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Title: Structure and Function of G-Quadruplexes and Their Interactions with Proteins and Small Molecules

Abstract:

Even though double-stranded DNA commonly folds into the well-known double-helix structure, other types of secondary structures are also possible. DNA is particularly vulnerable to fold into such 'non-canonical' structures when the double helix is unwound by proteins during DNA replication, repair, or transcription. During these cellular events, unwound single strands of DNA could explore different structures, including those that involve base-pairing with other nucleotides within the same strand. G-quadruplex (GQ) structures are prominent examples of such structures and focus our research. GQ structures are best known for their role in protecting chromosome ends (telomeres), which are otherwise vulnerable against enzymatic activity. Due to overarching involvement of telomeres in various cancers, GQ structures and small molecules that stabilize them are of particular significance in cancer research. GQ structures have also been shown to form at non-telomeric sites, particularly regulatory sites such as promoters. When they form in such sites, they typically inhibit gene expression. Unless such non-telomeric GQs are unwound by proteins, they result in DNA breaks and genomic instability as they act as roadblocks against critical cellular machinery. How different proteins and small molecules interact with GQ structures and the underlying kinetics of these interactions are the primary focus of our research. Single molecule fluorescence methods are our preferred tools in these studies as they provide access to interaction kinetics and system heterogeneities with high spatial and temporal resolution. In this talk, I will provide a broad overview of the field and talk about the particular research conducted in my laboratory.