

**Table S1.** Hydrogen bonding contacts ( $\leq 3.2 \text{ \AA}$ ) between the E2s epitope and the 8G12 Fab

8G12's epitope on E2s <sup>1</sup>	8G12 Fab residues	Distance ( $\text{\AA}$ ) <sup>2</sup>
Glu479 <sup>E2s(A)</sup> (OE1)	Lys <sup>H63</sup> (NZ)	2.6
(OE1)	Gln <sup>H60</sup> (OE1)	3.2
Arg542 <sup>E2s(B)</sup> (NH1)	Gly <sup>H102</sup> (O)	3.0
Glu549 <sup>E2s(A)</sup> (OE1)	Glu <sup>L93</sup> (OE1)	2.6
(OE1)	Thr <sup>L94</sup> (N)	3.1
(OE2)	Thr <sup>L94</sup> (OG1)	2.9
(OE2)	Tyr <sup>H105</sup> (OH)	2.8
Gly551 <sup>E2s(A)</sup> (O)	Gly <sup>H102</sup> (O)	3.0
(O)	Asn <sup>H104</sup> (N)	2.9
Thr553 <sup>E2s(A)</sup> (N)	Asn <sup>H104</sup> (OD1)	2.7
(OG1)	(OD1)	3.2
(OG1)	(ND2)	3.0
Lys554 <sup>E2s(A)</sup> (NZ)	Glu <sup>L93</sup> (OE1)	2.6
Thr564 <sup>E2s(B)</sup> (OG1)	Trp <sup>L92</sup> (NE1)	2.8
Ser590 <sup>E2s(A)</sup> (N) <sup>3</sup>	Asp <sup>L1</sup> (OD1)	2.9
Gly591 <sup>E2s(A)</sup> (O)	Gln <sup>H60</sup> (OE1)	2.7
Pro592 <sup>E2s(A)</sup> (O)	Gln <sup>H58</sup> (N)	2.9

<sup>1</sup> The residues are labeled to indicate their location on E2s dimer molecule (A or B)

<sup>2</sup> The calculation is based on the E2s<sup>HEV-4</sup>:8G12 Fab complex structure (2.3  $\text{\AA}$  resolution)

<sup>3</sup> For residue 590, a serine residue in genotype 4 but an alanine residue in the other genotypes