



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP101016

Project Title:
Understanding the Activity of a Potent Anticancer Agent

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Nature produces small molecules that profoundly benefit human health. Natural products can be produced by bacteria (e.g. doxorubicin), fungi (e.g. tetracyclins) or plants (e.g. paclitaxel). The treatment of cancer, in particular, has benefited from Nature's arsenal of small molecules. For this reason, newly discovered natural products present exciting opportunities for interdisciplinary research involving chemical and biological studies. Recently, it was discovered that bacteria produce a small molecule named simaomicin. By itself, simaomicin has no effect on normal or human cancer cell lines. However, in combination with agents that damage DNA, simaomicin kills cancer cells selectively. Currently, little is known about the details of this process. Several proteins which are known to regulate cell growth and division are not the targets of simaomicin. We hope to determine the mechanism by which simaomicin synergizes with other anti-cancer agents. If the project is successful, we will learn how a potential therapeutic agent functions. Of greater importance, we may uncover new strategies to target human cancers. To identify how simaomicin functions, we will pursue three strategies simultaneously. First, we will see if simaomicin inhibits the function of several enzymes known to be involved in DNA repair and replication. Second, we will look for proteins that physically interact with simaomicin. Finally, we will evolve cell lines that are resistant to the effects of simaomicin. By determining how resistant cell lines differ from sensitive cell lines, we may reveal the biochemical pathway targeted by simaomin.