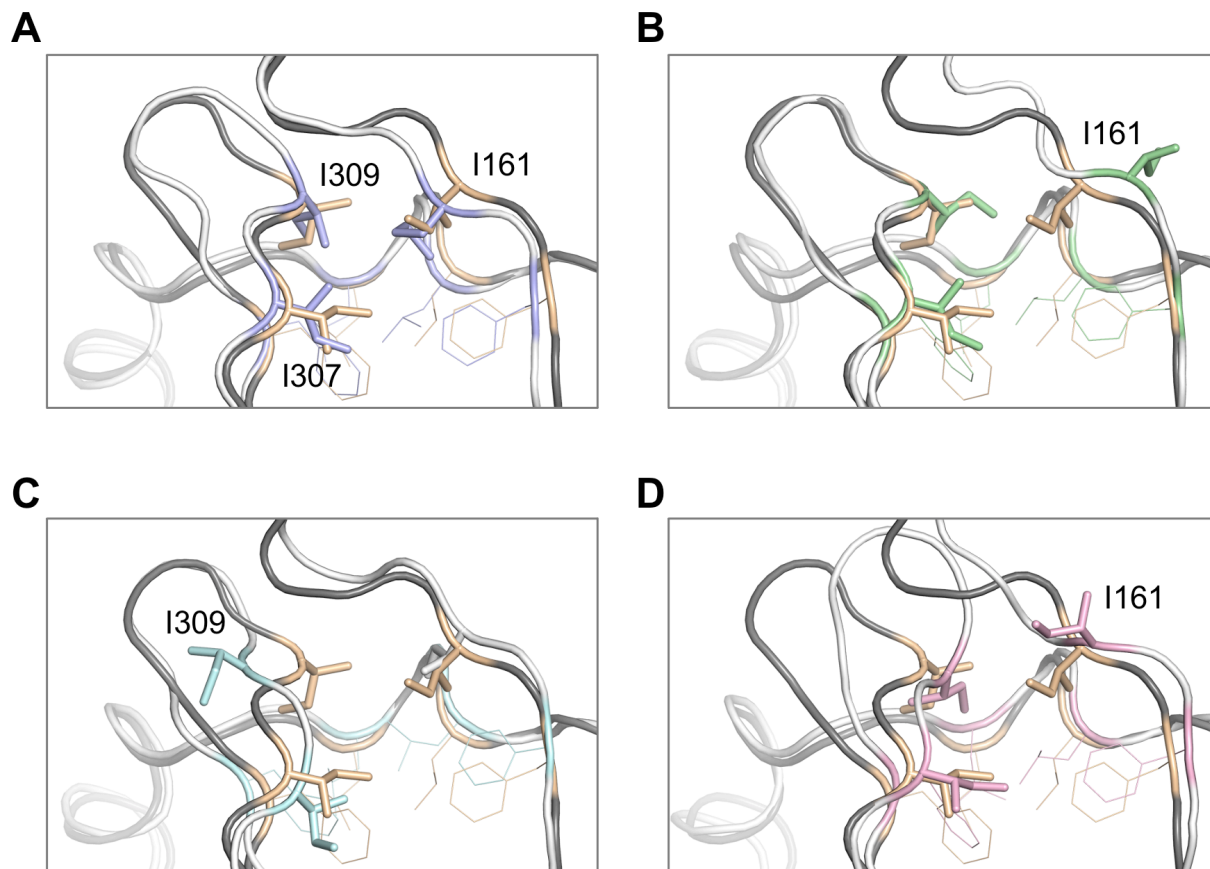


Figure S4



**FIG S4 Structural explanation for anomalous behavior of I307 in the AMC011 Env  $\Delta\Delta G$  calculations.** (A) Structural alignment of gp120 from the HIV-1 BG505 trimer (PDB ID: 6NNJ; light grey ribbon) to that of the JR-FL trimer (PDB ID: 5FYK; dark grey, ribbon). Selected hydrophobic cluster-2 residues are shown in stick representation and colored in blue (6NNJ) or tan (5FYK). (B) Structural alignment of gp120 from the HIV-1 AMC011 trimer chain A (PDB ID: 6OLP; light grey ribbon) to that of the JR-FL trimer (PDB ID: 5FYK; dark grey, ribbon). Selected hydrophobic cluster-2 residues are shown in stick representation and colored in green (6OLP) or tan (5FYK). (C) Structural alignment of HIV-1 AMC011 trimer chain C to JR-FL. Selected hydrophobic cluster-2 residues are colored in cyan (6OLP) or tan (5FYK). (D) Structural alignment of HIV-1 AMC011 trimer chain E to JR-FL. Selected hydrophobic cluster-2 residues are colored in pink (6OLP) or tan (5FYK). The altered orientations of I161 in 6OLP chains A and E and I309 in 6OLP chain C perturb the hydrophobic interactions about I307, which manifests in a diminished effect of mutating I307 to alanine for AMC011 in the  $\Delta\Delta G$  calculations performed in this study.