

G-Quadruplex Secondary Structures and DNA Dynamics

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Abstract

DNA is structurally dynamic in ways that can have a consequence for biological processes. I will discuss a class of four-stranded DNA structure, called the G-Quadruplex that can be formed from certain G-rich single stranded DNA. There is now a good level of understanding on the structural biophysics of G-quadruplexes along with a large body of work on the design and synthesis of small organic molecules that can target such structures. Some such molecules have been found to have anti-proliferative effects on human cancer cells along with specific effects on the transcriptional activity of certain genes, raising hypotheses about their existence and function in cells. I will present recent results from my laboratory that provide new insights into when and where such non-Watson-Crick structures may exist in cellular DNA together with a perspective on how such structures may interact with chromatin structure and the epigenome.

Biography

Sir Shankar Balasubramanian is the Herchel Smith Professor of Medicinal Chemistry at the University of Cambridge and senior group leader at the Cambridge Institute. He works on the chemistry, structure and function of nucleic acids. He is a co-inventor of the leading next generation DNA sequencing methodology, Solexa sequencing (now Illumina) that has made routine, accurate, low-cost sequencing of human genomes a reality and has revolutionised biology. He has invented chemistry to decode several modified (epigenetic) DNA bases and DNA secondary structures (G-quadruplexes) in the genome and has made seminal contributions towards the understanding of their dynamics and function. His work on small molecule recognition of nucleic acids has revealed molecular mechanisms that can be exploited to modulate the biology of cancer. His collective contributions span fundamental chemistry and its application to the biological and medical sciences. Sir Shankar was knighted in the Queen's New Year's Honours in 2017 for his services to science and medicine and awarded the Royal Society's Royal Medal in 2018.