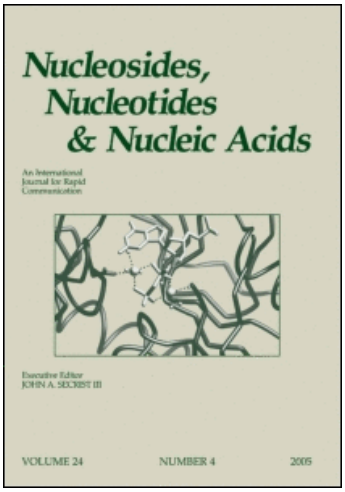

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Crystal Structure of a Left-Handed Z-DNA Hexamer, $d(CG)_3$, Duplex Complexed with Synthetic Polyamine Reveals Binding of a Polyamine in the Minor Groove

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CRYSTAL STRUCTURE OF A LEFT-HANDED Z-DNA HEXAMER, $d(CG)_3$, DUPLEX COMPLEXED WITH SYNTHETIC POLYAMINE REVEALS BINDING OF A POLYAMINE IN THE MINOR GROOVE

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ABSTRACT: As a series of X-ray structural studies of Z-DNA Polyamine complex, the crystal structure of Z-DNA hexamer, $d(CG)_3$, duplex complexed with a synthetic polyamine, N,N'-bis(2-aminoethyl)-1,2-ethanediamine, NH_2-$(CH_2)_2$-NH-$(CH_2)_2$-NH-$(CH_2)_2$-NH_2 [PA(222)], has been determined.

Under certain environment conditions (salt and ethanol concentration etc.), a double-helical DNA adopts not only the right-handed B-form, but also the left-handed Z-form which was confirmed by single crystal X-ray diffraction studies of oligonucleotide (1). Furthermore, polyamines such as spermine induce condensation agregation and conformational B-Z transition of DNA (2), and play a significant role in the regulation of normal and malignant cell proliferation. We have recently determined several crystal structures of Z-DNA oligomer complexes with several polyamines (3-7). Here briefly we report the crystal structure (resolution 1A) of $d(CG)_3$ and PA(222) complex, where $d(CG)_3$ is a left-handed Z-form DNA hexamer and PA(222) is a synthetic polyamine. Single crystal was obtained within 2 weeks according to the similar procedure as described in references (5-7). The cell dimensions were :a=17.93(1)A, b=31.36(2)A,

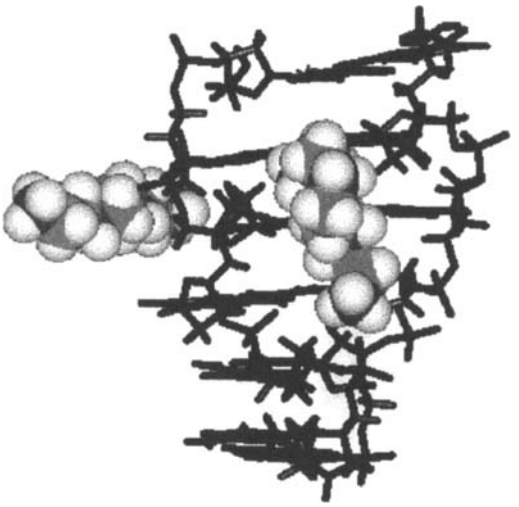

Fig. 1 The Crystal structure of $d(CG)_3$ and PA(222) complex

c=44.62(2)A, with space group P212121. The structure was determined by molecular replacement method because the unit cell dimensions were isomorphous to the other $d(CG)_3$ polyamine complex crystals. The least-squares refinement was performed by using the program CCP4 and X-PLOR (a final R=0.20). An asymmetric unit contains one $d(CG)_3$ duplex, two PA(222) molecules, one magnesium cation and twenty-nine water molecules, in which five water molecules are coordinated to magnesium ion. The backbone conformation of $d(CG)_3$ hexamer duplex shows a commonly observed ZI-conformation except G4 nucleotide resisue which is distinguishable as a ZII-conformation, and two PA(222) molecules are used for stabilization of the Z-DNA conformation, and two PA(222) molecules are used for stabilization of the Z-DNA conformation in such a way that one "interhelix" PA(222) molecule mediates contacts between neighboring duplexes with various interactions, and the other "intrahelix" polyamine molecule is tightly bound in the minor groove formed by the double-stranded left-handed $d(CG)_3$ duplex with several hydrogen bonds (Fig. 1). The latter interaction is the first finding in the Z-DNA polyamine complex structure at room temperature.

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