

Nucleic Acids Chemistry beyond the Watson-Crick Double Helix (74): Effect of DNA modifications on the transition between canonical and non-canonical DNA structures in CpG island

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DNA modifications play crucial roles in biochemistry. 5-methylcytosine (5mC) and 5-hydroxymethylcytosine (5hmC) target CpG dinucleotides in CpG island. Importantly, CpG island has quite GC-rich sequences, which have the potential to fold non-canonical DNA structures such as i-motif and G-quadruplexes. The transition between duplex and quadruplex are drastically affected by molecular crowding and cations.¹ Therefore, it is required to consider the molecular environment for investigating the effect of modifications of 5mC and 5hmC on the changes of transition between duplex and quadruplexes in cellular environments.

In this study, we investigated the effect of 5mC and 5hmC modifications on the transition between a duplex and quadruplexes in the presence of NaCl or KCl with or without poly(ethylene glycol) with an average molecular weight of 200 (PEG200). As a result, the modifications changed the transition. Unmodified DNA preferred to fold into quadruplexes, whereas DNA with 5mC and 5hmC preferred to fold into duplexes in the absence of PEG200 (Figure, left). On the other hand, DNA with or without modifications tended to fold i-motifs under molecular crowding conditions (Figure, right).² Furthermore, an investigation of quadruplexes forming sequences in CpG islands, followed by gene ontology enrichment analysis for gene groups classified by the presence of quadruplexes, showed a difference in function between genes with and without quadruplexes in the CpG region.² These results indicate that it is important to consider the effects of DNA modifications on the transition between canonical and non-canonical DNA structures to understand gene regulation by epigenetic modification.

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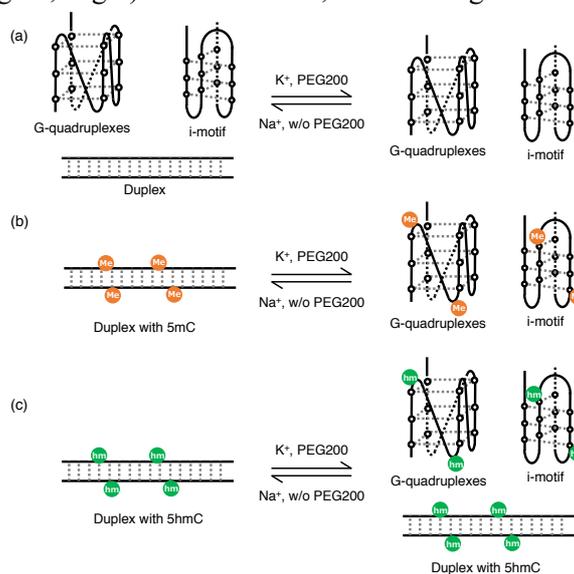


Figure. Schematic representation of the transition between duplex and i-motif and G-quadruplexes (a) without modifications, (b) with 5mC, and (c) with 5hmC.