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.


We have determined the structure of a serotype C (isolate C-S81) 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 O2BFS (Acharya, R. et al. 1989, Nature (London), 347, 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-S81 structure include visualization 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 POLO virus; Cloow, M. et al. 1987, Nature (London), 347, 452-460) as an immature density bound to the N-terminal of VP4. The GI 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 disulfide bond in type O2 virus (the loop becomes ordered, and therefore visible crystallographically on reduction of the disulfide; Logan, D. et al. 1993, Nature (London). In press). Despite lacking the disulfide 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 roles 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. J. 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. A49, 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 particle is all in the same relative orientation but the choice is random between crystals. Each crystal may therefore be indexed as k,l,m or n,l,m. By comparison to a reference set the data can be divided into two streams and processed separately until (following post-refinement) the indices of one of the streams are modified and the 2 data sets merged. Data collected from a MAb-escape derived FMDV mutant (507) appeared to crystallize isomorphously with the parent virus (O2K) (Curry, S. et al. 1993, J. Mol. Biol. 228, 1263-1298); 123, 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 a isomorphous virus. However, statistically the data appeared to belong to point group 422. Assuming that each crystal all viral 2-folds are arranged randomly with respect to all other 2-folds with the ratio of the two orientations 59:41 the data would have apparent 4-fold symmetry. Processing