Evaluation of the properties of a cyclic pyrrole–imidazole polyamide, which specifically binds to CAG/CTG repeat DNA

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Trinucleotide repeat sequences widely exist in the human genome. And abnormal expansion of the repeat often leads to a variety of diseases.[1] The abnormal elongation of CAG/CTG repeat sequences causes Huntington's disease, spinocerebellar ataxia, and myotonic dystrophy. In order to develop therapeutic methods for these diseases, many compounds targeting CAG/CTG repeat sequences have been developed.[2] Our group have been studied hairpin pyrrole–imidazole polyamides (hPIPs), which sequence specifically bind to the minor groove of CAG/CTG sequences.[3]

Although hPIPs have been mainly used in many studies, cyclic PIPs (cPIPs) have been developed and reported to have higher DNA-binding affinity and sequence specificity than the corresponding hPIPs.[4] Therefore, we have developed a CAG/CTG-targeting cPIP in this study. We evaluated its DNA-binding property by using double-stranded DNA melting temperature (T_m) measurements and surface plasmon resonance (SPR) assays. Additionally, the next-generation sequencing study revealed the high sequence specificity of the cPIP.[5] The results of each experiment will be reported in detail in the presentation.

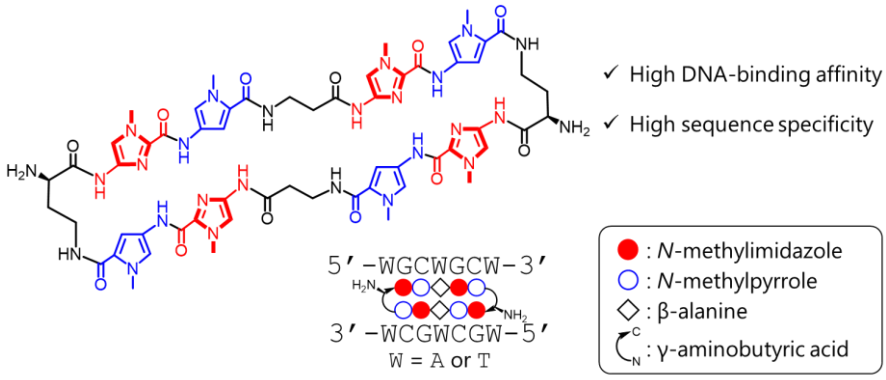

Figure. The chemical structure and ball-and-stick notation of the cPIP.

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