Optimized DNA targeting using \(N,N\)-bis(2-pyridylmethyl)-\(\beta\)-alanyl 2'-amino-LNA

B. Ravindra Babu, Patrick J. Hrdlicka, Christine J. McKenzie and Jesper Wengel*

Nucleic Acid Center and Department of Chemistry, University of Southern Denmark, DK-5230 Odense M, Denmark

Electronic supplementary information (ESI)

**Table S1** 13-mer ONs synthesized and thermal denaturation studies at different concentrations of divalent metal ions

<table>
<thead>
<tr>
<th>ON</th>
<th>5'-CGT GAT ATA XAA A 3'-GCA CAX AXT ATT T</th>
<th>DNA</th>
<th>DNA</th>
<th>+ EDTA</th>
<th>Ni(^{2+})</th>
<th>Cu(^{2+})</th>
<th>Zn(^{2+})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>5'-CGT GAT ATA TAA A 3'-GCA CTA TAT ATT T</td>
<td>DNA</td>
<td>DNA</td>
<td>1 equiv.</td>
<td>excess</td>
<td>1 equiv.</td>
</tr>
<tr>
<td>ON6</td>
<td>31 (ref)</td>
<td>50 (ref)</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>ON7</td>
<td>37 (+6)</td>
<td>47 (+16)</td>
<td>48</td>
<td>17</td>
<td>40</td>
<td>9</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>48 (+17)</td>
<td>49</td>
<td>18</td>
<td>40</td>
<td>9</td>
<td>40</td>
</tr>
<tr>
<td>ON8</td>
<td>38 (+7)</td>
<td>48 (+17)</td>
<td>48</td>
<td>17</td>
<td>40</td>
<td>9</td>
<td>40</td>
</tr>
<tr>
<td>ON6</td>
<td>39 (+8)</td>
<td>47 (+16)</td>
<td>48</td>
<td>17</td>
<td>40</td>
<td>9</td>
<td>40</td>
</tr>
<tr>
<td>ON7</td>
<td>42 (+11)</td>
<td>54 (+23)</td>
<td>29</td>
<td>(-2)</td>
<td>52</td>
<td>21</td>
<td>19</td>
</tr>
<tr>
<td>ON6</td>
<td>49 (+18)</td>
<td>59 (+28)</td>
<td>63</td>
<td>(+32) 51</td>
<td>20</td>
<td>48</td>
<td>17</td>
</tr>
<tr>
<td>ON8</td>
<td>51 (+20)</td>
<td>63 (+32)</td>
<td>63</td>
<td>(+32) 51</td>
<td>20</td>
<td>48</td>
<td>17</td>
</tr>
</tbody>
</table>

\(T_m(\Delta T_m) / ^{\circ C}\)

Molecular Modelling Procedure. A standard B-type DNA-DNA duplex was built using the SPARTAN '02 program and subsequently modified within the MacroModel V7.2 suite of programs (R. D. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, C. Chang, T. Hendrickson and W. C. Still, *J. Comput. Chem.*, 1990, 11, 1301). The charge from the phosphodiester backbone was neutralized with Na\(^{+}\)-ions, which were placed approximately 3 Å from the negatively charged oxygens. Zn\(^{2+}\)-ions were initially placed approximately 3 Å from the nitrogen atoms of the metal chelator. All atoms were frozen except those of the sugar moiety, linker.
and metal chelator part of monomer X and Zn$^{2+}$-ions. The duplexes were minimized using the Polak-Ribiere conjugate gradient method and static Merck Mechanical Force Field (T. A. Halgreen, *J. Comput. Chem.*, 1990, **11**, 1301) as implemented in MacroModel V7.2. A dielectric constant of 80 relative to vacuum was applied. Non-bonded interactions were treated with extended cut-offs (van der Waals 8.0 Å, electrostatic 20.0 Å). The minimized structure was then, using the same constraints as described above, submitted to 2 ns of stochastic dynamics (300 K, timestep of 2 fs, SHAKE all H), during which 100 structures were sampled and minimized.

**Fig. S1** Low energy structure of **ON1**:DNA including one Zn$^{2+}$-ion. For clarity hydrogens, sodium ions and bond orders have been omitted. Colouring scheme: nucleobases, yellow; sugar-phosphate backbone, red; $N,N$-bis(2-pyridylmethyl)-β-alanyl ligand, blue; Zn$^{2+}$-ion, black.

**Fig. S2** Lowest energy structure of **ON1**:DNA including one Zn$^{2+}$-ion. Colouring scheme as in Fig S1.
**Fig. S3** Thermal denaturation curves measured at 260 nm. See Table 1 for sequence key and other details.