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Photoactivatable Porphyrin Oligonucleotide Derivatives for Sequence Specific Chemical Modification and Cleavage of DNA

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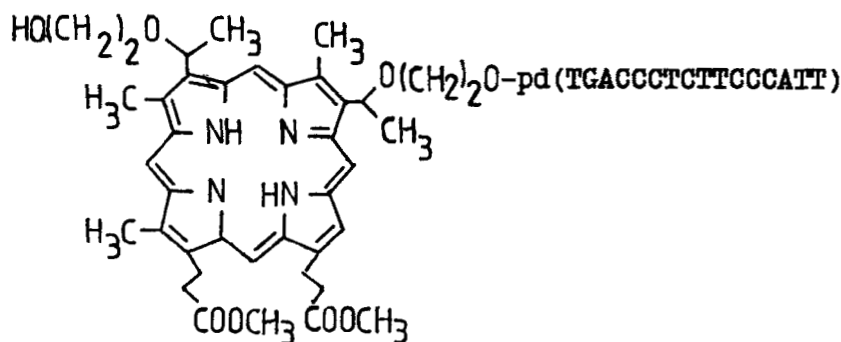
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PHOTOACTIVATABLE PORPHYRIN OLIGONUCLEOTIDE DERIVATIVES
FOR SEQUENCE SPECIFIC CHEMICAL MODIFICATION AND
CLEAVAGE OF DNA

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Abstract: Oligonucleotide derivatives bearing porphyrin groups cause site-specific modification of DNA after irradiation with visible light.

Oligonucleotide derivative bearing a porphyrin group: dimethyl ester of 2,4-di[α -(2-hydroxyethyl)oxyethyl]-deuteroporphyrin IX (R) at the 5'-theminus was synthesized.



Reaction of this derivative with a single-stranded DNA fragment containing a nucleotide sequence complementary to this oligonucleotide was investigated. Irradiation of the complex formed by this oligonucleotide and the DNA with visible light (350-450 nm, 2.8 W/m²) resulted in sequence specific chemical modification of the target at two consecutive guanosines near the binding site. The modified DNA could be cleaved at the modified residues by the hot piperi-

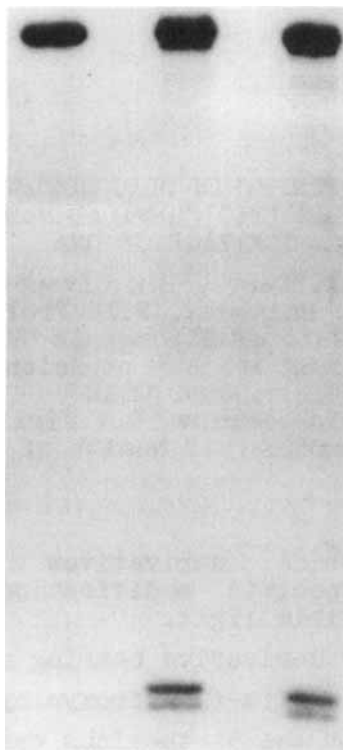


FIGURE 1 Modification of the ssDNA fragment by a porphyrin derivatives of oligonucleotide pd(TGACCCTCTTCCCATT).

Lane 1 -incubation in the dark;

Lane 2 -incubation under irradiation for 1 hour in the presence of oxygen;

Lane 3 -incubation under irradiation for 1 hour in the absence of oxygen.

Modification conditions: 10^{-8} M 32 P-labelled ssDNA fragment; 10^{-5} M oligonucleotide derivative;

Buffer: 0.05 M Tris-HCl, pH 7,5; 0.1 M NaCl.

dine treatment. Quantum yield of the reaction (calculated as a ratio of the DNA modification extent to the number of photons absorbed by one porphyrin group) was 10^{-3} at the reagent concentration of 10^{-5} M. S-shaped reaction kinetic curve suggested a complex, at least two-step, mechanism of the process. The existence of the secondary conversions was confirmed by the increase of the reaction yield in the course of the incubation of the reaction mixture in the dark after short exposure to the light.

It is believed, that the nucleic acids modification caused by porphyrins includes formation of the singlet molecular oxygen as a damaging species. However, reaction of the oligonucleotide derivative with DNA was apparently oxygen independent: it was not affected by the removal of oxygen from the reaction mixture (Fig.1) and by the introduced quencher of the singlet oxygen, sodium azide. The results obtained suggest that direct interaction of the excited porphyrin group and guanosine in the target DNA are responsible for the modification.