# Oligonucleosides as Prospective Therapeutic Drugs

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In recent years, development of synthetic oligonucleotides which bind in a sequence-specific way to RNA or DNA aiming at the inhibition of gene expression has been the focus of intensive research. This novel strategy which has become known as "antisence" or "antigene" approach, respectively, opens up new possibilities in research and drug development.

A number of new mono- and bifunctional derivatives of oligonucleotides (deoxyribo- and ribo-series, as well as their 2'-O-methyl- and thiophosphate analogues) are designed. They contained reactive (alkylating, cleaving (bleomycin A5 or peptides), or photoactive), stabilizing (phenazinium), or hydrophobic steroid (cholesterol, estrone, testosterone) groups [1]. The oligonucleotide bearing only the bleomycin residue causes the catalytic site-directed cleavage of DNA [1]. Photoreactive perfluoroaryl azide conjugated with oligonucleotide has the high quantum yield and modifies the DNA and RNA-targets with high efficiency [2]. Peptidyl oligonucleotides bearing alternated hydrophobic and basic amino acids turn out the promising artificial ribonucleases [3]. The phenazinium residue linked to an oligonucleotide stabilizes the complexes of the latter with DNA or RNA targets.

We have also synthesized a number of bifunctional derivatives containing simultaneously reactive and stabilizing groups; reactive and steroid groups; stabilizing and steroid groups; two stabilizing groups. Disubstituted derivatives of oligonucleotides acquire the package of the new unique properties for their particular application. Thus, the ability of the phenazinium derivatives of short oligonucleotides to form stable complementary complexes with nucleic acids and to stabilize the complexes of adjacent short oligonucleotides allow us to develop the new and perspective approach for DNA recognition by short oligonucleotides [4].

The short oligonucleotides (tetra-, hexamers) form stable complexes with DNA and RNA in the presence of flanking effectors that are oligonucleotides or their derivatives containing phenazinium or steroid groups. Tandems of short oligonucleotides and their derivatives selfassembled on DNA are more sensitive to one point mutations than extended oligonucleotides. The proposed approach opens new opportunities to design therapeutic drugs, superspecific chemical nucleases, and DNA diagnostic and sequencing methods.

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