

EXECUTIVE SUMMARY [NON-CONFIDENTIAL, NON-TECHNICAL ABSTRACT FOR PUBLIC INFORMATION OR PROGRAM PROMOTION]: State in layman's terms the application's broad, long-term objectives and specific aims, making reference to the potential public benefits of the project relevant to California. Do not include proprietary or confidential information. This may be distributed before the funding decision has been finalized.

The design and synthesis of drug candidates with new and cheaper technology to treat medical diseases continues to be a major emphasis in biotechnological research as the cost of health care continues to increase. One new emerging treatment utilizes light to convert pro-drugs into their active form. Among the advantages of light activated pro-drugs include minimal damage to healthy cells by controlled delivery of light along with little to no surgical procedures by employing fiber optic or external light sources for activation. This proposal describes the synthesis of enediyne anti-cancer pro-drugs that will bind to and, once properly activated, cleave DNA leading to cell death. The proposed enediyne pro-drugs will be activated with light to trigger a chemical transformation to generate the active intermediate responsible for DNA strand scission and ultimately cell death. Synthetic methodology to prepare a series of enediyne pro-drugs will be developed and their thermal stability under physiological temperatures will be examined. Analogs that display good thermal stability will be irradiated with light to monitor activation of the drug. This study will identify lead candidates to pursue DNA binding and light-activated cleavage of double-strand DNA.