

INDIAN ASSOCIATION FOR THE CULTIVATION OF SCIENCE

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Citation (summary) on the outstanding research work

Professor Benu Brata Das has been awarded the Sun Pharma Science Foundation Research Award in Medical Science Basic Research. Top1 inhibitors are frontline drugs used clinically in cancer therapy. Prof. Das has made outstanding contributions in basic research to understanding the molecular mechanism of DNA topoisomerase I (Top1)-induced DNA damage response and repair by Tyrosyl-DNA-phosphodiesterase (TDP1) both in the nucleus and mitochondria. Prof. Das's outstanding discoveries also include the identification of novel therapeutic targets like PRMT5 and PARP1 that play a critical role in the repair of trapped Top1-DNA lesions and act as resistance determinants in cancer chemotherapy. Prof. Das's group discovered a novel role for PARP1 in the regulation of Top1-nuclear mobility through Top1-PARylation, which provides rationale for the combination of Top1 and PARP inhibitors in cancer. Prof. Das research shows that PRMT5 is the critical modulator of the DNA repair function of TDP1 for the resection of trapped Top1-DNA complexes. CRISPR-mediated PRMT5 KO cells were generated to show that loss of TDP1 arginine methylation results in compromised TDP1 proteostasis and CPT-induced cytotoxicity. Finally, Prof. Das group provides the first evidence for connecting mitochondrial dysfunction with the etiology of neurodegenerative disease (SCAN1) due to a point mutation in human TDP1. These studies are highly relevant for the ongoing clinical trials and also promise precision medicine in cancer. All this work is performed at the Indian Association For the Cultivation of Science, India.

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