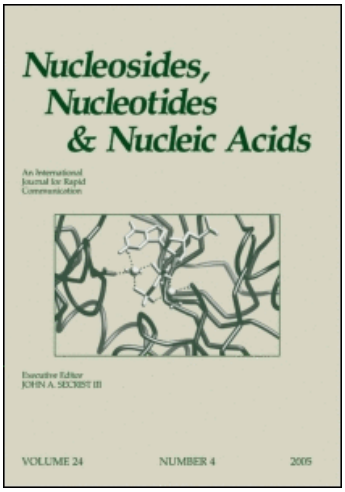

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ENHANCEMENT OF STABILITY OF DOUBLE AND TRIPLE STRANDED DNA BY CATIONIC AMPHIPHILIC α-HELIX PEPTIDE

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ABSTRACT

It was found that synthetic amphiphilic α-helix peptide could bind stabilize double or triple stranded DNA. The stabilization effect was significant for cationic α-helix peptides which indicated the importance of electrostatic interaction of positive charge of peptide and negative charge of DNA. It was also pointed out that α-helix content was increased in the presence of DNA.

It was found that synthetic amphiphilic α-helix peptide could bind stabilize double or triple stranded DNA. The stabilization effect was significant for cationic α-helix peptides which indicated the importance of electrostatic interaction of positive charge of peptide and negative charge of DNA. It was also pointed out that α-helix content was increased in the presence of DNA. Since it was shown that cationic amphiphilicα-helix peptide protect DNA against nuclease digestion and accelerate membrane permeability of DNA, the present study can provide a solution for the problems of antisense or triplex oligonucleotide in their practical application.

peptide **1** : $HO(LKAL)_3NH_2$ (ESIMS M/Z = 1295.0 ($M+H^+$))
peptide **2** : $HO(LRAL)_3NHAc$ (ESIMS M/Z = 1421.1($M+H^+$))

The UV melting curves revealed that peptide **1** bearing three lysine residues could slightly stabilize dsDNA at neutral pH (DTm = 0 - +2.7 °C). It could be attributed to

the simple relief of anionic repulsion between phosphate backbones on DNA by cationic property of peptide **1**, because CD spectra (not shown) did not show α-helical structure of the peptide in the presence or absence of DNA.

In contrast, peptide **2** bearing three arginine moieties could stabilize dsDNA to a larger extent (ΔTm = 0 - + 6.0 °C). CD spectra showed predominance of α-helical structure of the peptide in the presence of DNA.

he difference of stabilization effects on dsDNA between peptide **1** and **2** can be referred to the secondary structures of these peptides. Since the peptide **2** has amphiphilic properties in its α-helical structure, it can be possible to assume the larger enhancement of stabilization of DNA could be caused by hydrophobic contact of the peptide in the major or minor groove of DNA as well as electrostatic interaction of phosphate backbone and cationic arginine residues.

It is notable that the peptide **2** could significantly stabilize triple stranded DNA at pH 6.0. (ΔTm = + 6.4 °C) It should be pointed out that the shape of the melting curve for triple stranded DNA-peptide hybrid was quite different from that for dsDNA-peptide hybrid. The observation indicated the binding of the peptide **2** to triple stranded DNA in the major groove was hindered by the third strand of DNA.

These results strongly suggest that cationic amphiphilic a-helix peptides can be used for improved antisense and triplex strategy.

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REFERENCES

1) M. Fujii, K. Yamamoto, J. Hidaka, and T. Ohtsu.*Tetrahedron Letters*, **38 (3)**, 417 (1997).; M. Fujii, K. Yoshida, J. Hidaka, and T. Ohtsu. *Bioorg. & Med.Chem.Lett.*, **7 (5)**, 637 (1997).; M. Fujii, K. Yoshida, J. Hidaka, and T. Ohtsu, *J. Chem. Soc., Chem. Commun.*, **1998**, 717.

2) T. Niidome, N. Ohmori, A. Ichinose, A. Wada, H. Mihara, T. Hirayama, and H. Aoyagi, *J. Bio. Chem.*, **272**, 15307 (1977).