[P10] Determination of the affinity parameters of Z-DNA binding protein to DNA via single-molecule measurements

Sook Ho Kim, Korea University

Left-handed Z-DNA is an unusual conformation of DNA, which can form under special chemical and physical conditions. Nearly two decades ago, several proteins were found to recognize, bind to, and stabilize Z-DNA, which strongly supports the idea that Z-DNA has a biological role in gene regulatory processes. Human ADAR1, prototypic Z-DNA binding protein (ZBP), binds to Z-DNA with high affinity, each covering ~ 6 nucleotides and a pair of them wrapping the 6-bp segment from the opposite sides. Despite comprehensive structural studies for ZBP-DNA interactions, physical and energetic details on their interactions still remain largely elusive.

Utilizing single-molecule assays that measure thermodynamic populations of ADAR1-bound DNA conformations in both GC and TG repeat sequences and the statistical physics model based on the grand canonical ensemble, we determined quantitatively the affinities of ADAR1 to Z-DNAs formed by these sequences as well as B-DNA. We also revealed what pathways it takes to induce the B-Z transition in those sequences. From this study, we gain physical insights into how DNA binding proteins bind to and act on DNA to effect downstream functions.