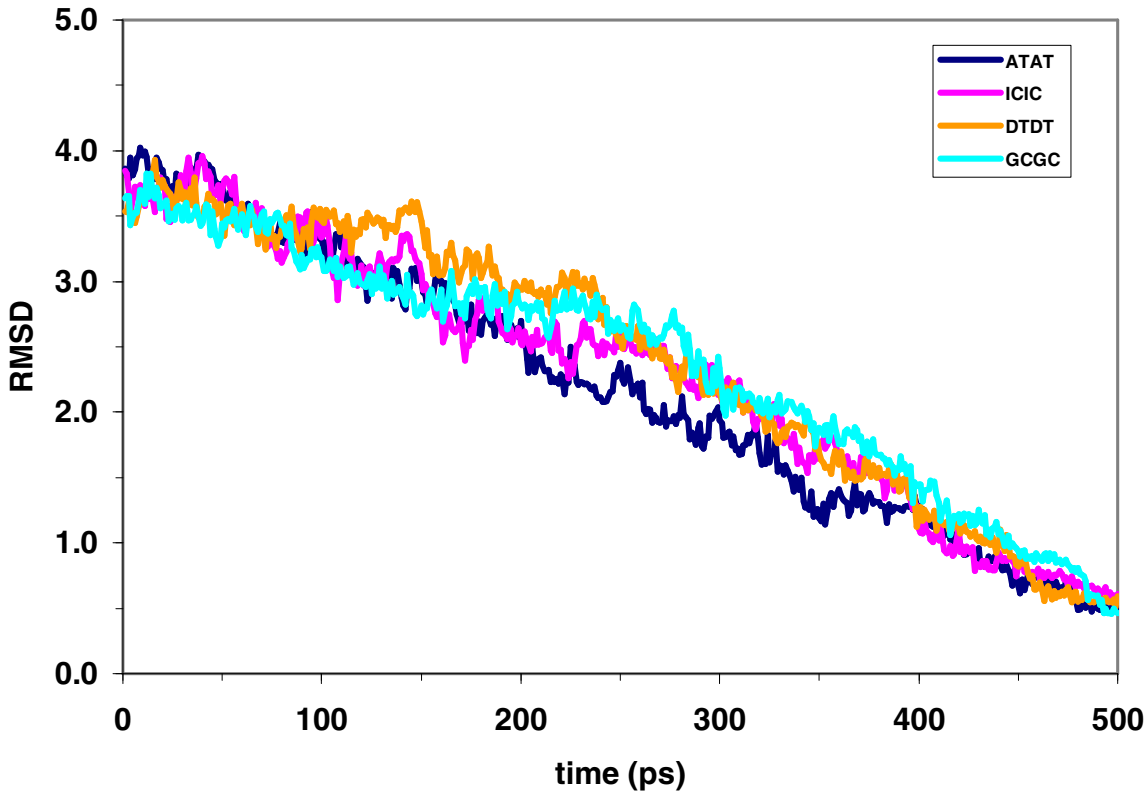

Figure S1. Time evolution of the root-mean-square deviation (RMSD) of the atoms that make up the central tetranucleotide where the bis-intercalators bind along the targeted MD simulations. Similar results were obtained when the simulation lasted 5 ns.

Table S1. Intermolecular Distances and Angles Between Hydrogen Bonding Donor and Acceptor Atoms[a] in the Equilibrated Complexes of 2QN and CysMeTANDEM with Each of its Target Decanucleotides.[b]

Donor-Acceptor	2QN: d(GCGG**CG**CCGC)$_2$		2QN: d(GCGD**TD**TCGC)$_2$	
	d (Å)	Angle (º)	d (Å)	Angle (º)
N2 D6/G6–O Ala2	3.5 ± 0.5 (44%)	157.3 ± 9.4	3.5 ± 0.5 (40%)	158.7 ± 9.7
N Ala2–N3 D6/G6	3.4 ± 0.3 (40%)	152.2 ± 11.5	3.4 ± 0.3 (34%)	151.2 ± 12.1
N2 D16/G16–O Ala1	3.2 ± 0.3 (71%)	159.7 ± 8.7	3.1 ± 0.2 (76%)	159.0 ± 9.1
N Ala1–N3 D16/G16	3.7 ± 0.4 (16%)	145.3 ± 12.3	3.5 ± 0.3 (31%)	149.1 ± 11.2
	CysMeTANDEM: d(CTCA**TA**TCAG)$_2$		CysMeTANDEM: d(CTCI**CI**CCAG)$_2$	
	d (Å)	Angle (º)	d (Å)	Angle (º)
N Ala2–N3 A6/I6	3.4 ± 0.4 (93%)	123.7 ± 31.0	3.3 ± 0.3 (57%)	144.0 ± 15.8
N Ala1–N3 A16/I16	3.4 ± 0.3 (35%)	119.3 ± 30.1	4.4 ± 0.5 (0%)	113.8 ± 18.2
N Val1/O Ala2	3.4 ± 0.4	138.4 ± 23.7	3.5 ± 0.4	131.3 ± 21.6
N Val2/O Ala1	3.2 ± 0.2	149.9 ± 13.7	3.1 ± 0.2	145.9 ± 20.1

[a] Residue numbering scheme as in Figure 3.

[b] Percentages in brackets indicate the percent of snapshots in which these intermolecular distances fulfill the criterion for hydrogen-bond formation ($d \leq 3.2$ Å).

AMBER PREP file for 5-methyl-cytosine

```
0    0    2

5-methyl-cytosine for TI calculations; 6-31G* RESP charges
cytC.data
DUC  INT     1
CORR OMIT DU   BEG
0.0
   1   DUMM  DU    M    0  -1  -2    0.00      0.00      0.00       0.0000
   2   DUMM  DU    M    1   0  -1    1.00      0.00      0.00       0.0000
   3   DUMM  DU    M    2   1   0    1.00     90.00      0.00       0.0000
   4   P     P     M    3   2   1    1.60    119.04    200.00       1.1659
   5   O1P   O2    E    4   3   2    1.48    109.61    150.00      -0.7761
   6   O2P   O2    E    4   3   2    1.48    109.58     20.00      -0.7761
   7   O5'   OS    M    4   3   2    1.60    101.43    -98.89      -0.4954
   8   C5'   CT    M    7   4   3    1.44    119.00    -39.22      -0.0069
   9   H5'1  H1    E    8   7   4    1.09    109.50     60.00       0.0754
  10   H5'2  H1    E    8   7   4    1.09    109.50    -60.00       0.0754
  11   C4'   CT    M    8   7   4    1.52    110.00    180.00       0.1629
  12   H4'   H1    E   11   8   7    1.09    109.50   -200.00       0.1176
  13   O4'   OS    S   11   8   7    1.46    108.86    -86.31      -0.3691
  14   C1'   CT    B   13  11   8    1.42    110.04    105.60      -0.0116
  15   H1'   H2    E   14  13  11    1.09    109.50   -240.00       0.1963
  16   N1    N*    S   14  13  11    1.49    108.10   -127.70      -0.0339
  17   C6    CM    B   16  14  13    1.36    121.10     81.59      -0.0183
  18   H6    H4    E   17  16  14    1.08    120.00      0.00       0.2293
  19   C5    CM    B   17  16  14    1.36    121.00    180.00      -0.3185
  20   C7    CT    3   19  17  16    1.09    120.00    180.00      -0.3646
  21   H71   HC    E   20  19  17    1.08    109.50     60.00       0.1157
  22   H72   HC    E   20  19  17    1.08    109.50    180.00       0.1157
  23   H73   HC    E   20  19  17    1.08    109.50    300.00       0.1157
  24   C4    CA    B   19  17  16    1.43    116.90      0.00       0.8439
  25   N4    N2    B   24  19  17    1.32    120.10    180.00      -0.9773
  26   H41   H     E   25  24  19    1.01    117.70    180.00       0.4314
  27   H42   H     E   25  24  19    1.01    120.27      0.00       0.4314
  28   N3    NC    B   24  19  17    1.33    121.70      0.00      -0.7748
  29   H3    D3    E   28  24  19    0.40    116.77    180.00       0.0000
  30   C2    C     S   28  24  25    1.36    120.50      0.00       0.7959
  31   O2    O     E   30  28  24    1.24    122.40    180.00      -0.6548
  32   C3'   CT    M   11   8   7    1.53    115.78   -329.11       0.0713
  33   H3'   H1    E   32  11   8    1.09    109.50     30.00       0.0985
  34   C2'   CT    B   32  11   8    1.53    102.80    -86.30      -0.0854
  35   H2'1  HC    E   34  32  11    1.09    109.50    120.00       0.0718
  36   H2'2  HC    E   34  32  11    1.09    109.50    240.00       0.0718
  37   O3'   OS    M   32  11   8    1.42    116.52   -203.47      -0.5232

IMPROPER
 C6   C2   N1   C1'
 N1   N3   C2   O2
 C4   H41  N4   H42
 N1   C5   C6   H6
 C6   C4   C5   C7
 N3   C5   C4   N4
 C2   C4   N3   H3

LOOP CLOSING EXPLICIT
 C1'  C2'
 C2   N1

DONE
STOP
```

AMBER PREP file for inosine

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0   0   2

Inosine for TI calculations; 6-31G* RESP charges
ipe.data
IPE  INT     1
CORR OMIT DU   BEG
   0.00000
   1   DUMM  DU    M    0  -1  -2    0.0000    0.0000    0.0000    0.00000
   2   DUMM  DU    M    1   0  -1    3.0000    0.0000    0.0000    0.00000
   3   DUMM  DU    M    2   1   0    3.0000   90.0000  -90.0000    0.00000
   4   P     P     M    3   2   1    1.60    119.04    200.00       1.1659
   5   O1P   O2    E    4   3   2    1.48    109.61    150.00      -0.7761
   6   O2P   O2    E    4   3   2    1.48    109.58     20.00      -0.7761
   7   O5'   OS    M    4   3   2    1.60    101.43    -98.89      -0.4954
   8   C5'   CT    M    7   4   3    1.44    119.00    -39.22      -0.0069
   9   H5'1  H1    E    8   7   4    1.09    109.50     60.00       0.0754
  10   H5'2  H1    E    8   7   4    1.09    109.50    -60.00       0.0754
  11   C4'   CT    M    8   7   4    1.52    110.00    180.00       0.1629
  12   H4'   H1    E   11   8   7    1.09    109.50   -200.00       0.1176
  13   O4'   OS    S   11   8   7    1.46    108.86    -86.31      -0.3691
  14   C1'   CT    B   13  11   8    1.42    110.04    105.60       0.0431
  15   H1'   H2    E   14  13  11    1.09    109.50   -240.00       0.1838
   8   N9    N*    S    4   3   2    1.4798   37.8434  205.2975    -0.0138
   9   C8    CK    B    8   4   3    1.3867  126.9832  119.9587     0.0783
  10   H8    H5    E    9   8   4    1.0625  121.8634    0.0287     0.1773
  11   N7    NB    S    9   8   4    1.2976  111.9036  180.0196    -0.5367
  12   C5    CB    S   11   9   8    1.3858  105.6528    0.0000     0.1663
  13   C6    C     B   12  11   9    1.4327  130.4467  179.9769     0.5066
  14   O6    O     B   13  12  11    1.5387  130.6550    0.1288    -0.5472
  15   H61   D6    E   14  13  12    0.4     120.0290  359.9088     0.0000
  16   H62   D6    E   14  13  12    0.4     119.9751  179.8939     0.0000
  17   N1    NA    B   13  12  11    1.4196  109.5335  180.0248    -0.4092
  18   H1    H     E   17  13  12    1.0013  114.5060  179.9724     0.3234
  19   C2    CQ    B   17  13  12    1.3614  125.8243    0.0740     0.2284
  20   H2    H5    E   19  17  13    1.0691  116.4181  179.8593     0.1571
  21   N3    NC    S   19  17  13    1.2829  123.7782  359.9587    -0.5392
  22   C4    CB    E    8   4   3    1.3540  126.9783  299.9951     0.3033
  31   C3'   CT    M   11   8   7    1.53    115.78   -329.11       0.0713
  32   H3'   H1    E   30  11   8    1.09    109.50     30.00       0.0985
  33   C2'   CT    B   30  11   8    1.53    102.80    -86.30      -0.0854
  34   H2'1  HC    E   32  30  11    1.09    109.50    120.00       0.0718
  35   H2'2  HC    E   32  30  11    1.09    109.50    240.00       0.0718
  36   O3'   OS    M   30  11   8    1.42    116.52   -203.47      -0.5232

IMPROPER
 C8   C4   N9   C1'
 N9   N3   C4   C5
 N3   N1   C2   H2
 C2   C6   N1   H1
 N1   C5   C6   O6
 N7   N9   C8   H8
 C6   H61  O6   H62

LOOP
 C1'  C2'
 C4   C5
 C4   N9

DONE
STOP
```

AMBER PREP file for 2,6-diamino-purine

```
0    0    2

2,6-diamino-purine for TI calculations, 6-31G* RESP charges
dapab.data
DAP  INT     1
CORR OMIT DU   BEG
0.0
   1   DU   DU    M   0  -1  -2   0.0000   0.0000   0.0000   0.00000
   2   DU   DU    M   1   0  -1   8.8730   0.0000   0.0000   0.00000
   3   DU   DU    M   2   1   0   2.3079  90.0000 -90.0000   0.00000
   4   P    P     M   3   2   1   0.7800  64.3232  90.0000   1.16590
   5   O1P  O2    E   4   3   2   1.4760 114.4963  80.5727  -0.77610
   6   O2P  O2    E   4   3   2   0.9501  56.7517 291.4063  -0.77610
   7   O5'  OS    M   4   3   2   1.5945 132.5370 282.2855  -0.49540
   8   C5'  CT    M   7   4   3   1.4498 118.7822 228.3665  -0.00690
   9   H5'1 H1    E   8   7   4   1.0900 109.7613  93.9934   0.07540
  10   H5'2 H1    E   8   7   4   1.0895 109.7582 333.9654   0.07540
  11   C4'  CT    M   8   7   4   1.5109 109.7677 213.9796   0.16290
  12   H4'  H1    E  11   8   7   1.0901 107.7608 156.3397   0.11760
  13   O4'  OS    S  11   8   7   1.4632 108.6489 279.1130  -0.36910
  14   C1'  CT    B  13  11   8   1.4145 109.7846 106.4011   0.04311
  15   H1'  H2    E  14  13  11   1.0901 107.9285 115.7842   0.18380
  16   N9   N*    S  14  13  11   1.4877 107.7679 232.4945   0.00498
  17   C8   CK    B  16  14  13   1.3685 128.2779  82.2317   0.12688
  18   H8   H5    E  17  16  14   1.0905 123.1877   0.2565   0.16505
  19   N7   NB    S  17  16  14   1.2997 113.6206 180.2646  -0.59650
  20   C5   CB    S  19  17  16   1.3836 103.8157 359.3635   0.12491
  21   C6   C     B  20  19  17   1.3661   9.5850 285.5802   0.59450
  22   N6   N2    B  21  20  19   1.3342  53.0502  56.7783  -0.87871
  23   H61  H     E  22  21  20   1.0296  58.6492 172.7085   0.40649
  24   H62  H     E  22  21  20   1.0301 178.3823 136.8361   0.40649
  25   N1   NA    B  21  20  19   1.3412  60.4955 223.2029  -0.74502
  26   H1   D1    E  25  21  20   0.4000 117.3600 179.9000   0.00000
  27   C2   CA    B  25  21  20   1.3296 118.9288 178.9914   0.90381
  28   N2   N2    B  27  25  21   1.4798 115.2686 180.3182  -0.97652
  29   H21  H     E  28  27  25   1.0306 119.9936   0.0000   0.42014
  30   H22  H     E  28  27  25   1.0296 120.0279 179.9898   0.42014
  31   N3   NC    S  27  25  21   1.3159 129.4640   0.3197  -0.65999
  32   C4   CB    E  31  27  25   1.3459 110.2047 359.7759   0.17788
  33   C3'  CT    M  11   8   7   1.5272 116.3826  36.3615   0.07130
  34   H3'  H1    E  33  11   8   1.0901 111.1425  33.6094   0.09850
  35   C2'  CT    B  33  11   8   1.5202 102.8645 273.6140  -0.08524
  36   H2'1 HC    E  35  33  11   1.0903 111.3657 205.0801   0.07180
  37   H2'2 HC    E  35  33  11   1.0894 111.3650  85.0665   0.07180
  38   O3   OS    M  33  11   8   1.4265 112.1694 156.4746  -0.52320

IMPROPER
 C6   H61  N6   H62
 C2   H21  N2   H22
 N7   N9   C8   H8
 N1   N3   C2   N2
 C5   N1   C6   N6
 N1   N3   C2   N2
 N7   N9   C8   H8
 C6   C2   N1   H1

LOOP
 C1'  C2'
 C4   C5
 C4   N9

DONE
STOP
```

AMBER PREP file for quinoxaline

```
0   0   2

CysMeTANDEM quinoxaline chromophore; 6-31G* RESP charges
qxn.data
QXN  INT     1
CORR OMIT DU   BEG
   0.00000
   1  DUMM  DU      M    0  -1  -2   0.0000   0.0000   0.0000   0.000000
   2  DUMM  DU      M    1   0  -1   3.0000   0.0000   0.0000   0.000000
   3  DUMM  DU      M    2   1   0   3.0000  90.0000 -90.0000   0.000000
   4  C1    CA      M    1   2   3   3.0000  90.0000  90.0000   0.282326
   5  H2    HA      E    4   1   2   1.0670  90.0000 270.0000   0.058160
   6  N3    NC      M    4   1   2   1.2993  29.6628  90.0000  -0.541737
   7  C4    CB      M    6   4   1   1.3662 118.6143 180.0000   0.411620
   8  C5    CA      M    7   6   4   1.4097 120.1383 180.0000  -0.324433
   9  H6    HA      E    8   7   6   1.0707 117.8403   0.0000   0.185916
  10  C7    CA      M    8   7   6   1.3574 119.7937 180.0000  -0.137170
  11  H8    HA      E   10   8   7   1.0716 120.1759 180.0000   0.163712
  12  C9    CA      M   10   8   7   1.4165 120.6362   0.0000  -0.137170
  13  H10   HA      E   12  10   8   1.0710 119.1897 180.0000   0.163712
  14  C11   CA      M   12  10   8   1.3565 120.5247   0.0000  -0.324433
  15  H12   HA      E   14  12  10   1.0708 122.2935 180.0000   0.185916
  16  C13   CB      M    7   6   4   1.3996 120.3973   0.0000   0.411620
  17  N14   NC      M   16   7   6   1.3643 119.5362   0.0000  -0.510937
  18  C15   CA      M   17  16   7   1.2960 118.8597   0.0000   0.083498
  19  C16   C       M   18  17  16   1.4964 120.1073 180.0000   0.597300
  20  O17   O       E   19  18  17   1.2228 120.3004 180.0000  -0.567900

IMPROPER
 C15  N3   C1   H2
 N3   C5   C4   C13
 C4   C7   C5   H6
 C5   C9   C7   H8
 C7   C11  C9   H10
 C13  C9   C11  H12
 N14  C11  C13  C4
 C16  N14  C15  C1
 C15  +M   C16  O17

LOOP
 C4  C13
 C15 C1

DONE
STOP
```

AMBER PREP file for quinoline

```
0    0    2

2QN quinoline chromophore; 6-31G* RESP charges
2qn.data
2QN INT 1
CORRECT OMIT DU BEG
0.0
   1  DU   DU     M   0  -1  -2   0.0000   0.0000   0.0000   0.000000
   2  DU   DU     M   1   0  -1   2.4495   0.0000   0.0000   0.000000
   3  DU   DU     M   2   1   0   2.0000 144.7356 -90.0000   0.000000
   4  H5   HA     M   3   2   1   3.7912  86.7944 319.6216   0.165641
   5  C5   CA     M   4   3   2   1.0808 118.7887  43.9467  -0.253310
   6  C6   CA     M   5   4   3   1.4059 119.8764 270.5244  -0.133851
   7  H6   HA     E   6   5   4   1.0802 120.1480 359.9331   0.143678
   8  C7   CA     M   6   5   4   1.4057 119.7328 179.6767  -0.087290
   9  H7   HA     E   8   6   5   1.0808 120.0570 180.6633   0.143583
  10  C8   CA     M   8   6   5   1.4058 119.8135   0.9029  -0.359955
  11  H8   HA     E  10   8   6   1.0806 119.8615 179.8028   0.180070
  12  C9   CB     M  10   8   6   1.4083 119.9120 359.5544   0.519497
  13  C10  CB     M  12  10   8   1.3831 120.2566 359.6219   0.055632
  14  C4   CA     M  13  12  10   1.3617 119.8069 180.8568  -0.178854
  15  H4   HA     E  14  13  12   1.0895 119.7083 179.5981   0.166755
  16  C3   CA     M  14  13  12   1.3469 120.5991 359.6021  -0.143611
  17  H3   HA     E  16  14  13   1.0805 119.0838 179.6788   0.124858
  18  C2   CA     M  16  14  13   1.4115 119.8436 359.2852   0.197612
  19  N1   NC     E  18  16  14   1.3503 119.0634   1.2107  -0.569855
  20  C    C      M  18  16  14   1.4491 121.3476 180.9885   0.597300
  21  O    O      E  20  18  16   1.2297 119.5463 357.6658  -0.567900

IMPROPER
 C3   N1   C2   C
 C2   +M   C    O

LOOP
 C10  C5
 C9   N1

DONE
STOP
```

Additional AMBER parameters for mutated DNA bases

Atom types

```
D6 1.008              Dummy atom of guanine bonded to O6
D5 1.008              Dummy atom of cytosine bonded to H5
D3 1.008              Dummy atom of cytosine bonded to N3
D1 1.008              Dummy atom of DAP bonded to N1
D4 1.008              Dummy atom of thymine bonded to O4
DH 1.008              Cytosine H to be mutated to methyl carbon
```

Bonds

```
O -D6  434.     0.400       guanine for TI
DH-D5  340.     1.090       cytosine for TI
NC-D3  434.     0.400       cytosine for TI
O -D4  434.     0.400       thymine
NA-D1  434.     0.400       DAP
CM-DH  317.     1.080       cytosine for TI
```

Angles

```
CM-DH-D5    50.0      109.50     cytosine with dummy atoms
D5-DH-D5    35.0      109.50     cytosine with dummy atoms
CA-NC-D3    50.0      118.00     cytosine with dummy atoms
D3-NC-C     50.0      116.80     cytosine with dummy atoms
C -O -D6    50.0      120.0      guanine with dummy atoms
D6-O -D6    35.0      120.00     guanine with dummy atoms
D4-O -D4    35.0      120.00     thymine with dummy atoms
CA-O -D4    50.0      120.0      thymine with dummy atoms
CA-NA-D1    50.0      118.00     DAP with dummy atoms
D1-NA-CA    50.0      116.80     DAP with dummy atoms
C -NA-D1    50.0      116.8      DAP with dummy atoms
CM-CM-DH    50.0      119.70     cytosine for TI
DH-CM-CA    50.0      123.30     cytosine for TI
```

Dihedrals

```
X -CD-CD-X    4    4.00        180.0            2.
X -CD-CT-X    6    0.00          0.0            2.
X -CD-CM-X    4   26.60        180.0            2.
X -CM-DH-X    6    0.00          0.0            3.
```

Improper dihedrals

```
X -X -O -D6          1.0          180.          2.          guanine for TI
X -X -O -D4          1.0          180.          2.          thymine for TI
X -X -NC-D3          1.0          180.          2.          cytosine for TI
X -X -NA-D1          1.0          180.          2.          adenine for TI
CM-CA-CM-DH          1.1          180.          2.          cytosine for TI
```

Non-bonded parameters

```
MOD4      RE
  D3          0.0     0.0               dummy atom
  D4          0.0     0.0               dummy atom
  D5          0.0     0.0               dummy atom
  D6          0.0     0.0               dummy atom
  DH          1.4590  0.0150            H to be mutated to C
```