

Investigating mechanisms of genome maintenance through protein and chromatin interactions

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In humans, *RECQ1* is the most abundant of the five helicases (*RECQ1*, *BLM*, *WRN*, *RECQL4*, and *RECQ5β*) belonging to the RecQ family associated with rare genetic diseases of premature aging and cancer predisposition. Our earlier work has revealed a unique requirement of *RECQ1* for genome stability maintenance. However, the mechanisms by which *RECQ1* executes its functions in genome maintenance have remained largely elusive. My lab is utilizing an unbiased proteomic approach to identify novel protein interactions of *RECQ1*. We have discovered a direct interaction of *RECQ1* with *PARP-1* and characterized its functional implications in cellular response to oxidative stress. Moreover, we have identified that *RECQ1* physically interacts and modulates the activity of Ku70/80 proteins which are part of *DNA-PK* complex for the repair of DNA double strand breaks. *PARP-1* and *DNA-PK* are molecular targets for anti-cancer. Our results demonstrating *RECQ1*'s ability to modulate the activities of *PARP-1* and Ku70/80 of *DNA-PK* complex suggest chemotherapeutic potential of *RECQ1*. *RECQ1* is uniquely important for the proliferation of cancer cells. We have used quantitative chromatin immune-precipitation to show that replication stress induces specific enrichment of *RECQ1* at common fragile sites *FRA3B* and *FRA16D* where replication forks have stalled following aphidicolin treatment. Fragile loci are fork stalling sites that occur naturally in genome and often coincide with chromosomal breakpoints in tumors. Current efforts are directed towards identifying what functional sub-modules of repair machinery are associated with *RECQ1* at specific genomic loci and how it participates in dynamic response to challenges under genotoxic stress.

Biography

Sudha Sharma received her Ph.D. in Biochemistry from Banaras Hindu University, India and served for a brief period as Assistant Professor at the Hyderabad Central University, India. She received her Postdoctoral training under the guidance of Dr. Robert M. Brosh at National Institute on Aging, NIH; and Dr. Bruce Yankner at Harvard Medical School. She has a broad interest in the field of DNA repair and its implications in cancer and aging; and specific background in RecQ helicases. She has served on the review panel for agencies including National Science Foundation and her research is funded by the NIH/NIGMS.

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