

protruding quite prominently, forming deep valleys at the pseudo-threefold axes between the A, B, and C subunits. The quasi-equivalent A, B, and C subunits adopt the jellyroll fold and are very similar in structure. The N termini, which had been found on the outside of the virion immunogenically, are found in the interior of the virion, and the first 26 residues of the A subunit are disordered. The N termini of the B and C subunits, which are completely visible, interact at the interior of the pseudo 6-fold axes, forming annuli. The C termini are exterior to the virion. All three histidines present in the coat protein are found on the inside of the virion, and may confirm the prediction that these residues bind RNA.

MS04.09.06 STRUCTURE OF HUMAN RHINO VIRUS 50 AT 1.8 Å E. Blanc¹, R. S. Alexander², M. McMillan³, D. C. Pevear⁴, V. Giranda⁵, M. S. Chapman¹, ¹Institute for Molecular Biophysics and Department of Chemistry, Florida State University, Tallahassee, FL 32306, ²Dupont Merck Pharmaceutical Co., Wilmington, DE 19880, ³Eastman Kodak Co., Rochester, NY 14650, ⁴Viropharma Inc., Malvern, PA 19335, ⁵Abbott Laboratories, Abbott Park, IL 60064-3500

Human Rhino Virus 50 (HRV50) belongs to one of the largest and most important families of viral pathogens: the picornaviridae. Rhinoviruses are among the smallest RNA-containing viruses; their genome is surrounded by a protein shell made of 60 copies of the asymmetric unit, each containing 4 polypeptide chains. As the major cause of the common cold, these viruses have already been extensively studied, and several structures have been determined. HRV50 is of special interest for two reasons: firstly, it is one of the more representative serotypes, of use in the design of broad spectrum drugs against all rhinoviruses. Secondly, there is the opportunity to study the structure and drug interactions at unusually high resolution, 1.8 Å.

The structure refinement has been performed mainly in real-space, using a new technique [Chapman (1995) *Acta Crystallogr. A* 51: 69-80] that accounts for the resolution of the experimental data, and can be 50 times faster than conventional reciprocal-space refinement. The method takes advantage of accurate phases that result from application of 15-fold non-crystallographic symmetry. Moreover, the method makes it tractable to refine such large structures against all experimental data simultaneously. Prior comparisons [Chapman & Rossmann (1996) *Acta Crystallogr. D*: in press] with canine parvovirus have demonstrated that the quality of a real-space refined virus is at least as good as refined in reciprocal space.

MS04.09.07 STRUCTURE-BASED DESIGN OF PEPTIDE PRESENTATION ON A VIRAL SURFACE: THE CRYSTAL STRUCTURE OF A PLANT/ANIMAL VIRUS CHIMERA AT 2.8 Å RESOLUTION T. Lin¹, C. Porta², G. Lomonosoff², J. E. Johnson¹ ¹Department of Molecular Biology, The Scripps Research Institute, 10666 N. Torrey Pines Rd., La Jolla, CA and ²Department of Virus Research, John Innes Centre, Colney Lane, Norwich NR4 7UH, UK

A genetically engineered icosahedral plant virus, cowpea mosaic virus (CPMV), was employed as an expression and presentation system to display a 14 amino acid linear antigenic epitope found in a capsid protein of human rhinovirus 14 (HRV14). Gram quantities of the CPMV/HRV14 chimera were made in plants and purified particles were crystallized in a form isomorphous with wild-type CPMV. The 2.8 Å resolution structure of the chimera shows that the inserted loop is well ordered and that, if the loop were intact, a PHE residue of CPMV would be placed in a hydrophilic environment. The resultant strain must make the loop an attractive substrate for endogenous plant proteases, as roughly 80%

of the inserted polypeptides are cleaved, allowing the PHE to be partially buried. Altering the PHE to an ARG should relieve the stress, reducing the propensity for cleavage and increasing the likelihood that the peptide will assume a structure closely similar to its structure in HRV14. Successful crystallization of other CPMV chimeras in forms isomorphous with the native virus suggests that this is a viable system for structure-based design of peptide presentation.

PS04.09.08 STRUCTURAL STUDIES OF AN HRV14:HIV-1 V3 LOOP CHIMERA THAT INDUCES NEUTRALIZING ANTIBODIES AGAINST HIV-1. Edward Arnold, Dawn A. Resnick, Jianping Ding, Sheila C. Geisler, Greg Kamer, and Gail Ferstandig Arnold, CABM and Rutgers University Chemistry Department, 679 Hoes Lane, Piscataway, NJ 08854

Human rhinovirus 14 (HRV14) has been engineered for use as a live-virus vaccine against human immunodeficiency virus (HIV-1). An HRV14:HIV-1 chimeric virus, designated DN-6, contains an immunogenic region from the V3 loop of the gp120 surface glycoprotein of HIV-1 transplanted into the neutralizing immunogenic site II of HRV14. DN-6 is strongly neutralized by anti-HIV-1 antibody preparations and elicits the production of antisera that potently neutralize HIV-1 in cell culture (Resnick *et al.*, 1995). The crystal structure of DN-6 will reveal the conformation of a V3 loop epitope that is able to elicit a neutralizing response against HIV-1.

Crystals of DN-6 were obtained that diffract X-rays to 2.8 Å resolution. A native dataset measured at CHESS from cooled crystals is 44.8% complete to 3.5 Å resolution (238,364 independent reflections, $R_{\text{merge}}=11.7\%$) and from a flash-frozen crystal is 61.4% complete to 3.5 Å resolution (322,463 independent reflections, $R_{\text{merge}}=14.7\%$). The crystal symmetry and unit cell dimensions are similar to those of the orthorhombic crystal forms of HRV14 (Erickson *et al.*, 1983) and poliovirus type 1 Mahoney (Hogle *et al.*, 1985). Surprisingly, although the cell dimensions are very similar, the packing is different from that of the poliovirus 1 Mahoney crystals and the space group is P2₁2₁ instead of P2₁2₁2. The reflections were indexed accordingly for the standard space group choice P2₁2₁2 with a=378.4, b=354.7, and c=317.7 Å.

Rotation and translation functions indicated a particle rotation of 93.0° (cooled) or 94.2° (frozen) around the z axis relative to a standard icosahedral orientation and the particle center position to be close to z=0.25. Rigid body refinement using the HRV14 native coordinates (Rossmann *et al.*, 1985; Arnold & Rossmann, 1988) yielded an R-factor of 0.34 for 15-3.5 Å resolution for the cooled dataset. Phase improvement by 30-fold noncrystallographic symmetry averaging is underway. Electron density is well ordered for the majority of the protein shell. We are in the process of interpreting the density in the chimeric region in terms of the structure of the transplanted HIV-1 V3 loop immunogen.

PS04.09.09 STRUCTURE OF COXSACKIEVIRUS B1 COMPLEXED WITH AN ANTIVIRAL AGENT. Karen N. Lentz¹, Allen D. Smith¹, Sheila C. Geisler¹, Stu Cox², Jason DeMartino², V. Girjavallabhan², John O'Connell², and Edward Arnold¹, ¹Center for Advanced Biotechnology and Medicine, and Rutgers University Department of Chemistry, 679 Hoes Lane, Piscataway, NJ 08854, ²Antiviral Chemotherapy, Schering-Plough Research Institute, 2015 Galloping Hill Road, Kenilworth, NJ 07033

Coxsackievirus B1 (CVB1) is a member of the picornavirus family and causes a wide variety of human diseases. These include common colds, mild febrile illness, encephalitis, and acute myocarditis. The picornaviruses are small (approximately 300 Å