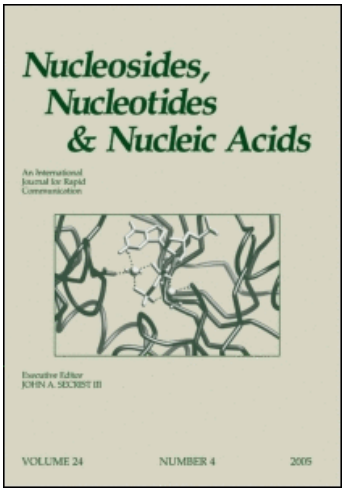


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Superactive Oligonucleotide Derivatives

D. S. Sergeyev[a]; P. E. Vorobjev[a]; V. F. Zarytova[a]
[a] Siberian Division of RAS, Novosibirsk Institute of Bioorganic Chemistry, Novosibirsk, Russia

To cite this Article Sergeyev, D. S. , Vorobjev, P. E. and Zarytova, V. F.(1997) 'Superactive Oligonucleotide Derivatives', Nucleosides, Nucleotides and Nucleic Acids, 16: 7, 1575 — 1577
To link to this Article: DOI: 10.1080/07328319708006233
URL: http://dx.doi.org/10.1080/07328319708006233

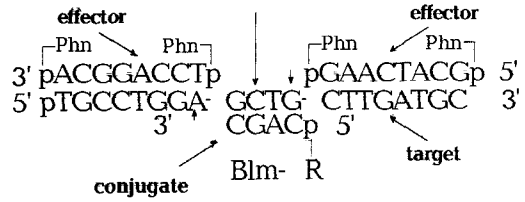
NUCLEOSIDES & NUCLEOTIDES, 16(7-9), 1575-1577 (1997)

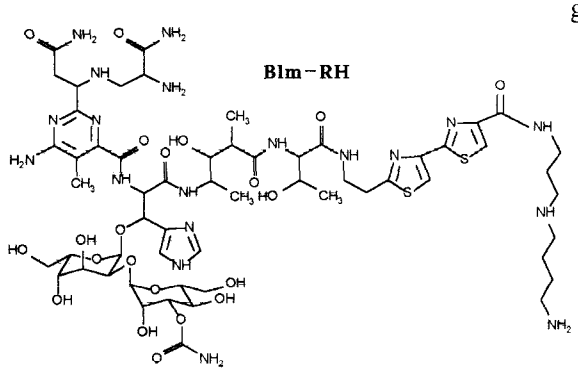
SUPERACTIVE OLIGONUCLEOTIDE DERIVATIVES

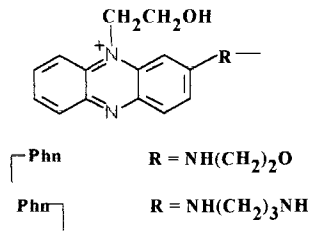
Sergeyev D.S., Vorobjev P.E., Zarytova V.F.*
Novosibirsk Institute of Bioorganic Chemistry, Siberian Division of RAS,
Novosibirsk 630090, Russia

ABSTRACT The conjugate of antitumor antibiotic bleomycin A5 with the tetranucleotide catalytically cleaves 20-mer ssDNA target in the presence of flanking octanucleotides. Each molecule of the conjugate cleaves on the average three molecules of the target.

Previously we reported that conjugates of antitumor antibiotic bleomycin A_5 can form duplexes[1] and ternary complexes[2] and site-specifically cleave ss and ds DNA targets respectively. It was demonstrated that bleomycin covalently bound to the oligonucleotide preserves its ability to degrade a ssDNA target in catalytic manner[3]. It was shown[4] that alkylating reagents on the basis of short oligonucleotides can perform site-specific modification of a ssDNA target in the presence of flanking oligonucleotides (effectors). The main respect of this work was to cleave 20-mer ssDNA target site-specifically using the conju-







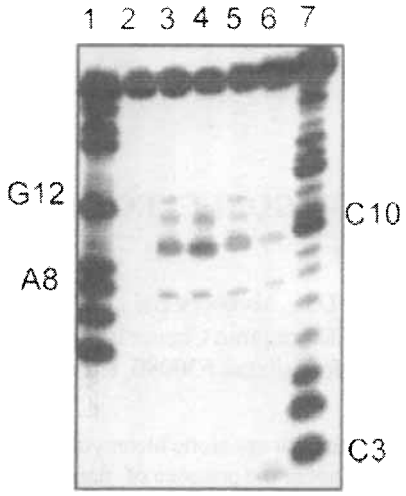


FIG. 1. Autoradiogram of a 20% sequencing gel showing the DNA target cleavage by the conjugate. Reaction conditions: 0.2 M LiCl, 0.01 M Tris-HCl (pH 7.5), $[Fe^{2+}]=5x10^{-5}$ M, $[SHC_2H_4OH]=0.05$ M, [target]=$2x10^{-5}$ M, [conjugate]= $2x10^{-6}$ M, [effector]=$1x10^{-5}$ M. Lanes: 1,7, A+G and T+C Maxam-Gilbert markers respectively; lane 2, the target alone under reaction conditions; lanes 3-5, target degradation by the conjugate in the presence of effectors (3, natural effectors at 20°C; 4, diphenazinium effectors at 20°C; 5, natural effectors at 37°C); lane 6, target degradation by bleomycin A_5 in the presence of pd(CAGC) and diphenazinium effectors.

gate of bleomycin with oligonucleotide as short as tetranucleotide. Two sets of effectors with different stabilizing strength were used: the octanucleotides and their derivatives, bearing on terminal phosphate groups residues of 2-N-(hydroxyethyl)phenazinium.

The DNA target was ^{32}P-labeled on 5'-end. Reactions were carried out using 10-fold excess of the target over the conjugate. The extent of cleavage of the target by conjugate in the presence of natural octanucleotides as effectors at 20°C amounts 31% (FIG. 1, lane 3). So each molecule of the conjugate cleaves on average three molecules of the target. The use of diphenazinium effectors instead of natural octanucleotides increased the extent of cleavage up to 34% (FIG. 1, lane 4). The main site of cleavage in all cases was C^{10} base. Free bleomycin in the same conditions cleaved only 14% of the target, the sites of cleavage were substantially different - C^3, C^{10} (FIG.1, lane 6). Site-specific cleavage of the DNA target

was also observed at higher temperatures. The extent of cleavage of the target by conjugate in the presence of natural octanucleotides at 37°C was 25% (FIG.1, lane 5).

The data obtained allow to consider such conjugates as potential antivirus agents.

The research described in this publication was supported in part by Grant from the Interuniversity Scientific and Technical Program "Biotechnology".

REFERENCES

1. V.F.Zarytova, D.S.Sergeyev, T.S.Godovikova. *Bioconjugate Chem.*, **1993**, *4*, 189-193.
2. Sergeyev D.S.; Godovikova T.S.; Zarytova V.F. *bioorg. Khim.*, **1995**, *21*, 188-196.
3. Sergeyev D.S.; Godovikova T.S.; Zarytova V.F. *nucleic Acids Res.* **1995**, *23*, 4400-4406.
4. Kutyavin I.V., Podyminogin M.A., Bazhina Yu.N., Fedorova O.S., Knorre D.G., Levina A.S., Mamaev S.V., Zarytova V.F. FEBS *Lett*, **1988**, *238*, 35-38.