Neuraminidase (NA) is one of the two glycoproteins on the influenza virus membrane. Its role is to enhance viral mobility via hydrolysis of the glycosidic linkage between a terminal sialic acid residue and the adjacent carbohydrate moiety on the host receptor. We have determined the crystal structure of native type B neuraminidase and the type B neuraminidase-sialic acid complex from several type B influenza strains. The native crystal type B neuraminidase structure is similar to the six β-sheet propeller fold found in type A neuraminidase. The sialic acid complex crystal structure indicates that the bound sialic acid is in the half-chair conformation, with planar density around C2, and no density for OH2. The complex structure supports the hypothesis that the enzymatic hydrolysis of terminal sialic acid by neuraminidase may be catalyzed by formation of a stabilized transition state species, not by nucleophilic attack from a proton donor. Further structural studies of type B neuraminidase complexed to several Abbott compounds showing neuraminidase inhibition activities are ongoing.

MS-03.02.06

CD4-HIV RECEPTOR by Jia-huai Wang*, You-wei Yan, P.J.Garrett,Jin-huan Liu and Stephen C. Harrison, Departmentof Biochemistry and Molecular Biology, Harvard University, Howard Hughs Medical Institute

The CD4 transmembrane glycoprotein on the surface of T-cell is a critical component in the cellular immune responce machinary. Ironically, human CD4 has become better known, because it is the receptor for HIV. We have been carrying out structural studies of various fragments by x-ray crystallographic method. The structure of N-terminal two domain fragment (CD4 (1-182) fragment) has been determined and refined to 2.2A resolution.

The CD4(1-182) contains two abutting immunoglobulin-like domains. Domain 1(D1) bears typical Ig V-type character, whereas domain 2(D2) is an interesting variation. It has an intrasheet disulfide bond instead of a usual intersheet bond across β-barrel. The relative packing of two sheet also shifts compared to the normal Ig fold. Between two domains there is an extensive hydrophobic interface. The last β-strand of D1 extends uninterruptedly to form the first strand of the D2. Together it makes a distict rigid concatenated domain connection. It is belived that this kind of domain organization should exists in other cell surface proteins as well.

The interaction between CD4 and HIV envelop protein gp120 is restricted to the very N-terminal domain of CD4 molecule. Key components of the binding site include :(a)The unique protrusion of C'-C" corner (in particular the Phe43), supported by the bulky sidechain of Trp62. This Trp62 is situated in the middle of an α-helix, which is a insertion in CD4 as opposed to any other Ig superfamily members. (b)A patch of positively charged residues surrounding Phe43. The MHC molecule binding site is, on the other hand, much more extended, involving both D1 and D2. We propose that the zigzagged surface of the first two domains of CD4 is complementary to a notched surface of class II MHC molecule, formed by two domains in its β-chain.

MS-03.02.07 THE STRUCTURE OF A TYPE C FOOT-AND-MOUTH DISEASE VIRUS AT 3.5Å. R. Abu-Ghazaleh‡, W. Blakemore‡, S. Curry‡, E. Domingo§, E. Fry†, T. Jackson‡, A. King‡, S. Lea†, M. Mateu§, J. Newman‡ and D. Stuart*†. †Laboratory of Molecular Biophysics, Oxford University, U.K. ‡AFRC Institute for Animal Health, Pirbright, Woking, U.K. §Centro de Biología Molecular, Madrid, Spain.

We have determined the structure of a serotype C (isolate C-S8c1) foot-and-mouth disease virus (FMDV) at 3.5Å resolution by X-ray crystallography. The overall structure of the virus is seen to be similar to that previously determined for O_1BFS (Acharya, R. *et al.* (1989), *Nature (London)*, **337**, 709-716.). There are significant changes in the structure of some antigenically important external loops and in some of the less well ordered regions involved in protomer-protomer contacts. The structure aids interpretation of a mass of antigenic results. New features seen in the C-S8c1 structure include visualisation of the N-terminal residues of VP2 and extra density around the interior of the 5-fold axes of the virion which may be interpreted (by comparison with the structure of Polio virus; Chow, M. *et al.* (1987), *Nature (London)*, **327**, 482-486.) as the myristate moiety bound to the N-terminus of VP4.

The GH loop of VP1 (the 'FMDV loop') is of major interest as the dominant antigenic site and location of the putative receptor binding residues. The flexibility of this loop is regulated by a disulphide bond in type O_1 virus (the loop becomes ordered, and therefore visible crystallographically on reduction of the disulphide; Logan, D. *et al.* (1993), *Nature (London)*, In press.). Despite lacking the disulphide this loop is disordered in the C virus (and also in two serotype A FMDVs we have studied) suggesting flexibility of the loop is advantageous to the virus. Possible rôles for this flexibility will be discussed.

PS-03.02.08 DECONVOLUTION OF DATA FROM INTIMATELY TWINNED CRYSTALS OF FMDV. By S. M. Lea* and D. I. Stuart. Laboratory of Molecular Biophysics, Oxford University, U.K.

Processing of FMDV data in space group I23 requires division of the data into two subsets (Fry, E., Acharya, A. and Stuart, D. (1993). *Acta Cryst.* A**49**, 45-55.) corresponding to the two ways of indexing the I23 lattice which are geometrically indistinguishable (i.e. placing the virion on a specific 3-fold axis related by a 90° rotation about a particle 2-fold). Within a crystal particles are all in the same relative orientation but the choice is random between crystals. Each crystal may therefore be indexed as h,k,l or k,h,l. By comparison to a reference set the data can be divided into two streams and processed separately until (following postrefinement) the indices of one of the streams are modified and the 2 data sets merged. Data collected from a mAb-escape derived FMDV mutant (G67) appeared to crystallize isomorphously with the parent virus (O_1K) (Curry, S. *et al.* (1993), *J. Mol. Biol.* **228**, 1263-1268); I23, a=345Å, however data from these crystals correlated poorly with the reference set, the correlation coefficient for either indexing scheme against the parent virus data being less than 0.5. This suggested extra 4-fold symmetry which is geometrically impossible for an icosahedral virus. However, statistically the data appeared to belong to point group 432. Assuming that in each crystal all viral 2-folds are arranged randomly with respect to all other 2-folds with the ratio of the two orientations 50:50 the data would have apparent 4-fold symmetry. Processing

