### Fiscal Year:
FY 2016

### PI Name:
Lau, Anthony G Ph.D.

### Project Title:
Whole Joint Health: Investigating Modeled Spaceflight Changes in Mice (Postdoctoral Fellowship)

### Division Name:
Human Research

### Program/Discipline:
NSBRI

### Program/Discipline--Element/Subdiscipline:
NSBRI--Musculoskeletal Alterations Team

### Joint Agency Name:
TechPort: No

### Human Research Program Elements:
1. **HHC**: Human Health Countermeasures

### Human Research Program Risks:
1. **Fracture**: Risk of Bone Fracture due to Spaceflight-induced Changes to Bone (IRP Rev F)

### Space Biology Element:
None

### Space Biology Cross-Element Discipline:
None

### Space Biology Special Category:
None

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### PI Organization Type:
UNIVERSITY

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University of North Carolina at Chapel Hill

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Chapel Hill

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NC

### Zip Code:
27599

### Congressional District:
4

### Comments:
NOTE: As of Fall 2015, Dr. Lau is at The College of New Jersey.

### Project Type:
GROUND

### Solicitation:
2012 NSBRI-RFA-12-02 Postdoctoral Fellowships

### Start Date:
11/01/2012

### End Date:
10/31/2015

### No. of Post Docs:
0

### No. of PhD Degrees:
0

### No. of PhD Candidates:
1

### No. of Master' Degrees:
0

### No. of Master's Candidates:
0

### No. of Bachelor's Degrees:
2

### No. of Bachelor's Candidates:
4

### Monitoring Center:
NSBRI

### Contact Monitor:

### Contact Phone:

### Project Type:

### Funding:

### Key Personnel Changes/Previous PI:

### COI Name (Institution):
Bateman, Ted (MENTOR/ University of North Carolina)

### Grant/Contract No.:
NCC 9-58-PF03003

### Performance Goal No.:

### Performance Goal Text:

**POSTDOCTORAL FELLOWSHIP**

**Original Aims**

Aim 1: Further develop the image analysis technology for assessing changes to mouse knee joint soft tissue with microCT, including cartilage, meniscus, ligaments, and tendons.

Aim 2: Assess whole-joint changes in the knee, including bone and soft tissues, from both unloading and reloading using the established hindlimb unloading (HLU) model. This will be accomplished with two studies:

Aim 2a: Study the effects of HLU on integrated joint properties, mimicking the STS-135 Space Shuttle flight profile.

**NOTE:** End date changed to 10/31/2015 per NSBRI submission (Ed., 12/12/14)
Hypothesis: Degradation of bone strength, as assessed by computational finite element analysis (FEA), will be similar to that observed in mice flown on STS-135 (13-days of unloading). Similarly, degradation of meniscus volume and density will also be observed with few changes in tendon and ligaments.

Aim 2b: Study the effects of longer-term unloading followed by reloading on whole-joint structural and functional properties. Hypothesis: Longer periods of unloading cause greater degradation in bone volume and strength, as well as larger changes in the connective soft tissues. There will be limited recovery after 4-weeks of reloading.

Key Findings

Analysis of the proximal tibia from skeletally mature mice flown on SPX-4, Rodent Research-1, found that ~21 days of spaceflight resulted in a decline in trabecular bone volume fraction (~45%) and total bone volume (~20% for combined cortical and trabecular bone) in the proximal tibia. Finite Element modeling of this region found this corresponded to a decline in compressive structural stiffness (~28%) which corresponded to a 12% decline in bone structural efficiency. Separation of the cortical and trabecular bone compartments found the majority of loss in the bone strength was in the cortical compartment. These findings are consistent with those observed from FE Analysis of the mouse proximal tibia from STS-135 as well as the complementary Hind Limb Unloading study, which were both previously reported.

Results from the HLU study had similar overall trends that were observed in spaceflight. One major difference is that while both HLU and spaceflight caused a 17% decline in proximal tibia bone volume, HLU caused a 22% decline in bone strength, compared to the 34% decline from spaceflight.

Impact of Key Findings

The use of skeletally mature mice and having the mice sacrificed while in orbit reduce the confounding factors of reloading as well as skeletal growth of the animal during the study. Thus, the majority of the observed decline in bone can be attributed to the microgravity conditions, with some possible loss due to aging. Even in skeletally mature mice (32 weeks old), the 21 days of spaceflight caused a decline in proximal tibia structural efficiency. Using older mice could better model spaceflight related bone loss in astronauts, as the average astronaut has achieved skeletal maturity. The FE modeling provides a more detailed assessment of bone health compared to the traditional microCT analysis and should be considered in future assessments of bone quality.

Proposed research plan for the coming year

While the post-doctoral fellowship has ended, Dr. Lau is planning on applying the computational techniques developed over the past 3 years in a collaboration with Dr. Jeff Willey at Wake Forest to look at bone strength changes in some of his animal studies.