Bankhead-Coley Cancer Research Program

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Biochemistry and Molecular Biology — *2008 Program*
University of Miami — *New Investigator (3-year project)*

Project Title: RecQ Family of DNA Helicases in Human DNA Mismatch Repair

Project Summary: The long-term objective of this grant is to understand the molecular mechanism of human mismatch repair (MMR) and its impact on human health. MMR is extremely important to maintain genome stability, whose defects directly lead to hereditary non-polyposis colon cancer and sporadic cancers. To find a cure for these deadly diseases, many fundamental questions about this repair pathway need to be answered. One such question is which DNA helicase(s) participates in MMR in humans. Given the fact that members of the RecQ family of DNA helicases interacts with MMR proteins, it is hypothesized that RecQ helicases are directly involved in human MMR by increasing repair efficiency. To test this hypothesis, we will first determine the involvement of all five RecQ helicases in MMR in the precisely defined in vitro reconstituted MMR system. Second, we will dissect the physical and functional interactions between RecQ helicases and MMR proteins and their involvement in MMR. Third, we will test the involvement of RecQ helicases in MMR through helicase-deficient cell lines and stable siRNA knockdown of the candidate helicases and measurement of microsatellite instability that is the established biomarker for loss of mismatch repair in tumor cells. These research studies should provide important insights into the development of novel diagnostic markers and the design of effective strategies against cancers resulting from MMR deficiency.