

**A**

mAb	Tier 1A		Global Neutralization Panel										SHIV Panel					SIVcpz						
	MW995-26	TH023-6	TR011	25710	CNE8	X2278	BJDX01000	X1632	Ce1176	246F3	CH119	Ce0217	CNE55	Q23	CRF-260	WITO	ZM233	CAP266SU	CH505	CH848	BG05 N332	MT145K		
<b>T927 lineage 1</b>																								
w32 P2D12	>250	>250	<b>6.6</b>	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250
<b>T927 lineage 2</b>																								
w24 P1D08	>250	<b>0.04</b>	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	<b>194</b>	>250	>250	>250	>250	>250	>250	>250
w24 P2D06	>250	<b>0.02</b>	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	<b>119</b>	>250	>250	>250	>250	>250	>250	>250
w24 P1D09	>250	<b>0.02</b>	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	<b>119</b>	>250	>250	>250	>250	>250	>250	>250
<b>T927 lineage 3</b>																								
w62 P1C05	>250	<b>0.05</b>	<b>0.80</b>	>250	<b>59</b>	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	<b>82</b>	>250	>250	>250	>250	>250	>250	>250
w62 P1C01	>250	<b>0.04</b>	<b>6.9</b>	>250	<b>20.2</b>	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	>250	<b>40.5</b>	>250	>250	>250	>250	>250	>250	>250
<b>T925 lineage 2</b>																								
w24 P1G03	>250			>250											>250		>250							
w24 P1E11	>250			>250											>250		>250							
w24 P1F01	>250			>250											>250		>250							
w24 P2C12	>250			>250											>250		>250							
w24 P1F12	>250			>250											>250		>250							

IC<sub>50</sub> 250-50µg/ml 49.9-10.0µg/ml 9.9-1.0µg/ml 0.99-0.01µg/ml

**B**

mAb	CAM13K								ZM233							MW995-26						
	CAM13K	CAM13K-K130N	CAM13K-N156K	CAM13K-N160K	CAM13K-R166S	CAM13K-K168E	CAM13K-K171Q	CAM13K-S186N	ZM233	ZM233-N160K	ZM233-R166S	ZM233-K168E	ZM233-K169E	ZM233-K171E	MW995-26	MW995-26-N160K	MW995-26-R166A	MW995-26-K168E	MW995-26-Q171K			
<b>T927 lineage 1</b>																						
w32 P2D12	<b>188</b>	<b>140</b>	<b>2.3</b>	<b>141</b>	<b>87</b>	<b>162</b>	>250	<b>233</b>														
<b>T927 lineage 2</b>																						
w24 P1D08	<b>11.5</b>	<b>56</b>	<b>0.05</b>	<b>0.36</b>	>250	>250	>250	<b>40.4</b>														
w24 P2D06	<b>9.2</b>	<b>34.6</b>	<b>0.03</b>	<b>0.12</b>	>250	>250	>250	<b>174</b>	<b>30.1</b>													
w24 P1D09	<b>10.1</b>	<b>12.4</b>	<b>0.01</b>	<b>0.57</b>	>250	>250	>250	<b>78</b>	<b>27.4</b>													
<b>T927 lineage 3</b>																						
w62 P1C05	>250	>250	<b>9.5</b>	>250	>250	>250	>250	>250	>250													
w62 P1C01	>250	>250	<b>11.4</b>	>250	>250	>250	>250	>250	>250													
<b>T927 lineage 4</b>																						
w62 P1B01	>250	>250	<b>6.9</b>	>250	>250	>250	>250	>250	>250													
w62 P1B10	>250	>250	<b>17.1</b>	>250	n.d.	>250	>250	>250	>250													
w62 P3E08	>250	>250	<b>7.2</b>	<b>170</b>	<b>165</b>	<b>169</b>	>250	>250	>250													
w62 P1H10	>250	>250	<b>19.0</b>	>250	>250	>250	>250	>250	>250													
w62 P1F05	>250	>250	<b>6.1</b>	>250	>250	>250	>250	>250	>250													
w62 P3C02	<b>215</b>	<b>142</b>	<b>1.7</b>	<b>141</b>	<b>110</b>	<b>231</b>	<b>233</b>	<b>198</b>														
w62 P1C07	>250	>250	<b>5.0</b>	>250	>250	>250	>250	>250	>250													
w62 P3A11	>250	>250	<b>5.8</b>	>250	>250	>250	>250	>250	>250													
<b>T927 lineage 5</b>																						
w24 P2B12	>250	>250	<b>50.0</b>	>250	>250	>250	>250	>250	<b>14.0</b>	<b>48.0</b>	>250	>250	>250	>250	<b>1.4</b>	>10	>10	>10	>10	<b>0.91</b>		
w24 P1C02	>250	>250	<b>41.2</b>	>250	>250	>250	>250	>250	<b>68</b>	<b>61</b>	>250	>250	>250	>250	<b>3.5</b>	>10	>10	>10	>10	<b>1.0</b>		
w24 P1D03	>250	>250	<b>100</b>	>250	>250	>250	>250	>250	<b>10.1</b>	<b>21.3</b>	>50	>50	>50	>50	<b>0.76</b>	<b>6.8</b>	>10	>10	>10	<b>0.22</b>		
w24 P1A11	<b>13.6</b>	<b>100</b>	<b>1.4</b>	>250	>250	>250	>250	<b>48.0</b>	<b>0.52</b>	<b>1.2</b>	>50	>50	>50	>50	<b>0.09</b>	<b>0.73</b>	>10	>10	>10	<b>0.01</b>		
w62 P1B05	<b>157</b>	>250	<b>1.3</b>	>250	>250	>250	>250	>250	<b>0.62</b>	<b>5.3</b>	>50	>50	<b>46.0</b>	>50	<b>0.01</b>	<b>0.30</b>	>10	>10	>10	<b>0.01</b>	<b>0.003</b>	
w62 P3G11	<b>161</b>	>250	<b>1.2</b>	>250	>250	>250	>250	>250	<b>2.0</b>	<b>5.3</b>	>50	>50	>50	>50	<b>0.14</b>	<b>2.5</b>	>10	>10	>10	<b>0.37</b>	<b>0.02</b>	
<b>T925 lineage 1</b>																						
w24 P1E09	<b>1.2</b>	<b>3.3</b>	<b>0.04</b>	>250	>250	>250	>250	<b>6.6</b>	<b>0.78</b>	<b>9.5</b>	<b>17.8</b>	>50	>50	>50	<b>4.0</b>	>10	>10	>10	>10	<b>0.007</b>		
w24 P1D09	<b>1.1</b>	<b>6.8</b>	<b>0.09</b>	>250	>250	>250	>250	<b>4.6</b>	<b>5.0</b>	<b>2.5</b>	>50	>50	>50	>50	<b>9.0</b>	>10	>10	>10	>10	<b>0.009</b>		
w24 P2B11	<b>2.3</b>	<b>14.0</b>	<b>0.10</b>	<b>102</b>	>250	>250	>250	<b>5.9</b>	<b>0.77</b>	<b>18.7</b>	<b>17.0</b>	>50	>50	>50	<b>4.9</b>	>10	>10	>10	>10	<b>0.02</b>		
w24 P1A12	<b>0.6</b>	<b>4.4</b>	<b>0.05</b>	<b>219</b>	>250	>250	>250	<b>3.7</b>	<b>0.28</b>	<b>13.0</b>	<b>13.0</b>	>50	>50	>50	<b>22.9*</b>	>10	>10	>10	>10	<b>0.006</b>		
w24 P1C08	<b>6.6</b>	<b>48.3</b>	<b>0.46</b>	>250	>250	>250	>250	<b>45.4</b>	<b>2.0</b>	<b>9.7</b>	>50	>50	>50	>50	>10	>10	>10	>10	>10	<b>0.05</b>		
<b>T925 lineage 2</b>																						
w24 P1G03	>250			>250				>250														
w24 P1E11	>250			>250				>250														
w24 P1F01	>250			>250				>250														
w24 P2C12	>250			>250				>250														
w24 P1F12	>250			>250				>250														

IC<sub>50</sub> 250-50µg/ml 49.9-10.0µg/ml 9.9-1.0µg/ml 0.99-0.01µg/ml <0.01µg/ml

**FIG S7 Neutralization properties of antibody lineages isolated from SCIV-infected RMs. (A)**

Expanded antibody lineages isolated from SCIV.CAM13K infected RMs with no or very limited tier 2 neutralization breadth. 50% inhibitory concentrations (IC<sub>50</sub>) are shown (µg/ml) for representative members of T927 lineages 1-3 and T925 lineage 2 (listed on the left) against

pseudovirus panels carrying HIV-1 and SIVcpz Envs as well as replicating SHIVs (indicated on top). The highest antibody concentration used was 250  $\mu\text{g/ml}$  (coloring indicates the relative neutralization potency). (B) Epitope mapping of SCIV-induced cross-neutralizing antibodies. Representative members of all isolated antibody lineages (listed on the left) were tested against panels of CAM13K, ZM233 and/or MW965.26 mutants (indicated on top). Given the patterns of early sequence evolution, we mutagenized residues at or near the V2-apex, with an emphasis on key N-linked glycosylation sites and C strand residues. 50% inhibitory concentrations ( $\text{IC}_{50}$ ) are shown ( $\mu\text{g/ml}$ ). An asterisk denotes an estimated  $\text{IC}_{50}$  value (as determined by the Prism software). Only the two most potent and cross-reactive lineages were tested against heterologous ZM233 and MW965.26 mutants. All viruses represent pseudotypes generated by transfection of 293T cells. The highest antibody concentration used was 250  $\mu\text{g/ml}$  (colors indicate the relative neutralization potency).