ESRF	**Experiment title:** BAG Barcelona - Structure of Human Rhinovirus Serotype 2 (HRV2)	**Experiment number:** LS1522
Beamline: ID14-2	**Date of experiment:** from: 13-Feb-00 to: 15-Feb-00	**Date of report:** 1-Aug-00
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Report:

Human rhinoviruses are classified into a major and minor group based on their bonding to ICAM-1 or to members of the LDL-receptor family, respectively. They can also be divided into groups A and B, according to their sensitivity towards a panel of antiviral compounds. The structure of human rhinovirus 2, that uses the LDL receptor for cell attachment and is included in antiviral grup B, has been solved and refined at 2.6 A resolution. Three different crystal forms were obtained depending on the crystallization conditions (1). Orthorrombic I222 crystals, with unit cell parameters a=308.7 A, b=352.2 A, c=380.5 A, diffracted beyond 2.0 A resolution and were used for the structure determination presented here. From these orthorrombic crystals, a partial data set (2.5 A resolution, obtained from 30 crystals) was collected at the beam line ID14.2 (ESRF,Grenoble) on a MARCCD detector and merged with a previous data collected at the beam line X11 (EMBL, Desy Hamburg) on a MAR345 Image Plate detector.The final data was 60% complete with and R-merge of 10.8 %.

The Main structural differences between HRV2 and other rhinoviruses are located at the internal protein shell surface and at the external antigenic sites. In the interior, the N-termini of VP1 and VP4 form a three stranded β-sheet in an arrangement similar to that present in enteroviruses, although myristate was not visible at the amino terminus of VP4 in the HRV2 structure. The βE-βF loop of VP2, a linear epitope within antigenic site B recognized by monoclonal antibody 8F5, adopts a conformation considerably different from that found in the complex of 8F5 with a synthetic peptide of the same sequence. This either points to considerable structural changes impinged on this loop upon antibody binding or to the existence of more than one single conformation of the loop when the virus is in solution. The hydrophobic pocket of VP1 was found to be occupied by a pocket factor apparently identical to that present in the major receptor group virus HRV16. Structure and sequence comparisons between the two HRV receptor groups revealed clusters of positive charges at the north wall of the canyon in minor group viruses (Figure 1) which were largely absent in major group viruses. These clusters might be involved in LDL receptor binding. Electron density, consistent with the presence of a viral RNA fragment, is seen stacket against a conserved tryptophan residue.

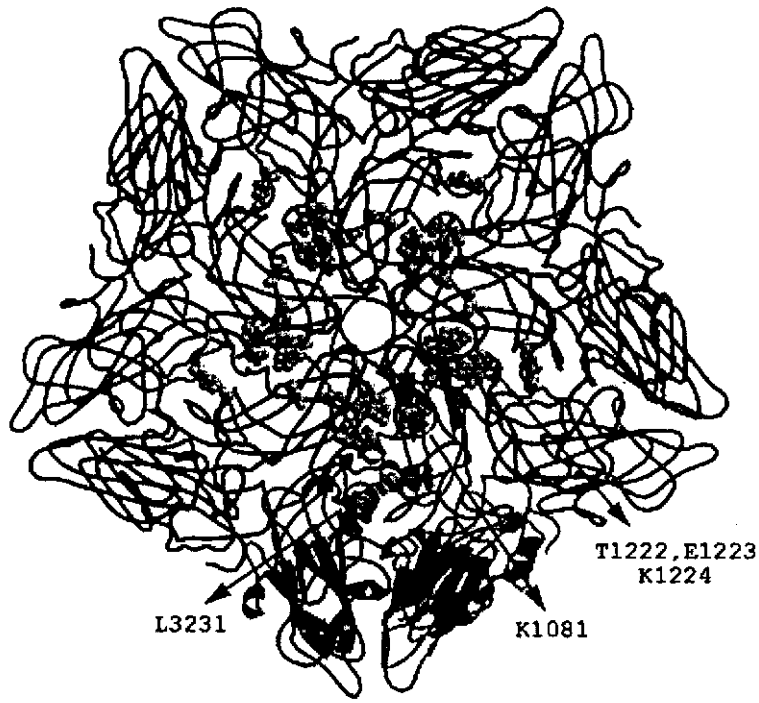

Figure 1. View down the 5-fold axis of HRV2 showing the disposition of the conserved residues among minor group rhinoviruses. The location of K1081, TEK (1222-1224) and L3231, that when modified, result in lethal viral variants are shown in yellow.

References

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