

## Alkynylated purine-pyridazine base pairs with enhanced orthogonality by utilizing non-classical hydrogen bond

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The development of unnatural base pairs (UBPs) is considered as one of the most promising methods to expand the functionality as well as genetic information of DNA. Over the past decades, researchers have reported different types of UBPs which exhibit orthogonal pairing and enzymatic replication in the presence of canonical A-T and G-C base pairs.<sup>1)</sup> We also have very recently created a new type of UBPs, namely alkynylated purine-pyridazine pairs, bearing additional hydrogen bonding units (pseudo-nucleobases) in the major groove; our idea was that the selectivity against the canonical bases can be acquired by translocating the hydrogen-bonding units of UBP to distant position. We have shown that the duplex DNAs containing the alkynylated purine-pyridazine pairs exhibit the selective and stable pairing through the formation of complementary hydrogen bonds in the major groove (Fig. 1A).<sup>2)</sup>

In this study, we aimed to further optimize these alkynylated purine-pyridazine base pairs, especially in terms of increasing the selectivity against the canonical nucleobases. To this end, we removed the hydrogen bonding N-H moiety from the Watson-Crick interface of alkynylated pyridazine structure and changed it to C-H group by adopting pyrazinone and pyridone structures (Fig. 1B). These nucleosides were expected to form non-classical C-H:N hydrogen bond and weaken the interaction with the canonical nucleobases, thereby increasing the selectivity in base pairing. Each nucleoside was successfully incorporated into DNA strands by solid phase DNA synthesis, and their pairing properties were investigated by UV melting measurement. It was revealed that these newly designed nucleosides exhibit improved selectivity against canonical nucleobases while maintaining affinity toward the alkynylated purine nucleoside. The details of the molecular design, synthesis of the nucleosides and the base pairing properties will be reported in the presentation.

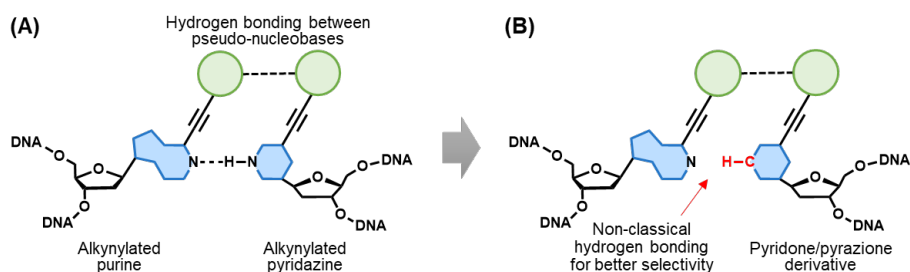


Figure 1. Our design of alkynylated purine-pyridazine base pairs

1) M. Kimoto, I. Hirao, *Chem. Soc. Rev.*, **2020**, *49*, 7602.

2) Manuscript under preparation.