Comparing the Properties of DNA-Binding Pyrrole−Imidazole Polyamides with Different Structures (Linear versus Cyclic)

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Pyrrole−Imidazole Polyamides (PIPs) are a class of oligopeptides, which bind to the minor groove of B-DNA in a sequence-specific manner. Their sequence-specificity is defined by a unique recognition rule: an antiparallel pair Im/Py recognizes a G/C base pair and an antiparallel pair Py/Py recognizes an A/T or T/A base pair (Figure 1). Taking advantage of their high binding affinity and sequence-specificity, we can design PIPs, which target various sequences and function as regulators of the expression of disease-associated genes and diagnostic probes.[1, 2]

Connecting two arrangements of Py and Im by one or two γ-aminobutyric acid turns can create two architectures of PIPs: hairpin[3] and cyclic[4] PIPs (hPIPs and cPIPs, Figure 1). hPIPs have been mainly used so far, whereas cPIPs have been less studied. However, because cPIPs have shown high affinity and specificity,[4–6] a better understanding of their properties is critical for the development of more potent gene regulators.

In this study, we compared the properties of a cPIP and hPIP, such as DNA binding, gene regulation in cells, and cellular uptake. The results to date will be reported here.

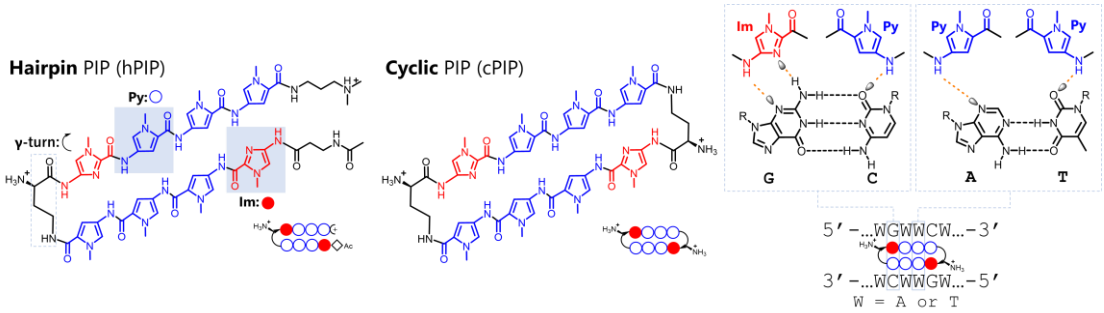

Figure 1. Chemical structures of a hPIP and cPIP, and an illustration of DNA sequence recognition by a cPIP.

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