Summer Student Research Program
Project Description

FACULTY SPONSOR'S NAME AND DEGREE: ***David N. Paglia, Ph.D.***
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PROJECT TITLE (200 Characters max):

Postnatal systemic loss of Cox2 signaling leads to spinal degeneration in a mouse model

HYPOTHESIS:

As COX-2 is the key enzyme in the biosynthesis of prostaglandin, we hypothesize that the disc degenerative pathologies in overexpression and loss of function lead to unique pathologic phenotypes.

PROJECT DESCRIPTION **(Include design, methodology, data collection, techniques, data analysis to be employed and evaluation and interpretation methodology)**

It has been estimated that over 80% of the population experiences some form of back pain over the course of their lives, making this a leading health concern. The precise pathogenesis of degenerative disc disease (DDD) is characterized by decreased cell populations (predominantly via apoptosis), metabolic derangements such as decreased production of important matrix proteins (i.e., collagen II, aggrecan),4 and the release of proteolytic enzymes such as matrix metalloproteinases (MMPs). Thus, identifying molecules that can delay disc degeneration is paramount. Treatment strategies are symptomatically targeted, rather than based on genetics due to limited literature on the pathomechanisms of disc degeneration. Current treatment approaches for spinal degeneration include fusion and disc of replacement procedures, though neither have proven to be ideal. Therefore, there is a critical need to better understand the disease etiology of disc degeneration, to enable the development of preventative treatment strategies. Our recent work in mice has implicated Cox2 signaling in maintenance of cartilage and disc architecture in the spine. In global postnatal Cox2 knockout mice (Rosa 26 Cre ERT2; Cox2 $^{F/F}$), induced by postnatal tamoxifen administration, we found OA-like fissures in the spinal growth plate and cartilage endplate with vascular infiltration of the annular space vis histology, as early as 4 weeks after Cox2 loss of function. Further, others have found that overexpression of COX-2 in osteoblasts is sufficient to cause spinal curvature in mice. In global postnatal Cox2 knockout mice (Rosa 26 Cre ERT2; Cox2 $^{F/F}$), induced by postnatal tamoxifen administration, we found OA-like fissures in the spinal growth plate and cartilage endplate with vascular infiltration of the annular space, as early as 4 weeks after Cox2 loss of function. This is a unique phenotype compared to discs we have evaluated from Prg4 null mice, which show the classic sequence of disc degeneration. Outcomes for this study include histology scoring for disc degeneration, disc height measurements from X-ray, and immunohistochemistry.

SPONSOR'S MOST RECENT PUBLICATIONS RELEVANT TO THIS RESEARCH:

Paglia DN, Kanjilal D, Kadkoy Y, Moskonas S, Wetterstrand C, Lin A, Galloway J, Tompson J, Culbertson MD, O'Connor JP. Naproxen treatment inhibits articular cartilage loss in a rat model of osteoarthritis. J Orthop Res. 2021 Oct;39(10):2252-2259. doi: 10.1002/jor.24937. Epub 2020 Dec 15. PMID: 33274763; PMCID: PMC8175455.

Paglia DN, Singh H, Karukonda T, Drissi H, Moss IL. PDGF-BB Delays Degeneration of the Intervertebral Discs in a Rabbit Preclinical Model. Spine (Phila Pa 1976). 2016 Apr;41(8):E449-58. doi: 10.1097/BRS.0000000000001336. PMID: 27064336.

Presciutti SM, Paglia DN, Karukonda T, Soung do Y, Guzzo R, Drissi H, Moss IL. PDGF-BB inhibits intervertebral disc cell apoptosis in vitro. J Orthop Res. 2014 Sep;32(9):1181-8. doi: 10.1002/jor.22638. Epub 2014 May 20. PMID: 24841673.

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THIS PROJECT IS: ☐ **Clinical** ☒ **Laboratory** ☐ **Behavioral** ☐ **Other**

THIS PROJECT IS CANCER-RELATED ☐
Please explain Cancer relevance

THIS PROJECT IS HEART, LUNG & BLOOD- RELATED ☐
Please explain Heart, Lung, Blood relevance

THIS PROJECT INVOLVE RADIOISOTOPES? ☐

THIS PROJECT INVOLVES THE USE OF ANIMALS ☒
PENDING ☐ **APPROVED** ☒ **IACUC PROTOCOL #201800006**

THIS PROJECT INVOLVES THE USE OF HUMAN SUBJECTS? ☐
PENDING ☐ **APPROVED** ☐ **IRB PROTOCOL # M**

THIS PROJECT IS SUITABLE FOR:

UNDERGRADUATE STUDENTS	☐	ENTERING FRESHMAN	☐
SOPHMORES	☐	ALL STUDENTS	☒

THIS PROJECT IS WORK-STUDY: **Yes** ☐ **or** **No** ☒

THIS PROJECT WILL BE POSTED DURING ACADEMIC YEAR FOR INTERESTED VOLUNTEERS: **Yes** ☐ **or** **No** ☒

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?
The student will learn the basics of histology and immunohistochemistry, the anatomy and physiology of the spine, as well as standard lab practices.