

MIXING CHEMISTRY WITH NANOTECHNOLOGY
TO REWRITE THE MODERN RECIPE FOR CANCER CHEMOTHERAPEUTICS

By

KARINA MARIE GONZALEZ

A Thesis Submitted to The W.A. Franke Honors College

In Partial Fulfillment of the Bachelors degree
With Honors in

Physiology & Medical Sciences

THE UNIVERSITY OF ARIZONA

M A Y 2 0 2 2

Approved by:

Dr. Jianqin Lu
Department of Pharmacology & Toxicology

Abstract

Cancer is one of the top leading causes of death in the United States, contributing to an estimated average of 600,000 deaths per year. Chemotherapy has proven to be the most effective anti-cancer drug in modern medicine today, but the downfall of this form of treatment is its debilitating side effects that significantly suppresses the body's immune system, killing off vital immune system protectors such as white blood cells in its effort to eliminate the immature and rapidly reproducing cancer cells. To combat this, the Lu lab is working to develop a nanotechnology-enabled chemotherapeutic drug that can specifically recognize and target the patient's cancer rather than toxify the entire immune system itself. The goal is to increase the efficacy of this self-assembling pro-drug in its ability to inhibit the cancer growth in all stages compared to modern methods whose efficacy is dependent on the degree of progression of the cancer as well as the degree of aggression of the treatment. We are currently testing our developed drugs by treating various types of cancer cells with drug-loaded liposomes that have proven effective in their ability to transport drugs and control their release in the body without inducing an immune response. Through our research, we aspire to develop more efficacious, clinically translatable, combination cancer chemotherapies through the use of nanotechnology that has the potential to change the face of modern chemotherapeutics as well as the lives of the hundreds of thousands that are fighting cancer every year.

Introduction

- Cancer is one of the top leading causes of death in the United States, contributing to an estimated average of 600,000 deaths per year with colorectal, pancreatic, and breast cancer being 3 of the top 5 deadliest forms.
- Chemotherapy has proven to be the most effective anti-cancer treatment today, but the downfall of this form of treatment is its debilitating side effects that suppress the body's immune system, killing off vital immune system protectors in its effort to eliminate the immature and rapidly reproducing cancer cells, as it cannot distinguish the two types of cells.
- To combat this, the Lu lab is working to develop a nanotechnology-enabled chemotherapeutic drug that can specifically recognize and target the patient's cancer rather than the toxify the entire immune system itself.
- The goal is to increase the efficacy of this self-assembling pro-drug in its ability to inhibit the cancer growth in all stages via drug-loaded liposomes that have proven effective in their ability to transport drugs and control their release in the body without inducing an immune response.
- Through our research, we aspire to develop more efficacious, clinically translatable, combination cancer chemotherapies through the use of nanotechnology that has the potential to change the face of modern cancer treatment as well as the lives of the hundreds of thousands that are fighting cancer every year.

Objective

Determine the safest, yet most effective concentrations of drug-loaded liposomes for treatment of various cancer cell lines

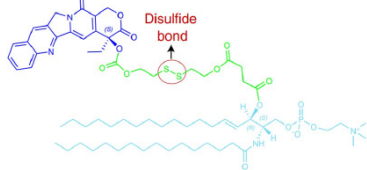


Figure 1. SM-derived CPT with disulfide bond and longer linker (SM-CSS-CPT)

Liposome Preparation

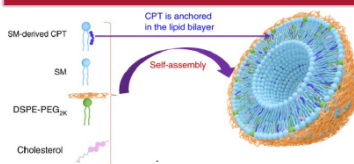


Figure 2. Self-assembly of SM-CPT into Camptothosome

1. Combine appropriate amounts of listed lipid components with organic solvent
2. Evaporate organic solvent to obtain thin lipidic film in a round-bottom flask
3. Rehydrate with polar solvent and sonicate to obtain pure liposome
4. Measure to ensure appropriate lipid nanovesicle (liposome) size and charge for experimentation

Methods

1. Culture and digest cancer cell line to transfer to experimental 96-well microplate
2. Treat cells with increasing concentrations of drug-loaded liposome to cell culture medium
3. Incubate and treat with MTT followed by DMSO for analysis of cellular metabolic activity

Results

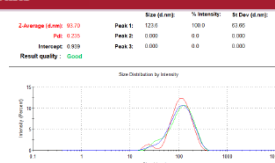


Figure 3. Measurement of Appropriate Liposome Size in 4T1 breast cancer cells for 72 h

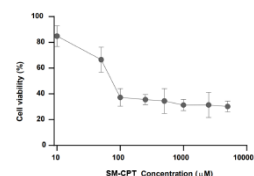


Figure 4. Results of Cellular Metabolic Activity Assay

This curve allows us to quantitatively analyze cancer cell viability, proliferation, and the cytotoxicity of our nanotechnology-enabled chemotherapeutic drug

Acknowledgements

National Institute of Environmental Health Sciences, Grant #2-R25-ES025494.
Wang, Z., N., Chen, J. et al. . *Nat. Nanotechnol.* 16, 1130-1140 (2021).

This research is supported by the Western Alliance to Expand Student Opportunities (WAESO) Louis Stokes Alliance for Minority Participation (LSAMP) National Science Foundation (NSF) Cooperative Agreement No. HRD-1619524



Thesis Poster -
Karina Gonzalez.pdf