NUCLEIC ACID STRUCTURES CONTAINING G-QUADRUPLEX AND DUPLEX MOTIFS: A STRUCTURAL STUDY AND POTENTIAL TARGETING APPROACH

Guanine-rich nucleic acid sequences have the propensity to assume four-stranded DNA structures known as G-quadruplex. G-quadruplex-forming sequences were identified at important regulatory regions in the human genome such as the telomere, gene promoter, and 5'-untranslated region of mRNA. Important biological processes such as telomere maintenance, transcription, translation, and replication can be influenced by the presence of G-quadruplex.

Quadruplex-duplex hybrid motifs, which contain both G-quadruplex and duplex segments, are also gaining increasing interest as potential therapeutic targets, with potential application in nanotechnology. This thesis explores structural features of different types of quadruplex-duplex motifs to provide important structural knowledge for G-quadruplex-based drug design and development. Two novel quadruplex-duplex hybrids including the multi-stem-loop quadruplex and a duplex-bulged quadruplex are presented in this thesis. This study also investigated a telomeric quadruplex-duplex structure in which the G-quadruplex adopts a basket-type G-quadruplex with two G-tetrads. Additionally, a specific targeting approach toward quadruplex-duplex hybrid structures is proposed based on the simultaneous recognition of duplex and quadruplex motifs. These findings provide structural insights and potential strategies which could be useful for the future design and development of drugs for G-quadruplex targeting. In addition, novel hybrid structures discovered in this thesis could have potential application in DNA nanotechnology.

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