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Genome maintenance by RECQ1 helicase and its implication in cancer biology

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Humans have five known RecQ helicase homologs (RECQ1, BLM, WRN, RECQL4, and RECQ5 β) but the functional loss of any one is sufficient to cause genomic instability. Our work has focused on RECQ1, the most abundant but least characterized human RecQ homolog. We have demonstrated that RECQ1 is important for the repair of endogenous and exogenously induced DNA damage, and governs basic cellular functions ranging from DNA replication, repair and genome integrity to gene transcriptional changes. My earlier work revealed that the loss of RECQ1 is sufficient to cause genomic instability in mouse and human cells. Subsequent work from my lab identified novel interactions of RECQ1 implicating critical roles in replication fork progression and DNA strand break repair mechanisms. In addition, RECQ1 is involved in telomere maintenance, responds to oxidative DNA damage, and performs a mechanistic role in base excision repair pathway which removes chemical alterations to DNA bases such as oxidation and alkylation. These findings provided a strong rationale to investigate RECQ1 mutations in cancer patients that ultimately lead to its recent discovery as a breast cancer susceptibility gene. The RECQ1 expression is significantly correlated with clinical outcomes of sporadic breast cancer patients, and depletion of RECQ1 in breast cancer cells has a significant effect on gene expression associated with tumorigenesis. Ongoing efforts are to gain a more complete understanding of RECQ1 functions in genome maintenance mechanisms of DNA repair and transcriptional regulation, and exploring its broader significance in cellular homeostasis.

Biography

Sudha Sharma has a broad interest in DNA repair and its implications in cancer and aging; and a specific background in molecular roles of DNA helicases. Her independent research program on mechanisms of genome maintenance is funded by NIH, and she is a co-investigator on a Canadian Institutes of Health Research (CIHR) funded project investigating breast cancer susceptibility, and an investigator on NIH funded training grant on aging. She serves on national and international review panels for grants and fellowships and is an editorial board member of the journal "Scientific Reports" (Nature publication group).

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