CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160667

Project Title:
DNA-Protein Crosslink Repair Pathways and Cancer Therapy

Award Mechanism:
Multi-Investigator Research Awards (Version 2)

Principal Investigator:
Chen, Junjie

Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Human cells have to cope with DNA damage that occurs naturally or is induced by exogenous sources like sunlight exposure. There are many types of DNA damage, one of which is DNA-protein crosslinks (DPCs; proteins trapped on DNA). DPCs are one of the most toxic types of damage in the cell, since they act as roadblock and prevent any event that takes place on DNA. It is now known that several commonly used chemotheraputic agents kill tumor cells by inducing abundant DPC lesions. This list includes irinotecan, topotecan, camptothecin, etoposide (VP-16), doxorubicin, daunorubicin and anthracycline. These drugs have been approved by FDA for the treatment of ovarian, lung, colon, and many other types of cancers. While DNA repair has been studied in basic research for several decades, there is little information about the mechanisms of DPC removal in any organism. Thus, we do not understand how DPCs are recognized, how the protein component of the lesion is processed, how the protein is ultimately removed from the DNA, or how the DNA is repaired following this removal. These events must take place in cells that are exposed to radiation and chemotherapeutic agents that induce DPCs, and it is widely known that resistance often occurs over time in patients. To understand the potential resistance pathways and survival mechanisms that cancer cells use, an understanding of DPC repair is critically important. This program brings together experts from across Texas to determine how cancer cells utilize specific pathways to deal with DPCs when they are confronted with the anti-cancer drugs described above. The studies proposed in this program will provide important knowledge that are likely to be translated into new opportunities for cancer treatment and overcoming drug resistance.