Folding dynamics, kinetics and ion exchange of DNA G-quadruplexes

Zi-Fu Wang,[1,2] Ming-Hao Li,[1,3] Ta-Chau Chang,[1,2,3,] and Shang-Te Danny Hsu[4,5]

([1] Institute of Atomic and Molecular Sciences, Academia Sinica, Taipei, Taiwan, [2] Department of Chemistry, National Taiwan University, Taipei, Taiwan, [3] Institute of Biophotonics, National Yang-Ming University, Taipei, Taiwan, [4] Institute of Biological Chemistry, Academia Sinica, Taipei, Taiwan, [5] Institute of Biochemical Sciences, National Taiwan University, Taipei, Taiwan)

e-mail: sthsu@gate.sinica.edu.tw

Guanine-rich DNA sequences with the ability to form quadruplex structures are enriched in human telomeres, which are associated with oncogenesis. G-quadruplexes (G4s) are structurally polymorphic and their folding topologies can depend on the sample conditions. Understanding the mechanism of Na^+/K^+-dependent spectral conversion of human telomeric G4 sequences has been limited not only because of the structural polymorphism but also the lack of sufficient structural information at different stages along the conversion process for one given oligonucleotide. Using solution state NMR spectroscopy, we investigate the structural conversion of a telomeric G4, Tel23, from Na^+ form to K^+ form during Na^+/K^+ exchange. Despite the large spectroscopic changes in the respective CD and NMR spectra. Time-resolved NMR experiments of hydrogen-deuterium exchange (HDX) and hybridization exclude involvement of the global unfolding for the fast Na^+/K^+ spectral conversion. In addition, the K^+ titration monitored by NMR reveals that the Na^+/K^+ exchange in Tel23 G4 is a two-step process. The addition of K^+ stabilizes the unfolding kinetics of Tel23 G4. These results offer a possible explanation of rapid spectral conversion of Na^+/K^+ exchange and insight into the mechanism of Na^+/K^+ structural conversion in human telomeric G4s.

References

1) Hsu *et al.*, *JACS* (2009) **131**:13399