Translational Research Scholars Program
Personal Statement

I have joined Mechanical and Biomedical Engineering Department at Boise State as an Assistant Professor in August 2016. Within first year of my appointment, I have established Mechanical Adaptations Laboratory and recruited a research team. My current research team consists of two PhD students, one Master Student and five undergraduate researchers. Before starting my research group, my training included a BS in physics, MS in mechanical engineering, and a Biomedical Engineering PhD focusing on tissue and cell level mechanical regulation of bone. Most recently, I was a post-doctoral researcher in the Endocrinology Division of department of Medicine at the University of North Carolina, Chapel Hill. I have worked on the mechanical control of stem cell structure, function and fate in relation to bone health. In particular, I have identified a novel mechanosensory function of LINC complexes, and how their interactions with the cytoskeleton regulate cellular structure and β-catenin trafficking to induce anabolic bone responses. While these diverse research experiences provide me a unique skill set and a strong scientific foundation, establishing a successful research program requires clear articulation of these concepts to a broader audience and compelling new evidence to form the basis of new NIH proposals. Participation in Translational Research Scholars Program will provide a number of major and long-term benefits to my career development.

- My unique advantage of being the only group with basic/pre-clinical research agenda within college of engineering is also makes it challenging to connect with NIH oriented researchers on campus. This pilot funding will serve as a mechanism to strengthen ties between my group, my department and NIH funded community in campus.
- Grant writing is a skill that you never stop learning. Mentoring, feedback and support provided through this mechanism will not only help me to generate a competitive R01 proposal, but will be transformative for my career trajectory by providing a strong foundation and a mindset to write compelling arguments to further my research agenda in coming years.
- This pilot funding will facilitate the generation, validation and preliminary testing of a novel mouse model will serve as a nucleation point for my research program to understand how function of nuclear envelope controls the musculoskeletal health. As mutations of nuclear envelope is implicated in clinical conditions such as progeria, muscular dystrophies and aging, this pilot data will be critical basis for a new R01 application with a possible interest from NIGMS, NIAMS and NIA.

In short-term, ITHS translational research program will provide a strong, competitive NIH proposal. In longer-term, grant writing skills and mentoring will be critical to align my career goals with NIH interests by providing me tools to conceptualize compelling proposals.

My long-term translational goals are to establish a research program that **connects** the structure-function relationship at cellular level to musculoskeletal health. Our focus is on nuclear envelope that serves as both barrier and mechanical connection between nucleus and outside world. This connection is critical because it is poised to control both epigenetics and cytoplasmic signaling in cells. More specifically, how mutations of nuclear envelope as seen in progeria, muscular dystrophies and aging envelope lead to musculoskeletal problems by disrupting mechanosignaling at cellular level. This TSRP will serve as the first critical step towards understanding how disrupting this nuclear envelope connectivity in stem cells will limit the bone accrual in response to exercise in a pre-clinical setting.

Translational Research Scholars Program
Research Proposal

SPECIFIC AIMS

Poor musculoskeletal health is one of the primary contributors to disability among aged individuals. During aging, **mesenchymal stem cells (MSC)** that maintain the musculoskeletal system lose their potency. Declining MSC health in aging skeleton results in increased adipocyte output and decreased osteoblast number.[1,2] This contributes to increased fatty infiltration of bone-marrow and skeletal frailty associated with osteoporosis.[3,4]

A principal source of mechanical signals that are universally recognized to combat adiposity, and to maintain a healthy musculoskeletal system is exercise[1] but exercise is not the only factor, as skeletal decline will occur even in aged individuals that maintain a highly active lifestyle.[5] Our team has shown that MSC mechanotransduction in response to mechanical signals relies on **LINC (Linker of Nucleoskeleton and Cytoskeleton) complexes**[6] that connect the cytoskeleton to the nuclear lamina.[7] We have found that inducing LINC deficiency accelerates MSC adipogenesis[7]and halts osteogenesis in both MSC and at the organism level by impeding nuclear function of βcatenin and YAP(Yorkie Homolog-1). This outcome suggests **that LINC-mediated connectivity between nucleus and cytoskeleton may be a key aspect of MSC health – such that its loss during aging contributes to a degraded mechanoresponse**.

Aim1 will test the hypothesis that disconnecting LINC from the nucleus disrupts MSC mechanotransduction by preventing nuclear translocation and function of βcatenin and YAP. As deletion of either βcatenin and YAP results in inferior skeletal phenotype[8,9] **Aim 2** will utilize a novel CAG-LacZ/EGFP KASH2$^{fl/fl}$/Prx1-CreER (EGFP-KASH2) mice model to determine if MSC specific de-activation of LINC function is sufficient to inhibit exercise-induced bone accrual due to limiting βcatenin and YAP endpoints. Our preliminary data shows that expression levels of LINC elements decline with progressing age. **Aim 3** will determine if aging decreases MSC LINC expression *in vivo*.

Successful identification of mechanisms of how LINC connectivity regulates MSC health and its response to exercise during aging will drive the discovery of molecular and synthetic approaches to regulate LINC to extend treatment options for afflictions associated with aging or other conditions affecting nuclear envelope.

SIGNIFICANCE

Given the success in improving human longevity, aging itself has become a “disease” with its own personal and fiscal costs. In stem cells, a basic understanding of the aging phenotype may come from looking at the sum of its parts: reduced differentiation capacity, slowed proliferation (senescence) and transcriptional instability.[10] While knowledge about individual processes are exceedingly detailed, strategies to combat aging at cellular level suffer from the lack of a unifying theme. The nucleus, central to all cellular activity, respond to external stimuli by regulating intra-nuclear chromatin organization that ultimately determine cell function and fate. Thus, failure to transmit this information to nucleus would lead to breakdown of these processes. Looking through a unifying lens, we ask **if aging is a process that limits information flow into the nucleus.** Absence of LINC complex, instigates phenotypes associated with aging, including, epigenetic instability and poor DNA repair.[11] As we will show, **aging reduces LINC** and genetic deletion of LINC elements impair mechanosensitivity by affecting βcatenin and YAP signaling. This leads to decreased proliferation and differentiation of mesenchymal stem cells. Thus, focusing on this understudied aspect of cell structure may lead to targeted strategies to improve MSC and ultimately musculoskeletal health in aging.

INNOVATION

Novel Examination of Aging Cell. This proposal provides a novel examination of how connections between the nucleus and the cytoskeleton change during aging. Diminished mechano-sensitivity and multipotentiality under reduced LINC-connectivity may offer new targets to regulate aging-induced MSC failure.

Extending Knowledge of the LINC Complex Functional Role. Using a novel, MSC specific LINC OFF scheme, we will study how LINC function regulate βcatenin and YAP signaling *in vitro* and bone phenotype in *in vivo*. Our findings have a potential to uncover previously unknown roles of LINC complex at integrating the function of well-known mechanoresponders βcatenin and YAP.

Uncovering Potential Therapeutic Targets for Aging. Clinicians have long prescribed exercise as a mechanism to maintain physical health. Our proposed studies have a potential uncover LINC regulatory targets for exercise and exercise mimetics.

APPROACH

We have reported that functional LINC complex is critical for maintaining MSCs multipotentiality and mechanoresponse[7] but the mechanisms by which MSC signaling is altered when LINC is disconnected is unknown. This section lists our proposed experiments to elucidate LINC-mediated βcatenin and YAP mechanotransduction in MSCs. First aim focuses on translocation and transcription aspects of mechanotransduction. As we argue that LINC dysfunction is a factor contributing to aging, second aim will test if MSC-specific LINC dysfunction is sufficient to impede exercise bone accrual in mice. Final aim will test if LINC complexes are indeed reduced in aging to negatively impact βcatenin and YAP signaling in aging MSCs.

Aim1 tests if functional LINC is necessary for mechanotransductive functions of βcatenin and YAP: Nuclear entry of βcatenin and YAP will be compared between intact and LINC-OFF MSCs using cell fractionation and FRAP microscopy. Secondly, we will determine if disabling LINC function interferes with βcatenin and YAP binding to their transcriptional targets via ChIP assays. **We expect** that LINC-OFF cells to have reduced nuclear entry of both βcatenin and YAP after mechanical challenge. If cell fractionation proves to be not as sensitive, we will focus on immunostaining and PCR against βcatenin (Axin-2) and YAP transcriptional targets (Ccna-2). ChIP experiments expected to show altered βcatenin and YAP binding to DNA in LINC-OFF MSCs as preliminary data shows decreased levels of heterochromatin protein HP1β in Sun1&2 co-depleted MSCs.

Aim 2 test if disabling LINC in Prx-1+ MSCs decreases efficacy of exercise to improve bone mass: As deletion of either βcatenin or YAP results in inferior skeletal phenotype[8,9] a possible decrease in LINC function in aging may contribute impediment of βcatenin & YAP mediated mechanosignaling. MSC-specific LINC deficiency effects in bone are unknown, which precludes us from making such observations. This aim will determine if MSC specific de-activation of LINC function is sufficient to inhibit exercise-induced bone accrual in mice. In order to inactivate the LINC complex, Tamoxifen (TAM) will be administered into transgenic EGFP-KASH2 mice for 5 consecutive days prior to the start of 4wk exercise regimen[12] which should inactivate LINC complex via overexpression of KASH2 fragment.[13] **We expect** EGFP-KASH2 mice to have diminished response to exercise in terms of bone modeling and present reduced activity of βcatenin and YAP transcriptional targets. Targets will include but not are not necessarily limited to Collagen-I, Cyclin-2, Axin-2, MYC, Runx2. [14-16]

Aim 3 determines if aging decreases LINC elements in MSCs: Flow cytometry will compare age (telomere length) as well as expression and protein levels of LINC elements (Nesprin-1&2, Sun-1&2) of MSCs isolated from 8 and 32 week old bone marrow. **We expect** reduced LINC expression in aged cells. While expectation is to use real aged MSCs, we are using *in vitro* model as an alternative. Another alternative is to use $p16^{INK4a}$ overexpressing transgenic mice to induce cell senescence[17] which shown to promote bone loss.[18]

TRANSLATIONAL IMPACT

This proposal is designed to examine that the loss of mechanical perception encountered in aging might be, in-part, due to decreased communication to the nucleus. The premise that intra-cellular connectivity maintained by "Linker of Nucleoskeleton and Cytoskeleton" complexes may be the key aspect regulating the nuclear mechanotransduction is of paramount interest for potential therapeutic interventions and poised to lay the foundation for novel advances in treatment and prevention of musculoskeletal decline as seen in aging, obesity, bedrest and other musculoskeletal conditions.

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8 Kegelman, C. D. *et al.* Skeletal Cell YAP And TAZ Redundantly Promote Bone Development By Regulation Of Collagen I Expression And Organization. *bioRxiv*, doi:10.1101/143982 (2017).
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16 Herbst, A. *et al.* Comprehensive analysis of beta-catenin target genes in colorectal carcinoma cell lines with deregulated Wnt/beta-catenin signaling. *BMC genomics* **15**, 74, doi:10.1186/1471-2164-15-74 (2014).
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ITHS | Institute of Translational Health Sciences
Accelerating Research. Improving Health.

ITHS Translational Research Scholars Program
Budget
Gunes Uzer

BUDGET

Applicant Name (Last, First, Middle):Uzer, Gunes

ITHS | Institute of Translational Health Sciences — Accelerating Research. Improving Health.

DETAILED BUDGET

FROM 03/01/18 THROUGH 02/28/19

List PERSONNEL *(Applicant Organization Only)*
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

Use Cal, Acad, or Summer to Enter Months Devoted to Project

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Gunes Uzer	PI		1.30	-	$9388/month	$0 (15% of PI effort will be provided through department release time)	0	
Undergraduate Student	Research Assistant		30weeks		$10/hr	3,500	70	3,570
Undergraduate Student	Research Assistant			10weeks	$10/hr	4,000	360	4,360
SUBTOTALS →						7,500	430	7,930
CONSULTANT COSTS								
EQUIPMENT *(Itemize)*								
SUPPLIES *(Itemize by category)*								
Animal genotyping	500							
PCR supplies	500							
Biochemistry Supp	500							
TRAVEL								
OTHER EXPENSES (Itemize by category)								

CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS		
SUBTOTAL DIRECT COSTS FOR BUDGET PERIOD		**$**	9,430
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATION COSTS		570
TOTAL DIRECT COSTS FOR BUDGET PERIOD		$	10,000
TOTAL INDIRECT COSTS FOR BUDGET PERIOD		$	
TOTAL COSTS FOR BUDGET PERIOD		**$**	**10,000**

BUDGET JUSTIFICATION

Gunes Uzer, PhD. – Principal Investigator (15% effort) – Dr. Uzer will oversee all phases of the experiments, and will take responsibility for each of its aspects including generation and exercise response in genetically modified CAG-LacZ/EGFP KASH2fl/fl/Prx1-CreER mouse model. Dr. Uzer will oversee aspects relating to quantifying LINC complex and LINC mediated mechanosignaling research asistant directly to coordinate the technical aspects of the proposed in vivo and in vitro experiments, ChIP assays, cell fractionation, PCR and Protein analyses.

TBD– Student Research Assistant, (100% effort) – Student will work closely with Dr. Uzer and will oversee the animal breeding, genotyping and perform, sample collection and analysis the data generated from in vivo exercise experiments. Research Assistanr will provide data to research team and participate in writing manuscripts.

Boise State Supplies– Supplies are requested this project, include molecular biology supplies for animal genotyping, ChIP and qPCR approaches. Antibodies and vital dies are required and must be continuously replenished for flow cytometry, microscopic imaging and microscopy fees (confocal, immunofluorescence, and FRAP data analysis). Tamoxifen, and tissue processing are a cost.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Uzer, Gunes

eRA COMMONS USER NAME (credential, e.g., agency login): gunes_uzer

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Celal Bayar University,, Manisa	BS	08/2005	Physics
Stony Brook University, Stony Brook, NY	MS	07/2008	Mechanical Engineering
Stony Brook University, Stony Brook, NY	PhD	01/2013	Biomedical Engineering
University of North Carolina, Chapel Hill, NC	Post-doc	01/2016	Cell Mechanobiology

A. Personal Statement

In the past 12 years I have been focused on the mechanical factors that modulate the molecular signaling pathways in cells and animals. Early on, I have identified the physiological mechanical environment of cells under external mechanical stimuli and established experimental and computational models to understand the mechanical factors that modulate wide variety of cell functions under external stimuli, including osteoblasts, osteocytes and mesenchymal stem cells. Over the years I have developed *in vitro* and *in vivo* models that apply mechanical challenges including high frequency vibrations, extracellular matrix strain, fluid shear stress and unloading regimes such as hindlimb suspension and microgravity. Our findings led to a fundamental question of how intracellular structure could work as a mechanosensory organelle in response to mechanical challenges to control stem cell fate- a common progenitor for musculoskeletal tissues. Notably, I discovered that sensation of mechanical signals required nucleo-cytoskeletal coupling facilitated by LINC (Linker of Nucleus and Cytoskeleton) complexes. We have further identified that this coupling was also essential for preserving MSC multipotentiality as disabling nucleo-cytoskeletal connectivity augmented pro-adipogenic programs and decreased osteogenesis in MSC. Our current studies focus on how LINC complexes and intranuclear organizers such as LaminA/C and actin polymerization contribute to MSC fate and mechanosignaling. If supported, this proposal will give my team a chance to further our work on this understudied aspect of stem cell biology and how deficiencies in LINC complexes may contribute to aging related loss of MSC health.

1. **Uzer G**, Thompson WR, Sen B, Xie Z, Yen SS, Miller S, Bas G, Styner M, Rubin CT, Judex S, Burridge K, Rubin J. Cell Mechanosensitivity to Extremely Low-Magnitude Signals Is Enabled by a LINCed Nucleus. Stem Cells. 2015 Jun;33(6):2063-76. PubMed PMID: 25787126; PubMed Central PMCID: PMC4458857.

2. **Uzer G**, Pongkitwitoon, Rubin J, Judex S, Cytoskeletal Configuration Modulates Mechanically Induced Changes in Mesenchymal Stem Cell Osteogenesis, Morphology and Stiffness, Scientific Reports. 2016 Oct;6:34791 Pubmed Central PMID: 27708389 ; PubMed Central PMCID: PMC5052530

3. Sen B, **Uzer G**, Samsonraj RM, Xie Z, McGrath C, Styner M, Dudakovic A, van Wijnen AJ, Rubin J. Intranuclear Actin Structure Modulates Mesenchymal Stem Cell Differentiation. Stem Cells. 2017 Jun;35(6):1624-1635. PubMed PMID: 28371128; PubMed Central PMCID: PMC5534840.

4. **Uzer G**, Pongkitwitoon S, Ete Chan M, Judex S. Vibration induced osteogenic commitment of mesenchymal stem cells is enhanced by cytoskeletal remodeling but not fluid shear. J Biomech. 2013 Sep 3;46(13):2296-302. PubMed PMID: 23870506; PubMed Central PMCID: PMC3777744.

B. Positions and Honors

Positions and Employment

2005 – 2008	Teaching/Research Assitant, Mechanical Engineering, Stony Brook University, Stony Brook
2008 – 2013	Research Assistant, Biomedical Engineering, Stony Brook University, Stony Brook
2013 – 2016	Postdoctoral Fellow, Endocrinology Division, University of North Carolina, Chapel Hill
2016 –	Assistant Professor, Department of Mechanical/Biomedical Engineering, Boise State University
2016 –	Adjunct Assistant Professor, Department of Medicine, University of North Carolina, Chapel Hill
2016 –	Affiliate, Biomolecular Research Center, Boise State University, Boise, ID

Other Experience and Professional Memberships

2006 -	Member, Society of Experimental Mechanics
2008-	Member, American Society for Bone and Mineral Research
2015-	Member, Orthopaedic Research Society
2016-	Advisory Board Member, ORS Musculoskeletal Biology Workshop
2017-	Editorial Board Member, Scientific Reports

Honors

2009	NASA New York City Research Initiative (NYCRI) Achievement Award, NASA
2012	Sigma Xi Research travel Award, Sigma Xi, Stony Brook Chapter
2013	President's Poster Award, American Society of Bone and Mineral Research
2014	Young Investigator Travel Award, American Society of Bone and Mineral Research
2014	IBFF Travel Award, 14th International Bone Fluid Flow Workshop
2015	Harold Frost Young Investigator Award, American Society of Bone and Mineral Research
2015	NSBRI First Award Fellowship, National Space Biomedical Research Institute
2016	STEM CELLS Young Investigator Award, STEM CELLS

C. Contribution to Science

1) My research considers the internal cellular structure as a mechanosensory element within cells that can both sense and adapt to various types of mechanical challenges. Changes in the cytoskeletal architecture not only modulate the intracellular connectivity but also direct the repositioning of the mechanosensory signaling mechanisms within the cells and provide the context by which cells will respond to their mechanical environment. To understand how cells sense external stimuli, we recently identified nuclear envelope bound LINC complexes as critical components for sensing of mechanical signals. We further found that the mesenchymal stem cell adipogenesis, which is usually increased in catabolic conditions like aging and osteoporosis, was accelerated in mesenchymal stem cell without LINC connectivity. As such, the LINC complex and intra-nuclear cell architecture may serve as a critical regulator of stem cell fate.

   a. **Uzer G**, Thompson WR, Sen B, Xie Z, Yen SS, Miller S, Bas G, Styner M, Rubin CT, Judex S, Burridge K, Rubin J. Cell Mechanosensitivity to Extremely Low-Magnitude Signals Is Enabled by a LINCed Nucleus. Stem Cells. 2015 Jun;33(6):2063-76. PubMed PMID: 25787126; PubMed Central PMCID: PMC4458857.

   b. Sen B, **Uzer G**, Samsonraj RM, Xie Z, McGrath C, Styner M, Dudakovic A, van Wijnen AJ, Rubin J. Intranuclear Actin Structure Modulates Mesenchymal Stem Cell Differentiation. Stem Cells. 2017 Jun;35(6):1624-1635. PubMed PMID: 28371128; PubMed Central PMCID: PMC5534840.

   c. Thompson WR, Guilluy C, Xie Z, Sen B, Brobst KE, Yen SS, **Uzer G**, Styner M, Case N, Burridge K, Rubin J. Mechanically activated Fyn utilizes mTORC2 to regulate RhoA and adipogenesis in mesenchymal stem cells. Stem Cells. 2013 Nov;31(11):2528-37. PubMed PMID: 23836527; PubMed Central PMCID: PMC4040149.

   d. Sen B, Xie Z, Case N, Thompson WR, **Uzer G**, Styner M, Rubin J. mTORC2 regulates mechanically induced cytoskeletal reorganization and lineage selection in marrow-derived mesenchymal stem cells. J Bone Miner Res. 2014 Jan;29(1):78-89. PubMed PMID: 23821483; PubMed Central PMCID: PMC3870029.

2) Bone cells populations of mesenchymal origin provide regenerative capacity to bone by replacing and reinforcing the skeleton at load bearing sites. The ability of cells to respond to mechanical cues generated during functional loading is critical for this capacity. My research is focused on identifying relevant components of mechanical signals that modulate a wide variety of bone cell functions, including mesenchymal stem cells, osteoblasts and osteocytes. More specifically these studies focus on if the dynamic fluid shear created during the high frequency vibration events contributed to the overall cell response. We used both experimental high speed photometry, particle image velocimetry, dynamic finite element modeling and in-vtro models to identify the cell-level mechanical environment during high frequency oscillations. Our studies established that vibration-induced acceleratory motions modulate a wide variety of bone cell functions independent of secondary signals such as fluid shear and strain.

a. **Uzer G**, Manske SL, Chan ME, Chiang FP, Rubin CT, Frame MD, Judex S. Separating Fluid Shear Stress from Acceleration during Vibrations in Vitro: Identification of Mechanical Signals Modulating the Cellular Response. Cell Mol Bioeng. 2012 Sep 1;5(3):266-276. PubMed PMID: 23074384; PubMed Central PMCID: PMC3466610.

b. **Uzer G**, Pongkitwitoon S, Ete Chan M, Judex S. Vibration induced osteogenic commitment of mesenchymal stem cells is enhanced by cytoskeletal remodeling but not fluid shear. J Biomech. 2013 Sep 3;46(13):2296-302. PubMed PMID: 23870506; PubMed Central PMCID: PMC3777744.

c. **Uzer G**, Pongkitwitoon S, Ian C, Thompson WR, Rubin J, Chan ME, Judex S. Gap junctional communication in osteocytes is amplified by low intensity vibrations in vitro. PLoS One. 2014;9(3):e90840. PubMed PMID: 24614887; PubMed Central PMCID: PMC3948700.

d. **Uzer G**, Pongkitwitoon, Rubin J, Judex S, Cytoskeletal Configuration Modulates Mechanically Induced Changes in Mesenchymal Stem Cell Osteogenesis, Morphology and Stiffness, Scientific Reports. 2016 Oct;6:34791 Pubmed Central PMID: 27708389 ; PubMed Central PMCID: PMC5052530

3) At the organismal level we have studied the effects presence of absence mechanical challenges on musculoskeletal system using preclinical animal models. Approximately 25% my scientific work consists of animal models, focusing on hindlimb unloading and exercise models in rat & mice. More specifically, we studied how extended periods of unloading alter muskeloskeletal physiology and how mechanical therapies like low intensity vibrations can be utilized to alleviate the catabolic changes in bone and intervertebral disc. Recently, we have been able to demonstrate that running exercise not only stimulates osteogenesis, but also halts the fatty infiltration in both muscle and bone marrow under high fat diet.

a. Holguin N, **Uzer G**, Chiang FP, Rubin C, Judex S. Brief daily exposure to low-intensity vibration mitigates the degradation of the intervertebral disc in a frequency-specific manner. J Appl Physiol (1985). 2011 Dec;111(6):1846-53. PubMed PMID: 21960658; PubMed Central PMCID: PMC3233878.

b. Gupta S, Vijayaraghavan S, **Uzer G**, Judex S. Multiple exposures to unloading decrease bone's responsivity but compound skeletal losses in C57BL/6 mice. Am J Physiol Regul Integr Comp Physiol. 2012 Jul 15;303(2):R159-67. PubMed PMID: 22592559; PubMed Central PMCID: PMC3404633.

b. Styner M, Pagnotti GM, McGrath C, Wu X, Sen B, **Uzer G**, Xie Z, Zong X, Styner MA, Rubin CT, Rubin J. Exercise Decreases Marrow Adipose Tissue Through ß-Oxidation in Obese Running Mice. J Bone Miner Res. 2017 Aug;32(8):1692-1702. PubMed PMID: 28436105; PubMed Central PMCID: PMC5550355.

a. Styner M, Pagnotti GM, Galior K, Wu X, Thompson WR, **Uzer G**, Sen B, Xie Z, Horowitz MC, Styner MA, Rubin C, Rubin J. Exercise Regulation of Marrow Fat in the Setting of PPARγ Agonist Treatment in Female C57BL/6 Mice. Endocrinology. 2015 Aug;156(8):2753-61. PubMed PMID: 26052898; PubMed Central PMCID: PMC4511140.

4) Optically-based experimental methodologies provide flexibility in both advanced material characterization and in biomedical research where standardized material characterization modalities fall short. My work in speckle photography is focused on optical experimental mechanics approaches to non-invasive mechanical characterization. Using high speed speckle photometry we quantified the acceleration transmitted to lower back of animals via a vertically vibrating plate in a rat model. In an in vitro system, we identified the fluid behavior in horizontally vibrating containers at both macro and cell level. I also extended these

methodologies to novel material characterization where we characterized fracture propagation in TiAl alloys, mechanical behavior of auxetic foams. I further, extended the speckle photography technique to three dimensional objects and high speed modalities which serves as pivotal techniques for my research today.

a. **Uzer G**, Chiang F. Mapping Full Field Deformation of Auxetic Foams using Digital Speckle Photography. Physica Status Solidi B. 2008; 245(11):2391.
b. **Uzer G**, Chiang F, Krukenkamp IB. Measuring Shape and Surface Strain of 3D Objects Using Digital Speckle Photography. Strain. 2008; 45(5):409.
c. Holguin N, **Uzer G**, Chiang FP, Rubin C, Judex S. Brief daily exposure to low-intensity vibration mitigates the degradation of the intervertebral disc in a frequency-specific manner. J Appl Physiol (1985). 2011 Dec;111(6):1846-53. PubMed PMID: 21960658; PubMed Central PMCID: PMC3233878.
d. **Uzer G**, Chiang F, Rosenberger AH. Cracked Brazilian Tests of Lamellar Tial. In:Gdoutos EE, editor. Proceedings of the 13th International Conference on Experimental Mechanics, Alexandroupolis, Greece, July 1–6, 2007. International Conference on Experimental Mechanics; 2007 July 01; Alexandroupolis, Greece. Springer Netherlands; c2007.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/1FEyaa_3rsTAx/bibliography/47488932/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Current Research Support

Organization: National Institutes of Health, NIGMS, 1P20GM109095-01
Title: COBRE in Matrix Biology
Project: Nucleoskeleton regulation of the Chromatin Dynamics and Cell Fate in Response to Mechanical Signals
Role: Junior Investigator
Dates: 9/1/16 – 8/31/19
Amount: $150,000 per year

Organization: NASA EPSCoR
Title: Role Cellular Connectivity in Maintaining Osteogenesis
Role: PI
Dates: 4/15/17 - 4/30/18
Amount: $37,000 per year

Completed Research Support

Organization: National Space Biomedical Research Institute, PF04304
Title: Role of LINC complex in Maintenance of MSC βcatenin Signaling Under Microgravity
Role: PI
Dates: 11/01/15-7/31/16
Amount: $50,000 per year

Organization: The Scientific and Tech. Research Council of Turkey, 2214-A
Title: Age related changes in LINC mediated nuclear coupling
Role: PI
Dates: 12/30/15 – 11/31/16
Amount: $27,000 per year