FRED & PAMELA BUFFETT CANCER CENTER

American Cancer Society

2016 ACS IRG Recipients

Gargi Ghosal, PhD
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PROJECT TITLE
Spartan maintains genome integrity in human mesenchymal stem cells and prevents cellular aging and early-onset tumorigenesis

LAY ABSTRACT
DNA is the blueprint of life in all living beings and it is important to transfer all the information in the DNA without any errors from one generation to the next. Any damage to the DNA, disturbs DNA metabolic process causing errors, leading to cell death, cancer and/or age-related disorders. Previously, we showed that Spartan is required for survival of cells when exposed to UV light. Patients identified with mutation in Spartan gene, develop cancer and age rapidly. Our preliminary data shows that Spartan is also required for cell survival upon treatment with chemotherapeutic drug etoposide, which generates DNA-protein crosslinks (DPCs). We propose that Spartan is important to remove damages in the DNA caused by exposure to UV rays and chemotherapeutic drugs that generate DPCs, mediate accurate DNA replication and cell survival. This study aims at investigating the novel role of Spartan and Spartan mediated DPC repair in the maintenance of genome integrity of stem cells. A successful outcome of our studies will provide for a better understanding of DPC repair and will open new avenues for targeting Spartan and DPC repair pathway alone or in a synthetic lethal approach with the existing therapeutic interventions in cancer.

Nicholas Woods, PhD
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PROJECT TITLE:
CTDP1 Regulation of NF1 in MPNST

LAY ABSTRACT
Malignant peripheral nerve sheath tumors (MPNST) are a rare form of soft tissue sarcoma that arise from specialized nerve cells, called Schwann cells, that maintain the myelin sheath. The 5-year survival for cases of MPNST is approximately 50%, and this cancer is resistant to both chemotherapy and radiation therapy. The NF1 gene is mutated in half of sporadic MPNST, but the underlying causes for the remaining cases are poorly defined. Our research has identified a physical interaction between NF1 and a specialized phosphatase, CTDP1. Interestingly, mutation of CTDP1 leads to the rare CCFDN disease that affects Schwann cells, and the CTDP1 gene locus is amplified in 20% of MPNST. The association between CTDP1 expression defects and Schwann cell dysfunction leads us to propose that CTDP1 overexpression is likely an oncogenic event in MPNST through its interaction with NF1. This proposed research will assess the expression profiles of CTDP1 in MPNST and determine the effects on NF1 and downstream Ras signaling. Targeted knockdown of CTDP1 will be used to determine the effects on MPNST growth and response to therapies. The results of these studies will be to establish CTDP1 as a target for small molecule inhibitor development to improve MPNST survival.