CALIFORNIA STATE SCIENCE FAIR
2010 PROJECT SUMMARY

Name(s)

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Project Number

S1825

Project Title

Sensitization of CD44+ Cancer Stem Cell Apoptosis by Sequential Inhibition of the S-Phase

Abstract

Objectives/Goals

Although there are multiple reasons for the lack of response to cancer therapy, the emergence of cancer stem cell populations, subsets of cancer cells with self-renewable properties, has been thought to be a crucial reason for the poor response to conventional cancer therapy. The goal of this study was to sensitize these cancer stem cells in order to enhance apoptosis, and thereby improve response to cancer therapy. Cell cycle regulation is one of the central mechanisms for controlling cell growth and cell death in cancer cells. In this study, we targeted the S-phase of the cell cycle, in which DNA synthesis occurs, in a sequential manner. We first arrested the cell cycle of the cancer stem cells in the S-phase, in order to block DNA synthesis, and then exposed the cells to cisplatin, an apoptosis agent.

Methods/Materials

CCL-30, human airway epithelial carcinoma cells were obtained and cultured. Cancer stem cells were sorted by using surface marker CD44+, a possible surface marker for cancer stem cells, by a fluorescence-activated cell sorter. Sorted CD44+ cells were treated with Cdc7 inhibiting drug, C75 for 24 hours followed by cisplatin, an apoptosis agent. Inhibition of Cdc7, by C75, results in the arrest of DNA synthesis in the S-phase. Immunoflourescence staining, Alamar Blue Assay, and TUNEL Assay were used in order to assess apoptosis.

Results

Induction of arrest in the S-phase of the cell cycle by Cdc7 inhibitor, C75, followed by treatment with cisplatin, significantly enhanced cancer cell apoptosis in CD44+ cancer stem cells and decreased cell proliferation as assessed by TUNEL and Alamar Blue assays. Immunoflourescence staining showed that sequential sensitization of cancer stem cells caused enhanced apoptosis via a mitochondrial death pathway.

Conclusions/Discussion

Sequential sensitization by induction of growth arrest followed by an exposure to an apoptosis agent may enhance the efficacy of currently available cancer therapies. The use of such an approach can not only improve response to therapy in cancer of airway disease, but it can also revolutionize the therapeutic approaches in all types of human cancer worldwide.

Summary Statement

Sequential sensitization by induction of growth arrest followed by an exposure to an apoptosis agent significantly increase apoptosis in CD44 cancer cells and may enhance the efficacy of currently available cancer therapies.

Help Received

Conducted project under the mentorship of Dr. Daya Upadhyay in her lab at the Stanford Medical Center; received lab training from Research assistants Dr. Wei Le and Dr. Weihua Wang, who directly supervised lab work; Project was generated as an extension to on-going studies in the Upadhyay lab.