

CRYOEM STRUCTURE OF HIV-1 CAPSID ASSEMBLY REVEALS NOVEL INTERSUBUNIT INTERFACES CRITICAL FOR HIV-1 CAPSID FUNCTION

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The type 1 human immunodeficiency virus (HIV-1) can form a conical capsid that surround RNA genome, which is crucial for infectivity. The capsid is composed of hexameric viral capsid protein (CA) and performs essential functions at early stages of viral replication. Previous structural analysis from two- and three-dimensional hexagonal arrays provided a molecular model of the CA hexamer and revealed three stabilizing interfaces in the capsid lattice. Here, we present a cryoEM density map of the HIV-1 CA tubular assembly at 16 Å resolution and a high resolution NMR structure of the CA C-terminal domain (CTD) dimer. The atomic model of the CTD solution dimer agrees well with the EM density map, suggesting that the dimer interface is retained in the assembled capsid. In addition to three previously characterized intermolecular interfaces, we further identified an additional, novel CTD-CTD interface at the local three-fold axis. This interface is primarily made of three pairs of helices 10 and 11, with each of the helix in the pair contributed from neighboring hexamers. The intersubunit interactions in this interface play a critical role in capsid stability, as evident by the available mutational data and new structural based mutational and cross-linking data. While the CTD dimer interfaces in tubular assemblies vary slightly to accommodate slightly different environments for each subunit, the combined action of two distinct CTD-CTD interfaces assures a flexible, but controlled asymmetric HIV capsid assembly from hexameric lattice network.