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Human DNA repair helicases and their roles in genome stability and disease.

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The Section on DNA Helicases in the Laboratory of Molecular Gerontology at the National Institute on Aging, NIH, led by Dr. Robert Brosh, is focused on age-related genetic diseases arising from mutations in genes encoding DNA helicases, a class of motor ATPases that unwind structured nucleic acids and play important roles in DNA metabolism. Dr. Brosh's group uses molecular and genetic approaches to study helicases and their hereditary diseases, frequently associated with premature aging (e.g., Werner syndrome), cancer (e.g., Fanconi Anemia, Bloom syndrome), or mitochondrial dysfunction. Current studies are focused on the characterization of novel helicase protein interactions and pathways in order to yield insight into how DNA repair helicases contribute to genome stability, healthy aging, and tumor resistance. Early and late functions of the FA Complementation Group J (FANCJ) helicase in double strand break repair, and its prominent role in G-quadruplex DNA metabolism will be discussed. Dr. Brosh's group was the first to employ small molecules to target a DNA helicase in human cancer cells. This strategy provided fresh insights to the role of the Werner syndrome helicase in the DNA damage response. Continued studies in this area are geared toward elucidating the consequences of helicase modulation in living cells to acquire a better understanding of the molecular defects of helicase genetic disorders and potential approaches to therapeutic targeting this important class of enzymes implicated in DNA repair and the replication stress response.

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