

THE GRADUATE COLLEGE OF THE  
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

# Kaitlin Calhoun

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE  
GRADUATE COLLEGE  
DEPARTMENT OF PHARMACEUTICAL SCIENCES



Monday, December 4, 2017, 9:30 am  
College of Pharmacy Building, Room 339, OUHSC

## *Phenotypic and Genetic Influences Upon the Cutaneous Inflammatory Response*

COMMITTEE IN CHARGE: Randle M. Gallucci, PhD,  
Robert Dale Foreman, PhD, Michael A. Ihnat, PhD, William Michael McShan, PhD,  
Kent Teague, PhD

ABSTRACT: Irritant contact dermatitis (ICD) is a cutaneous inflammatory response generated following topical irritant exposure. However, the intrapersonal and interpersonal variability observed with ICD, hinders effective clinical treatment and risk assessment. Our laboratory postulates that Th1- versus Th2-phenotypic dominance, and interleukin 6 (IL-6) deficiency influence the pathophysiology of ICD. To determine how these factors modulate the pathomechanism of ICD, denuded skin of C57BL/6J (“Th1 dominant”), Balb/c (“Th2 dominant”), and IL-6 deficient (IL-6KO) mice were exposed to the occupational irritants, benzalkonium chloride (BKC) and JP-8 jet fuel. Histopathology showed cutaneous inflammation, indicated by cellular infiltration and epidermal hyperplasia, following irritant exposure. Flow cytometric analysis showed that C57 skin is characterized by a pronounced neutrophil population compared to Balb/c and IL-

population of dendritic cells as compared to C57 skin. Multiplex protein analysis of skin cytokine and chemokine expression revealed up-regulation of IL-1 $\beta$  TNF- $\alpha$ , G-CSF, CCL4, CCL5, and CXCL2 in C57 skin after BKC exposure, but following JP-8 exposure these cytokines and chemokines had higher expression in Balb/c skin. In comparison to an IL-6 deficient immune response, C57 skin had increased expression of IL-18, CCL3, and CCL5 after BKC exposure, but decreased IL-10 following JP-8 exposure. The current findings illustrate that different immune phenotypes and IL-6 deficiency modulate the pathomechanism of ICD, which may explain the clinical variability associated with ICD patients. Overall, these findings suggest that evaluation of immune phenotypes and IL-6 deficiency in humans might assist with predicting of an individual's response to irritant exposure.