Molecular design of the PNA-PEG conjugate as an antisense nucleic acid model and the regulation of gene expression

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The functional analysis has been pushed since the sequence of the human genome was decided, and the causal agent gene sequencing such as many disease genes, the oncogene were already clarified. Peptide nucleic acid (PNA)[1] is a synthetic DNA/RNA analogue repeating N-(2aminoethyl)glycine with nucleobases. In genetic engineering, PNA as the antisense mRNA has been designed for the gene therapy[2], but there are very few examples used for the regulation of gene expression caused by many problems such as the low solubility, the coexistence of the temperature region and single base recognition ability. From some years, we have studied inchworm-type PNA-PEG conjugate (Fig. 1) and it showed a remarkable single base recognition around 30˚C for gene expression using a cell-free protein synthesis system (Fig. 2). This mechanism was induced by the inchworm-type structure of PNA-PEG conjugate which was amplified the difference of single base pair against the one side of 8 base PNA. In addition, PNA-PEG conjugate was taken into the cell with macropinocytotic pathway, and it indicates a possibility to control the gene expression in vivo.

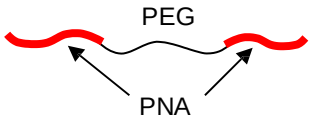

Fig.1 Schematic illustration of inchworm-type PNA-PEG conjugate.

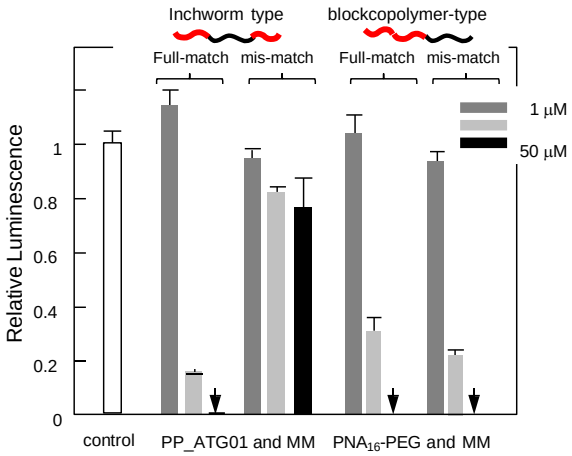

Fig. 2 Luminescence intensity ratio of luciferase in cell free protein synthesis system with inchworm-type and block-copolymer-type PNA-PEG conjugates.

References

1) Nielsen, P.E., Equholm, E., Berg, R.H., Buchardt, O. (1991) Science, 254, 1479-1500.

2) Komiyama, M., Aiba, Y., Ishizuka, T., Sumaoka, J. (2008) *Nat. Protoc.* **3**, 646-654.