HIV-1 Gp120 and the V3 Loop

Human Immunodeficiency Virus 1 (HIV-1) is arguably one of the most deeply studied and known biological entities: since its first discovery in 1986, hundreds of researchers have devoted years of studies to the features of the virus and of its relationship with the infected cells. HIV-1 is also one of the relatively simplest life forms: it is only about 120 nm small, it has a genome of 8.2 kb, containing a dozen genes, all of which have been characterized in some detail.

Beside the RNA genome (of which every virus carries two copies), viral particles are composed of several structural proteins that make up the core and the capside, and of an envelope derived from the cellular membrane. The surface is therefore a typical eukaryotic double layered lipid membrane in which are embedded and protruding trimeric structures, called spikes, composed of 6 viral proteins: 3 gp41 (trans-membrane) and 3 gp120. The viral surface also contains a number of cell-derived proteins, peptides and sugars.

When a mature particle is released from producing cell, it travels in the extracellular fluid until it meets with a target cell. The surface protein gp120 makes the first contact with the target, by binding to the major cellular receptor CD4. This interaction triggers a conformational change that exposes a formerly hidden site, able to engage in a second interaction with one of two cellular co-receptors, either CCR5 or CXCR4. Once the virus if firmly attached via multiple interactions between viral envelope and cellular receptors, subsequent steps occur that eventually lead to endocytosis of the virus and release of its infectious material into the cytoplasm. The following events of retro-transcription, maturation of the pre-integration complex, nuclear entry and genomic integration will, if successfully completed, lead to productive cellular infection.

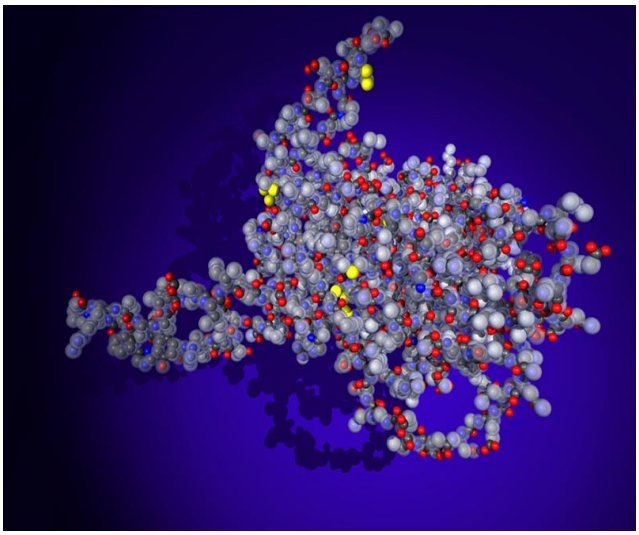

Image of the entire Gp120 strucutre, as derived from pdb file 2b4c.

Gp120 structure has been solved in different conformations either unbound or bound to CD4. Its interaction with the receptor CD4 triggers a major movement of parts of the protein, in particular the V3 loop. V3 loop is implicated in the selection of co-receptor and in the subsequent step of co-receptor binding.

Twenty conformers of V3, derived from NMR studies and available from the public database were used for our simulation using the 3D animation program Maya (Autodesk).