CHARACTERIZATION OF G-QUADRUPLEXES IN DNA REPAIR PROTEIN GENE SEQUENCES AND THE EFFECTS OF OXIDIZED GUANINE LESIONS ON DNA BASE INSERTION AND ELONGATION

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Guanine (G) is one of the four nucleobases that make up the complex macromolecule deoxyribonucleic acid (DNA). In addition to its ability to Watson-Crick base pair with cytidine (C), guanine can base pair with itself via non-canonical, Hoogsteen base pairing and form a secondary structure of DNA called a G-quadruplex (G4). Addressed in chapter 1, these structures, composed of four contiguous runs of at least three guanines each, are typically found in the telomeric sequence of chromosomes, but can be found in other DNA sequences and have also been implicated in transcriptional regulation of oncogenes. Using circular dichroism, thermal-melting analysis, and thioflavin T fluorescence, 8 possible G4s were identified and characterized in DNA sequences associated with base excision repair proteins (BER). The presence of G4s in these sequences can affect the transcription of these proteins.

Guanine is also easily oxidized to a number of products. These products can cause base transversions and thus induce mutations that can drastically affect an organism. In chapter 2, the effect of oxidized guanine lesions was determined by examining which DNA bases each lesion inserted opposite, as well as the percent elongation past the lesion when located in a DNA strands. The two research directions intersect where BER proteins have the role of repairing mutations in DNA, such as those that result from oxidized guanine lesions.