Molecular Insights into the Specific Targeting of *c-MYC* G-quadruplex by Cell-Penetrating Peptides: An in silico Study

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**Supplementary tables**

**Table S1.** Sequence of the promotor G4s.

|  |  |
| --- | --- |
| G4s | Sequence |
| *c-MYC* | TGAGGGTGGGTAGGGTGGGTAA |
| *c-KIT1* | GGGAGGGCGCTGGGAGGAGGG |
| *c-KIT2* | GGGCGGGCGCTAGGGAGGGG |
| *BCL2* | GGGCGCGGGAGGAATTGGGCGGG |

**Table S2.** Hoogsteen hydrogen bonds of the apo and the peptides bound G4s.1,2

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | | | | |
| G4 | Acceptor | Donor | Ocpy. (%) | Dist. (Å) | Ang. (°) |
| *c-MYC* | dG4@O6 | dG17@H1 dG17@N1 | 99.23% | 2.93 | 155.26 |
| dG8@O6 | dG4@H1 dG4@N1 | 99.29% | 2.98 | 160.52 |
| dG13@O6 | dG8@H1 dG8@N1 | 99.71% | 2.92 | 158.36 |
| dG17@O6 | dG13@H1 dG13@N1 | 99.67% | 2.94 | 158.37 |
| dG4@N7 | dG17@H21 dG17@N2 | 98.56% | 3.04 | 158.08 |
| dG8@N7 | dG4@H21 dG4@N2 | 99.58% | 2.98 | 159.01 |
| dG13@N7 | dG8@H21 dG8@N2 | 99.30% | 3.00 | 159.33 |
| dG17@N7 | dG13@H21 dG13@N2 | 99.72% | 2.97 | 160.09 |
| dG5@O6 | dG18@H1 dG18@N1 | 89.97% | 3.17 | 138.95 |
| dG9@O6 | dG5@H1 dG5@N1 | 91.91% | 3.19 | 141.05 |
| dG14@O6 | dG9@H1 dG9@N1 | 90.04% | 3.19 | 139.53 |
| dG18@O6 | dG14@H1 dG14@N1 | 94.25% | 3.17 | 141.01 |
| dG5@N7 | dG18@H21 dG18@N2 | 99.42% | 2.96 | 158.53 |
| dG9@N7 | dG5@H21 dG5@N2 | 99.53% | 2.99 | 157.49 |
| dG14@N7 | dG9@H21 dG9@N2 | 99.48% | 2.98 | 157.52 |
| dG18@N7 | dG14@H21 dG14@N2 | 99.51% | 3.00 | 156.55 |
| dG6@O6 | dG19@H1 dG19@N1 | 99.64% | 2.95 | 158.25 |
| dG10@O6 | dG6@H1 dG6@N1 | 99.78% | 2.97 | 158.98 |
| dG15@O6 | dG10@H1 dG10@N1 | 99.75% | 2.94 | 159.30 |
| dG19@O6 | dG15@H1 dG15@N1 | 99.61% | 2.98 | 161.50 |
| dG6@N7 | dG19@H21 dG19@N2 | 99.59% | 2.96 | 157.03 |
| dG10@N7 | dG6@H21 dG6@N2 | 99.89% | 2.97 | 161.24 |
| dG15@N7 | dG10@H21 dG10@N2 | 99.24% | 2.99 | 155.25 |
| dG19@N7 | dG15@H21 dG15@N2 | 99.92% | 2.96 | 158.96 |
| *c-MYC* (**TH1)** | dG4@O6 | dG17@H1 dG17@N1 | 99.79% | 2.94 | 159.07 |
| dG8@O6 | dG4@H1 dG4@N1 | 99.76% | 2.94 | 159.53 |
| dG13@O6 | dG8@H1 dG8@N1 | 99.86% | 2.93 | 159.62 |
| dG17@O6 | dG13@H1 dG13@N1 | 99.86% | 2.93 | 159.63 |
| dG4@N7 | dG17@H21 dG17@N2 | 99.70% | 2.99 | 159.48 |
| dG8@N7 | dG4@H21 dG4@N2 | 99.64% | 2.98 | 159.16 |
| dG13@N7 | dG8@H21 dG8@N2 | 99.70% | 2.99 | 160.78 |
| dG17@N7 | dG13@H21 dG13@N2 | 99.83% | 2.98 | 160.00 |
| dG5@O6 | dG18@H1 dG18@N1 | 95.69% | 3.12 | 142.71 |
| dG9@O6 | dG5@H1 dG5@N1 | 95.48% | 3.14 | 143.38 |
| dG14@O6 | dG9@H1 dG9@N1 | 96.02% | 3.12 | 143.93 |
| dG18@O6 | dG14@H1 dG14@N1 | 95.64% | 3.14 | 143.09 |
| dG5@N7 | dG18@H21 dG18@N2 | 99.79% | 2.95 | 161.21 |
| dG9@N7 | dG5@H21 dG5@N2 | 99.67% | 2.98 | 160.48 |
| dG14@N7 | dG9@H21 dG9@N2 | 99.76% | 2.96 | 161.04 |
| dG18@N7 | dG14@H21 dG14@N2 | 99.77% | 2.96 | 159.66 |
| dG6@O6 | dG19@H1 dG19@N1 | 99.58% | 2.96 | 162.03 |
| dG10@O6 | dG6@H1 dG6@N1 | 99.77% | 2.95 | 161.75 |
| dG15@O6 | dG10@H1 dG10@N1 | 99.90% | 2.92 | 162.32 |
| dG19@O6 | dG15@H1 dG15@N1 | 99.05% | 2.99 | 157.81 |
| dG6@N7 | dG19@H21 dG19@N2 | 98.45% | 3.02 | 152.95 |
| dG10@N7 | dG6@H21 dG6@N2 | 99.58% | 3.00 | 157.96 |
| dG15@N7 | dG10@H21 dG10@N2 | 99.49% | 3.00 | 156.51 |
| dG19@N7 | dG15@H21 dG15@N2 | 99.45% | 3.01 | 156.47 |
| *c-MYC* (**TH3**) | dG4@O6 | dG17@H1 dG17@N1 | 99.87% | 2.92 | 158.85 |
| dG8@O6 | dG4@H1 dG4@N1 | 99.84% | 2.92 | 161.90 |
| dG13@O6 | dG8@H1 dG8@N1 | 99.92% | 2.92 | 160.79 |
| dG17@O6 | dG13@H1 dG13@N1 | 99.92% | 2.93 | 161.55 |
| dG4@N7 | dG17@H21 dG17@N2 | 99.47% | 3.01 | 157.05 |
| dG8@N7 | dG4@H21 dG4@N2 | 99.33% | 3.01 | 156.87 |
| dG13@N7 | dG8@H21 dG8@N2 | 99.79% | 2.98 | 158.05 |
| dG17@N7 | dG13@H21 dG13@N2 | 99.87% | 2.97 | 159.84 |
| dG5@O6 | dG18@H1 dG18@N1 | 95.09% | 3.13 | 141.84 |
| dG9@O6 | dG5@H1 dG5@N1 | 94.55% | 3.16 | 142.59 |
| dG14@O6 | dG9@H1 dG9@N1 | 95.55% | 3.14 | 143.08 |
| dG18@O6 | dG14@H1 dG14@N1 | 94.38% | 3.16 | 141.68 |
| dG5@N7 | dG18@H21 dG18@N2 | 99.69% | 2.96 | 161.20 |
| dG9@N7 | dG5@H21 dG5@N2 | 99.82% | 2.98 | 160.63 |
| dG14@N7 | dG9@H21 dG9@N2 | 99.55% | 2.98 | 157.84 |
| dG18@N7 | dG14@H21 dG14@N2 | 99.52% | 2.97 | 157.08 |
| dG6@O6 | dG19@H1 dG19@N1 | 99.37% | 2.98 | 159.53 |
| dG10@O6 | dG6@H1 dG6@N1 | 99.91% | 2.93 | 160.87 |
| dG15@O6 | dG10@H1 dG10@N1 | 99.96% | 2.91 | 162.87 |
| dG19@O6 | dG15@H1 dG15@N1 | 99.37% | 2.99 | 160.53 |
| dG6@N7 | dG19@H21 dG19@N2 | 99.38% | 2.98 | 155.92 |
| dG10@N7 | dG6@H21 dG6@N2 | 99.68% | 3.00 | 158.54 |
| dG15@N7 | dG10@H21 dG10@N2 | 99.75% | 3.00 | 156.65 |
| dG19@N7 | dG15@H21 dG15@N2 | 99.73% | 2.98 | 155.76 |
|  |  |  |  |  |
| *c-KIT1* | dG1@O6 | dG12@H1 dG12@N1 | 98.61% | 2.96 | 153.94 |
| dG5@O6 | dG1@H1 dG1@N1 | 99.15% | 2.97 | 157.35 |
| dG9@O6 | dG5@H1 dG5@N1 | 99.42% | 2.94 | 156.91 |
| dG12@O6 | dG9@H1 dG9@N1 | 99.59% | 2.94 | 161.03 |
| dG1@N7 | dG12@H21 dG12@N2 | 98.93% | 3.00 | 158.84 |
| dG5@N7 | dG1@H21 dG1@N2 | 99.10% | 2.99 | 158.79 |
| dG9@N7 | dG5@H21 dG5@N2 | 98.62% | 3.03 | 160.29 |
| dG12@N7 | dG9@H21 dG9@N2 | 99.25% | 3.01 | 159.41 |
| dG2@O6 | dG13@H1 dG13@N1 | 95.67% | 3.11 | 142.44 |
| dG6@O6 | dG2@H1 dG2@N1 | 97.11% | 3.11 | 144.74 |
| dG13@O6 | dG20@H1 dG20@N1 | 96.34% | 3.12 | 144.18 |
| dG20@O6 | dG6@H1 dG6@N1 | 96.68% | 3.12 | 144.75 |
| dG2@N7 | dG13@H21 dG13@N2 | 99.58% | 2.97 | 161.79 |
| dG6@N7 | dG2@H21 dG2@N2 | 99.79% | 2.96 | 162.51 |
| dG13@N7 | dG20@H21 dG20@N2 | 99.73% | 2.97 | 163.30 |
| dG20@N7 | dG6@H21 dG6@N2 | 99.88% | 2.95 | 162.62 |
| dG3@O6 | dG14@H1 dG14@N1 | 99.44% | 2.99 | 156.30 |
| dG7@O6 | dG3@H1 dG3@N1 | 99.30% | 2.98 | 156.69 |
| dG14@O6 | dG21@H1 dG21@N1 | 99.68% | 2.98 | 158.08 |
| dG21@O6 | dG7@H1 dG7@N1 | 99.36% | 2.98 | 155.34 |
| dG3@N7 | dG14@H21 dG14@N2 | 99.77% | 2.96 | 160.53 |
| dG7@N7 | dG3@H21 dG3@N2 | 99.70% | 2.99 | 161.74 |
| dG14@N7 | dG21@H21 dG21@N2 | 99.80% | 2.99 | 161.17 |
| dG21@N7 | dG7@H21 dG7@N2 | 99.65% | 3.00 | 160.02 |
| *c-KIT1* (**TH1**) | dG1@O6 | dG12@H1 dG12@N1 | 98.59% | 2.97 | 151.97 |
| dG5@O6 | dG1@H1 dG1@N1 | 99.42% | 2.98 | 155.92 |
| dG9@O6 | dG5@H1 dG5@N1 | 99.57% | 2.96 | 157.74 |
| dG12@O6 | dG9@H1 dG9@N1 | 99.24% | 2.97 | 158.23 |
| dG1@N7 | dG12@H21 dG12@N2 | 99.42% | 2.98 | 159.85 |
| dG5@N7 | dG1@H21 dG1@N2 | 99.84% | 2.97 | 162.11 |
| dG9@N7 | dG5@H21 dG5@N2 | 99.46% | 3.00 | 162.04 |
| dG12@N7 | dG9@H21 dG9@N2 | 99.60% | 2.99 | 161.73 |
| dG2@O6 | dG13@H1 dG13@N1 | 97.10% | 3.11 | 144.37 |
| dG6@O6 | dG2@H1 dG2@N1 | 97.38% | 3.11 | 144.84 |
| dG13@O6 | dG20@H1 dG20@N1 | 97.75% | 3.10 | 145.24 |
| dG20@O6 | dG6@H1 dG6@N1 | 97.32% | 3.11 | 145.04 |
| dG2@N7 | dG13@H21 dG13@N2 | 99.85% | 2.95 | 162.93 |
| dG6@N7 | dG2@H21 dG2@N2 | 99.88% | 2.96 | 163.15 |
| dG13@N7 | dG20@H21 dG20@N2 | 99.76% | 2.98 | 164.01 |
| dG20@N7 | dG6@H21 dG6@N2 | 99.89% | 2.95 | 163.39 |
| dG3@O6 | dG14@H1 dG14@N1 | 99.61% | 2.98 | 157.65 |
| dG7@O6 | dG3@H1 dG3@N1 | 97.96% | 3.00 | 156.42 |
| dG14@O6 | dG21@H1 dG21@N1 | 99.49% | 2.98 | 156.45 |
| dG21@O6 | dG7@H1 dG7@N1 | 99.38% | 2.98 | 156.02 |
| dG3@N7 | dG14@H21 dG14@N2 | 99.77% | 2.96 | 161.66 |
| dG7@N7 | dG3@H21 dG3@N2 | 99.84% | 2.98 | 162.00 |
| dG14@N7 | dG21@H21 dG21@N2 | 99.80% | 2.98 | 161.02 |
| dG21@N7 | dG7@H21 dG7@N2 | 99.79% | 3.00 | 162.27 |
| *c-KIT1* (**TH3**) | dG1@O6 | dG12@H1 dG12@N1 | 99.59% | 2.92 | 158.85 |
| dG5@O6 | dG1@H1 dG1@N1 | 99.30% | 2.96 | 157.70 |
| dG9@O6 | dG5@H1 dG5@N1 | 99.44% | 2.94 | 154.52 |
| dG12@O6 | dG9@H1 dG9@N1 | 99.54% | 2.93 | 161.54 |
| dG1@N7 | dG12@H21 dG12@N2 | 98.99% | 3.02 | 158.20 |
| dG5@N7 | dG1@H21 dG1@N2 | 99.70% | 2.96 | 158.60 |
| dG9@N7 | dG5@H21 dG5@N2 | 99.44% | 3.00 | 160.18 |
| dG12@N7 | dG9@H21 dG9@N2 | 99.44% | 3.00 | 160.34 |
| dG2@O6 | dG13@H1 dG13@N1 | 97.82% | 3.09 | 146.78 |
| dG6@O6 | dG2@H1 dG2@N1 | 98.71% | 3.07 | 144.64 |
| dG13@O6 | dG20@H1 dG20@N1 | 98.13% | 3.06 | 146.42 |
| dG20@O6 | dG6@H1 dG6@N1 | 96.61% | 3.08 | 143.46 |
| dG2@N7 | dG13@H21 dG13@N2 | 99.85% | 2.91 | 161.39 |
| dG6@N7 | dG2@H21 dG2@N2 | 99.50% | 2.96 | 157.70 |
| dG13@N7 | dG20@H21 dG20@N2 | 99.82% | 2.97 | 164.07 |
| dG20@N7 | dG6@H21 dG6@N2 | 99.85% | 2.94 | 160.96 |
| dG3@O6 | dG14@H1 dG14@N1 | 99.56% | 2.97 | 161.13 |
| dG7@O6 | dG3@H1 dG3@N1 | 99.94% | 2.94 | 163.63 |
| dG14@O6 | dG21@H1 dG21@N1 | 99.97% | 2.86 | 162.90 |
| dG21@O6 | dG7@H1 dG7@N1 | 99.96% | 2.90 | 165.45 |
| dG3@N7 | dG14@H21 dG14@N2 | 98.79% | 3.04 | 148.14 |
| dG7@N7 | dG3@H21 dG3@N2 | 99.56% | 3.03 | 157.43 |
| dG14@N7 | dG21@H21 dG21@N2 | 99.77% | 2.97 | 154.23 |
| dG21@N7 | dG7@H21 dG7@N2 | 94.95% | 3.12 | 151.15 |
|  |  |  |  |  |
| *c-KIT2* | dG1@O6 | dG17@H1 dG17@N1 | 99.33% | 2.94 | 156.72 |
| dG5@O6 | dG1@H1 dG1@N1 | 99.67% | 2.95 | 158.79 |
| dG13@O6 | dG5@H1 dG5@N1 | 99.85% | 2.91 | 159.92 |
| dG17@O6 | dG13@H1 dG13@N1 | 99.60% | 2.94 | 161.07 |
| dG1@N7 | dG17@H21 dG17@N2 | 99.22% | 3.01 | 159.15 |
| dG5@N7 | dG1@H21 dG1@N2 | 99.19% | 3.00 | 157.78 |
| dG13@N7 | dG5@H21 dG5@N2 | 99.58% | 3.00 | 160.38 |
| dG17@N7 | dG13@H21 dG13@N2 | 99.29% | 2.99 | 157.67 |
| dG2@O6 | dG18@H1 dG18@N1 | 94.55% | 3.13 | 141.19 |
| dG6@O6 | dG2@H1 dG2@N1 | 93.57% | 3.17 | 141.99 |
| dG14@O6 | dG6@H1 dG6@N1 | 94.92% | 3.14 | 142.37 |
| dG18@O6 | dG14@H1 dG14@N1 | 93.16% | 3.18 | 141.42 |
| dG2@N7 | dG18@H21 dG18@N2 | 99.62% | 2.96 | 160.26 |
| dG6@N7 | dG2@H21 dG2@N2 | 99.53% | 2.98 | 158.85 |
| dG14@N7 | dG6@H21 dG6@N2 | 99.79% | 2.95 | 160.88 |
| dG18@N7 | dG14@H21 dG14@N2 | 99.53% | 3.00 | 158.01 |
| dG3@O6 | dG19@H1 dG19@N1 | 99.47% | 2.97 | 158.72 |
| dG7@O6 | dG3@H1 dG3@N1 | 99.61% | 2.98 | 159.30 |
| dG15@O6 | dG7@H1 dG7@N1 | 99.64% | 2.97 | 158.53 |
| dG19@O6 | dG15@H1 dG15@N1 | 99.83% | 2.96 | 159.87 |
| dG3@N7 | dG19@H21 dG19@N2 | 99.41% | 2.99 | 157.10 |
| dG7@N7 | dG3@H21 dG3@N2 | 99.76% | 2.98 | 160.33 |
| dG15@N7 | dG7@H21 dG7@N2 | 99.61% | 2.98 | 158.44 |
| dG19@N7 | dG15@H21 dG15@N2 | 99.90% | 2.96 | 160.90 |
| *c-KIT2* (**TH1**) | dG1@O6 | dG17@H1 dG17@N1 | 99.60% | 2.94 | 157.68 |
| dG5@O6 | dG1@H1 dG1@N1 | 99.26% | 2.97 | 158.54 |
| dG13@O6 | dG5@H1 dG5@N1 | 99.45% | 2.93 | 156.49 |
| dG17@O6 | dG13@H1 dG13@N1 | 99.47% | 2.96 | 158.36 |
| dG1@N7 | dG17@H21 dG17@N2 | 99.51% | 3.00 | 160.91 |
| dG5@N7 | dG1@H21 dG1@N2 | 99.44% | 2.98 | 159.88 |
| dG13@N7 | dG5@H21 dG5@N2 | 99.55% | 3.00 | 161.05 |
| dG17@N7 | dG13@H21 dG13@N2 | 99.40% | 2.97 | 158.83 |
| dG2@O6 | dG18@H1 dG18@N1 | 95.21% | 3.14 | 142.87 |
| dG6@O6 | dG2@H1 dG2@N1 | 93.84% | 3.17 | 141.85 |
| dG14@O6 | dG6@H1 dG6@N1 | 94.91% | 3.13 | 141.55 |
| dG18@O6 | dG14@H1 dG14@N1 | 94.77% | 3.15 | 142.71 |
| dG2@N7 | dG18@H21 dG18@N2 | 99.80% | 2.95 | 161.29 |
| dG6@N7 | dG2@H21 dG2@N2 | 99.67% | 2.97 | 158.32 |
| dG14@N7 | dG6@H21 dG6@N2 | 99.67% | 2.97 | 160.36 |
| dG18@N7 | dG14@H21 dG14@N2 | 99.63% | 2.98 | 159.84 |
| dG3@O6 | dG19@H1 dG19@N1 | 99.65% | 2.97 | 159.65 |
| dG7@O6 | dG3@H1 dG3@N1 | 99.80% | 2.95 | 160.70 |
| dG15@O6 | dG7@H1 dG7@N1 | 99.64% | 2.96 | 159.65 |
| dG19@O6 | dG15@H1 dG15@N1 | 99.60% | 2.96 | 158.03 |
| dG3@N7 | dG19@H21 dG19@N2 | 99.50% | 2.99 | 157.43 |
| dG7@N7 | dG3@H21 dG3@N2 | 99.80% | 2.98 | 159.07 |
| dG15@N7 | dG7@H21 dG7@N2 | 99.75% | 2.98 | 158.93 |
| dG19@N7 | dG15@H21 dG15@N2 | 99.76% | 2.99 | 159.04 |
| *c-KIT2* (**TH3**) | dG1@O6 | dG17@H1 dG17@N1 | 99.75% | 2.94 | 158.59 |
| dG5@O6 | dG1@H1 dG1@N1 | 99.36% | 2.95 | 159.97 |
| dG13@O6 | dG5@H1 dG5@N1 | 99.43% | 2.92 | 154.02 |
| dG17@O6 | dG13@H1 dG13@N1 | 99.73% | 2.95 | 161.15 |
| dG1@N7 | dG17@H21 dG17@N2 | 99.50% | 3.00 | 159.45 |
| dG5@N7 | dG1@H21 dG1@N2 | 99.88% | 2.97 | 160.49 |
| dG13@N7 | dG5@H21 dG5@N2 | 99.12% | 3.02 | 159.90 |
| dG17@N7 | dG13@H21 dG13@N2 | 99.57% | 2.98 | 158.22 |
| dG2@O6 | dG18@H1 dG18@N1 | 95.65% | 3.13 | 142.67 |
| dG6@O6 | dG2@H1 dG2@N1 | 94.59% | 3.16 | 142.42 |
| dG14@O6 | dG6@H1 dG6@N1 | 94.43% | 3.13 | 141.22 |
| dG18@O6 | dG14@H1 dG14@N1 | 95.16% | 3.15 | 142.84 |
| dG2@N7 | dG18@H21 dG18@N2 | 99.75% | 2.94 | 160.40 |
| dG6@N7 | dG2@H21 dG2@N2 | 99.75% | 2.96 | 159.23 |
| dG14@N7 | dG6@H21 dG6@N2 | 99.69% | 2.97 | 160.42 |
| dG18@N7 | dG14@H21 dG14@N2 | 99.70% | 2.98 | 159.86 |
| dG3@O6 | dG19@H1 dG19@N1 | 99.78% | 2.95 | 159.91 |
| dG7@O6 | dG3@H1 dG3@N1 | 99.75% | 2.97 | 160.58 |
| dG15@O6 | dG7@H1 dG7@N1 | 99.54% | 2.97 | 158.15 |
| dG19@O6 | dG15@H1 dG15@N1 | 99.88% | 2.95 | 159.95 |
| dG3@N7 | dG19@H21 dG19@N2 | 99.64% | 2.99 | 158.48 |
| dG7@N7 | dG3@H21 dG3@N2 | 99.82% | 2.98 | 159.80 |
| dG15@N7 | dG7@H21 dG7@N2 | 99.55% | 2.98 | 157.90 |
| dG19@N7 | dG15@H21 dG15@N2 | 99.90% | 2.97 | 160.55 |
|  |  |  |  |  |
| *BCL-2* | dG1@O6 | dG9@H1 dG9@N1 | 99.96% | 2.93 | 161.16 |
| dG9@O6 | dG17@H1 dG17@N1 | 99.91% | 2.93 | 162.12 |
| dG17@O6 | dG21@H1 dG21@N1 | 99.93% | 2.93 | 159.65 |
| dG21@O6 | dG1@H1 dG1@N1 | 99.82% | 2.92 | 159.16 |
| dG1@N7 | dG9@H21 dG9@N2 | 99.94% | 2.96 | 160.22 |
| dG9@N7 | dG17@H21 dG17@N2 | 99.69% | 3.00 | 154.48 |
| dG17@N7 | dG21@H21 dG21@N2 | 99.63% | 3.00 | 160.74 |
| dG21@N7 | dG1@H21 dG1@N2 | 99.44% | 3.04 | 155.38 |
| dG2@O6 | dG22@H1 dG22@N1 | 91.87% | 3.18 | 141.17 |
| dG8@O6 | dG2@H1 dG2@N1 | 87.10% | 3.22 | 140.12 |
| dG18@O6 | dG8@H1 dG8@N1 | 94.12% | 3.14 | 142.46 |
| dG22@O6 | dG18@H1 dG18@N1 | 92.35% | 3.18 | 141.19 |
| dG2@N7 | dG22@H21 dG22@N2 | 99.74% | 2.98 | 158.56 |
| dG8@N7 | dG2@H21 dG2@N2 | 99.01% | 3.03 | 160.84 |
| dG18@N7 | dG8@H21 dG8@N2 | 99.68% | 2.99 | 162.50 |
| dG22@N7 | dG18@H21 dG18@N2 | 99.84% | 2.96 | 160.50 |
| dG3@O6 | dG23@H1 dG23@N1 | 99.86% | 2.97 | 161.57 |
| dG7@O6 | dG3@H1 dG3@N1 | 98.98% | 3.00 | 154.06 |
| dG19@O6 | dG7@H1 dG7@N1 | 99.97% | 2.89 | 159.63 |
| dG23@O6 | dG19@H1 dG19@N1 | 99.21% | 2.99 | 152.93 |
| dG3@N7 | dG23@H21 dG23@N2 | 99.90% | 2.96 | 158.88 |
| dG7@N7 | dG3@H21 dG3@N2 | 99.93% | 2.96 | 162.45 |
| dG19@N7 | dG7@H21 dG7@N2 | 99.96% | 2.96 | 160.15 |
| dG23@N7 | dG19@H21 dG19@N2 | 99.49% | 3.00 | 160.56 |
| *BCL-2* (**TH1**) | dG1@O6 | dG9@H1 dG9@N1 | 99.97% | 2.92 | 161.20 |
| dG9@O6 | dG17@H1 dG17@N1 | 99.91% | 2.92 | 162.15 |
| dG17@O6 | dG21@H1 dG21@N1 | 99.92% | 2.93 | 159.31 |
| dG21@O6 | dG1@H1 dG1@N1 | 99.82% | 2.92 | 159.11 |
| dG1@N7 | dG9@H21 dG9@N2 | 99.94% | 2.95 | 160.30 |
| dG9@N7 | dG17@H21 dG17@N2 | 99.68% | 3.00 | 154.20 |
| dG17@N7 | dG21@H21 dG21@N2 | 99.56% | 3.01 | 160.54 |
| dG21@N7 | dG1@H21 dG1@N2 | 99.46% | 3.04 | 155.38 |
| dG2@O6 | dG22@H1 dG22@N1 | 91.81% | 3.18 | 140.78 |
| dG8@O6 | dG2@H1 dG2@N1 | 87.78% | 3.22 | 140.37 |
| dG18@O6 | dG8@H1 dG8@N1 | 93.34% | 3.16 | 142.18 |
| dG22@O6 | dG18@H1 dG18@N1 | 92.25% | 3.19 | 141.18 |
| dG2@N7 | dG22@H21 dG22@N2 | 99.70% | 2.98 | 158.11 |
| dG8@N7 | dG2@H21 dG2@N2 | 99.04% | 3.03 | 161.21 |
| dG18@N7 | dG8@H21 dG8@N2 | 99.69% | 2.99 | 162.21 |
| dG22@N7 | dG18@H21 dG18@N2 | 99.82% | 2.96 | 160.28 |
| dG3@O6 | dG23@H1 dG23@N1 | 99.92% | 2.95 | 161.06 |
| dG7@O6 | dG3@H1 dG3@N1 | 99.57% | 2.97 | 155.82 |
| dG19@O6 | dG7@H1 dG7@N1 | 99.96% | 2.91 | 160.96 |
| dG23@O6 | dG19@H1 dG19@N1 | 99.32% | 3.00 | 154.05 |
| dG3@N7 | dG23@H21 dG23@N2 | 99.91% | 2.97 | 159.43 |
| dG7@N7 | dG3@H21 dG3@N2 | 99.93% | 2.96 | 162.08 |
| dG19@N7 | dG7@H21 dG7@N2 | 99.95% | 2.97 | 159.76 |
|  | dG23@N7 | dG19@H21 dG19@N2 | 99.59% | 3.00 | 161.14 |
| *BCL-2* (**TH3**) | dG1@O6 | dG9@H1 dG9@N1 | 99.97% | 2.93 | 161.09 |
| dG9@O6 | dG17@H1 dG17@N1 | 99.90% | 2.93 | 162.01 |
| dG17@O6 | dG21@H1 dG21@N1 | 99.94% | 2.93 | 159.84 |
| dG21@O6 | dG1@H1 dG1@N1 | 99.84% | 2.92 | 158.85 |
| dG1@N7 | dG9@H21 dG9@N2 | 99.95% | 2.95 | 160.42 |
| dG9@N7 | dG17@H21 dG17@N2 | 99.69% | 3.00 | 154.34 |
| dG17@N7 | dG21@H21 dG21@N2 | 99.75% | 3.00 | 160.70 |
| dG21@N7 | dG1@H21 dG1@N2 | 99.36% | 3.04 | 155.08 |
| dG2@O6 | dG22@H1 dG22@N1 | 92.86% | 3.17 | 141.33 |
| dG8@O6 | dG2@H1 dG2@N1 | 88.24% | 3.21 | 140.13 |
| dG18@O6 | dG8@H1 dG8@N1 | 94.65% | 3.14 | 142.62 |
| dG22@O6 | dG18@H1 dG18@N1 | 93.12% | 3.18 | 141.43 |
| dG2@N7 | dG22@H21 dG22@N2 | 99.80% | 2.97 | 158.52 |
| dG8@N7 | dG2@H21 dG2@N2 | 99.18% | 3.02 | 160.95 |
| dG18@N7 | dG8@H21 dG8@N2 | 99.73% | 2.98 | 162.65 |
| dG22@N7 | dG18@H21 dG18@N2 | 99.86% | 2.96 | 160.84 |
| dG3@O6 | dG23@H1 dG23@N1 | 99.88% | 2.96 | 162.44 |
| dG7@O6 | dG3@H1 dG3@N1 | 99.10% | 2.99 | 154.74 |
| dG19@O6 | dG7@H1 dG7@N1 | 99.97% | 2.89 | 160.24 |
| dG23@O6 | dG19@H1 dG19@N1 | 99.40% | 2.98 | 153.55 |
| dG3@N7 | dG23@H21 dG23@N2 | 99.91% | 2.96 | 158.41 |
| dG7@N7 | dG3@H21 dG3@N2 | 99.91% | 2.97 | 161.56 |
| dG19@N7 | dG7@H21 dG7@N2 | 99.95% | 2.96 | 159.63 |
| dG23@N7 | dG19@H21 dG19@N2 | 99.56% | 3.00 | 160.31 |

1 Hydrogen bonds located in the top, central, and bottom G-tetrads are colored in green, orange, and purple, respectively.

2 Ocpy., Dist., and Ang. mean the occupancy, bond length, and bond angle of the Hoogsteen hydrogen bonds, respectively.

**Supplementary figures**

**Figure S1**



**Figure S1.** RMSD profiles of the **TH1** bound promotor G4s (a)−(d) and the eigenvalue profiles constructed by the first 30 eigenvectors of the **TH1** bound G4s (e).

**Figure S2**



**Figure S2.** RMSD profiles of the **TH3** bound promotor G4s (a)−(d) and the eigenvalue profiles constructed by the first 30 eigenvectors of the **TH3** bound G4s (e).

**Figure S3**



**Figure S3.** The variations of distance between the polar hydrogen and the hydrogen bond receptor atoms throughout the MD simulations.