

M & I
Microbiology
and Immunology
University of North Carolina at Chapel Hill

DISSERTATION SEMINAR

Laurel Kartchner

“Generation Of Clinically Relevant Models Of Burn-Associated Comorbidities For Analysis Of Immune Dysfunction After Burn Injury.”

Monday, April 23, 2018
1:30 p.m.
2004 Marsico Hall

Dissertation Advisors: Drs. Bruce Cairns and Rob Maile

Presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy

Abstract

Laurel Kartchner: : Generation Of Clinically Relevant Models Of Burn-Associated Comorbidities For Analysis Of Immune Dysfunction After Burn Injury
(Under the direction of Drs. Cairns and Maile)

Burn injury is a significant form of trauma that leads to alterations in the functionality of multiple body systems. One vital system that promotes both healing and protection from invasive pathogens is the immune system. After burn injury the immune system is severely impeded. However, models of burn injury are unable to successfully recapitulate phenotypes seen among burn-injured patient populations. Studies indicate that presence of burn-associated comorbidities can greatly improve the translatability of models and that study of comorbidities is essential for improving treatment of patients.

Here we report the development of a model of repeated bacterial exposure after burn injury. This model is able to recapitulate immune cell recruitment and alterations in cytokine production that mimic those seen among patient populations. Namely, we found that repeated infections lead to increased bacterial burden after burn injury, and the loss of a lab-derived burn “protection” phenotype that is common in the literature late after burn injury. We found that this phenotype corresponds with burn-dependent alterations in pulmonary innate immune cell numbers and function. We believe that these cells represent a potential target for therapeutic intervention.

Additionally, we have worked to establish a model of inhalation injury to examine inhalation-dependent alterations in the immune profile that take place both independently and concomitant with burn injury. We have found that inhalation and burn injury independently contribute to damage in our murine model of inhalation. We examined the pulmonary compartment and found that burn and inhalation independently affect the recruitment of neutrophils to either the airspace or the lung tissue. We also found that inhibition of nitric oxide production can ameliorate damage that takes place after inhalation injury, representing a potential target for therapeutic intervention among the patient population.