Nucleic Acids Chemistry beyond the Watson-Crick Double Helix (78) : Analysis of structural dynamics of *c-Myc* G-quadruplex DNA using high pressure

(*[1]FIBER, Konan Univ., [2]Sun Yat-sen Univ., [3]FIRST, Konan Univ.*) ○Shuntaro Takahashi[1], Tatsuya Ohyama[1], Shuo-Bin Chen[2], Jia-Heng Tan[2], Naoki Sugimoto[1,3]

Keywords: Nucleic acids; Thermodynamics; High pressure; Guanine quadruplex; Mg^{2+} ion

Nucleic acids (DNA and RNA) form not only duplexes but also non-duplexes such as the guanine quadruplex (G4). These structural changes between these structures regulate the function of proteins that interact with nucleic acids. Thus, the formation of G4 regulates reactions such as gene replication and transcription.[1,2] The interaction of cations is also highly important in such changes in nucleic acid structure. In cells, the concentration of cations (Na^+, K^+, Mg^{2+}, etc.) changes dynamically, which may affect physical properties of G4 and regulate gene expression. We studied previously the dynamics of hydration during the G4 formation using high pressure.[3] In this study, we investigated the effect of Mg^{2+} on G4 formation using high pressure.

The results of CD melting curves of G4 from the *cMyc* gene under ambient pressure showed that there was little change in stability for both Mg^{2+} concentrations of 0 and 8 mM. Under high pressure, a tendency for the structural stability of *cMyc* G4 to decrease with increasing pressure was observed under both conditions (Fig. 1). This indicates that the volume of the G4 structure including hydration is larger than the single-stranded state. On the other hand, the decrease in stability was greater in the 8 mM condition than in the absence of Mg^{2+}. The CD spectral analysis showed no conformational change of *cMyc* G4 with Mg^{2+} concentration. Therefore, the Mg^{2+}-dependent of the volume change of *cMyc* G4 was not due to a change in the overall G4 structure, but rather to dehydration associated with the specific binding of Mg^{2+} to *cMyc* G4. The replication inhibition by *cMyc* G4 in the presence of 8 mM Mg^{2+} was strongly observed. These results suggest that *cMyc* G4 may regulate the gene expression by altering the mechanism of its formation and melting without changing the stability of G4 depending on the Mg^{2+} concentration.

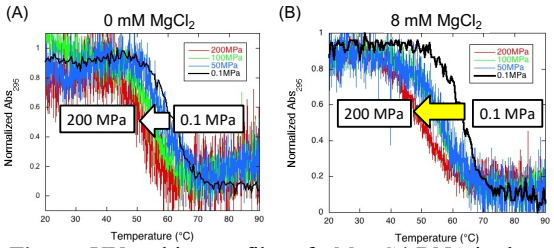

Figure. UV melting profiles of *cMyc* G4 DNA in the absence (A) or presence (B) of 8 mM $MgCl_2$. The measurements were carried out in 10 mM Tris-HCl pH 7.5, 2 mM KCl, and 0 or 8 mM $MgCl_2$. The solution contained 10 uM DNA.

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