

**New Jersey State Commission on Cancer Research
LAY ABSTRACT OF RESEARCH PROJECT**

NAME OF PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR: **Yao-Ping Lu**

Project Title: **Selectivity for proapoptotic effects of caffeine**

Description: **Topical application of caffeine selectively enhances apoptosis by specifically inhibiting ATR-mediated Chk1 phosphorylation, thereby preventing UVB-induced skin tumors.**

Sunlight-induced skin cancer is the most prevalent cancer in the United States, and strategies to prevent these cancers would save lives and have significant social impact. In earlier studies, we found that oral administration of green tea, black tea or caffeine or topical applications of caffeine inhibited ultraviolet B light (UVB)-induced skin carcinogenesis in mice. Our studies also indicated a stimulatory effect of caffeine administration on UVB-induced apoptosis (programmed cell death) in the epidermis of p53 tumor suppressor gene knockout mice and in tumors. Caffeine administration did not affect apoptosis in normal non-UVB treated mice or in non-tumor areas of tumor bearing mice. In the present study, we plan to investigate mechanisms of the proapoptotic effect of caffeine by studying its effect on ATR-mediated Chk-1 phosphorylation, which is an important regulator of programmed cell death. We hypothesize that caffeine enhances apoptosis by inhibiting Chk-1 phosphorylation in UVB-treated epidermis and in UVB-induced tumors but not in non-UVB treated epidermis or in areas of the epidermis away from tumors in tumor-bearing mice. The proposed studies will provide a better understanding of in vivo mechanisms of cancer chemoprevention by caffeine and may help in the development of a more active stimulator of apoptosis in DNA-damaged skin or in tumors that acts by inhibiting ATR-mediated phosphorylation of Chk1.