

Structural characterization of neutralizing antibody lineages from an HIV-infected donor

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HIV broadly neutralizing antibody (bNAb) responses develop in chronic infection in only approximately 25% of HIV-1-infected individuals. Understanding how bNAbs develop has been a major focus in HIV vaccine research in recent years. The aim of this study is to solve the structures of co-evolving strain-specific and bNAbs from an HIV-infected donor, CAP314. We have recently isolated three antibody lineages from this donor. The first lineage is an N332/glycan-dependent lineage which matured from being strain-specific to broadly neutralizing through the course of infection. Comparison of early and late antibodies by X-ray crystallography techniques may thus provide insight into the differences between the binding of broadly neutralizing and strain-specific antibodies within a single lineage. Preliminary data suggest the second lineage of interest can be classified as a “helper” lineage which aided in the development of the broad N332/glycan-dependent lineage. Therefore, using X-ray crystallography to obtain the structures of these antibodies will aid in understanding how this lineage shaped viral populations and drove the development of neutralization breadth. The third lineage identified from this participant recognizes an undefined epitope consisting of elements of both the N332/glycan and the CD4 binding site. Therefore, solving the structure of this antibody by X-ray crystallography will provide insight into the binding of a neutralizing antibody lineage targeting a novel epitope. Collectively, structural data for three antibody lineages from a single HIV-infected individual represents a unique opportunity to investigate the underlying mechanisms used by the humoral immune response in responding to swarms of HIV variants.

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