CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

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Project Number

S0518

Project Title

DNA Damage Induced by a Novel Drug Cocktail Regulates Chemokine Production in Leukemia through Cytosolic DNA Sensing

Abstract

Objectives/Goals

This research investigates the mechanism of action for chemokine production induced by a novel cancer drug cocktail to induce DNA damage in precursor-B acute lymphoblastic leukemia (ALL). Preliminary data supports a model in which DNA damage caused by this drug cocktail leads to DNA leakage into the cytoplasm and the activation of innate immune DNA sensing pathways, modulating the production of inflammatory cytokines, chemokines, and interferons.

Methods/Materials

200,000 p185BCR-ABL Arf-/- pre-B ALL cells (p185) were injected into mice via tail vein. Mice in the cancer group were administered the three drugs orally.

p185 cells in the treatment group were grown in DMEM with three drugs alone or in combination for 4 days. p185 cells in the vehicle group was grown in DMEM media for 4 days.

60-80% confluent p185 cells in a 6 well plate were transfected with small interfering RNA against STING and MyD88 (Life Technology) using Lipofectaminer RNAiMAX Transfection Reagent (Life Technology) for 72 hours. The cell culture was composed of two groups of three wells; a treated and not-treated group. Each group had a STING transient knockdown, a MyD88 transient knockdown, and a vehicle/ control group.

Samples were analyzed using the Multi-Analyte ELISArray (Qiagen) according to the protocol provided with the kit.

Results

This project establishes the dependence on these proteins for production of chemokines in vitro and long term in vivo: treatments in vitro exhibit an increased production of Eotaxin and KC after 1 day of treatment, and Eotaxin, MIP-1a, MIP-1b, and SDF-1 after 4 days of treatment. Knockdowns for STING and MyD88 in vitro results in decreased expression of MCP-1, MIP-1b, MIG, Eotaxin, and TARC in both treated and non-treated groups.

Conclusions/Discussion

Exploring the role of innate immunity in cancer models is crucial to understanding the dynamic interaction between the immune system and tumors and may lead to novel methods to treat cancer.

Summary Statement

This project investigates the possible immunostimulatory effect of this novel drug combination on chemokine production in treated ALL cells and treated mice xenografted with ALL cells.

Help Received

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