CALIFORNIA STATE SCIENCE FAIR
2013 PROJECT SUMMARY

Name(s)

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Project Number

S0504

Project Title

Preventing Cancer Metastasis by Targeting the Epithelial-to-Mesenchymal Transition

Abstract

Objectives/Goals

The goal of this study is to establish a model system for screening potential compounds that can selectively inhibit cancer stem cells (CSCs), using the mesenchymal cells generated by an established method of inducing epithelial-to-mesenchymal transition (EMT) in cell lines in vitro.

Methods/Materials

Cell lines H358 (lung cancer) and LIM 1863 (colon cancer) were treated with cytokines TNF-=CE=B1 and TGF-=C3=9F for 3 days; and the analytical procedures such as phase contrast and fluorescent microscopy, Western Blot, Taqman qPCR, Immunocytochemistry, and cell proliferation assay were used to quantitatively assess the molecular and phenotypic change that occurred within the cells to verify that they underwent EMT. Mesenchymal and epithelial H358 cells were then treated with Salinomycin, using a pan-cytotoxic compound- Staurosporine as comparison, and the data collected was analyzed using IC50 graphs as well as a pair-wise student t-test to assess selectivity of the hypothesized CSC inhibitor, Salinomycin.

Results

After treatment with the cytokines for 3 days, the cells acquired morphological characteristics such as elongation and dissemination out of colonies, as well as a many fold increase in mesenchymal markers and no change in the epithelial marker for RNA expression, an increase in mesenchymal markers and a decrease in the epithelial marker for protein expression, and a greater than 50% decrease in proliferation. After treatment with the two drugs, the mesenchymal cells were inhibited at the same rate as the epithelial cells by salinomycin at roughly a 10 fold lower concentration, while there was no statistically significant difference for inhibition of the two cell types by staurosporine.

Conclusions/Discussion

In this study, it was demonstrated that cancer cells can be induced to pass through EMT by treatment with cytokines. The induced mesenchymal cells have reduced proliferation rate, increased expression of mesenchymal markers, and increased resistance to cytotoxic compounds, and are extremely similar to CSCs. However, they became more sensitive to salinomycin. The model systems established in this study can potentially be used to screen for small molecule compounds or biological agents that target EMT and cancer stem cells.

Summary Statement

A model system was established and validated for discovery of medicines specific for cancer stem cells to prevent metastasis

Help Received

Used lab facility at UCSD under the supervision of Ping Jiang sponsored by Dr. Kun-Liang Guan