

Structural basis for evolution of HIV-1 neutralization breadth in the DH270 lineage antibodies

In this project we are interested in investigating the structural basis for the development of HIV-1 neutralization efficacy in an antibody lineage isolated from an HIV-1-infected individual. We have determined structures at 4.1 and 4.4 Å, respectively of two antibodies -the unmutated common ancestor, which is an early progenitor with very limited neutralization breadth, and a mature antibody.

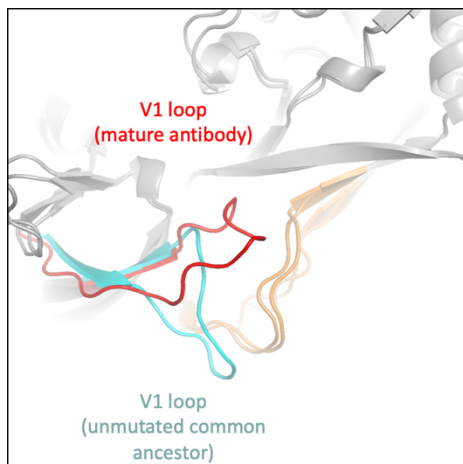
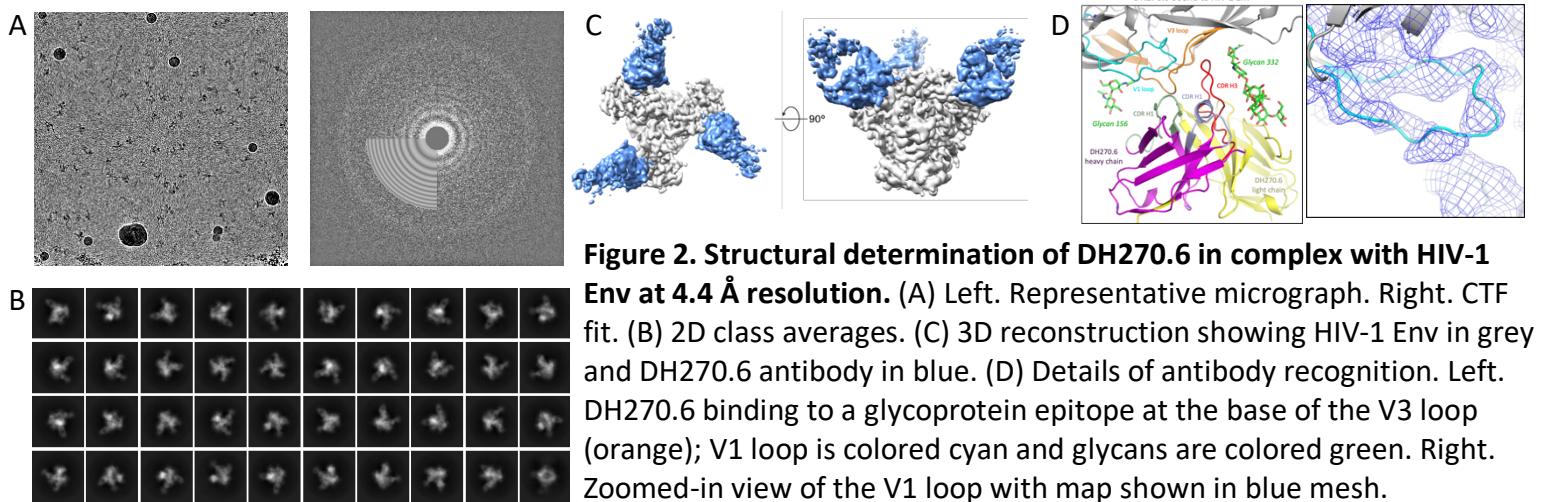
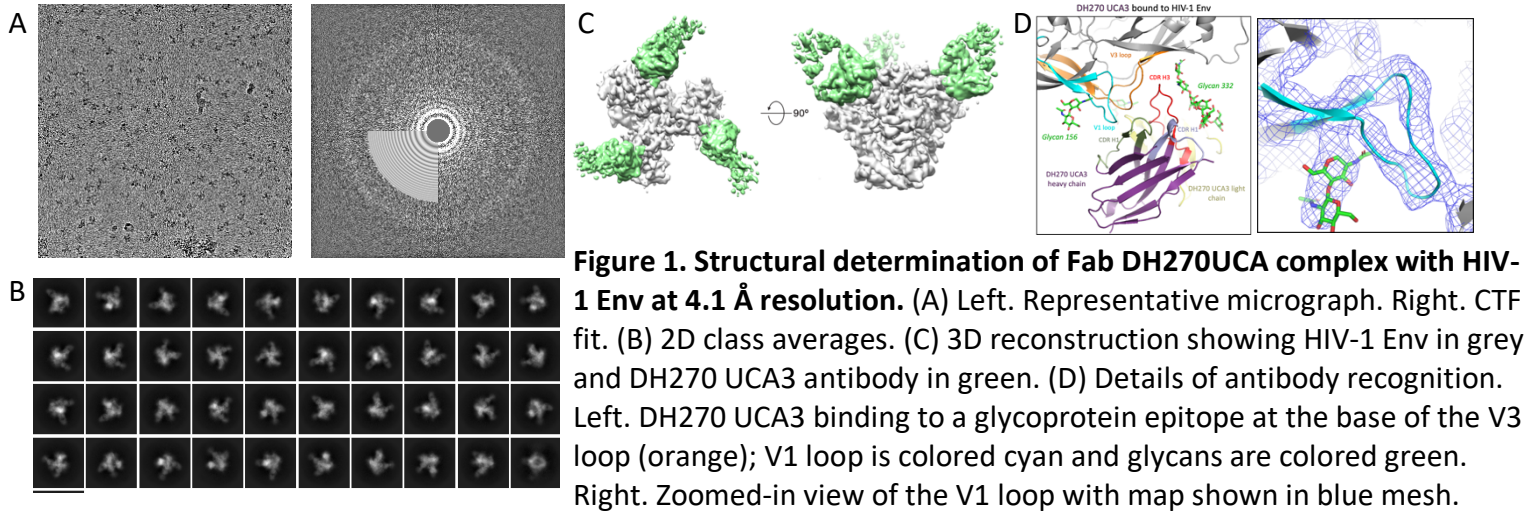


Figure 3. Structural changes in the HIV-1 Env V1 loop induced by binding of DH270 lineage antibodies. The HIV-1 Env variable region 1 (V1) loop is part of the epitope of the DH270-like antibodies. A large movement of the bound V1 loop was observed between the unmutated common ancestor (early progenitor) (cyan V1 loop) and the mature antibody (red V1 loop). The bound antibodies have been removed from these images for clarity.

We hypothesize that accommodation of the HIV-1 Env V1 loop is critical for the maturation of the DH270 antibody lineage.

The **goal** of this study is to structurally characterize the HIV-1 Env binding of 10 intermediates along the DH270-lineage maturation pathway, to elucidate the structural basis for development of neutralization efficacy in this lineage.