Metal ion-Responsive Structural Switch of G-Quadruplexes

Daisuke Miyoshi¹, Zhong-Ming Wang¹, Hisae Karimata², Mamiko Inoue², and Naoki Sugimoto¹,²

¹Frontier Institute for Biomolecular Engineering Research (FIBER), and ²Department of Chemistry, Faculty of Science and Engineering, Konan University
8–9–1 Okamoto, Higashinada-ku, Kobe 658–8501, Japan

G-rich sequences, which are abundant throughout the genomes of most organisms, can fold into G-quadruplexes. Although there is little direct evidence for the formation of G-quadruplexes in vivo, there is growing interest in their potential roles in many biological systems. In addition, various functional molecules can form G-quadruplex structures in vitro. G-rich sequences have extraordinary structural polymorphism depending on the sequence and the environmental conditions. Importantly, the polymorphic nature of the G-quadruplex is promising as a nanomolecular material because a regulated structural transition between different types of G-quadruplex can provide the basis for switchable molecular devices. Moreover, the G-rich sequences are attracting interest as functional elements in molecular electronics. Previously, we reported that structure and function of various DNAs can be regulated by the surrounding condition such as pH, molecular crowding, and divalent metal ions.

In this study, we studied quantitatively effects of divalent cations on the antiparallel G-quadruplex of d(G₄T₄G₄), and found that Ca²⁺ induces a structural transition from the antiparallel to parallel G-quadruplex, and finally G-wire. It was also found that Ca²⁺ and Mg²⁺ can inhibit the duplex formation of the telomere DNAs, which consist of the G-rich oligonucleotide and its complementary C-rich oligonucleotide.

Although the G-wire developed here is promising as molecular electronics, switches are essential for electronics and their size dictates that of the entire circuit. Therefore, possibility of the switches that undergo a structural transition induced by metal ions based on a chemical modification with a structural scaffold of G-quadruplexes, will be also discussed in this study.