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**TRIPLEX FORMATION OF α -OLIGODEOXYNUCLEOTIDES
CONTAINING 5-Me- α -dC(N-4-SPERMINE)**

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ABSTRACT : Pyrimidine α -ODNs containing 5-Me- α -dC(N-4-spermine) at the 5'-end or in the sequence were synthesized. The corresponding $\alpha\beta\beta$ triple helices were strongly stabilized by Mg^{2+} cations. Unlike in β -series these triplexes were not stabilized at pH 7.

Triplex oligodeoxynucleotide (ODN) has therapeutic importance (1) and depends on Hoogsteen hydrogen bonds between a duplex DNA and a third DNA strand, T*A:T triplets are formed at neutral pH and C⁺*G:C are favored at acidic pH. It was demonstrated that spermine conjugation at N-4 of 5-Methyl-deoxycytidine in ODNs lead to triplexes stable at physiological pH (2). However since natural ODNs are rapidly degraded by nucleases and nuclease resistant PS-ODNs exhibited poor triplex ability, we developed the same strategy with the nuclease resistant α -ODNs (3).

Di-*O*-3',5'-acetyl- α -thymidine was converted in three steps into *O*-4-(2,6-dimethylphenyl)- α -thymidine. After 5'-dimethoxytritylation the 2,6-dimethylphenyl group was then displaced by spermine to yield 5-methyl- α -deoxycytidine(N-4-spermine) derivative which was finally converted, after protection of their amino functions by trifluoroacetyl groups, into the desired phosphoramidite building block.

Pyrimidine α -ODNs (**Table**) containing 5-Me- α -dC(N-4-spermine) at the 5'-end or in the sequence were synthesized and the stability of the corresponding $\alpha\beta\beta$ triple helices were studied, by UV melting experiments, at pH 6 and 7 in absence and in presence of Mg^{2+} .

Table : Sequence of α -oligonucleotides third strand and $\beta\beta$ -target.

	α -oligonucleotides third strand
<u>I</u>	α -5'-TCTCTCTCTCTTTT-3'
<u>II</u>	α -5'-T ^{me} CT ^{me} CT ^{me} CT ^{me} CTTTT-3'
<u>III</u>	α -5'-T ^{me} C ^{Sper} TCTCTCTCTTTT-3'
<u>IV</u>	α -5'-TCTCTCTCT ^{me} C ^{Sper} TTTT-3'
<u>V</u>	α -5'-T ^{me} C ^{Sper} T ^{me} CT ^{me} CT ^{me} CTTTT-3'
	β -Double-Stranded DNA Target
<u>VI</u>	3'-GCTAGAGAGAGAGAAAAATCG-5'
<u>VII</u>	5'-CGATCTCTCTCTCTTTTATAGC-3'

The presence of 20mM Mg²⁺ strongly stabilized the triple helices at pH 6 and 7. As expected introduction of 5-methyl cytosine (II and V) increased the T_m values ($\Delta T_m + 9^\circ\text{C}$). In contrary to what was found in β -series introduction of spermine into α -ODNs (III and V) destabilized the resulting triplexes ($\Delta T_m - 11^\circ\text{C}$). The destabilization was more pronounced ($\Delta T_m - 20^\circ\text{C}$) when spermine was conjugated in the sequence of the ODN (IV) than at its 5'-end (III and V).

Furthermore we showed at pH 7 that α -ODNs have a propensity to form self-hybridization that competes with triplex formation.

At pH 7 no enhancement of triplexes stability was observed in contrary to what was found in β -series. This discrepancy may be due to the difference of sequence since the sequence reported in β -triplexes contained only three cytosines.

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