Table S1

| Pattern | P $_{2}$ | Drugs | p-value |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 2 electrostatic mutations |  |  | $<10^{-7}$ |  |  |
| D30N, N88D | $2.7 \times 10^{-2}$ | NFV | $<10^{-7}$ |  |  |
| K20I, N37D | $6.1 \times 10^{-3}$ | IDV,NFV | $<10^{-3}$ |  |  |
| N37D, H69Q | $4.6 \times 10^{-3}$ | PI | $<10^{-3}$ |  |  |
| N37D, Q61E | $2.9 \times 10^{-3}$ | RTV,SQV,PI | $<10^{-7}$ |  |  |
| Q7E, N37D | $2.1 \times 10^{-3}$ | RTV,PI | $<10^{-7}$ |  |  |
| 3 electrostatic mutations |  |  |  |  |  |
| D30N, N37D, N88D | $4.7 \times 10^{-3}$ | IDV,NFV,RTV | $<10^{-7}$ |  |  |
| K20I, D30N, N88D | $3.1 \times 10^{-3}$ | IDV,NFV,PI | $<10^{-7}$ |  |  |
| D30N, H69Q, N88D | $2.7 \times 10^{-3}$ | IDV,NFV,RTV,SQV | $<10^{-7}$ |  |  |
| D30N, Q61E, N88D | $8.1 \times 10^{-4}$ | NFV | $<10^{-6}$ |  |  |
| Q7E, D30N, N88D | $7.4 \times 10^{-3}$ | NFV | $<10^{-7}$ |  |  |
|  | 4 electrostatic mutations | $<10^{-7}$ |  |  |  |
| K20I, D30N, N37D, N88D | $5.5 \times 10^{-4}$ | IDV,NFV | $<10^{-7}$ |  |  |
| D30N, N37D, H69Q, N88D | $3.0 \times 10^{-4}$ | APV,IDV,NFV,RTV,SQV | $<10^{-7}$ |  |  |
| K20I, D30N, H69Q, N88D | $2.4 \times 10^{-4}$ | NFV,RTV,PI | - |  |  |
| K20I, D30N, E35Q, N88D | $2.2 \times 10^{-4}$ | IDV,NFV |  |  |  |
| D30N, N37D, Q61E, N88D | $1.5 \times 10^{-4}$ |  |  |  |  |

