

Supplementary Materials

Self-aggregation and coaggregation of p53 core fragment and its aggregation gatekeeper variant

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This supplementary material contains three figures and 12 tables.

Three figures:

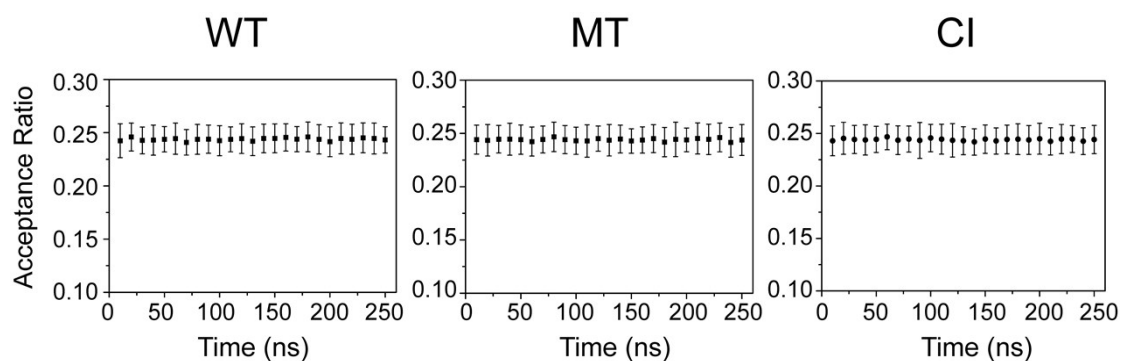


Fig. S1 Average acceptance ratio of three REMD systems. The acceptance ratio is ~ 24% for the WT, MT and CI systems.

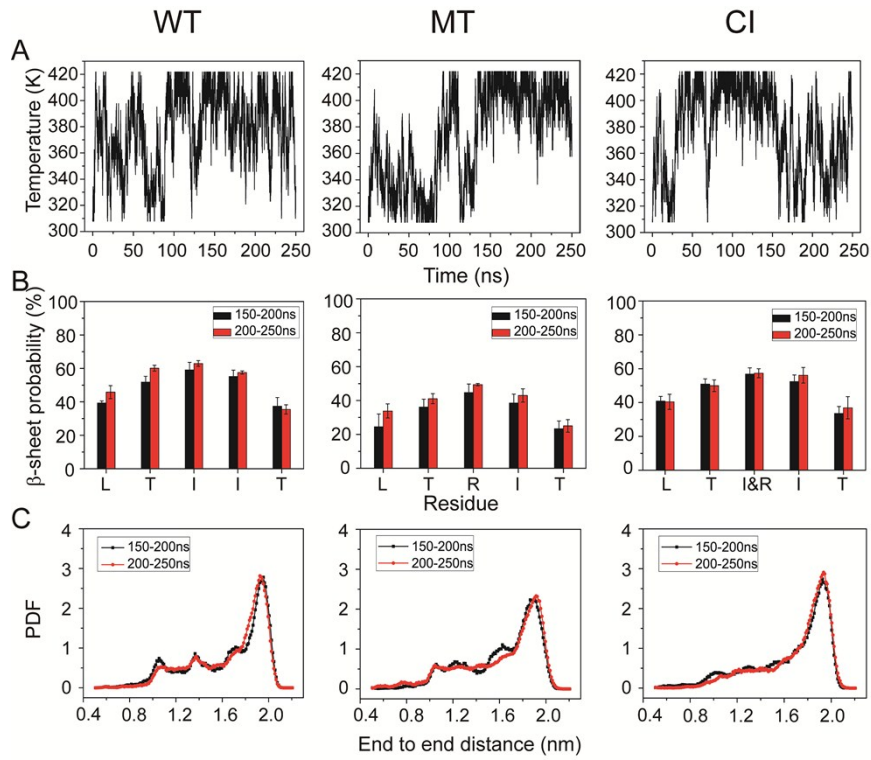


Fig. S2 Convergence check. The time evolution of a representative 310k replica (A). The β -sheet probability of each residue (B) and the probability density function (PDF) of end-to-end distance of each chain (C) within two different time intervals using the 150-200 ns and 200-250 ns data.

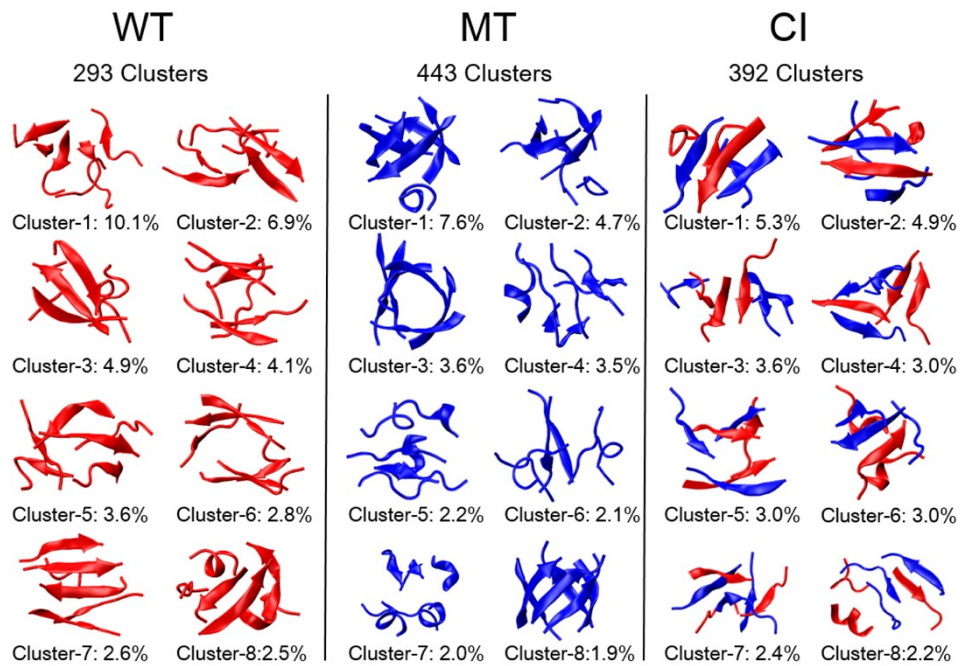


Fig. S3 Representative conformation of the first eight most-populated clusters. For the

CI hexamer, similar to the WT system, bilayer β -sheets structures, such as those in the first cluster (5.3%) and the fifth cluster (3.0%), are populated.

12 Tables:

Table S1. WT Main-chain—main-chain contact probabilities and corresponding errors (Fig. 5A)

| | | | | | | | |
|----------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| L | 0.060 ± 0.003 | 0.061 ± 0.001 | 0.060 ± 0.002 | 0.065 ± 0.002 | 0.047 ± 0.002 | 0.048 ± 0.004 | 0.046 ± 0.007 |
| T | 0.072 ± 0.005 | 0.094 ± 0.010 | 0.093 ± 0.003 | 0.081 ± 0.002 | 0.067 ± 0.001 | 0.052 ± 0.001 | 0.048 ± 0.004 |
| I | 0.087 ± 0.005 | 0.125 ± 0.017 | 0.139 ± 0.003 | 0.116 ± 0.004 | 0.114 ± 0.006 | 0.067 ± 0.001 | 0.047 ± 0.002 |
| I | 0.087 ± 0.003 | 0.096 ± 0.007 | 0.133 ± 0.008 | 0.127 ± 0.002 | 0.116 ± 0.004 | 0.081 ± 0.002 | 0.065 ± 0.002 |
| T | 0.049 ± 0.002 | 0.090 ± 0.003 | 0.131 ± 0.009 | 0.133 ± 0.008 | 0.139 ± 0.003 | 0.093 ± 0.003 | 0.060 ± 0.002 |
| L | 0.044 ± 0.001 | 0.065 ± 0.001 | 0.090 ± 0.003 | 0.096 ± 0.007 | 0.125 ± 0.017 | 0.094 ± 0.010 | 0.061 ± 0.001 |
| I | 0.042 ± 0.001 | 0.044 ± 0.001 | 0.049 ± 0.002 | 0.087 ± 0.003 | 0.087 ± 0.005 | 0.072 ± 0.007 | 0.060 ± 0.003 |
| Residues | I | L | T | I | I | T | L |

Table S2. MT Main-chain—main-chain contact probabilities and corresponding errors (Fig. 5B)

| | | | | | | | |
|----------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| L | 0.038 ± 0.001 | 0.054 ± 0.001 | 0.061 ± 0.001 | 0.060 ± 0.004 | 0.047 ± 0.004 | 0.039 ± 0.002 | 0.030 ± 0.005 |
| T | 0.063 ± 0.002 | 0.075 ± 0.010 | 0.090 ± 0.001 | 0.091 ± 0.007 | 0.086 ± 0.005 | 0.060 ± 0.005 | 0.039 ± 0.002 |
| I | 0.098 ± 0.001 | 0.111 ± 0.003 | 0.098 ± 0.003 | 0.098 ± 0.009 | 0.083 ± 0.014 | 0.086 ± 0.05 | 0.047 ± 0.004 |
| R | 0.111 ± 0.004 | 0.101 ± 0.005 | 0.110 ± 0.001 | 0.105 ± 0.004 | 0.098 ± 0.009 | 0.091 ± 0.007 | 0.060 ± 0.004 |
| T | 0.070 ± 0.002 | 0.080 ± 0.002 | 0.093 ± 0.002 | 0.110 ± 0.001 | 0.098 ± 0.003 | 0.090 ± 0.001 | 0.061 ± 0.001 |
| L | 0.037 ± 0.003 | 0.042 ± 0.007 | 0.080 ± 0.002 | 0.101 ± 0.005 | 0.111 ± 0.003 | 0.075 ± 0.010 | 0.054 ± 0.001 |
| I | 0.028 ± 0.002 | 0.037 ± 0.003 | 0.070 ± 0.002 | 0.111 ± 0.004 | 0.098 ± 0.001 | 0.063 ± 0.002 | 0.038 ± 0.001 |
| Residues | I | L | T | R | I | T | L |

Table S3. CI Main-chain—main-chain contact probabilities and corresponding errors (Fig. 5C)

| | | | | | | | |
|----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| L | 0.055 ±0.002 | 0.057 ±0.007 | 0.063 ±0.001 | 0.062 ±0.002 | 0.047 ±0.001 | 0.047 ±0.002 | 0.044 ±0.004 |
| T | 0.062 ±0.001 | 0.084 ±0.003 | 0.095 ±0.006 | 0.088 ±0.003 | 0.074 ±0.004 | 0.064 ±0.005 | 0.047 ±0.002 |
| I | 0.079 ±0.002 | 0.109 ±0.002 | 0.126 ±0.006 | 0.108 ±0.009 | 0.095 ±0.011 | 0.074 ±0.004 | 0.047 ±0.001 |
| I&R | 0.079 ±0.001 | 0.099 ±0.009 | 0.129 ±0.006 | 0.134 ±0.014 | 0.108 ±0.009 | 0.088 ±0.003 | 0.062 ±0.002 |
| T | 0.058 ±0.001 | 0.085 ±0.002 | 0.117 ±0.005 | 0.129 ±0.006 | 0.126 ±0.006 | 0.095 ±0.006 | 0.063 ±0.001 |
| L | 0.046 ±0.005 | 0.064 ±0.009 | 0.085 ±0.002 | 0.099 ±0.009 | 0.109 ±0.002 | 0.084 ±0.003 | 0.057 ±0.007 |
| I | 0.036 ±0.009 | 0.046 ±0.005 | 0.058 ±0.001 | 0.079 ±0.001 | 0.079 ±0.002 | 0.062 ±0.001 | 0.055 ±0.002 |
| Residues | I | L | T | I&R | I | T | L |

Table S4. WT Side-chain—side-chain contact probabilities and corresponding errors (Fig. 5D)

| | | | | | | | |
|----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| L | 0.087 ±0.001 | 0.101 ±0.005 | 0.087 ±0.001 | 0.118 ±0.010 | 0.098 ±0.017 | 0.067 ±0.001 | 0.083 ±0.001 |
| T | 0.093 ±0.008 | 0.111 ±0.003 | 0.096 ±0.005 | 0.103 ±0.001 | 0.097 ±0.008 | 0.082 ±0.007 | 0.067 ±0.001 |
| I | 0.110 ±0.006 | 0.158 ±0.009 | 0.135 ±0.013 | 0.201 ±0.015 | 0.165 ±0.018 | 0.097 ±0.008 | 0.098 ±0.017 |
| I | 0.147 ±0.008 | 0.166 ±0.013 | 0.149 ±0.015 | 0.209 ±0.008 | 0.201 ±0.015 | 0.103 ±0.001 | 0.118 ±0.010 |
| T | 0.076 ±0.011 | 0.110 ±0.011 | 0.118 ±0.015 | 0.149 ±0.015 | 0.135 ±0.013 | 0.096 ±0.005 | 0.087 ±0.001 |
| L | 0.112 ±0.001 | 0.123 ±0.001 | 0.110 ±0.010 | 0.166 ±0.013 | 0.158 ±0.009 | 0.111 ±0.003 | 0.101 ±0.005 |
| I | 0.106 ±0.009 | 0.112 ±0.009 | 0.076 ±0.011 | 0.147 ±0.008 | 0.110 ±0.006 | 0.093 ±0.008 | 0.087 ±0.001 |
| Residues | I | L | T | I | I | T | L |

Table S5. MT Side-chain—side-chain contact probabilities and corresponding errors (Fig. 5E)

| | | | | | | | |
|---|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| L | 0.105 ±0.014 | 0.097 ±0.009 | 0.103 ±0.001 | 0.090 ±0.002 | 0.133 ±0.006 | 0.060 ±0.005 | 0.090 ±0.003 |
| T | 0.082 ±0.003 | 0.091 ±0.013 | 0.102 ±0.005 | 0.108 ±0.006 | 0.099 ±0.001 | 0.092 ±0.002 | 0.060 ±0.005 |

| | | | | | | | |
|----------|-----------------|-----------------|-----------------|-----------------|------------------|-----------------|-----------------|
| I | 0.147 ±0.002 | 0.183 ±0.010 | 0.216 ±0.007 | 0.097 ±0.002 | 0.322 ±0.0043 | 0.099 ±0.001 | 0.133 ±0.006 |
| R | 0.126 ±0.002 | 0.114 ±0.007 | 0.110 ±0.001 | 0.077 ±0.003 | 0.097 ±0.002 | 0.108 ±0.006 | 0.090 ±0.002 |
| T | 0.064 ±0.006 | 0.112 ±0.008 | 0.118 ±0.005 | 0.110 ±0.001 | 0.216 ±0.007 | 0.102 ±0.005 | 0.103 ±0.001 |
| L | 0.087 ±0.007 | 0.133 ±0.014 | 0.112 ±0.008 | 0.114 ±0.007 | 0.183 ±0.010 | 0.091 ±0.013 | 0.097 ±0.009 |
| I | 0.086 ±0.011 | 0.087 ±0.007 | 0.064 ±0.006 | 0.126 ±0.002 | 0.147 ±0.002 | 0.082 ±0.003 | 0.105 ±0.014 |
| Residues | I | L | T | R | I | T | L |

Table S6. CI Side-chain—side-chain contact probabilities and corresponding errors (Fig. 5F)

| | | | | | | | |
|----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| L | 0.102 ±0.003 | 0.111 ±0.005 | 0.090 ±0.001 | 0.119 ±0.005 | 0.113 ±0.002 | 0.072 ±0.001 | 0.098 ±0.005 |
| T | 0.081 ±0.001 | 0.091 ±0.002 | 0.104 ±0.001 | 0.096 ±0.009 | 0.105 ±0.008 | 0.080 ±0.004 | 0.072 ±0.001 |
| I | 0.114 ±0.001 | 0.166 ±0.001 | 0.147 ±0.007 | 0.182 ±0.002 | 0.207 ±0.014 | 0.105 ±0.008 | 0.113 ±0.002 |
| I&R | 0.118 ±0.004 | 0.129 ±0.002 | 0.153 ±0.018 | 0.136 ±0.012 | 0.182 ±0.002 | 0.096 ±0.009 | 0.119 ±0.005 |
| T | 0.080 ±0.004 | 0.105 ±0.011 | 0.118 ±0.010 | 0.153 ±0.018 | 0.147 ±0.007 | 0.104 ±0.001 | 0.090 ±0.001 |
| L | 0.096 ±0.003 | 0.114 ±0.003 | 0.105 ±0.011 | 0.129 ±0.002 | 0.166 ±0.001 | 0.091 ±0.002 | 0.111 ±0.005 |
| I | 0.090 ±0.009 | 0.096 ±0.003 | 0.080 ±0.004 | 0.118 ±0.004 | 0.114 ±0.001 | 0.081 ±0.001 | 0.102 ±0.003 |
| Residues | I | L | T | I&R | I | T | L |

Table S7. WT-WT Main-chain—main-chain contact probabilities and corresponding errors in CI system (Fig. 7A)

| | | | | | | | |
|-----|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| L | 0.035 ±0.002 | 0.034 ±0.010 | 0.042 ±0.003 | 0.046 ±0.001 | 0.027 ±0.007 | 0.021 ±0.006 | 0.022 ±0.002 |
| T | 0.040 ±0.001 | 0.074 ±0.002 | 0.085 ±0.002 | 0.035 ±0.007 | 0.032 ±0.012 | 0.027 ±0.006 | 0.021 ±0.006 |
| I | 0.065 ±0.006 | 0.102 ±0.006 | 0.114 ±0.012 | 0.065 ±0.007 | 0.039 ±0.017 | 0.032 ±0.012 | 0.027 ±0.007 |
| I&R | 0.073 ±0.005 | 0.061 ±0.002 | 0.106 ±0.008 | 0.076 ±0.001 | 0.065 ±0.007 | 0.035 ±0.007 | 0.046 ±0.001 |
| T | 0.056 ±0.001 | 0.051 ±0.010 | 0.082 ±0.003 | 0.106 ±0.008 | 0.114 ±0.012 | 0.085 ±0.002 | 0.042 ±0.003 |

| | | | | | | | |
|----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| L | 0.031 ±0.001 | 0.027 ±0.023 | 0.051 ±0.010 | 0.061 ±0.002 | 0.102 ±0.006 | 0.074 ±0.002 | 0.034 ±0.010 |
| I | 0.025 ±0.005 | 0.031 ±0.001 | 0.056 ±0.001 | 0.073 ±0.005 | 0.065 ±0.006 | 0.040 ±0.001 | 0.035 ±0.002 |
| Residues | I | L | T | I&R | I | T | L |

Table S8. MT-MT Main-chain—main-chain contact probabilities and corresponding errors in CI system (Fig. 7B)

| | | | | | | | |
|----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| L | 0.032 ±0.013 | 0.019 ±0.007 | 0.032 ±0.013 | 0.036 ±0.007 | 0.031 ±0.005 | 0.036 ±0.025 | 0.025 ±0.008 |
| T | 0.035 ±0.007 | 0.047 ±0.014 | 0.034 ±0.003 | 0.040 ±0.010 | 0.046 ±0.008 | 0.047 ±0.034 | 0.036 ±0.025 |
| I | 0.068 ±0.007 | 0.084 ±0.001 | 0.061 ±0.004 | 0.039 ±0.013 | 0.046 ±0.026 | 0.046 ±0.008 | 0.031 ±0.005 |
| I&R | 0.062 ±0.004 | 0.050 ±0.001 | 0.071 ±0.004 | 0.070 ±0.032 | 0.039 ±0.013 | 0.040 ±0.010 | 0.036 ±0.007 |
| T | 0.051 ±0.004 | 0.049 ±0.015 | 0.074 ±0.003 | 0.071 ±0.004 | 0.061 ±0.004 | 0.034 ±0.003 | 0.032 ±0.013 |
| L | 0.034 ±0.015 | 0.047 ±0.016 | 0.049 ±0.015 | 0.050 ±0.001 | 0.084 ±0.001 | 0.047 ±0.014 | 0.019 ±0.007 |
| I | 0.030 ±0.001 | 0.034 ±0.015 | 0.051 ±0.004 | 0.062 ±0.004 | 0.068 ±0.007 | 0.035 ±0.007 | 0.032 ±0.013 |
| Residues | I | L | T | I&R | I | T | L |

Table S9. WT-MT Main-chain—main-chain contact probabilities and corresponding errors in CI system (Fig. 7C)

| | | | | | | | |
|----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| L | 0.047 ±0.006 | 0.045 ±0.001 | 0.035 ±0.001 | 0.039 ±0.004 | 0.033 ±0.003 | 0.039 ±0.007 | 0.042 ±0.010 |
| T | 0.055 ±0.011 | 0.057 ±0.003 | 0.075 ±0.012 | 0.069 ±0.004 | 0.065 ±0.004 | 0.053 ±0.005 | 0.048 ±0.009 |
| I | 0.065 ±0.001 | 0.083 ±0.011 | 0.084 ±0.001 | 0.089 ±0.009 | 0.077 ±0.005 | 0.051 ±0.003 | 0.039 ±0.005 |
| R | 0.050 ±0.004 | 0.102 ±0.021 | 0.129 ±0.002 | 0.117 ±0.013 | 0.098 ±0.007 | 0.085 ±0.006 | 0.054 ±0.011 |
| T | 0.048 ±0.004 | 0.099 ±0.005 | 0.119 ±0.009 | 0.125 ±0.010 | 0.098 ±0.007 | 0.091 ±0.009 | 0.064 ±0.005 |
| L | 0.050 ±0.007 | 0.073 ±0.011 | 0.084 ±0.003 | 0.113 ±0.008 | 0.092 ±0.002 | 0.066 ±0.001 | 0.049 ±0.011 |
| I | 0.034 ±0.012 | 0.045 ±0.018 | 0.066 ±0.004 | 0.085 ±0.004 | 0.082 ±0.003 | 0.057 ±0.002 | 0.042 ±0.005 |
| Residues | I | L | T | I | I | T | L |

Table S10. WT-WT Side-chain—side-chain contact probabilities and corresponding errors in CI system (Fig. 7D)

| | | | | | | | |
|----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| L | 0.073 ±0.007 | 0.108 ±0.015 | 0.072 ±0.010 | 0.132 ±0.014 | 0.093 ±0.014 | 0.053 ±0.001 | 0.073 ±0.024 |
| T | 0.071 ±0.009 | 0.110 ±0.008 | 0.113 ±0.005 | 0.089 ±0.017 | 0.093 ±0.018 | 0.040 ±0.009 | 0.053 ±0.001 |
| I | 0.088 ±0.012 | 0.165 ±0.003 | 0.112 ±0.012 | 0.205 ±0.022 | 0.133 ±0.030 | 0.093 ±0.018 | 0.093 ±0.014 |
| I | 0.129 ±0.017 | 0.147 ±0.039 | 0.171 ±0.023 | 0.179 ±0.020 | 0.205 ±0.022 | 0.089 ±0.017 | 0.132 ±0.014 |
| T | 0.067 ±0.003 | 0.108 ±0.011 | 0.074 ±0.018 | 0.171 ±0.023 | 0.112 ±0.012 | 0.113 ±0.005 | 0.072 ±0.010 |
| L | 0.100 ±0.014 | 0.079 ±0.015 | 0.108 ±0.011 | 0.147 ±0.039 | 0.165 ±0.003 | 0.110 ±0.008 | 0.108 ±0.015 |
| I | 0.058 ±0.002 | 0.100 ±0.014 | 0.067 ±0.003 | 0.129 ±0.017 | 0.088 ±0.012 | 0.071 ±0.009 | 0.073 ±0.007 |
| Residues | I | L | T | I | I | T | L |

Table S11. MT-MT Side-chain—side-chain contact probabilities and corresponding errors in CI system (Fig. 7E)

| | | | | | | | |
|----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| L | 0.091 ±0.005 | 0.086 ±0.009 | 0.084 ±0.020 | 0.080 ±0.015 | 0.133 ±0.001 | 0.071 ±0.023 | 0.083 ±0.003 |
| T | 0.061 ±0.005 | 0.068 ±0.005 | 0.068 ±0.006 | 0.053 ±0.021 | 0.084 ±0.028 | 0.063 ±0.031 | 0.071 ±0.023 |
| I | 0.115 ±0.009 | 0.186 ±0.010 | 0.160 ±0.028 | 0.099 ±0.021 | 0.270 ±0.056 | 0.084 ±0.028 | 0.133 ±0.001 |
| I&R | 0.109 ±0.009 | 0.080 ±0.004 | 0.097 ±0.020 | 0.084 ±0.028 | 0.099 ±0.021 | 0.053 ±0.021 | 0.080 ±0.015 |
| T | 0.062 ±0.001 | 0.107 ±0.018 | 0.089 ±0.026 | 0.097 ±0.020 | 0.160 ±0.028 | 0.068 ±0.006 | 0.084 ±0.020 |
| L | 0.084 ±0.005 | 0.090 ±0.015 | 0.107 ±0.018 | 0.080 ±0.004 | 0.186 ±0.010 | 0.068 ±0.005 | 0.086 ±0.009 |
| I | 0.085 ±0.016 | 0.084 ±0.005 | 0.062 ±0.001 | 0.109 ±0.009 | 0.115 ±0.009 | 0.061 ±0.005 | 0.091 ±0.005 |
| Residues | I | L | T | I&R | I | T | L |

Table S12. WT-MT Side-chain—side-chain contact probabilities and corresponding errors in CI system (Fig. 7F)

| | | | | | | | |
|---|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| L | 0.138 ±0.012 | 0.147 ±0.003 | 0.084 ±0.003 | 0.146 ±0.006 | 0.093 ±0.001 | 0.094 ±0.003 | 0.111 ±0.016 |
| T | 0.082 ±0.012 | 0.070 ±0.002 | 0.098 ±0.002 | 0.112 ±0.002 | 0.104 ±0.010 | 0.09 ±0.007 | 0.065 ±0.012 |

| | | | | | | | |
|----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| I | 0.128 ±0.013 | 0.162 ±0.008 | 0.144 ±0.007 | 0.266 ±0.013 | 0.211 ±0.006 | 0.130 ±0.004 | 0.134 ±0.001 |
| I&R | 0.106 ±0.013 | 0.113 ±0.007 | 0.135 ±0.013 | 0.140 ±0.005 | 0.139 ±0.005 | 0.113 ±0.002 | 0.118 ±0.003 |
| T | 0.074 ±0.001 | 0.107 ±0.012 | 0.142 ±0.002 | 0.195 ±0.017 | 0.165 ±0.011 | 0.135 ±0.003 | 0.119 ±0.014 |
| L | 0.094 ±0.014 | 0.134 ±0.015 | 0.101 ±0.004 | 0.165 ±0.016 | 0.152 ±0.011 | 0.116 ±0.005 | 0.103 ±0.007 |
| I | 0.103 ±0.011 | 0.105 ±0.002 | 0.107 ±0.012 | 0.128 ±0.009 | 0.125 ±0.013 | 0.110 ±0.006 | 0.104 ±0.003 |
| Residues | I | L | T | I&R | I | T | L |