CALIFORNIA STATE SCIENCE FAIR
2013 PROJECT SUMMARY

Name(s)

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Project Number

S1702

Project Title

Examination of Quorum Sensing Mechanisms in Glioblastoma Multiforme

Abstract

Objectives/Goals

Glioblastoma multiforme (GBM) is a prevalent and deadly primary brain tumor in humans. It is reported that glycoprotein Prominin 1 (CD133/1) expression is associated with a distinct population of stem/progenitor GBM cells that have increased capacities for self-renewal, sphere formation, and tumor initiation. Quorum sensing (QS) is a cell-signaling mechanism utilized by bacteria to track cell density and coordinate gene expression and population behavior based on said cell density. I hypothesized that a QS mechanism may be used by GBM cells to regulate populations of CD133-expressing cells, and attempted in this study to probe populations of GBM cells for behaviors consistent with a QS mechanism.

Methods/Materials

Phase I: Patient-derived brain tumor cells (cell line PBT003) were cultured in vitro for several passages, following which fluorescence-activated cell sorting (FACS) was used to separate CD133/1^+ cells from CD133/1^- cells. Cells of the top 5% of each group (selected to ensure purity) were cultured separately for twelve days. Cells were then reanalyzed for CD133/1 expression using flow cytometry. Phase II: PBT003 cells were cultured in the presence or absence of exogenous tumor necrosis factor-alpha (TNF-alpha) for six days, following which their CD133/1 expression was assayed by flow cytometry.

Results

Phase I: CD133/1^+ and CD133/1^- PBT003 cell populations responded differently to culture: the CD133/1^- population originally isolated by FACS remained almost entirely CD133/1^-, whereas the CD133/1^+ population returned to a "steady state" in which the ratio of CD133/1^+ to CD133/1^- cells mirrored that of the original unsorted cultures. Phase II: Preliminary results indicate that TNF-alpha, a putative autoinducer, increases extracellular and intracellular expression of CD133/1 (as compared to cultures without TNF-alpha). Such a change in cell state would be an expected result of the addition of an autoinducer in a QS mechanism.

Conclusions/Discussion

The reversion of CD133/1^+ cells to a "steady state" is consistent with a QS mechanism. TNF-alpha has been shown to increase CD133/1 expression and could possibly be driving populations of GBM cells towards a more disseminatory phenotype. These results are consistent with the hypothesis that TNF-alpha secreted by tumor cells may be functioning as an autoinducer in a QS model of CD133 expression/glioma proliferation.

Summary Statement

Glioblastoma multiforme exhibits behaviors consistent with a quorum-sensing mechanism.

Help Received

Dr. Michael Barish and Dr. Susan Kane helped me fine-tune my idea; Ms. Nousha Khosh and Mr. Bradley Huss trained me in the use of lab equipment at the City of Hope Beckman Research Institute and supervised me while I conducted my project; parents helped me commute to City of Hope.