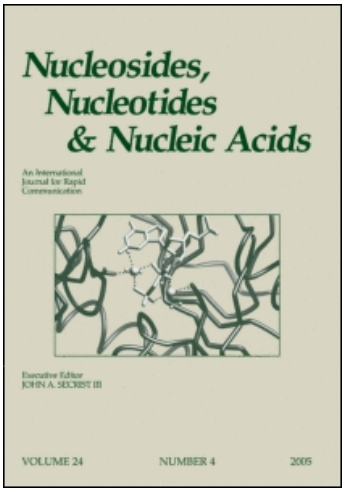

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Oligoribonucleotides with Functionalized Nucleobases as New Modifiers of Biopolymers

M. Repkova[ab]; M. Meshchaninova[a]; D. Pyshnyi[a]; A. Venyaminova[a]
[a] SB RAS, Novosibirsk Institute of Bioorganic Chemistry, Novosibirsk, Russia [b] SB RAS, Novosivirsk Institute of Bioorganic Chemistry, Novosibirsk, Russia

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Oligoribonucleotides with Functionalized Nucleobases as New Modifiers of Biopolymers

M. Repkova,* M. Meshchaninova, D. Pyshnyi, and A. Venyaminova

Novosibirsk Institute of Bioorganic Chemistry, SB RAS, Novosibirsk, Russia

ABSTRACT

Synthesis and evaluation of hybridization and modification abilities of the new types of photoactivatable oligoribonucleotide conjugates are presented.

Key Words: Oligoribonucleotides; Functionalized nucleobases; Perfluoroarylazide; Hybridization; Modification.

Oligoribonucleotides bearing modified nucleotides at certain positions of the chain are indispensable tools for studying RNA-nucleic acid and RNA-protein interactions in both basic and applied aspects. This communication describes the synthesis and properties of oligoribonucleotides bearing an aliphatic amino linker or photoactive *p*-azidotetrafluorobenzamide group at the heterocycle.

A solid-phase H-phosphonate synthesis of oligoribonucleotides[1] containing a convertible nucleoside with bromine atom or 4-chlorophenyl residue at the heterocycle as leaving groups, substituted afterwards by an aliphatic diamine, was developed. An acid-labile (in this case, 2′-O-tetrahydropyranyl) protective group is

*Correspondence: M. Repkova, Novosivirsk Institute of Bioorganic Chemistry, SB RAS, Lavrentyev Ave. 8, 630090 Novosibirsk, Russia; Fax: +7 383 233 3677; E-mail: repk@niboch.nsc.ru.

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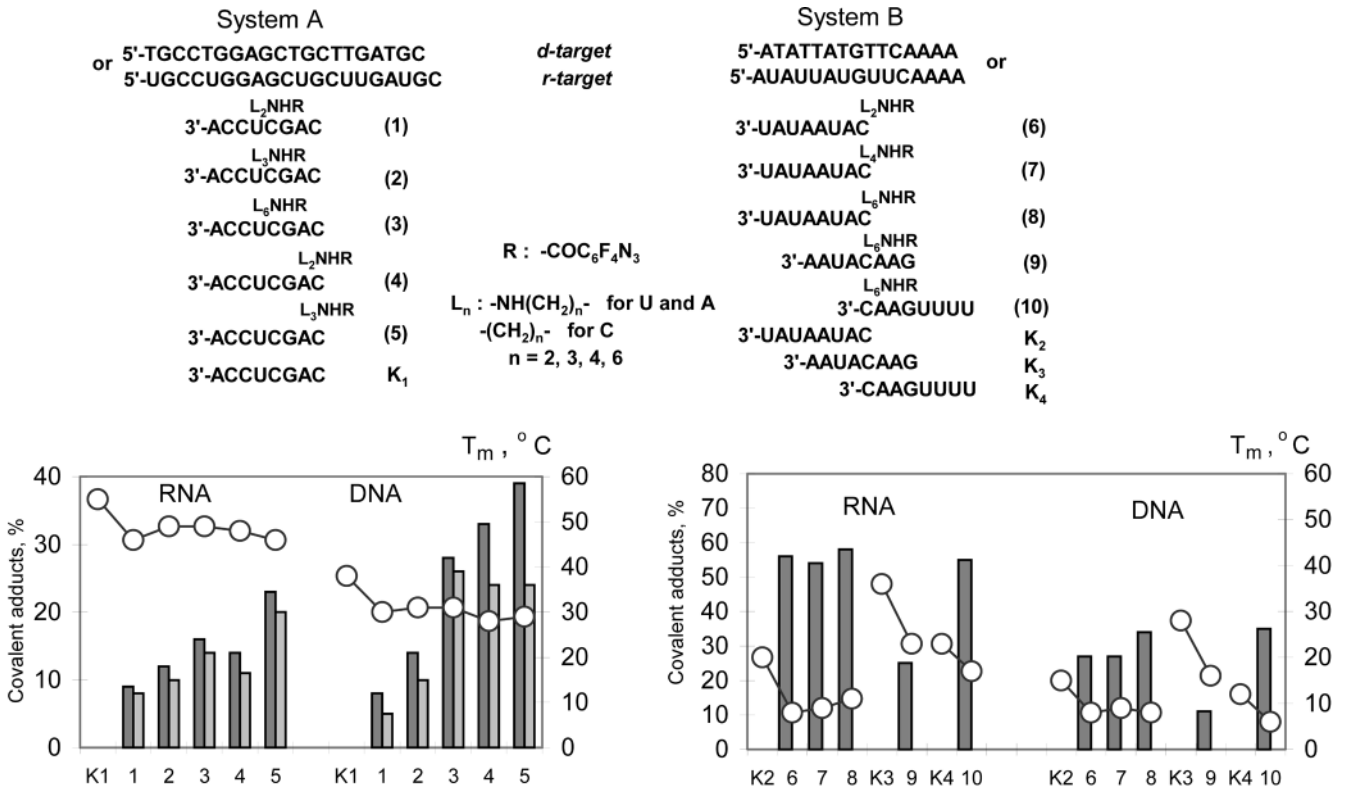

Figure 1. Hybridization and modification abilities of new photoactivatable reagents. Buffer for melting: 0.1 M NaCl, 10 mM Na cacodylate, 1 mM Na_2EDTA, pH 7.4; [oligonucleotide] = $1.3 \cdot 10^{-5}$ M. Irradiation conditions: 303-365 nm, $5 \cdot 10^{-4}$ W·cm^{-2}, 10 min, 5°C (■) or 20°C (□), buffer 0.1 M NaCl, 1 mM Na_2EDTA, 0.01 M Tris-HCl, pH 7.2; [target] = $1 \cdot 10^{-7}$ M, [reagent] = $1 \cdot 10^{-5}$ M.

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important to prevent the undesirable cleavage of oligoribonucleotides by aliphatic amines. The approach allows an oligoribonucleotide precursor to be converted into a family of modified ribooligomers differing only in the structure of the amino linkers. The series of oligoribonucleotides bearing the amino linkers at the C8 of adenine, C5 of uracil, and N4 of cytosine were synthesized. The presence of a highly nucleophilic aliphatic amino group allows different reactive groups (alkylating, photoactive, cleaving DNA and RNA chains, and other) to be easily introduced into oligoribonucleotides to create new reagents for affecting biopolymers. This was illustrated by synthesizing new types of photoactivatable oligoribonucleotide conjugates bearing *p*-azidotetrafluorobenzamide group at the heterocycle. The reagents based on perfluoroarylazides are of interest because they are easy to synthesize and have a high photodissociation quantum yield.[2]

Treatment of the amino-containing oligoribonucleotides with N-hydroxysuccinimide ester of *p*-azidotetrafluorobenzoic acid by analogy with[3] leads to the corresponding photoactivatable derivatives of oligoribonucleotides bearing *p*-azidotetrafluorobenzamide group at the C5 of uracil (reagents **1**–**3**), C8 of adenine (reagents **4**, **5**), and N4 of cytosine (reagents **6**–**10**). Photoactivatable oligoribonucleotide conjugates are of great interest for investigation of biological processes based on interactions of biopolymers. A number of synthesized oligoribonucleotides bearing a modified uracil at various positions of the chain are employed successfully for studying mRNA arrangement at the decoding center of human ribosomes.[4] A comparative study of hybridization and photomodification abilities of perfluoroarylazide conjugates of the oligoribonucleotides bearing modified adenine, uracil, and cytosine is presented here. The systems A and B for comparative study of the properties of the synthesized perfluoroarylazide conjugates of oligoribonucleotides were designed (Fig. 1). Ribo- and deoxyoligomers with the same sequence were used as targets, viz., eicosamers with sequence identical to the fragment of (+) strand of HIV-1 DNA (system A) and model pentadecamers (system B).

All the modified oligoribonucleotides bearing an aliphatic amino or *p*-azidotetrafluorobenzamide group at the heterocyclic base displayed higher binding affinity for the complementary RNA than for DNA. Modification of RNA and DNA in both systems with new photoactivatable conjugates proceeds site-specifically. There is a noticeable difference in the action of the photoreagents depending on the type of target, type of modified nucleoside, its location in the oligoribonucleotide chain, position of photoactive group, and structure of amino linkers. Comparison of the hybridization and modification abilities of the reagents studied demonstrates the absence of clear correlation between extent of formation of covalent adducts and T_m of duplexes. The guanosine closest to the reactive group is the major DNA modification site for all the reagents. The results obtained demonstrate that these photoactivatable oligoribonucleotide conjugates bearing *p*-azidotetrafluorobenzamide group at the heterocycle are promising effective modifiers of biopolymers.

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