

Nucleic Acids Chemistry beyond the Watson-Crick Double Helix (68) : Topological control of DNA G-quadruplexes in CpG islands by changes of surrounding environments during senescence

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Levels and patterns of DNA modification play crucial roles in senescence. Two major DNA modifications, 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 DNA non-canonical structures such as i-motifs and G-quadruplexes. The conformations and thermal stabilities of these structures are drastically affected by molecular crowding and cations.¹ Especially, the thermal stability of G-quadruplexes is stabilized by molecular crowding depending on their sequences.² Therefore, it is required to consider the molecular environment for investigating of the effect of modifications of 5mC and 5hmC on the conformations and thermal stabilities of these structures in senescent cells.

In this study, we investigated the conformations and thermal stabilities of i-motifs and G-quadruplexes with 5mC and 5hmC modifications in the presence of NaCl or KCl and with or without poly(ethylene glycol) with an average molecular weight of 200 (PEG200). Analyses of their thermal stability showed that both modifications did not drastically affect the stability. On the other hand, circular dichroism (CD) studies indicated that the surrounding environment regulate the topology of G-quadruplexes depending on the number, position, and type of modifications, although structures of i-motif with any modifications did not change. In the presence of NaCl, molecular crowding of PEG200 changed the topology of G-quadruplex from a hybrid to parallel conformation, while the combination of KCl and PEG200 changed the topology of G-quadruplex from parallel to hybrid conformation (Figure). This result suggested that changes in chemical conditions in senescent cells could modulate the topology of G-quadruplexes in CpG island depending on the modifications.

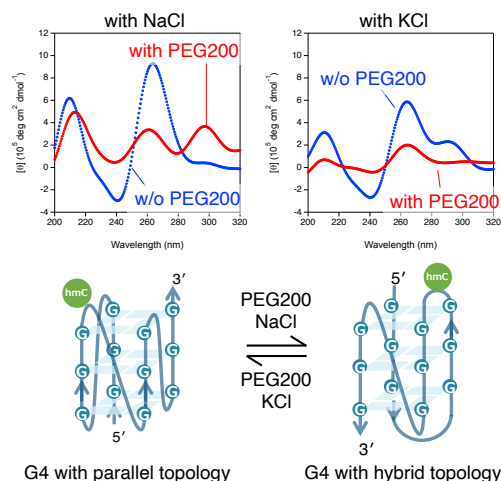


Figure. CD spectra of G-quadruplex with 5hmC modification in 100 mM NaCl or KCl and with and without PEG200 and schematic illustration of the topological transition of G-quadruplex with 5hmC.

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