Supplementary data

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Supplementary Table S1. Detail parameters of 2’-OCH₃ modified nonstandard nucleotides (DAO, DGO and DCO) in the established force field of DTA_OMe.

| Serial number | Atom name | Atom type | Atom charge | Atom name | Atom type | Atom charge | Atom name | Atom type | Atom charge |
|---------------|-----------|-----------|-------------|-----------|-----------|-------------|-----------|-----------|-------------|
| 1             | OP1       | O2        | -0.776100   | OP1       | O2        | -0.776100   | OP1       | O2        | -0.776100   |
| 2             | P         | P         | 1.165900    | P         | P         | 1.165900    | P         | P         | 1.165900    |
| 3             | OP2       | O2        | -0.776100   | OP2       | O2        | -0.776100   | OP2       | O2        | -0.776100   |
| 4             | O5’       | OS        | -0.495400   | O5’       | OS        | -0.495400   | O5’       | OS        | -0.495400   |
| 5             | C5’       | Cl        | -0.006900   | C5’       | Cl        | -0.006900   | C5’       | Cl        | -0.006900   |
| 6             | H5’       | H1        | 0.075400    | H5’       | H1        | 0.075400    | H5’       | H1        | 0.075400    |
| 7             | H5”       | H1        | 0.075400    | H5”       | H1        | 0.075400    | H5”       | H1        | 0.075400    |
| 8             | C4’       | CT        | 0.162900    | C4’       | CT        | 0.162900    | C4’       | CT        | 0.162900    |
| 9             | H4’       | H1        | 0.117600    | H4’       | H1        | 0.117600    | H4’       | H1        | 0.117600    |
| 10            | C3’       | CE        | 0.071300    | C3’       | CE        | 0.071300    | C3’       | CE        | 0.071300    |
| 11            | H3’       | H1        | 0.098500    | H3’       | H1        | 0.098500    | H3’       | H1        | 0.098500    |
| 12            | C2’       | CT        | 1.004252    | C2’       | CT        | 1.047946    | C2’       | CT        | -0.337646   |
| 13            | H2’       | H1        | 0.459992    | H2’       | H1        | 0.490953    | H2’       | H1        | 0.733344    |
| 14            | O2’       | OS        | -1.265496   | O2’       | OS        | -1.275964   | O2’       | OS        | 0.581614    |
| 15            | CM2       | CT        | 0.807210    | CM2       | CT        | 0.809411    | CM2       | CT        | -0.797516   |
| 16            | H11       | H1        | -0.172799   | H11       | H1        | -0.175796   | H11       | H1        | 0.001395    |
| 17            | H12       | H1        | -0.172799   | H12       | H1        | -0.175796   | H12       | H1        | 0.001395    |
| 18            | H13       | H1        | -0.172799   | H13       | H1        | -0.175796   | H13       | H1        | 0.001395    |
| 19            | O3’       | OS        | -0.523200   | O3’       | OS        | -0.523200   | O3’       | OS        | -0.523200   |
| 20            | O4’       | OS        | -0.369100   | O4’       | OS        | -0.369100   | O4’       | OS        | -0.369100   |
| 21            | C1’       | CT        | -0.381261   | C1’       | CT        | -0.450958   | C1’       | CT        | -0.137381   |
| 22            | H1’       | H2        | 0.183800    | H1’       | H2        | 0.174600    | H1’       | H2        | 0.196300    |
| 23            | N9        | N*        | -0.026800   | N9        | N*        | 0.057700    | N1        | N*        | -0.033900   |
| 24            | C8        | C1        | 0.160700    | C8        | CK        | 0.073600    | C6        | CM        | -0.018300   |
| 25            | H8        | H5        | 0.187700    | H8        | H5        | 0.199700    | H6        | H4        | 0.229300    |
| 26            | N7        | NB        | -0.617500   | N7        | NB        | -0.572500   | C5        | CM        | -0.522200   |
| 27            | C5        | CB        | 0.072500    | C5        | CB        | 0.199100    | H5        | HA        | 0.186300    |
| 28            | C6        | CA        | 0.689700    | C6        | C        | 0.491800    | C4        | CA        | 0.843900    |
| 29            | N6        | N2        | -0.912300   | O6        | O         | -0.569900   | N4        | N2        | -0.977300   |
| 30            | H61       | H         | 0.416700    | N1        | NA        | -0.505300   | H41       | H         | 0.431400    |
| 31            | H62       | H         | 0.416700    | H1        | H         | 0.352000    | H42       | H         | 0.431400    |
| 32            | N1        | NC        | -0.762400   | C2        | CA        | 0.743200    | N3        | NC        | -0.774800   |
| 33            | C2        | CQ        | 0.571600    | N2        | N2        | -0.923000   | C2        | C         | 0.795900    |
| 34            | H2        | H5        | 0.059800    | H21       | H         | 0.423500    | O2        | O         | -0.654800   |
| 35            | N3        | NC        | -0.741700   | H22       | H         | 0.423500    | -         | -         | -           |
| 36            | C4        | CB        | 0.380000    | N3        | NC        | -0.663600   | -         | -         | -           |
| 37            | -         | -         | -           | C4        | CB        | 0.181400    | -         | -         | -           |
**Supplementary Table S2.** Detail parameters of 2’-OCH₃ modified nonstandard nucleotides (DTO, GO5 and GO3) in the established force field of DTA_OMe.

| Serial number | DTO | GO5 | GO3 |
|---------------|-----|-----|-----|
|               | Atom name | Atom type | Atom name | Atom type | Atom name | Atom type |
| 1             | OP1 | O2  | -0.776100 | N2 | N2  | -0.923000 |
| 2             | P   | P   | 1.165900   | H21 | H   | 0.423500  |
| 3             | OP2 | O2  | -0.776100 | H22 | H   | 0.423500  |
| 4             | O5’ | OS  | -0.495400 | C2  | CA  | 0.743200  |
| 5             | C5’ | CI  | -0.066900 | N3  | NC  | -0.663600 |
| 6             | H5’ | H1  | 0.075400   | C4  | CB  | 0.181400  |
| 7             | H5” | H1  | 0.075400   | N1  | NA  | -0.505300 |
| 8             | C4’ | CT  | 0.162900   | H1  | H   | 0.352000  |
| 9             | H4’ | H1  | 0.117600   | C6  | C   | 0.491800  |
| 10            | C3’ | CE  | 0.071300   | O6  | O   | -0.569900 |
| 11            | H3’ | H1  | 0.098500   | C5  | CB  | 0.199100  |
| 12            | C2’ | CT  | 0.944391   | N7  | NB  | -0.572500 |
| 13            | H2’ | H1  | 0.472814   | C8  | CK  | 0.073600  |
| 14            | O2’ | OS  | -1.229256  | H8  | H5  | 0.199700  |
| 15            | CM2 | CT  | 0.679657   | N9  | N*  | 0.057700  |
| 16            | H12 | H1  | -0.137819  | C1’ | CT  | -0.450958 |
| 17            | H13 | H1  | -0.137819  | H1’ | H2  | 0.174600  |
| 18            | H14 | H1  | -0.137819  | O4’ | OS  | -0.369100 |
| 19            | O3’ | OS  | -0.523200  | C4’ | CT  | 0.162900  |
| 20            | O4’ | OS  | -0.369100  | C5’ | CI  | -0.066900 |
| 21            | C1’ | CT  | -0.327949  | O5’ | OH  | -0.631800 |
| 22            | H1’ | H2  | 0.180400   | HOS’ | HO  | 0.442200  |
| 23            | N1  | N*  | -0.023900  | H5’ | H1  | 0.075400  |
| 24            | C6  | C2  | -0.220900  | H5” | H1  | 0.075400  |
| 25            | H6  | H4  | 0.260700   | H4’ | H1  | 0.117600  |
| 26            | C5  | C2  | 0.002500   | C3’ | CE  | 0.071300  |
| 27            | C7  | CT  | -0.226900  | H3’ | H1  | 0.098500  |
| 28            | H71 | HC  | 0.077000   | O3’ | OS  | -0.523200 |
| 29            | H72 | HC  | 0.077000   | C2’ | CT  | 1.047946  |
| 30            | H73 | HC  | 0.077000   | H2’ | H1  | 0.490953  |
| 31            | C4  | C   | 0.519400   | O2’ | OS  | -1.27596 |
| 32            | O4  | O   | -0.556300  | CM2 | CT  | 0.809411  |
| 33            | N3  | NA  | -0.434000  | H12 | H1  | -0.175796 |
| 34            | H3  | H   | 0.342000   | H13 | H1  | -0.175796 |
| 35            | C2  | C   | 0.567700   | H14 | H1  | -0.175796 |
| 36            | O2  | O   | -0.588100  | H22 | H   | 0.423500  |
| 37            | -   | -   | -           | -   | -   | -         |
| 38            | -   | -   | -           | -   | -   | -         |
### Supplementary Table S3. Simulation details of protein, DNA aptamer and protein-DNA complex models in solvent.

| Simulation system   | Time (ns) | Number of atoms | Number of water molecules | Number of ions | Minimum distance (solute and box)(Å) |
|---------------------|-----------|----------------|---------------------------|----------------|-------------------------------------|
| DEK_N               | 40        | 1857           | 5598                      | 13×Cl⁻         | 10                                  |
| DEK_C               | 40        | 1198           | 6417                      | 3×Cl⁻          | 10                                  |
| DTA                 | 400       | 1300           | 8502                      | 40×Na⁺         | 10                                  |
| DTA_OMe             | 400       | 1464           | 8407                      | 40×Na⁺         | 10                                  |
| DEK_N/DTA           | 200       | 3132           | 12830                     | 27×Na⁺         | 12                                  |
| DEK_N/DTA_OMe       | 200       | 3308           | 14368                     | 27×Na⁺         | 12                                  |
| DEK_C/DTA           | 200       | 2394           | 13597                     | 37×Na⁺         | 12                                  |
| DEK_C/DTA_OMe       | 200       | 2570           | 13384                     | 37×Na⁺         | 12                                  |
**Supplementary Table S4.** Per-residue free energy decomposition of DEK_N/DTA and DEK_N/DTA_OMe complexes (only show the negative energy).

| Residue | DEK_N/DTA Energy (kcal/mol) | DEK_N/DTA_OMe Energy (kcal/mol) |
|---------|-----------------------------|---------------------------------|
| Phe78   | -4.29                       | Phe78 -3.56                     |
| Thr79   | -0.65                       | Thr79 -0.05                     |
| Ile80   | -2.12                       | Ile80 -1.27                     |
| Ala81   | -0.17                       | Ala81 -0.36                     |
| Gln82   | -0.49                       | Gln82 -0.74                     |
| Gly83   | -0.02                       | Gly83 -0.01                     |
| Lys84   | -2.60                       | Lys84 -4.82                     |
| Lys87   | -2.94                       | Gly85 -0.05                     |
| Leu88   | -0.13                       | Lys87 -2.57                     |
| Cys89   | -0.06                       | Leu88 -0.04                     |
| Arg93   | -2.06                       | Cys89 -0.02                     |
| Hip95   | -2.36                       | Arg93 -1.96                     |
| Phe97   | -0.04                       | Hip95 -2.15                     |
| Leu98   | -0.03                       | Lys100 -2.18                    |
| Lys100  | -2.51                       | Lys101 -3.24                    |
| Lys101  | -3.38                       | Lys102 -2.84                    |
| Lys102  | -3.08                       | Thr103 -0.02                    |
| Arg107  | -10.38                      | Arg107 -6.02                    |
| Asn108  | -1.48                       | Asn108 -0.17                    |
| Leu109  | -0.16                       | Hid110 -0.15                    |
| Hid110  | -0.17                       | Lys111 -4.62                    |
| Lys111  | -10.91                      | Leu112 -1.92                    |
| Leu112  | -0.91                       | Tyr114 -1.23                    |
| Leu113  | -0.10                       | Asn115 -0.95                    |
| Tyr114  | -0.29                       | Arg116 -11.31                   |
| Asn115  | -2.29                       | Pro117 -2.33                    |
| Arg116  | -9.44                       | Gly118 -0.63                    |
| Pro117  | -1.83                       | Thr119 -1.01                    |
| Gly118  | -0.28                       | Val120 -0.81                    |
| Thr119  | -0.08                       | Ser121 -0.13                    |
| Ser121  | -0.18                       | Ser122 -1.00                    |
| Leu123  | -0.02                       | Leu123 -0.16                    |
| Lys124  | -3.03                       | Lys124 -2.44                    |
| Lys125  | -7.75                       | Lys125 -2.65                    |
## Supplementary Table S4

| Residue  | Energy (kcal/mol) | Residue  | Energy (kcal/mol) |
|----------|------------------|----------|------------------|
| Asn126   | -0.07            | Asn126   | -0.39            |
| Val127   | -0.13            | Val127   | -0.06            |
| Gly128   | -0.38            | Gly128   | -0.04            |
| Gln129   | -4.16            | Gln129   | -0.11            |
| Phe130   | -0.40            | Phe130   | -0.14            |
| Ser131   | -0.14            | Phe135   | -0.32            |
| Phe133   | -0.33            | Lys137   | -2.57            |
| Pro134   | -0.27            | Ser139   | -0.28            |
| Phe135   | -0.34            | Val140   | -3.72            |
| Lys137   | -2.48            | Gln141   | -2.41            |
| Gly138   | -0.04            | Tyr142   | -0.16            |
| Ser139   | -0.16            | Lys143   | -4.44            |
| Val140   | -2.06            | Lys144   | -8.74            |
| Gln141   | -1.40            | Lys145   | -3.96            |
| Tyr142   | -0.03            | Met148   | -0.28            |
| Lys143   | -3.38            | Leu149   | -0.11            |
| Lys144   | -5.60            | Lys150   | -3.16            |
| Lys145   | -4.39            | Lys151   | -3.36            |
| Met148   | -1.41            | Phe152   | -0.08            |
| Leu149   | -0.23            | Arg153   | -2.36            |
| Lys150   | -3.24            | Lys158   | -1.86            |
| Lys151   | -3.92            | Val163   | -0.03            |
| Phe152   | -3.66            | Leu164   | -0.03            |
| Arg153   | -7.26            | Leu166   | -0.02            |
| Asn154   | -2.32            | Arg168   | -2.00            |
| Ala155   | -1.51            | Lys177   | -2.13            |
| Met156   | -0.39            | Arg178   | -1.97            |
| Leu157   | -0.07            | Hid185   | -0.05            |
| Lys158   | -3.22            | Pro186   | -0.02            |
| Ser159   | -0.13            | -        | -                |
| Ile160   | -0.13            | -        | -                |
| Cys161   | -0.15            | -        | -                |
| Val163   | -0.11            | -        | -                |
| Leu164   | -0.08            | -        | -                |
| Leu166   | -0.03            | -        | -                |
| Residue | Energy (kcal/mol) | Residue | Energy (kcal/mol) |
|---------|------------------|---------|-------------------|
| Arg168  | -4.10            | -       | -                 |
| Ser169  | -0.18            | -       | -                 |
| Val171  | -0.04            | -       | -                 |
| Asn172  | -0.07            | -       | -                 |
| Ser173  | -0.01            | -       | -                 |
| Leu175  | -0.07            | -       | -                 |
| Lys177  | -2.58            | -       | -                 |
| Arg178  | -2.23            | -       | -                 |
| Ile179  | -0.03            | -       | -                 |
| Phe182  | -0.04            | -       | -                 |
| Hid185  | -0.06            | -       | -                 |
| Pro186  | -0.06            | -       | -                 |
Supplementary Table S5. Per-residue free energy decomposition of DEK_C/DTA and DEK_C/DTA_OMe complexes (only show the negative energy).

| Residue | DEK_C/DTA Energy (kcal/mol) | Residue | DEK_C/DTA_OMe Energy (kcal/mol) |
|---------|----------------------------|---------|-------------------------------|
| Lys314  | -11.46                     | Lys314  | -13.32                        |
| Lys315  | -8.16                      | Lys315  | -4.93                         |
| Leu316  | -0.29                      | Leu316  | -1.11                         |
| Lys317  | -13.25                     | Lys317  | -7.95                         |
| Lys318  | -7.94                      | Lys318  | -4.84                         |
| Pro319  | -0.07                      | Pro319  | -0.30                         |
| Pro320  | -1.57                      | Pro320  | -0.17                         |
| Leu325  | -0.19                      | Lys326  | -2.80                         |
| Lys326  | -2.60                      | Lys330  | -3.02                         |
| Thr328  | -0.12                      | Lys331  | -4.05                         |
| Ile329  | -0.02                      | Leu332  | -0.65                         |
| Lys330  | -3.13                      | Leu333  | -0.06                         |
| Lys331  | -5.84                      | Ala334  | -0.14                         |
| Leu332  | -1.44                      | Ser335  | -0.16                         |
| Leu333  | -0.16                      | Ala336  | -0.16                         |
| Ala334  | -0.43                      | Asn337  | -0.08                         |
| Ser335  | -0.35                      | Leu338  | -0.05                         |
| Ala336  | -0.23                      | Val341  | -0.16                         |
| Asn337  | -0.01                      | Lys344  | -2.12                         |
| Leu338  | -0.06                      | Gln345  | -0.07                         |
| Val341  | -0.15                      | Lys348  | -2.62                         |
| Lys344  | -2.19                      | Lys349  | -8.99                         |
| Gln345  | -0.02                      | Val350  | -0.02                         |
| Lys348  | -2.94                      | Tyr351  | -0.03                         |
| Lys349  | -3.88                      | Tyr354  | -0.32                         |
| Asn353  | -3.19                      | Pro355  | -0.30                         |
| Tyr354  | -1.94                      | Thr356  | -0.31                         |
| Pro355  | -2.88                      | Tyr357  | -1.24                         |
| Tyr357  | -1.93                      | Leu359  | -0.09                         |
| Leu359  | -0.18                      | Thr360  | -0.11                         |
| Thr360  | -0.04                      | Arg362  | -2.87                         |
| Arg362  | -2.48                      | Lys363  | -2.54                         |
| Lys363  | -2.37                      | Phe365  | -0.04                         |
| Phe365  | -0.02                      | Ile366  | -0.03                         |
### Supplementary Table S5

| Residue  | Energy (kcal/mol) | Residue  | Energy (kcal/mol) |
|----------|-------------------|----------|-------------------|
| Ile366   | -0.04             | Lys367   | -2.27             |
| Lys367   | -2.17             | Thr368   | -0.04             |
| Thr368   | -0.03             | Thr369   | -0.04             |
| Thr369   | -0.04             | Val370   | -0.02             |
| Val370   | -0.03             | Lys371   | -2.10             |
| Lys371   | -1.98             | Leu373   | -0.04             |
| Leu373   | -0.04             | Ile374   | -0.01             |
| Ile374   | -0.01             | Ser375   | -0.02             |
| Ser375   | -0.03             | Leu376   | -0.03             |
| Leu376   | -0.04             | -        | -                 |
Supplementary Table S6. Detailed information of hydrogen bonds in DEK_N/DTA complex.

| H-bond acceptor | DonorH | H-bond donor | Occupancy (%) | Average distance (Å) |
|-----------------|--------|--------------|---------------|---------------------|
| Ile80@O         | DT10@H3 | DT10@N3      | 63.74         | 2.84                |
| DA40@OP2        | Arg153@HH12 | Arg153@NH1   | 63.67         | 2.79                |
| DA40@OP2        | Asn154@HD21 | Asn154@ND2   | 62.13         | 2.84                |
| DG3@OP2         | Arg107@HH22 | Arg107@NH2   | 52.41         | 2.82                |
| DT10@OP1        | Gln129@HE22 | Gln129@NE2   | 52.18         | 2.82                |
| DA40@OP1        | Arg153@HH22 | Arg153@NH2   | 49.99         | 2.83                |
| DG3@OP2         | Arg107@HH12 | Arg107@NH1   | 41.48         | 2.82                |
| DG2@OP1         | Arg107@HH21 | Arg107@NH2   | 39.34         | 2.82                |
| DA34@OP2        | Arg116@HH12 | Arg116@NH1   | 35.31         | 2.80                |
| DA34@OP2        | Arg116@HH22 | Arg116@NH2   | 34.53         | 2.81                |
| DC35@O2         | Lys111@HZ3 | Lys111@NZ    | 32.88         | 2.76                |
| DG2@OP1         | Lys111@HZ1 | Lys111@NZ    | 26.05         | 2.80                |
| DC35@O2         | Lys111@HZ1 | Lys111@NZ    | 25.40         | 2.77                |
| DT33@OP1        | Lys144@HZ1 | Lys144@NZ    | 25.18         | 2.79                |
| DT33@OP1        | Lys144@HZ3 | Lys144@NZ    | 24.62         | 2.79                |
| DT33@OP1        | Lys144@HZ2 | Lys144@NZ    | 23.43         | 2.80                |
| DC35@O2         | Lys111@HZ2 | Lys111@NZ    | 22.92         | 2.77                |
| Asn115@O        | DC35@H41 | DC35@N4      | 22.68         | 2.87                |
| DA37@OP1        | Asn108@HD21 | Asn108@ND2   | 22.62         | 2.86                |
| DT33@OP2        | Asn115@HD22 | Asn115@ND2   | 22.12         | 2.82                |
| DA9@OP2         | Lys125@HZ1 | Lys125@NZ    | 19.86         | 2.79                |
| DA9@OP2         | Lys125@HZ2 | Lys125@NZ    | 19.43         | 2.79                |
| DA9@OP2         | Lys125@HZ3 | Lys125@NZ    | 19.33         | 2.79                |
| DG2@OP1         | Lys111@HZ2 | Lys111@NZ    | 19.22         | 2.79                |
| DA36@O3'        | Asn108@HD21 | Asn108@ND2   | 18.40         | 2.89                |
| DA34@OP1        | Asn115@HD21 | Asn115@ND2   | 16.37         | 2.85                |
| DG2@OP1         | Lys111@HZ3 | Lys111@NZ    | 16.25         | 2.80                |
| DT10@O2         | Ile80@H | Ile80@N      | 15.69         | 2.87                |
| DT12@OP2        | Phe78@H2 | Phe78@N      | 13.44         | 2.79                |
| DA11@OP2        | Lys125@HZ1 | Lys125@NZ    | 10.88         | 2.79                |
| DT10@OP2        | Gln129@HE22 | Gln129@NE2   | 10.48         | 2.86                |
| DG3@OP2         | Arg107@HH21 | Arg107@NH2   | 10.35         | 2.80                |
**Supplementary Table S7.** Detailed information of hydrogen bonds in DEK_N/DTA_OMe complex.

| H-bond acceptor | DonorH   | H-bond donor | Occupancy (%) | Average distance (Å) (acceptor-donor) |
|-----------------|----------|--------------|---------------|---------------------------------------|
| DCO27@OP1       | Arg116@HH22 | Arg116@NH2  | 87.66         | 2.81                                 |
| DGO22@OP2       | Arg107@HH12 | Arg107@NH1  | 62.88         | 2.82                                 |
| DGO22@OP2       | Arg107@HH22 | Arg107@NH2  | 61.69         | 2.83                                 |
| DGO27@OP1       | Arg116@HH12 | Arg116@NH1  | 35.14         | 2.86                                 |
| DGO26@O2'       | Ser122@HG  | Ser122@OG   | 29.49         | 2.60                                 |
| DGO28@O4'       | Thr79@HG1  | Thr79@OG1   | 29.35         | 2.78                                 |
| DCO16@OP1       | Gln141@HE21 | Gln141@NE2 | 26.47         | 2.85                                 |
| DCO24@OP1       | Ser121@HG  | Ser121@OG   | 17.34         | 2.70                                 |
| DTO21@OP1       | Lys111@HZ1 | Lys111@NZ   | 15.88         | 2.78                                 |
| DTO21@OP1       | Lys111@HZ3 | Lys111@NZ   | 15.08         | 2.79                                 |
| DTO21@OP1       | Lys111@HZ2 | Lys111@NZ   | 14.86         | 2.79                                 |
| Gln82@OE1       | DCO29@H42  | DCO29@N4    | 14.47         | 2.86                                 |
| DGO26@O3'       | Arg116@HH12 | Arg116@NH1 | 13.85         | 2.87                                 |
| DGO22@O5'       | Arg107@HH22 | Arg107@NH2 | 13.67         | 2.88                                 |
| DCO30@OP2       | Asn115@HD22 | Asn115@ND2 | 12.03         | 2.82                                 |
| DCO16@OP1       | Gln141@HE22 | Gln141@NE2 | 11.93         | 2.84                                 |
| DGO3@O4'        | Lys144@HZ1 | Lys144@NZ   | 11.71         | 2.84                                 |
| DGO3@O4'        | Lys144@HZ3 | Lys144@NZ   | 11.42         | 2.84                                 |
| DGO3@O4'        | Lys144@HZ2 | Lys144@NZ   | 11.31         | 2.84                                 |
| DCO24@OP1       | Thr119@HG1 | Thr119@OG1  | 11.04         | 2.79                                 |
| Asn115@OD1      | DCO30@H42  | DCO30@N4    | 10.41         | 2.84                                 |
**Supplementary Table S8.** Detailed information of hydrogen bonds in DEK_C/DTA complex.

| H-bond acceptor | DonorH     | H-bond donor | Occupancy (%) | Average distance (Å) (acceptor-donor) |
|------------------|------------|--------------|---------------|---------------------------------------|
| DC29@OP1         | Lys318@H   | Lys318@N     | 59.27         | 2.84                                  |
| Thr321@O         | DC29@H42   | DC29@N4      | 45.27         | 2.86                                  |
| DC23@OP1         | Ser335@HG  | Ser335@OG    | 41.10         | 2.68                                  |
| Asn353@OD1       | DG22@H21   | DG22@N2      | 38.47         | 2.85                                  |
| Asn353@OD1       | DG22@H1    | DG22@N1      | 34.71         | 2.85                                  |
| Glu327@OE1       | DG26@H1    | DG26@N1      | 19.49         | 2.81                                  |
| DT5@OP1          | Lys315@H   | Lys315@N     | 15.18         | 2.84                                  |
| DG28@OP1         | Lys318@HZ1 | Lys318@NZ    | 15.16         | 2.78                                  |
| DC30@OP2         | Lys317@HZ2 | Lys317@NZ    | 14.65         | 2.81                                  |
| DC29@OP2         | Lys317@HZ3 | Lys317@NZ    | 14.31         | 2.83                                  |
| Glu327@OE2       | DG26@H21   | DG26@N2      | 13.78         | 2.85                                  |
| DG28@OP1         | Lys318@HZ3 | Lys318@NZ    | 13.10         | 2.78                                  |
| DC30@OP2         | Lys317@HZ1 | Lys317@NZ    | 12.55         | 2.81                                  |
| DC29@OP2         | Lys317@HZ2 | Lys317@NZ    | 11.91         | 2.83                                  |
| DC30@OP2         | Lys317@HZ3 | Lys317@NZ    | 11.84         | 2.81                                  |
| DC29@OP2         | Lys317@HZ1 | Lys317@NZ    | 11.57         | 2.83                                  |
| DG28@OP1         | Lys318@HZ2 | Lys318@NZ    | 11.16         | 2.78                                  |
**Supplementary Table S9.** Detailed information of hydrogen bonds in DEK\_C/DTA\_OMe complex.

| H-bond acceptor | DonorH | H-bond donor | Occupancy (%) | Average distance (Å) |
|-----------------|--------|--------------|---------------|---------------------|
| DTO10@O2' | Lys349@HZ3 | Lys349@NZ | 27.59 | 2.73 |
| DTO10@O2' | Lys349@HZ2 | Lys349@NZ | 27.38 | 2.73 |
| DTO10@O2' | Lys349@HZ1 | Lys349@NZ | 26.02 | 2.73 |
| DCO27@O2 | Lys315@H | Lys315@N | 24.05 | 2.86 |
| DCO14@OP1 | Lys314@H3 | Lys314@N | 20.43 | 2.81 |
| DCO14@OP1 | Lys314@H1 | Lys314@N | 19.47 | 2.80 |
| DCO29@O4' | Thr356@HG1 | Thr356@OG1 | 15.67 | 2.80 |
| DCO30@OP2 | Lys317@HZ3 | Lys317@NZ | 15.46 | 2.77 |
| DCO14@OP1 | Lys314@H2 | Lys314@N | 15.29 | 2.80 |
| DCO30@OP2 | Lys317@HZ1 | Lys317@NZ | 14.89 | 2.77 |
| DCO15@OP2 | Lys314@H2 | Lys314@N | 13.53 | 2.78 |
| DAO11@OP1 | Ser335@HG | Ser335@OG | 13.50 | 2.68 |
| DCO15@OP2 | Lys314@H3 | Lys314@N | 12.94 | 2.78 |
| DCO15@OP2 | Lys314@H1 | Lys314@N | 11.70 | 2.79 |
| DCO30@OP2 | Lys317@HZ2 | Lys317@NZ | 11.67 | 2.77 |
**Supplementary Table S10.** Sequences and modification schemes of mutants (the cyan boxes are mutation sites and red letters are nucleotides modified with 2′-OCH₃ in the deoxyribose sugar unit).

| Mutant  | Aptamer sequence (5’ to 3’)                                                                 |
|---------|--------------------------------------------------------------------------------------------|
| DTA     | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DT10DA  | GGG GTT AAA AAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DT10DC  | GGG GTT AAA CAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DT10DG  | GGG GTT AAA GAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DC35DA  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT AAA AAT AG                                       |
| DC35DG  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DC35DT  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DCO29DAO| GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DCO29DGO| GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DCO29DTO| GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DCO30DAO| GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DCO30DGO| GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DCO30DTO| GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DG22DA  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DG22DC  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DG22DT  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DG26DA  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DG26DC  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DG26DT  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DC29DA  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DC29DG  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DC29DT  | GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DCO27DAO| GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DCO27DGO| GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |
| DCO27DTO| GGG GTT AAA TAT TCC CAC ATT GCC TGC GCC AGT ACA AAT AG                                       |