CALIFORNIA STATE SCIENCE FAIR
2013 PROJECT SUMMARY

Name(s)

Ailis C. Dooner

Project Number

33123

Project Title

Targeting Lung Mutagenesis: Mycosporine-like Amino Acids as ROS Scavengers for Reduction of p53 Mutation and Scission

Abstract

Objectives/Goals

This study assesses the capacity of mycosporine-like amino acids (MAAs) Shinorine (SH) and Porphyra-334 (P-334),secondary metabolites synthesized by macro- and microalgae, to scavenge PAH o-quinone derived reactive oxygen species and reduce mutation and strand scission of the p53 tumor suppressor gene, the most frequently mutated gene in human lung cancer. Polycyclic aromatic hydrocarbons (PAH) are atmospheric pollutants found in tobacco smoke and products of incomplete combustion. The aldo keto reductase-catalyzed metabolic activation and autooxidation of PAH generates redox-cycling o-quinones, BPQ, BAQ, and PNQ, and induces oxidative stress and mutation of the p53 tumor suppressor gene. MAAs derived from marine algae were applied as ROS scavengers to protect p53 from deleterious mutation and degradation.

Methods/Materials

The efficacy of SH and P-334 was evaluated with a p53 mutagenesis assay, a yeast transcriptional reporter system; and a gel-electrophoresis strand scission assay. In the p53 mutagenesis assay, a YIG397 yeast reporter strain was transfected with p53 plasmid treated with o-quinone, redox cycling conditions, and MAAs in vitro. Wild-type p53 binds to the p21 promoter, activates an adenine reporter, and turns colonies white (ADE+), while p53 mutated in the binding domain turns colonies red (ADE-), allowing for quantification of o-quinone mutagenicity. In the strand scission assay, DNA degradation was detected with agarose gel electrophoresis.

Results

SH and P-334 lowered mutational frequency by 59% with BPQ at 0.5 ìM and 24% with BPQ at 0.25 ìM, and significantly reduced shearing with o-quinones BPQ, PNQ, and BAQ in the strand scission assay, supporting initial hypotheses.

Conclusions/Discussion

This study demonstrates the capacity of algae derived mycosporine-like amino acids to scavenge PAH o-quinone derived ROS and reduce scission and mutation of the p53 tumor suppressor gene. This study develops a novel biomedical application of MAAs in lung cancer pharmacology, and based on my results, MAAs could be applied as a critical active ingredient in a pharmacological agent in the prevention or treatment of the world's most fatal cancer.

Summary Statement

This study assess the capacity of mycosporine-like amino acids Shinorine and Porphyra-334, metabolites of aquatic algae, to scavenge PAH o-quinone derived ROS and reduce scission and mutation of the p53 tumor suppressor gene in lung cancer.

Help Received

I used laboratory equipment at University of Pennsylvania Perelman School of Medicine under the supervision of Dr. Jeffrey M. Field.

Preliminary