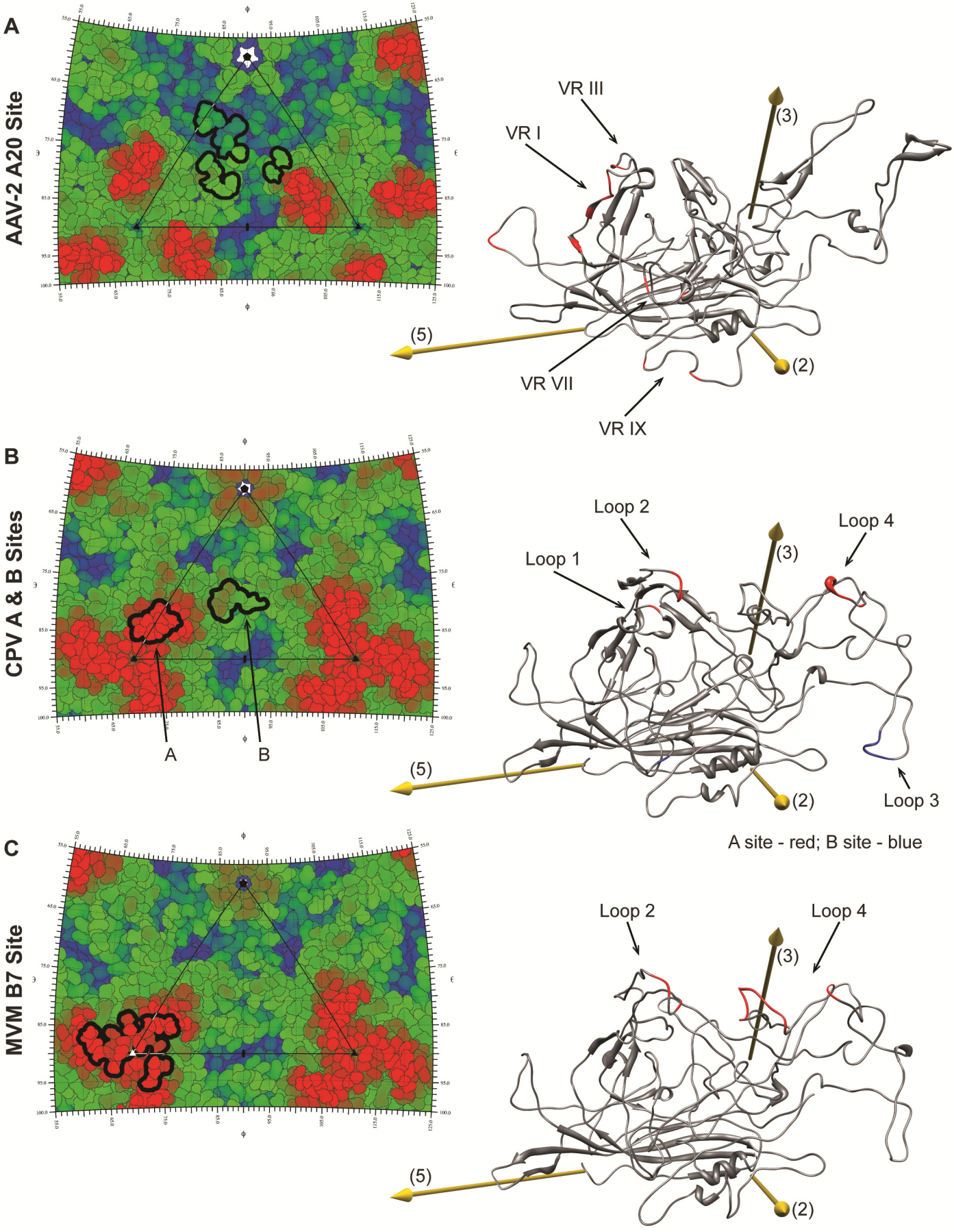
SUPPLEMENTARY DATA

Figure S 1 (Overleaf): Comparison of antibody-binding footprints in AAV-2, CPV/FPV and MVM. Panels A - C (left column) outline residues involved in antibody binding on stereographic surface projections of each virus similar to Figure 3. Panels D - F (right column) show the subunit backbone, framed by the 5-, 3- and 2-fold axes (arrows), and with antibody contact residues colored. Panels A & D (top row) show residues implicated in AAV-2/A20 binding (this paper). Panels B & E show the CPV and FPV residues common to the footprints of all "A" or "B" epitope viruses (Haffenstein et al., 2009). Panels C & F (bottom row) show residues implicated in the binding of B7 to MVM (Kauffman et al., 2007).

Figure S 1 (caption on previous page):



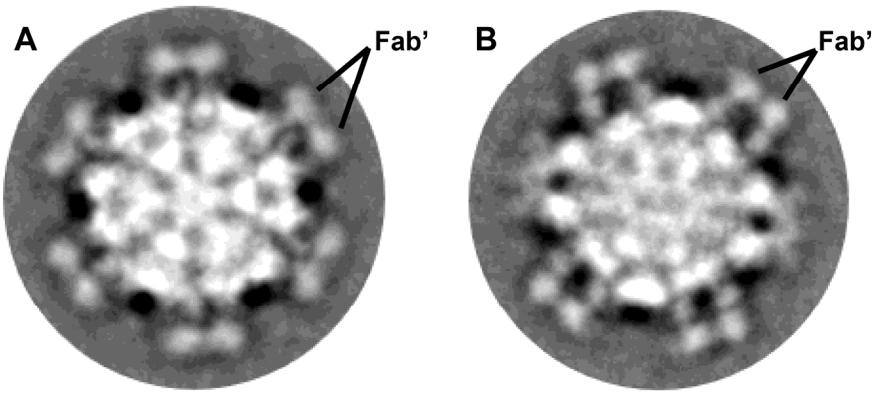


Figure S 2: Cryo-EM imaging of AAV-2 complexed with A20 Fab'. Class averages projected along 3-fold (A) and 2-fold (B) axes respectively, in which the variable and constant domains can be resolved most easily where they emanate radially in a near-equatorial plane. In panel A, viewed down a 3-fold, 6 clusters of 5 Fab' are near-equatorial . In panel B, viewed along a 2-fold, 4 clusters are in-plane and 2 are less well resolved, because we are looking at the superimposition of clusters pointing 30° above and below the plane.

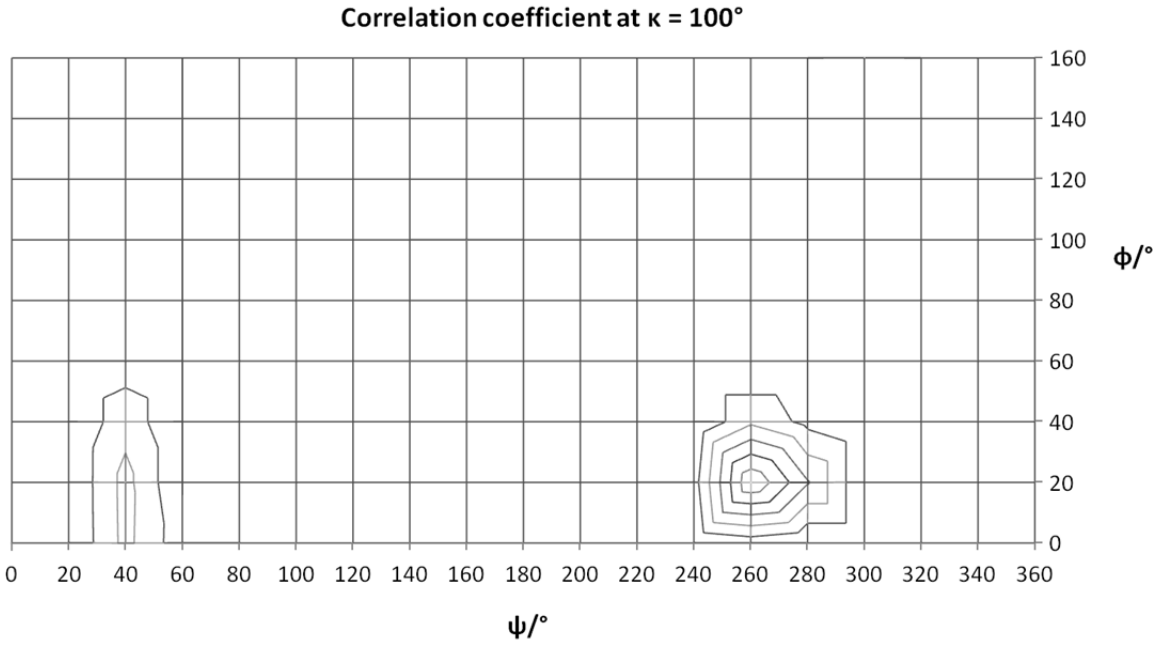


Figure S 3: Search for the orientation of the Fab' in the *cryo*-EM reconstruction. The structure of a representative Fab (PDB ID 1A6T) was rotated throughout spherical-polar space in 20° increments to get a preliminary model orientation prior to homology modeling. Correlation coefficients (between the atomic model and a difference map) above 0.5 are shown (increments of 0.05) for the match of model and experimental density. On this section, the highest and third highest peaks are visible at 0.75 and 0.57. Peaks 2 – 4 at correlation coefficients of 0.62, 0.57 and 0.47 are *pseudo*-symmetrical solutions related to the correct solution by 2-fold rotations about the principal axes of the approximately ellipsoid Fab' density. Peaks 3 & 4 would implausibly point the CDRs away from the virus. Clear distinction between peak 1 and these incorrect solutions provided confidence that the correct orientation could be found even with a model that only crudely represented Fab' A20.

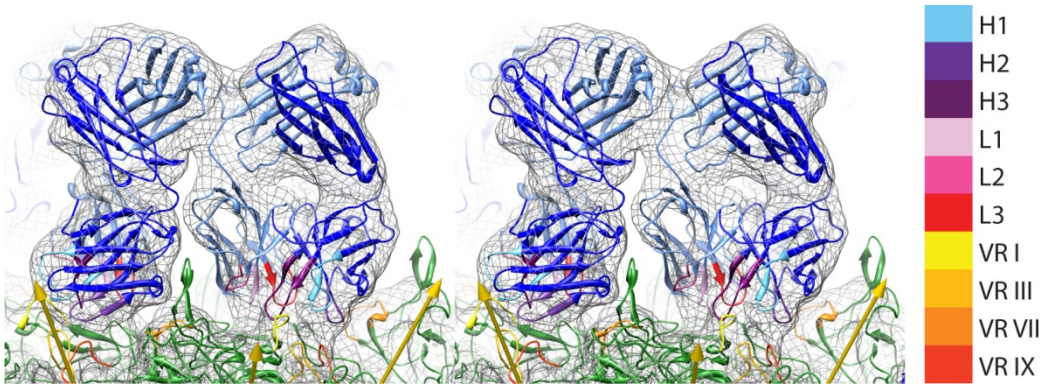


Figure S 4: Stereo pair, showing the fit of the homology model into the density of the *cryo*-EM reconstruction. Two symmetry-equivalent Fab fragments are shown in blue (pale for the light chain, dark for heavy) with CDRs highlighted according to the color key, H1-3 and L1-3. AAV-2 is shown in green with variable regions VR-I, -III, -VII and -IX, the main CDR contacts, highlighted in color. The view is tangential to the virus surface with yellow arrows indicating symmetry axes, 2-folds on each side, and looking from a 3-fold (front center) towards a 5-fold (out of view). Density is contoured at 2.5 σ.

			Density	***Homology model***	***CDR database***
			Solved excluded (●) & accessible (○) volumes		*Most likely cluster (●) & alternate H3 (○) loops*
Plateau	Ser	261	●	●	●
	Ser	262	●	●	●
	Gln	263	●	●	●
	Ser	264	●	●	●
	Gly	265	○		●
	Ala	266			○
	Ser	384	●	●	●
	Gln	385	●	●	●
	Ser	707	○		
	Val	708	●	●	●
	Asn	709	●		
	Thr	716	●		●
	Asn	717	●	●	●
Canyon wall	Lys	258	●	●	●
	Gln	259	●		
	Ile	260	●		
	Tyr	272			○
Canyon	Thr	251	○		●
	Tyr	252	●		
	Asn	253	●	●	●
	Asn	254	●	●	●
	Leu	256	○		
	Ser	276	○		
	Ser	658		●	
	Thr	659	●	●	●
	Thr	660		●	●
Spike	Glu	548	○	●	●
	Val	552	○		
	Lys	556	○	●	●

Table S 1: AAV-2 residues potentially within the MAb A20 footprint were identified three ways. (1) Those > 25% covered by Fab' *cryo*-EM density: density was contoured to give a volume equal to the solvent excluded (approx. van der Waals) volume or to the larger solvent accessible volume outlined by the center of a water probe rolled over the solvent excluded surface (Gerstein *et al.*, 2001); (2) Those with atoms within 4 Å of atoms in an A20 homology model fit to the *cryo*-EM density; (3) Those with atoms within 4 Å of a model spliced together from the CDR loops of appropriate sequence motif from Dunbrack's data base of CDR conformation (North *et al.*, 2011). Open circles denote additional residues implicated by an alternative CDR H3 conformer that cannot be excluded by sequence, but is 6-fold less frequent in the database, and, with six Cα clashing with AAV-2, is unlikely to be the relevant conformation. Usually, a fit homology model is considered to provide the most accurate footprint, but is subject to modeling errors, particularly in side chain rotamers. The membership of a core 12 residues in the footprint is validated by consistency between the three approaches. Residues implicated by a subset of approaches lie at the periphery of the footprint.

Literature cited:

Hafenstein, S., Bowman, V. D., Sun, T., Nelson, C. D., Palermo, L. M., Chipman, P. R., Battisti, A. J., Parrish, C. R., and Rossmann, M. G. (2009). Structural comparison of different antibodies interacting with parvovirus capsids. J Virol: 83, 5556-5566.

Kaufmann, B., Lopez-Bueno, A., Mateu, M. G., Chipman, P. R., Nelson, C. D., Parrish, C. R., Almendral, J. M., and Rossmann, M. G. (2007). Minute virus of mice, a parvovirus, in complex with the Fab fragment of a neutralizing monoclonal antibody. J Virol: 81(18), 9851-8.