Nucleic Acids Chemistry beyond the Watson-Crick Double Helix (84): Fluorescence light-up through binding of ligand molecules to specific loop sequences of i-motif DNA

([1]*FIBER, Konan University*, [2]*FIRST, Konan University*) ○Sinjan Das,[1] Shuntaro Takahashi,[1] Naoki Sugimoto[1,2]

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Nucleic acids (DNA and RNA) form not only duplexes but also tetraplexes such as the guanine quadruplex (G4) and i-motif. These structural changes regulate the gene expression to affect the reaction of proteins that interact with nucleic acids. The tetraplex formation creates loop region that links between the tetraplex forming tracts. We have reported that the loop regions of tetraplexes are functional units for gene expression by the ligand binding and solution environments.[1-3] Therefore, it is highly valuable to predict molecular interaction between the ligand of interest and the loops of these tetraplexes from the sequence information for the sensing or regulation of a specific tetraplex, although such technique is still unexplored.

In this work, we investigated loop regions of various i-motif DNAs to understand whether these regions specifically interact with fluorescent ligands. We found that crystal violet (CV) showed high fluorescence response with i-motif from the promoter region of human Bcl-2 gene. The sequence analysis indicated that CV bound to the site formed involving the first and third loop of the Bcl-2 i-motif (Figure 1). Thus, the microenvironment produced by these loops on the i-motif could be a specific site formed for binding and fluorescence emission of CV. Furthermore, the fluorescence intensity of CV on Bcl-2 i-motif was significantly higher than other structures such as other i-motifs, G4s and hairpin structures. Our finding suggests that the loops of i-motif is a novel platform for the specific binding of small molecules, which can be utilized to design the novel ligand to monitor and control biological reactions along i-motif DNAs.

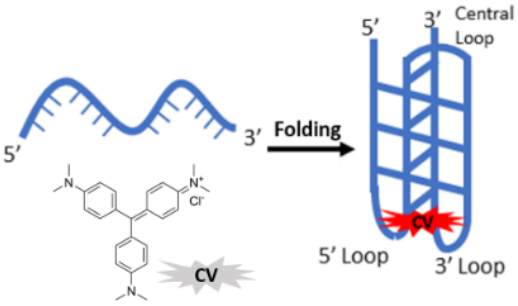

Figure 1. Schematic representation of interaction of CV with Bcl-2 i-motif.

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