OFFICE OF NAVAL RESEARCH

Grant N00014-92-J1052

R&T Code 4135018

Technical Report #7

"The Nonnatural Deoxyribonucleoside D_3 Incorporated in an Intramolecular DNA Triplex Binds Sequence Specifically by Intercalation"

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June 1, 1993

The Nonnatural Deoxyribonucleoside D_3 Incorporated in an Intramolecular DNA Triplex Binds Sequence Specifically by Intercalation

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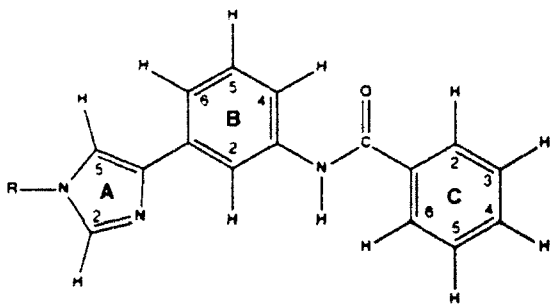
Abstract: The synthetic deoxyribonucleoside 1-(2-deoxy-β-D-ribofuranosyl)-4-(3-benzamido)phenylimidazole (D_3) has been shown to specifically recognize both T·A and C· G base pairs when incorporated into the Hoogsteen paired strand of pyrimidine·purine·pyrimidine triplexes. To further investigate the binding of D_3, a DNA oligonucleotide containing a single D_3 residue and designed to form intramolecular triplexes was synthesized and studied by one- and two-dimensional NMR spectroscopy. The oligonucleotide d(AGATAGAACCCCTTCTATCTTATATCTD$_3$TCTT) was found to form a stable intramolecular triplex, with a CCCC and a TATA loop connecting the Watson-Crick and Hoogsteen paired strands, respectively. Unlike other third strand bases, however, D_3 does not hydrogen bond with a Watson-Crick base pair. Instead, it intercalates between its associated base pair (T·A) and the adjacent 3' T·A·T triplet. The binding mode of D_3 is unique in that it not only binds by intercalation but skips a potential base pair to do so. Thus, non-purine bases can be accommodated in the purine strand of DNA triplexes in an entirely new way.

Figure Captions

Figure 1. (A) Chemical structure of the nonnatural deoxyribonucleoside D_3 with ring labeling and numbering scheme used. **R** is deoxyribose. (B) Schematic of the proposed folding of the 31 base intramolecular triplex with base numbering scheme used. Hydrogen bonds are indicated by (·) except for those of protonated C, indicated by (+).

Figure 2. Schematic illustrating the binding mode of D_3 and neighboring nucleotides.


R
N
A
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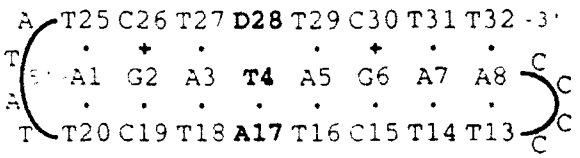
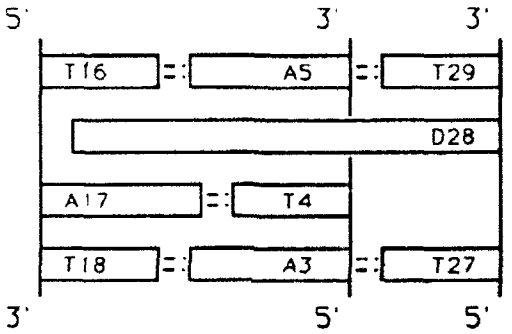

A T25 C26 T27 D28 T29 C30 T31 T32 -3'
T A1 G2 A3 T4 A5 G6 A7 A8 C C
A T20 C19 T18 A17 T16 C15 T14 T13 C C


5'
3'
3'
T16
A5
T29
D28
A17
T4
T18
A3
T27
3'
5'
5'