Development of the artificial triplex-forming oligonucleotides containing chemically modified nucleobases or sugar moieties

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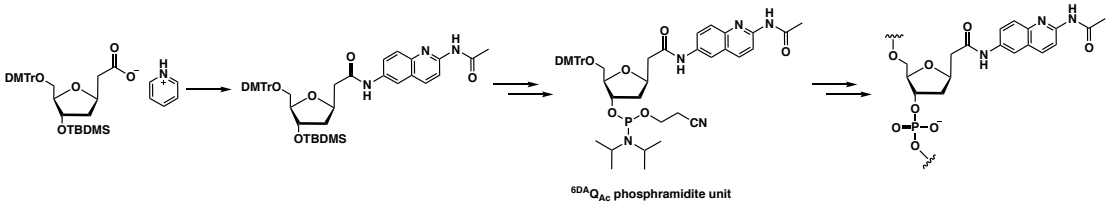
Triplex-forming oligonucleotides (TFOs), which can bind to the major groove of DNA duplex, are expected to be available for inhibition of the targeted gene expression in gene therapy. However, unmodified TFOs have three serious drawbacks: low binding ability to targeted DNA duplex, high dependency to homopurine sequence, and low nuclease resistance. To overcome these problems, many artificial nucleobases and sugar moieties have been reported. In our previous study we found that introduction of 4-thiotymidine ($_s$T) and 2′-deoxy 6-thioguanosine ($_s$G) into antiparallel-type TFOs remarkably increased their binding abilities by the stacking effects of thiocarbonyl groups.

In this study, we synthesized antiparallel TFOs containing *N*-acetyl-2,6-diamino-1,8-quinoline ($^{6DA}Q_{Ac}$) residues as modified nucleobases to improve sequence-dependencies. As a result, it was revealed that $^{6DA}Q_{Ac}$ incorporated into a TFO can selectively bind to T-A base Moreover, we evaluated their binding abilities and base recognition abilities of TFOs containing $^{6DA}Q_{Ac}$, $_s$T and $_s$G.



Furthermore, we carried out introduction of the sugar moieties with the cationic groups into TFOs in order to improve their nuclease resistance. In this paper, we will report the synthesis and the properties of antiparallel TFOs containing 5′-amino-5′-deoxy-5′-hydroxymethylthfymidine (^{R}T), as shown below.