CALIFORNIA STATE SCIENCE FAIR
2012 PROJECT SUMMARY

Name(s)

Nikhil Buduma

Project Number

S0505

Project Title

PTX-Mediated Inhibition of Lymphocyte Trafficking into the Lungs: Considerations for an Improved Whooping Cough Vaccine

Abstract

Objectives/Goals

Whooping cough, a disease characterized by a paroxysmal cough, is caused by the bacterium Bordetella pertussis. The current study aims to demonstrate that the pertussis toxin (PTX), a major component of the current vaccine against whooping cough, impairs the activation of the adaptive immune system. Specifically, this study intends to show that PTX inhibits lymphocyte recruitment to the lungs by downregulating the expression of lymphocyte trafficking receptors (TRs).

Methods/Materials

Four Balb/c murine models of human respiratory infections were implemented: uninfected mice, mice infected by B. pertussis, mice infected by B. pertussis TOX6 (A mutant for the PTX gene), and mice infected by B. parapertussis (a close relative that overlaps 90% of the virulence factor genes but does not express PTX). Lung cross-sections were taken at 5 days, 10 days, and 25 days post infection (p.i.) and analyzed using standard HE staining and immunofluorescence staining for neutrophils, macrophages, B cells, and T cells. In addition, peripheral blood was analyzed for the expression of alpha4beta7, alpha4beta1, CD11a, and Psel-L TRs using flow cytometry. Similar flow cytometric analyses were performed in vitro on T cells co-cultured with lung dendritic cells from infected mice 5 days p.i.

Results

HE staining and immunofluorescence labeling of lung cross-sections revealed that the recruitment of adaptive immune cells, in particular B cells and T cells, was severely delayed during infection by B. pertussis compared to both control groups. In addition flow cytometry analysis revealed two trafficking receptor populations, alpha4beta7 and alpha4beta1, that were downregulated on memory T cells at 5 days p.i. during B. pertussis infection. The in vitro co-culture demonstrated similar results, though the differences in alpha4beta7 expression were not revealed as significant by statistical analyses.

Conclusions/Discussion

This study demonstrates that PTX delays the recruitment of adaptive immune cells to the lungs. This observed delay is likely to be mediated by a PTX-dependent downregulation of alpha4beta7 and alpha4beta1 TR expression, due at least partly to defective communication between resident dendritic cells and T cells. These results suggest that vaccine formulations should avoid the use of PTX because of its potential for preventing the infant#s immune system from developing a sufficient defense.

Summary Statement

My project aims to demonstrate that the pertussis toxin, a major component of the current whooping cough vaccine, interferes with the proper functioning of the adaptive immune system.

Help Received

I conducted this research under the guidance of Dr. Tzvia Abramson at San Jose State University.