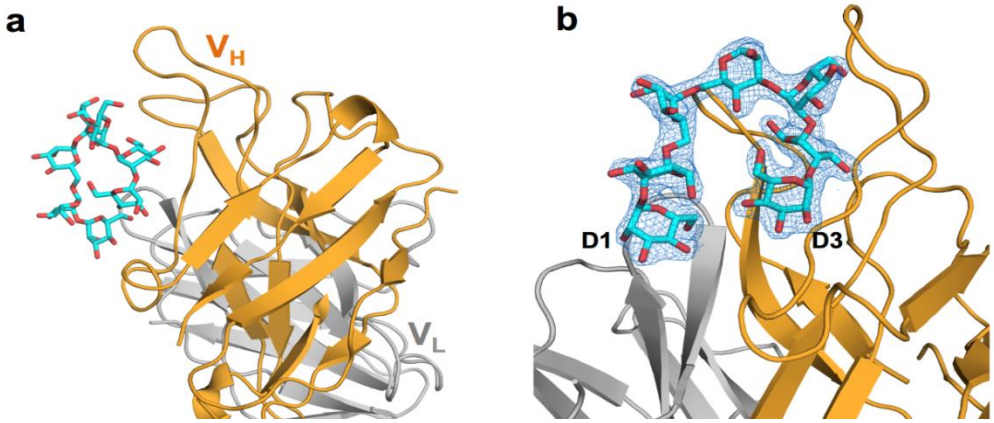
Synthetic mimetics induce HIV neutralising antibodies

Attempts to use the densely packed carbohydrate shield of the HIV envelope for the development of vaccines have met with very limited success over the last 30 years. The main reason is seen in the structural resemblance of the viral sugar coat with the mammalian glycans thereby preventing immune activation.

A recent proof-of-concept study shows how to overcome this immune tolerance by subtle variations of the basic oligomannosidic structures and thus opens a new perspective in the field of vaccine development against HIV. Based on the structure of a cell wall component from a plant-pathogenic bacterium, the Kosma lab in Vienna embarked on the synthesis of several mimetics followed by conversion into glycoconjugates which were used to generate specific anti-HIV antibodies. In a joint collaboration with research groups from Canada and the US, the authors could show that the immune sera had neutralizing activity against 5 out of 7 HIV strains. In addition, the molecular details of the binding motifs of a lead compound complexed to a broadly neutralizing antibody of the PGT family were determined.



X-ray structure of a mannoheptaoside complexed to the neutralising antibody PGT 128.

Pantophlet R, Trattnig N, Murrell S, Lu N, Chau D, Rempel C, Wilson I A, Kosma P. Bacterially derived synthetic mimetics of mammalian oligomannose prime antibody responses that neutralize HIV infectivity. ***Nature Comm***. 2017 (doi: 10.1038/s41467-017-01640-y)