Supplemental Material

Title

Nanobody binding to a conserved epitope promoted norovirus particle disassembly

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Supplementary Figures

Figure S1

Alternative conformations:

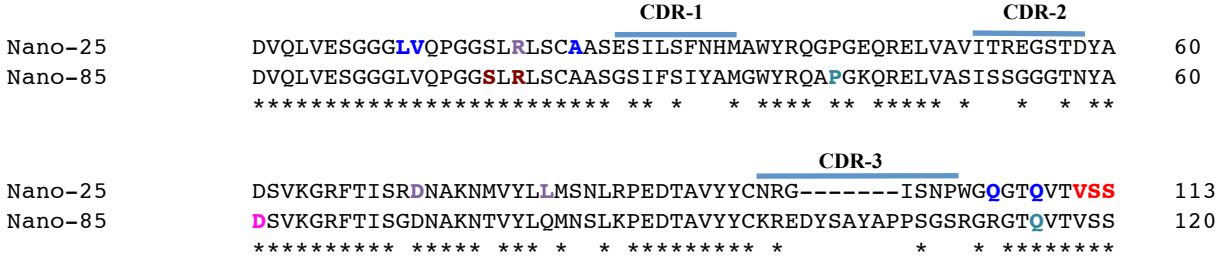


Figure S1. An amino acid alignment of Nano-25 and Nano-85 showing the alternative binding sites. The three CDRs (blue bars) were labeled. The Nanobody amino acids involved in alternative P domain binding were colored accordingly, GII.10 Nano-25 (blue, purple, red) and GII.10 Nano-85 (maroon, pink, and teal). The asterisks represent conserved amino acids.

Figure S2

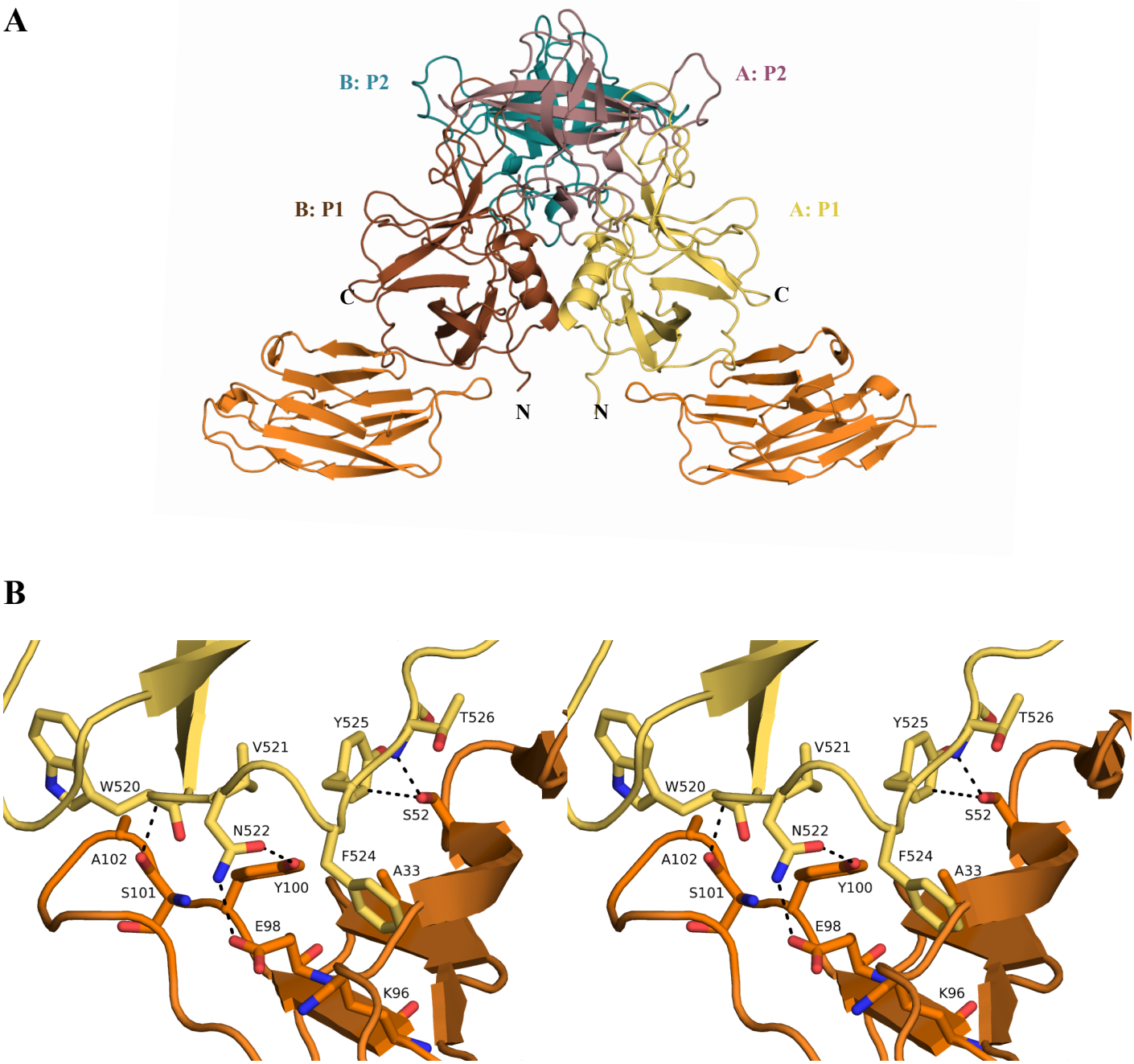
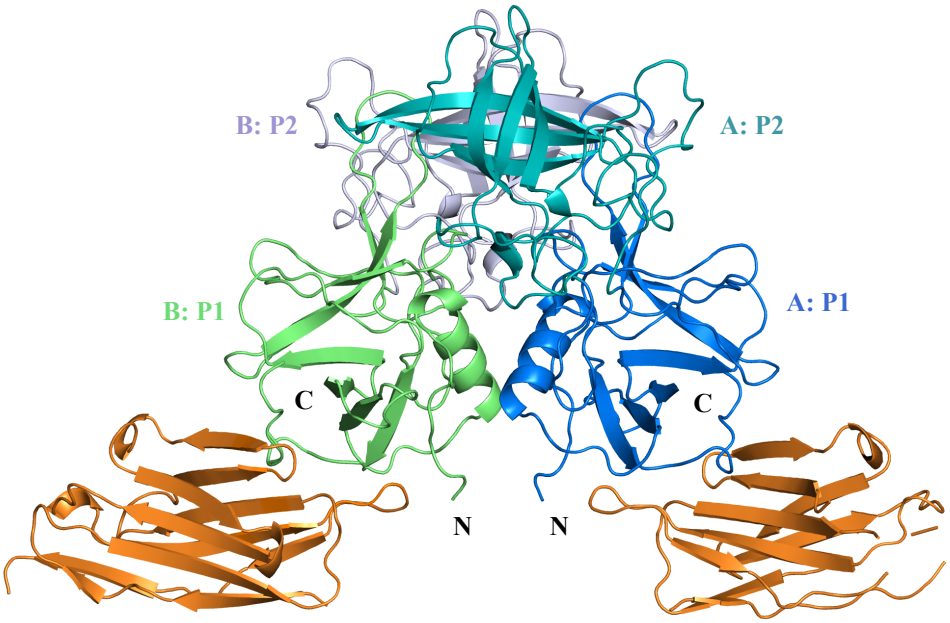


Figure S2. Structure of Saga-2006 GII.4 domain Nano-85 complex. (A) The X-ray crystal structure of the Saga-2006 GII.4 domain Nano-85 complex. Molecular replacement indicated one P dimer and two Nano-85 molecules in space group $P22_12_1$. The Nano-85 bound to the lower region of the P1 subdomain and involved a monomeric interaction. The complex was colored according to Saga-2006 GII.4 P domain monomers (chain A and B) and P1 and P2 subdomains, i.e., chain A: P1 (brown), chain A: P2 (deep teal), chain B: P1 (yellow orange), chain B: P2 (dirty violet), and Nano-85 (orange). (B) A close-up stereo view of (chain A) Saga-2006 GII.4 P domain residues interacting with Nano-85. The P domain hydrogen bond interactions included side-chain and main chain interactions (2.6-2.9 Å), one main chain of Trp520, two side chains of N522, and one main chain of T526. One π donor hydrogen bond interaction was formed between Y525 of the P domain and Nano-85. P domain hydrophobic interactions involved V521 and F524.

Figure S3

A



B

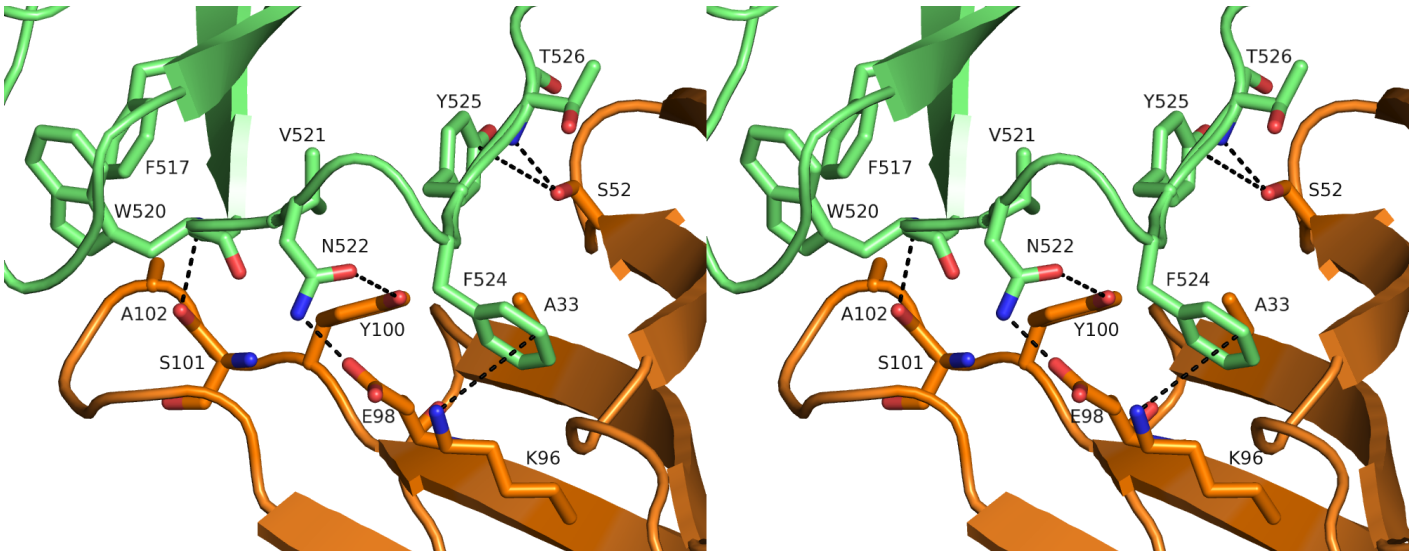


Figure S3. **Structure of NSW-2012 GII.4 domain Nano-85 complex.** (A) The X-ray crystal structure of the GII.10 domain Nano-25 complex. Molecular replacement indicated one P dimer and two Nano-85 molecules in space group $P2_12_12_1$. The Nano-85 bound to the lower region of the P1 subdomain and involved a monomeric interaction. The complex was colored according to NSW-2012 GII.4 P domain monomers (chain A and B) and P1 and P2 subdomains, i.e., chain A: P1 (lime), chain A: P2 (blue white), chain B: P1 (marine), chain B: P2 (teal), and Nano-85 (orange). (B) A close-up stereo view of (chain B) NSW-2012 GII.4 P domain residues interacting with Nano-85. The P domain hydrogen bond interactions included side-chain and main chain interactions (2.4-3.2 Å), one main and one side chain of W520, one side chain of N522, and one main chain of T526. One electrostatic interaction (F524) and one π donor hydrogen bond interaction (Y525) was also observed. P domain hydrophobic interactions involved F517, V521, and F524.