

**S1\_Table.** Free energy differences between beginning and end of simulations calculated using the MMGBSA method (kcal/mol)

| Simulation | wildtype | wildtype/weak restraints | G7aA     | G7aT     | G7abcA   | G7abcT   |
|------------|----------|--------------------------|----------|----------|----------|----------|
| 1          | -70.7    | -36.1                    | -80.2    | -58.6    | -57.8    | -21.7    |
| 2          | -82.3    | -57.9                    | -76.5    | -72.9    | -57.4    | -6.6     |
| 3          | -94.0    | -89.9                    | -36.2    | -49.9    | -16.6    | -40.9    |
| 4          | -68.9    | -70.8                    | -56.8    | -90.9    | -58.6    | -41.4    |
| 5          | -104.8   | -64.3                    | -73.9    | -64.3    | -44.4    | -78.0    |
| 6          | -87.4    | -77.7                    | -28.4    | -92.0    | -51.9    | -62.3    |
| 7          | -77.9    | -25.9                    | -66.3    | -50.7    | -44.5    | -25.6    |
| 8          | -68.3    | -19.0                    | -58.7    | -86.3    | -68.6    | -36.2    |
| 9          | -81.3    | -74.5                    | -95.8    | -101.7   | -38.6    | -28.0    |
| 10         | -92.0    | -91.6                    | -71.1    | -54.7    | -62.6    | -32.8    |
| average    | -83 ± 11 | -61 ± 24                 | -64 ± 19 | -72 ± 18 | -50 ± 14 | -30 ± 16 |