CALIFORNIA STATE SCIENCE FAIR
2012 PROJECT SUMMARY

Name(s)

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Project Number

S1720

Project Title

Smart Bomb to the Tumors: Clostridial-Directed Enzyme Prodrug Therapy (CDEPT) Enhanced with Vascular Targeting Agents

Abstract

Objectives/Goals

It has been known that tumor hypoxia is a major setback in standard cancer treatment of radiation therapy and chemotherapy. This project is focused on turning this setback into an advantage by employing clostridia, a nonpathogenic obligate anaerobe, as a tumor-specific prodrug-activating enzyme delivery system. The goal is to develop a system with high delivery efficiency, high specificity and highly selective cytotoxicity with the combination of transformed clostridia and prodrug targeting at the hypoxic/necrotic regions of the tumors.

Methods/Materials

Gene of prodrug activating enzyme was PCR amplified from genomic DNA of E. coli and incorporated into an E. coli-clostridia shuttle vector, the resulting vector was then transformed into a clostridial host. In vitro growth inhibition assay was used for assessing growth inhibition caused by the enzyme-mediated prodrug activation with cell cultures mixed with prodrugs and cell extracts from transformed clostridia. Finally, the animal model with transplanted tumor was used for evaluating the anticancer efficacy of the proposed treatment with clostridia-targeted enzyme-mediated prodrug therapy in combination with or without the use of a vascular-targeting agent.

Results

In the most optimal conditions, a 96% decrease in tumor volume at 7 days after the start of treatment was observed in our animal model with transplanted tumor, with a single administration of the combination of transformed clostridial spores, prodrug and a vascular targeting agent. Furthermore, there was no tumor regrowth during our entire experimental duration, hence the tumor was considered cured.

Conclusions/Discussion

This research has established a gene delivery system targeting tumor hypoxia with nonpathogenic anaerobic bacteria. The Clostridia Directed Enzyme Prodrug Therapy (CDEPT) provides specific targeting of anticancer drugs to solid tumors. The therapy yields antitumor activity in nude mice with CD (+ 5-FC) and NTR (+ CB1954) with no tumor lysis toxicity. Vascular targeting agents enhance CDEPT anticancer efficacy in tumors with CD or NTR- producing clostridia.

Summary Statement

This project has developed an enzyme/prodrug therapy using transformed Clostridia that will yield tumor-specific anticancer effects, which are enhanced by the inclusion of vascular targeting agents.

Help Received

Lab equipment was kindly provided by Stanford University under the supervision of Dr. Fred Lartey. Most animal model procedures, especially those involving surgical techniques, were performed by the supervising scientist, including tumor implantation, tissue extraction, clostridial spores and drug injection,