

|                        | library 1 | library 1 replicate | library 2 | library 3 |
|------------------------|-----------|---------------------|-----------|-----------|
| H17-L19 0.5 $\mu$ g/ml | 2.1%      | 2.5%                | 4.9%      | 5.4%      |
| H17-L19 1 $\mu$ g/ml   | 0.7%      | 0.7%                | 1.9%      | 1.8%      |
| H17-L19 10 $\mu$ g/ml  | 0.3%      | 0.2%                | 0.4%      | 0.4%      |
| H17-L10 3 $\mu$ g/ml   | 0.2%      |                     | 0.2%      | 0.2%      |
| H17-L7 15 $\mu$ g/ml   | 0.2%      |                     | 0.1%      | 0.1%      |
| H18-S415 3 $\mu$ g/ml  | 0.2%      |                     | 0.1%      | 0.2%      |

**S1 Table:** Percentage of each mutant virus library remaining infectious after antibody neutralization in each replicate selection experiment. Percent infectivity was measured by qRT-PCR of the influenza nucleoprotein gene and interpolated from a standard curve of infection prepared with serial dilutions of each virus library.