THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

TINA B. MCKAY

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE
GRADUATE COLLEGE
DEPARTMENT OF CELL BIOLOGY

Monday, January 30, 2017 | 10:30 am
Biomedical Research Center, Room 109

KERATOCONUS: *IN VITRO* AND *IN VIVO*

COMMITTEE IN CHARGE: Dimitrios Karamichos, Ph.D., Chair; James J. Tomasek, Ph.D.; Jody Summers, Ph.D.; Randy Gallucci, Ph.D.; Kenneth Humphries, Ph.D.

ABSTRACT: Keratoconus (KC) is a common corneal dystrophy that is caused by thinning of the extracellular matrix (ECM) within the corneal stroma. Various studies have shown that primary corneal fibroblasts derived from KC patients, termed HKCs, exhibit increased oxidative stress, upregulated aerobic glycolysis, and dysfunctional matrix deposition. Though KC is a result of thinning of the stromal ECM, our lab and others have found increased expression of fibrotic markers by HKCs with higher expression of Collagen III compared to healthy controls. Our previous studies led us to the hypothesis that KC is a corneal thinning disease characterized by altered cellular metabolism and elevated oxidative stress in HKCs that increases their sensitivity to environmental factors, such as hypoxia-induced cell stress, pro-inflammatory factors, and exogenous hormone levels, which may be central in promoting disease progression. This dissertation has focused on addressing two broad questions in the KC field: 1) Can we target the altered cellular metabolism exhibited in HKCs therapeutically to inhibit expression of fibrotic markers? and 2) Are there systemic features of KC that may correlate with clinical severity? This work describes a novel mechanism of KC pathogenesis revealing the susceptibility of HKCs to both internal and external oxidative stress, the identification of a novel therapeutic to rescue the metabolic phenotype exhibited in HKCs, and discovery of systemic factors that may contribute to KC severity.