

Direct observations of force-induced rupture of non-canonical DNA structures by magnetic tweezers and single-molecule FRET

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Watson and Crick discovered that DNA exists as a double helix of two strands and the two strands are joined by Watson-Crick base pairs (A-T and G-C). The double stranded DNA structure based on Watson-Crick base pairing is a fundamental structural element of life. With specific conditions met, non-canonical DNA structures such as hairpin, triplex, and quadruplex are thought to co-exist in vivo with B-DNA and to form during DNA metabolic processes such as transcription. While these structures may serve as recombination hotspots, often leading to deleterious genetic instability, it opens up a new opportunity for genetic diversity. Despite intensive chemical and biochemical studies on non-B DNA structures, their physical nature remains largely unknown. DNA hairpin and triplex being model systems, we investigated the mechanical and dynamical behaviors of Watson-Crick and Hoogsteen pairings. In order to monitor the nano-scale conformational transition upon force-induced unzipping of base pairs, we utilized the hybrid technique of single-molecule FRET and magnetic tweezers. We found that a few picoNewtons tension is sufficient to rupture the unusual DNA structures under various chemical conditions and observed frequent inter-conversions between zipped and unzipped states implying their dynamic nature under physiological conditions. †.