

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 β TNF- α , 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.