Biophysical Mechanism of Sequence-Dependent Attraction between Double-Stranded DNAs and Its Biological Significance

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Abstract

The chromosome spends most of its lifetime in the interphase in which it is only loosely condensed and hence viewed as a dynamic polymer. The physical properties of DNA in vitro have been rigorously studied but its structural organization in a living cell and the role of such structure in epigenetics have only started to be explored, leaving the physical mechanism behind largely unknown. From our recent studies combining molecular dynamics simulations and single molecule experiments, we suggest that polycation-driven electrostatic inter-DNA attraction might play a crucial role in determining the overall condensed structure of DNA. We found that the C5 methyl group of thymines, which methylated cytosines also have, induces sequence-dependent attraction between double stranded DNAs. Such behavior is consistent with the large scale structure of chromosomes from Hi-C measurements and the observed compactness of hyper-methylated chromosomes. In this talk, I will present our recent efforts to test the hypothesis from the molecular to the cellular level that may reveal the physical mechanism of controlling the chromosome structure and dynamics for epigenetic gene regulation.