

“Proteomic Screening Reveals PARylation Landscape of Base Excision Repair Proteins After β -lapachone Treatment in Colorectal Cancer Cell Line”



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Zoom Link

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Abstract: Poly (ADP-ribose) PAR is a protein post-translational modification catalyzed by a family of enzymes known as PARPs. Though PARylation is a well-defined phenomenon occurring after DNA damage, the downstream effects of PARylation on the target proteins and relevance in cancer treatment has not been well characterized. NQO1 overexpressed in most solid cancers bioactivates β -lap leading to ROS causing DNA single strand breaks and base-damage in a tumor specific manner which hyperactivates PARP1, a DNA repair enzyme that utilizes NAD^+ to generate PAR moieties. Proteomic screening after β -lap treatment in colorectal cancer cell line revealed PARylation landscape of base excision, mismatch and nucleotide excision repair proteins of which twenty proteins overlap with H_2O_2 treatment and one unique to β -lap. Moreover, depletion of two of the identified proteins RFC1 and PCNA enhanced β -Lapachone mediated cell death. Also, β -lap mediated cytotoxicity was independent of PARG or TOPO loss. Overall, our findings suggest that PARylation landscape is very crucial for understanding the key proteins involved in enhancing the drug efficacy, and overexpression or downregulation of these proteins can be a novel and effective way to designing effective anti-cancer drugs.

Bio: Dr. Naveen Singh is currently a Tenure Track Assistant Professor of Biochemistry at the Chemistry Dept, New Mexico Highlands University, Las Vegas, NM. Dr. Singh received his Ph.D. in Chemistry from New Mexico State University, Las Cruces, NM, where he worked on orphan P450s – drug metabolizing enzymes and ways to enhance drug metabolism under hypoxic conditions in tumor tissues. As a Postdoctoral researcher at the Dept. of Biochemistry and Molecular Biology, Indiana University, School of Medicine, Indianapolis, IN, he was trained with Dr. David A. Boothman, an internationally renowned cancer researcher and pioneer in the field of PARP inhibitors and NQO1 bio-activatable drugs. Dr. Singh's research interests include DNA repair pathways, Phase I/II drug metabolizing enzymes and ways to enhance synthetic lethality of anti-cancer drugs.



Department of Chemistry
Graduate Seminar
Host: Praveen Patidar