X-ray crystal structure analysis of a reverse binding orientation cyclic-PIP and DNA complex and structural comparison with forward binding orientation complex

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Pyrrole imidazole polyamide (PIP) is a molecule that binds to the DNA duplex in a sequence-specific manner, and because of this property it shows promise in drug discovery applications. PIP contains an N-terminus and a C-terminus, and when the N-terminus is oriented toward the 5' side of the DNA strand, it is called forward orientation, and when the C-terminus is oriented toward the 5' side of the DNA strand, it is called reverse orientation. Depending on the design of the PIP, there are some PIPs that cannot recognize this orientation and combine in both types of orientation. To design a PIP that specifically recognizes only a single orientation, it is necessary to elucidate the bonding mode in both orientations at the atomic level. The X-ray crystal structure of the forward binding orientation of the cPIP-DNA complex has been reported[1,2], but that of the reverse binding orientation has not been reported yet. In this presentation, we will report X-ray crystal structure analysis for the reverse binding orientation of cPIP-DNA[3]. In addition, comparisons were made with forward-oriented structures, and similarities and differences were highlighted. Based on this result, the factors of orientation priority were also considered using modeling.

Keywords : X-ray crystal structure analysis; DNA; PIP

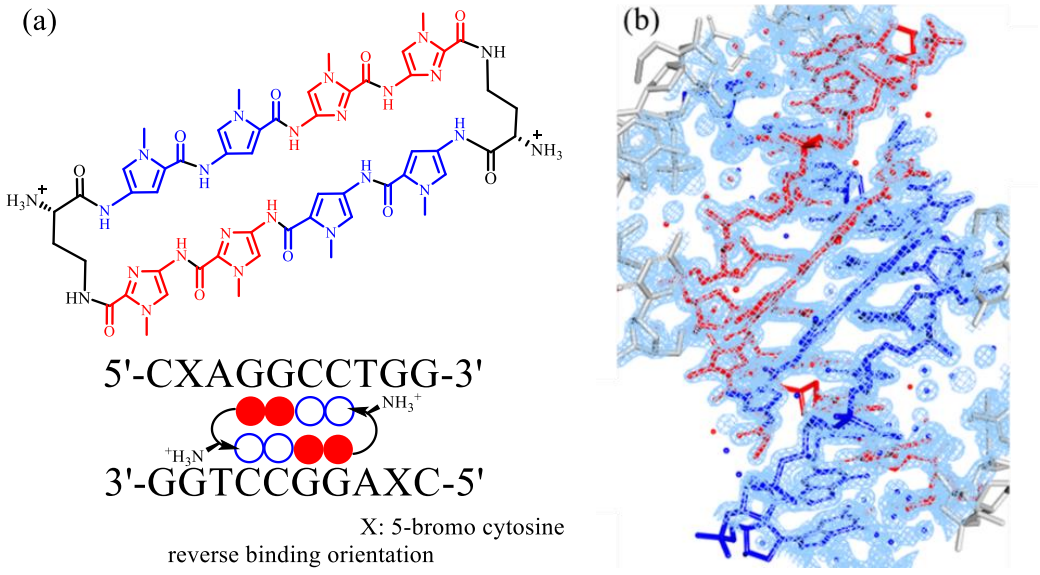

Figure 1. (a) Chemical structure and ball and stick notation of a cyclic PIP. (b) The crystal structure of the reverse binding orientation cPIP-DNA complex.

1) D. M. Chenoweth. *et al.*, *Proc. Natl. Acad. Sci.* **2009**, *106*, 13175-13179.
2) D. M. Chenoweth. *et al.*, *J. Am. Chem. Soc.* **2010**, *132*, 14521-14529.
3) K. Abe. *et al.*, *J. Am. Chem. Soc.* **2020**, *142*, 10544–10549.