Summer Student Research Program
Project Description

FACULTY SPONSOR'S NAME AND DEGREE: ***J. Patrick O'Connor, Ph.D.***
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PROJECT TITLE (200 Characters max):

Methods for Treating and Promoting Bone Regeneration

HYPOTHESIS:

Bone regeneration can be accelerated by use of novel local or systemic therapies.

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

Design: The effects of local or systemic drug treatments on promoting bone regeneration will be determined by comparing drug-treated cohorts to vehicle/placebo control cohorts. Variables to be assessed include drug dose, treatment regimen, and temporal effects on bone regeneration.
Methodology: Experiments will employ one or more animal models to assess different aspects of bone regeneration. Surgical models may include rat knee arthritis, a closed femur fracture model in rats, a femur segmental defect model in rats, cortical defect models in rats or rabbits, and posterolateral spinal fusion in rabbits.
Data Collection: Drug effects will be evaluated using multiple outcome measures that may include (a) measuring local or systemic drug levels, (b) drug effects on target pathways using molecular and cellular measures, (c) bone and cartilage formation by X-ray, μCT, and histological methods, (d) assessment of function using gait analysis, kinetic weight bearing, and X-ray videography, and (e) mechanical assessment of healing.
Data Analysis & Interpretation: Parametric and non-parametric statistical analyses of the data will be employed to identify drug effects. Improvements in mechanical integrity of the bone and improved functional use of the bone will be the principal outcomes. Secondary outcomes will include drug effects on molecular and cellular mechanisms.
Techniques to be used: Multiple methods will be used to conduct, collect, and analyze data. Prominent methods include: (a) animal surgery and care, (b) X-ray and radiographic image collection, (c) histological specimen collection and preparation, (d) functional analysis of animal movement, (e) mechanical testing, (f) molecular and cellular methods, and (g) statistical data analysis.

SPONSOR'S MOST RECENT PUBLICATIONS RELEVANT TO THIS RESEARCH:

1. Zhangab C, Feinberga D, Alharbia,M, Ding Z, Lua C, O'Connor JP, and Graves DT. (submitted) Chondrocytes promote vascularization in fracture healing through a FOXO1 dependent mechanism.
2. Alharbi MA, Zhang C, Lu C, Milovanova TN, Yi L, Ryu JD, Jiao H, Dong G, O'Connor JP, and Graves DT. (submitted) FOXO1 Deletion Reverses the Effect of Diabetic-Induced Impaired Fracture Healing.
3. Abraham S, Vives MJ, Cottrell JA, Mitchell AM, Shah N, Munoz W, Uko L, Nasser S, Iqbal E, Lin H-N, Jingar N, Todhe P, Shenouda M, Kim BD, Chaudhary SB, Lin SS, Benevenia J, O'Connor JP. (in revision) Local insulin application has a dose-dependent effect on lumbar fusion in a rabbit model. The Spine Journal.
4. Lin HN, O'Connor JP. (in revision) Effects of cyclooxygenase-2 deletion in osteoblasts, chondrocytes, and osteoclasts on fracture healing in mice. J. Orthopaedic Research.
5. Lin H-N and O'Connor JP. (2017) Osteoclast depletion with clodronate liposomes delays fracture healing in mice. J. Orthopaedic Research 35:1699-1706.

6. Ippolito JA, Krell ES, Cottrell J, Meyer R, Clark D, Nguyen D, Sudah S, Munoz M, Lim E, Lin A, Lee TJ, O'Connor JP, Benevenia J, Lin SS. (2017) Effects of local vanadium delivery on diabetic fracture healing. J. Orthopaedic Research 35:2174-2180.
7. Krell ES, Ippolito J, Montemurro N, Vincent R, Hreha J, Wey, A, Cottrell JA, Sudah S, Munoz M, Pacific K, Benevenia J, O'Connor JP, Lin SS. (2017) Local zinc chloride release from a calcium sulfate carrier enhances fracture healing. J. Orthopaedic Trauma 31:168-174.
8. Cottrell JA, Cardenas-Turner J, Livingston-Arinzeh T, and O'Connor JP. (2016) The biology of bone and ligament healing. Foot and Ankle Clinics of North America 21:739-761.
9. Streit A, Watson BC, Streit A, Granata JD, Philbin TM, Lin HN, O'Connor JP, and Lin SS. (2016) Effect on clinical outcome and growth factor synthesis with adjunctive use of pulsed electromagnetic fields for fifth metatarsal nonunion fracture: a double-blind randomized study. Foot & Ankle International 37:919-923.
10. Lin H-N, Cottrell JA, and O'Connor JP. (2016) Variation in lipid mediator and cytokine levels during mouse femur fracture healing. J. Orthopaedic Research 34:1883-1893.

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

THIS PROJECT IS CANCER-RELATED ☒
Please explain Cancer relevance: Bone tumors often manifest as fractures. Furthermore, tumor resection generally leaves large boney defects that require significant intervention to stabilize the bone and to promote bone formation to heal the defect caused by tumor resection.

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 #201800021, 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?
Student will learn bone biology and orthopaedic related methods for treating bone injuries at a basic level. The students should also gain significant, practical knowledge of the scientific method, experimentation related skeletal regeneration and tissue engineering, and data analysis.