Recognition of double-stranded DNA by using parallel-stranded PNAs

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Small molecules to recognize target sequences in double-stranded DNA (dsDNA) have been extensively studied because of their applicability. Peptide nucleic acid (PNA), a type of DNA analog (Fig. 1a),[1] has been utilized for the direct recognition of dsDNA via the formation of a unique invasion complex (Fig. 1b).[2] However, nucleobase modifications of PNAs are necessary to inhibit undesired PNA/PNA duplex formation and have been an obstacle to a wide range of applications of dsDNA recognition by PNAs. Recently, only using PNAs without any modifications of their nucleobases and backbones, we succeeded in efficient recognition of target dsDNA sequences.[3]

Herein, we have designed a pair of PNAs in not antiparallel but parallel to inhibit the binding between PNAs (Fig. 1c) and developed a new strategy for PNA invasion. The efficiency of invasion complex formation can be evaluated by electrophoretic mobility shift assay (EMSA), since the complex shows a lower mobility than corresponding dsDNA. The EMSA showed the formation of the invasion complex (lanes 3 & 4 in Fig. 1d) as well as high sequence selectivity, enabling discrimination of 1 base mismatch (lanes 5 & 6 in Fig. 1d). The melting temperature of the duplex with the parallel PNA/PNA was much lower than the antiparallel PNA/PNA duplex, suggesting destabilization of PNA/PNA duplex formation and improvement on the efficient formation of the invasion complex. Moreover, we succeeded in the X-ray crystal structure analysis of the parallel PNA/PNA duplex. Details of the structure and comparison with antiparallel one will be discussed in the presentation.

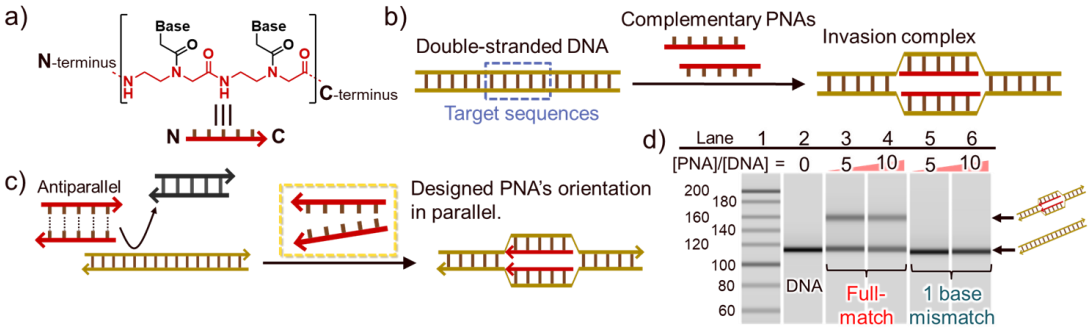

Fig. 1 (a) Structure and orientation of PNA. (b) Double-stranded DNA recognition of PNA via invasion complex formation. (c) Newly developed PNA invasion using parallel-stranded PNAs. (d) EMSA for evaluation of the sequence selectivity.

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