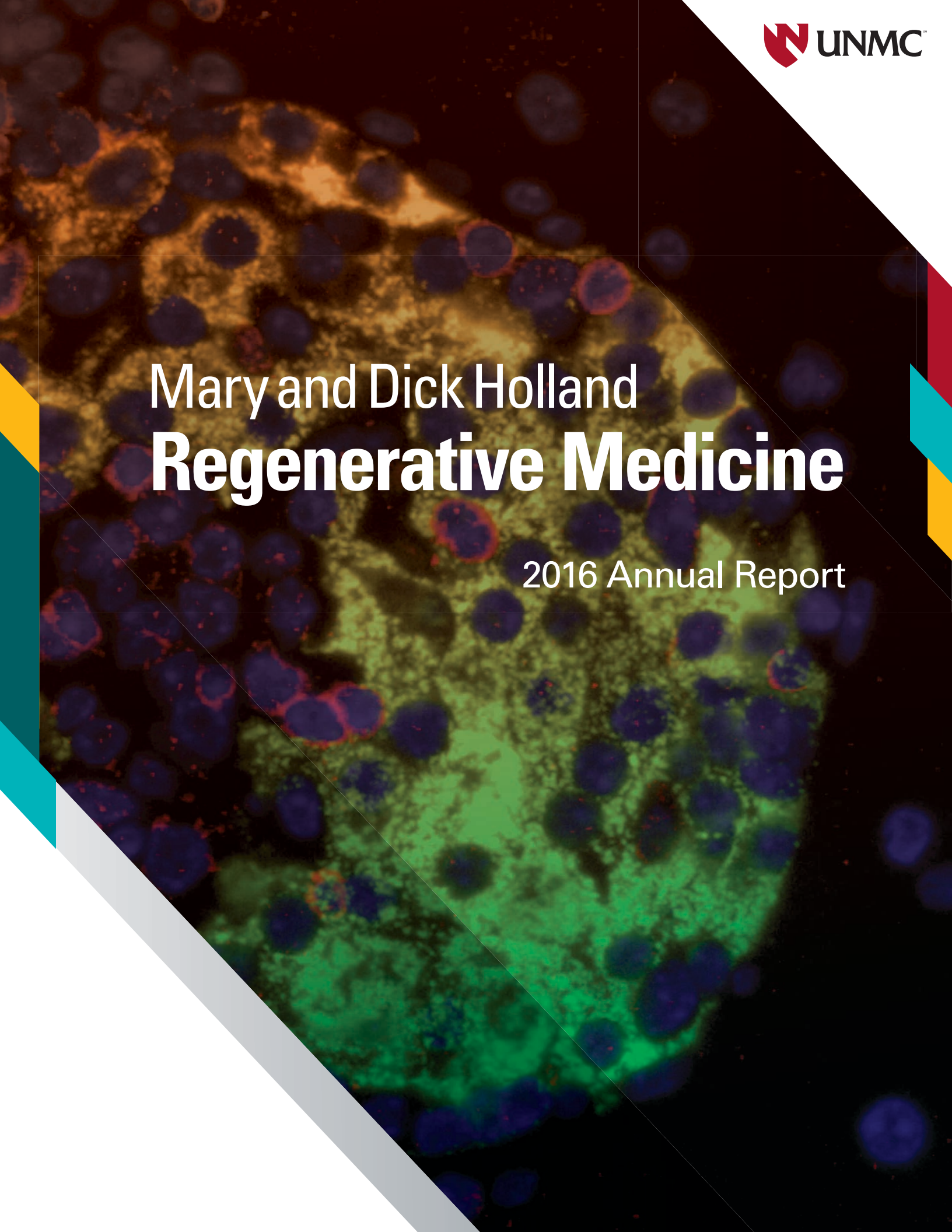

UNMC

# Mary and Dick Holland
# Regenerative Medicine

2016 Annual Report

*A very special thank you to our Donors*

**The Holland Family**

**&**

**The Durham Family**

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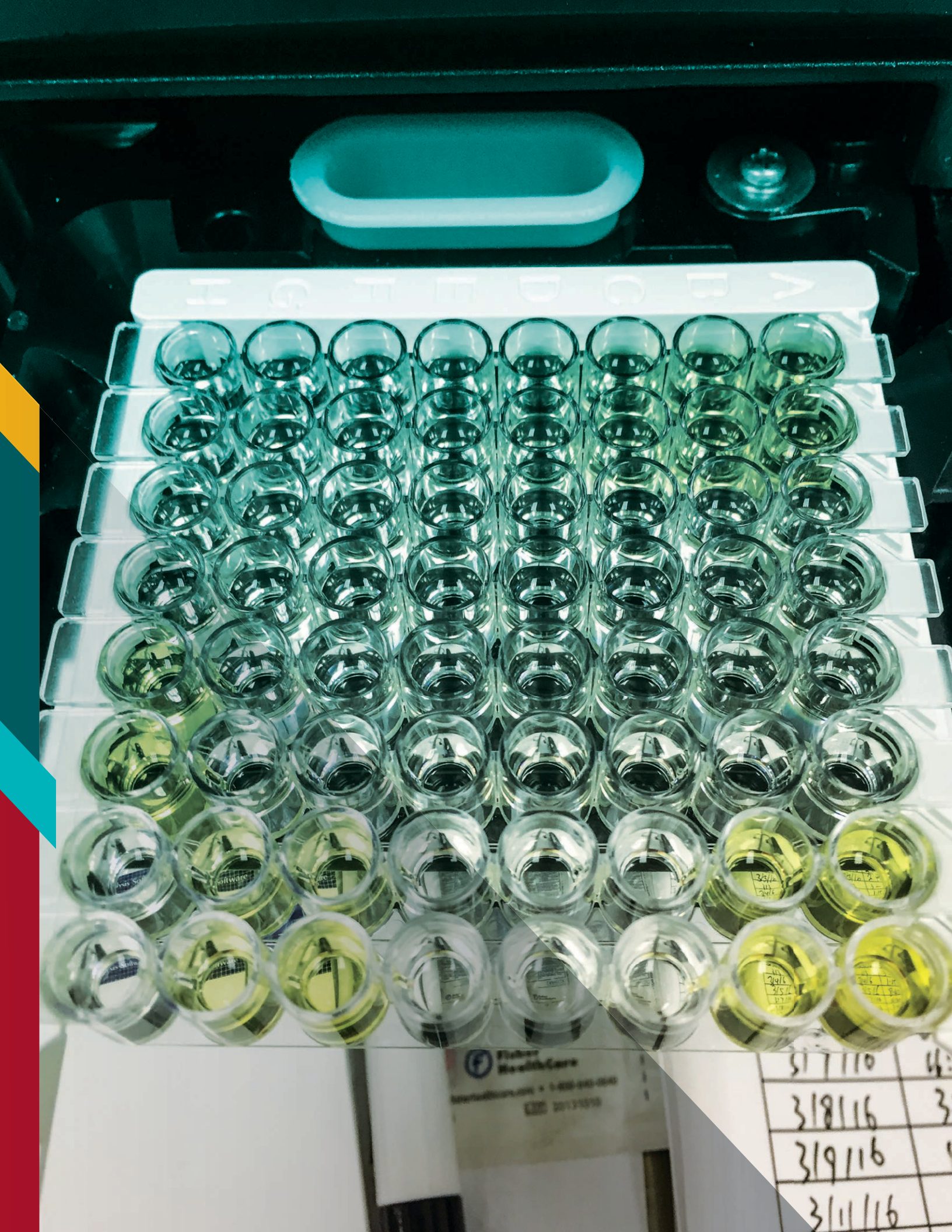
Mary and Dick Holland **Regenerative Medicine**

2016 Annual Report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# Letter from the Director

Driven by the needs of patients who seek treatment for their incurable diseases, The University of Nebraska Medical Center established the Mary and Dick Holland Regenerative Medicine Program. Our mission is focused on bringing together forward thinking scientists and clinicians who are committed to understanding the basic science behind tissue engineering and development. By translating these concepts we seek to pioneer regenerative therapies that can be taken into the clinic, spreading hope throughout the Nebraskan community and around the world. While still a new program, we are proud of our ongoing innovations and successes in the areas of bone and cartilage development and remodelling, vascular regeneration, pancreas development and diabetes, and biomaterials for tissue regeneration. We look forward to further evolving and adding new faculty, initiatives, and collaborations in 2016 and 2017.

The field of regenerative medicine involves innovative medical therapies that enable the body to repair, replace, restore and regenerate damaged or diseased tissues and organs. I am honored to have the opportunity to be involved in this cutting edge scientific field that holds so much potential to help those suffering from acute and chronic conditions.

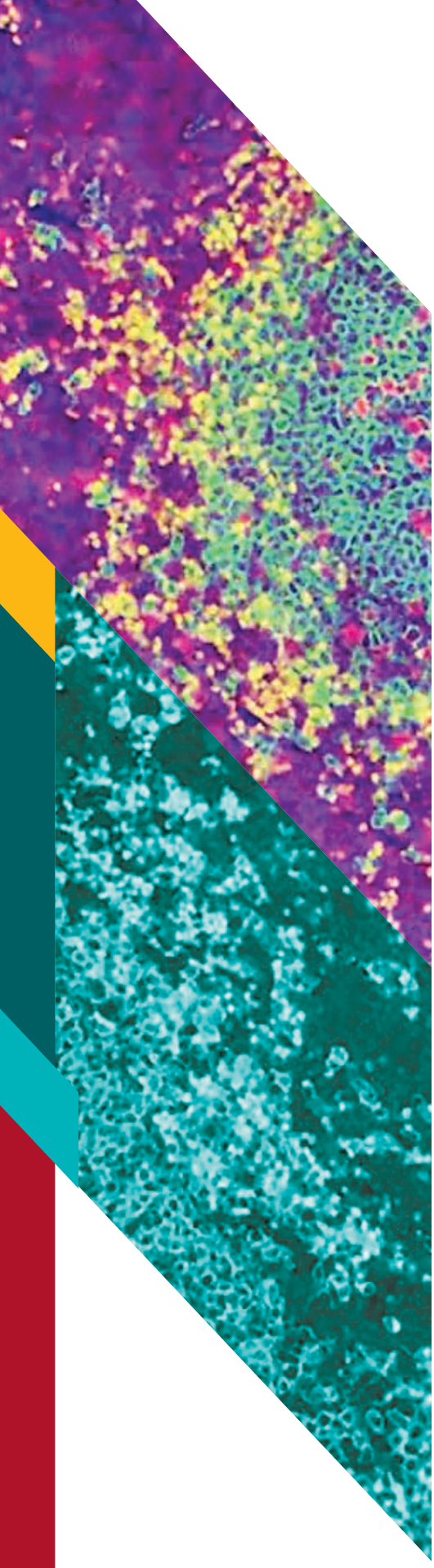
There are several avenues of Regenerative Medicine that will require many more years of research, but as we want to focus on developing therapies that can help treat patients now. This year we have added a number of excellent new faculty and staff to our program, started new initiatives and continued others into a second year, and added new equipment and facilities to advance our research and help us further towards this goal.

The last few months have seen the introduction of five new regenerative medicine initiatives, which are being given seed funding from the program. These extend the reach of the Regenerative Medicine Program, fostering new innovative projects. These initiatives bring together researchers and clinicians from UNMC and the engineering program at UNL to collaborate and develop novel research areas.

We are also excited to announce the development of a new Bioprinting core which will be run by one of our new faculty members. Bioprinting is literally the use of a printers to create cell matrixes to form organs. The Bioprinting Core will provide access to advanced imaging technologies enabling precise placement of cells, biomaterials, and biomolecules for regenerative medicine-related research. 3D bioprinting technology has emerged as a versatile and powerful tool for fabricating 3D tissue and organ analogs and it is thrilling to be part of this innovative research.

Overall it has been an exciting year for the Regenerative Medicine Program and I look forward to see what we achieve in the upcoming year!

Nora Sarvetnick, PhD, Director of Regenerative Medicine



# Regenerative Medicine

Regenerative Medicine is an emerging interdisciplinary field of research. The clinical applications resulting from this field focus on the repair, replacement or regeneration of cells, tissues, or organs to restore lost function that has been lost from any cause, including hereditary defects, disease, injury, and aging. Using methodologies from diverse scientific fields, Regenerative Medicine has the capacity to launch far ahead of traditional transplantation and replacement therapies.

The Regenerative Medicine Program has been established at UNMC to bring many areas of science and medicine together to provide those in Nebraska and surrounding areas more advanced therapies and treatments that can enhance their quality of life beyond what we are currently capable of providing. Researchers hope to develop strategies to grow bone and muscle tissue for amputees or new heart tissue for those who suffer from heart disease.

Here at UNMC, researchers and students have access to state of the art facilities and equipment to allow successful research to expand and grow.

A few of the UNMC Regenerative Medicine Focus Areas:

## Biomaterials for Regeneration

In regenerative medicine, biomaterials play an important role as they can act as not only a scaffold/substrate for supporting cell growth, forming certain structures and regulating cell behaviors but also a local delivery system for sustained delivery of signaling molecules and enhancement of cell functions and tissue regeneration. At UNMC, scientists are interested in development of novel biomaterials with multiple functions and understanding the interactions between materials and cells/tissues. The final goal is to use these designed biomaterials in studying tissue morphogenesis and patterning during development, forming tissues for in vitro drug screening, and regenerating tissues for treatment of diseases.

## Bone and Cartilage Development and Regeneration

What happens during embryonic development as our bones begin to form and how does our body regulate this to ensure appropriate tissue development? As we understand these patterns we can begin to apply them to human therapeutic applications as a means to regenerate bone tissue after major injury or disease has destroyed the primary functional bone.

## Pancreas Regeneration

Once damaged, the body's insulin-producing cells don't regenerate. UNMC scientists are working to make history by replacing those damaged cells with healthy tissue, thereby directly addressing one of the causative problems of diabetes.

## Vascular Regeneration

One of the major vascular accesses designed for long-term hemodialysis use is arteriovenous fistula, a connection, made by a vascular surgeon, of an artery to a vein. However, veins for a number of patients failed to reach maturation preventing their use for dialysis access. At UNMC, scientists are interested in understanding the mechanisms of vein maturation and finding ways to improve the success rate of vein maturation for dialysis patients.

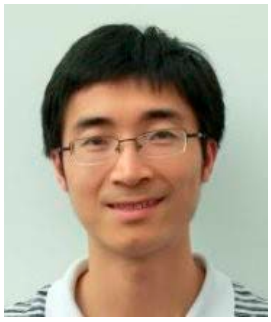
A necessary component for the success of this project is clinical translation. Without the help of involved/collaborative clinicians here at UNMC we cannot bring our current research into the clinic. By taking a collaborative, interdisciplinary group approach we have identified critical problems in different organs or diseases and actively work out ways to solve them. We hope to help grow the field of Regenerative Medicine at UNMC, and also give both junior and senior faculty the chance to participate in research and therapy development. By focusing on adult and embryonic stem cell research and utilizing UNMC's new Biologics Production Facility, we hope to develop new treatments that move quickly into clinical trials.

# New Faculty

## Shannon Buckley, PhD

*Assistant Professor,*
*Genetics, Cell Biology and Anatomy*
*University of Nebraska Medical Center*

Dr. Buckley's research interest centers on the molecular mechanisms regulating stem cell fate decisions that may also be linked to cancer. Her goal is to utilize genomic and proteomic approaches to identify key ubiquitin ligases and their substrates that regulate mechanisms of pluripotency, self-renewal, differentiation, and hematopoietic malignant transformation. The dynamic reversibility of the ubiquitin modification (by kinases, phosphatases, E3 ligases and de-ubiquitinases) and recent success of a UPS inhibitor (Velcade) for the treatment of multiple myeloma and mantle cell lymphoma proves the translational importance of the UPS system. This suggests that targeting of specific elements of the UPS could lead to future breakthroughs in both basic research and cancer therapy by creating a more efficient generation of induced pluripotent stem cells, promoting lineage differentiation for cell therapy, and providing potential targets for drug discovery.



## Bin Duan, PhD

*Assistant Professor, Internal Medicine*
*University of Nebraska Medical Center*

Dr. Duan has recently joined the regenerative medicine program as a faculty member in the department of Internal Medicine. Dr. Duan completed his PhD in Biomedical Engineering at the University of Hong Kong in 2010, where his thesis focused on developing calcium phosphate/poly(3-hydroxybutyrate-co-3-hydroxyvalerate) nanocomposite scaffolds via selective laser sintering for bone tissue engineering.

The focus of Dr. Duan's research integrates novel biomaterials, advanced biofabrication of tissue engineered scaffolds, bioprinting, tissue constructs and tissue models, controlled growth factor delivery strategy, and bioreactors. He has implemented rapid prototyping (RP) techniques to fabricate nanocomposite scaffolds with complex architectures and porous structures for bone tissue engineering and to generate living hydrogel valve conduits with anatomical architecture and mechanical heterogeneity for heart valve regeneration. He investigates the mechanisms through which the local microenvironment, including adhesion ligand density, matrix component and stiffness, regulates several aspects of valve interstitial cell (VIC, the most prevalent cells in the heart valve leaflets) behaviors like cell spreading, migration, and differentiation (both physiological and pathological). Duan uses this information to direct the differentiation of mesenchymal stem cells (MSC) towards valve specific phenotypes and compare the capacity and efficiency of different MSC sources. He is actively developing novel 3D hydrogel systems with biochemical and biophysical tunability for mimicking extracellular matrix (ECM) to appropriately control MSC fate and for precisely replicating in vivo pathological microenvironments in vitro.

# New Faculty

## Sung-Ho Huh, PhD

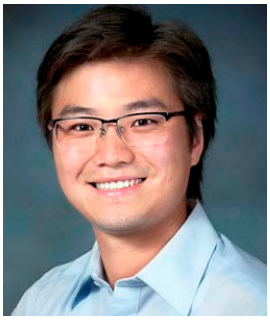
*Assistant Professor,*
*Munroe-Meyer Institute*
*University of Nebraska*
*Medical Center*

Dr. Huh has recently joined the regenerative medicine program as a faculty member of the Munroe-Meyer Institute. Dr. Huh was previously a research instructor at Washington University in St. Louis, where he also completed his Postdoc in 2012. His studies focus on identifying the molecular mechanisms that regulate hair cell progenitor development and maintenance in mammals using a mouse model system. This research will provide a framework to understand how a non-repairable organ develops and what pathways might be used to therapeutically induce regeneration. This is an important problem given that in humans 3 out of 1000 new-borns suffer from congenital hearing loss and many more people develop sensorineural hearing loss as a result of noise, antibiotics exposure, and aging. Sensorineural hearing loss primarily results from loss of sensory hair cells in the cochlea, which, once damaged, cannot repair under normal physiological conditions. The tools and discoveries Dr. Huh's lab will develop through the identification of cochlear progenitor growth and maintenance can be utilized for the development of new reparative gene/molecule/cell-based therapies. He believes that selective reactivation of signaling pathways that function during embryonic development will be an effective means to promote repair and regeneration of malformed or damaged organs such as the cochlea and may also prevent pathological responses that could further compromise organ function.

## Nicole Iverson, PhD

*Assistant Professor and*
*Biomedical Nanotechnology*
*Specialist, Biological Systems*
*Engineering Department*
*University of Nebraska-Lincoln*

Dr. Iverson was an NIH postdoctoral fellow at the Massachusetts Institute of Technology from 2010-2015 before becoming an assistance professor at UNL. Dr. Iverson's research interests include delivery, monitoring, and analysis of in vivo nanoparticles that act as biological sensors, DNA-wrapped single wall carbon nanotubes in alginate microparticles, modifying chemical structures of nanoparticles for use in non-invasive intravenous delivery. Iverson earned her PhD and master's degrees in biomedical engineering from Rutgers University and bachelor's in biomedical engineering from the University of Minnesota.



## Peng Jiang, PhD

*Assistant Professor, Munroe-Meyer Institute*
*Developmental Neuroscience*
*University of Nebraska*
*Medical Center*

Dr. Jiang focuses on differentiating pluripotent stem cells to neural cells for modeling and treating neurological disorders. Pluripotent stem cells, including embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs), can differentiate into all cell lineages of the body. Differentiation of human pluripotent stem cells to brain cells provides a new tool for studying human neural development. With iPSC technology, he also generates human iPSCs (hiPSCs) from human somatic cells through reprogramming. Neural differentiation of patient-derived hiPSCs allows him to study the pathogenesis of human neurological diseases with a human patient's own brain cells. Moreover, hiPSCs hold great promise for developing cell replacement therapy to treat CNS injury. His long-term goal is to dissect the development pathways and corresponding pathogenesis of neurodevelopmental diseases to develop stem cell regenerative medicine to combat CNS injury.

## Haitao Wen, PhD

*Assistant Professor, Pathology and Microbiology*
*University of Nebraska*
*Medical Center*

In August of 2015, Haitao Wen joined Faculty in the Department of Microbiology and Pathology at UNMC and became a member of the Regenerative Medicine Program. Dr. Wen comes to us from the University of North Carolina School of Medicine's Jaycee Burn Center where they focus on reconstruction and regeneration. Dr. Wen has a PhD from the University of Michigan Medical School in molecular and cellular pathology.

The Wen laboratory studies innate immunity and inflammatory-associated diseases. By employing various approaches, including gene deletion, biochemical, proteomics, and animal models, they aim to study the mechanisms by which immune receptors regulate inflammation and cell stress responses and their applications in inflammation-associated diseases. Two of his major research directions are Nrf2 regulation of cell stress response in polymicrobial sepsis and mitochondrial metabolism on immune signaling.

# Research Highlights

## Collaboration for Advanced Surgical and Engineering Applications (CASEA)

**Alexey Kamenskiy, PhD, and Jason MacTaggart, MD**

Jason MacTaggart, MD

Alexey Kamenskiy, PhD

### Vascular Ageing and Remodeling

Dr. MacTaggart, a vascular surgeon, and Alexey Kamenskiy, Ph.D., a biomedical engineer, both assistant professors in the UNMC Department of Surgery, are co-principal investigators of the research study.

Research is focused on the assessment of changes that occur in human arteries with ageing and disease in terms of their shape, internal structure, and mechanical properties. The human vascular system adapts to changing mechanical and biological environments undergoing changes in morphometry, arterial structure and mechanical properties. Detailed characterization of these changes with ageing and disease is important for understanding arterial pathophysiology and improving treatment modalities.

**Recent Publications**

**Kamenskiy AV**, Miserlis D, Adamson P, Adamson M, Knowles T, Neme J, Koutakis P, Phillips N, Pipinos I, **MacTaggart J**. Patient Demographics and Cardiovascular Risk Factors Differentially Influence Geometric Remodeling of the Aorta Compared to the Peripheral Arteries. Surgery. doi: 10.1016/j.surg.2015.05.013. 2015. PMID: 26096560.

**Kamenskiy AV**, Seas A, Bowen G, Deegan P, Desyatova A, Bohlim N, Poulson W, **MacTaggart J**. In Situ Longitudinal Pre-Stretch in the Human Femoropopliteal Artery. Acta Biomaterialia. doi: 10.1016/j.actbio.2016.01.002. 2016. PMID: 26766633.

**Kamenskiy AV**, Pipinos II, Carson JS, **MacTaggart JN**, Baxter BT. Age and Disease-Related Geometric and Structural Remodeling of the Carotid Artery. Journal of Vascular Surgery. 62(6):1521-8. 2015. PMID: 25499709.

**Kamenskiy AV**, Pipinos II, Dzenis YA, Phillips NY, Desyatova AS, Kitson J, Bowen R, **MacTaggart JN**. Effects of Age on the Physiological and Mechanical Characteristics of Human Femoropopliteal Arteries. Acta Biomaterialia. V11. P304-313. 2015. PMID: 25301303.

### Peripheral Arterial Disease

Research is focused on detailed understanding and quantification of the complex mechanical environment of the femoropopliteal arterial segment in order to determine optimal patient and lesion-specific treatment options for patients with Peripheral Arterial Disease. To achieve this researchers are utilizing human cadaver models, mechanical and structural characterization, as well as constitutive and computational modeling.

Researchers have recently received a five-year, $3.5 million grant funded by the National Institutes of Health to find out why stents don't work well for treating peripheral artery disease (PAD).

**Recent Publications**

**Kamenskiy AV**, Seas A, Bowen G, Deegan P, Desyatova A, Bohlim N, Poulson W, **MacTaggart J**. In Situ Longitudinal Pre-Stretch in the Human Femoropopliteal Artery. Acta Biomaterialia. doi: 10.1016/j.actbio.2016.01.002. 2016. PMID: 26766633.

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# Research Highlights

Jung Yul Lim, PhD

## Biomaterials and Mechanotransduction Research

**Jung Yul Lim, PhD**

### Traumatic Brain Injury (TBI) and Neuronal Regenerative Medicine

An in vitro impulsive cell pressurization device is developed to investigate TBI conditions of human neuronal cells. Neuronal regenerative medicine is pursued by utilizing micropatterned biomaterials and by applying cell stretch, fluid flow, and ultrasound to neuronal precursor cells.

### Microfluidics for Bone Cell Mechanotransduction and Stem Cell Migration

A novel multichannel microfluidic device mimicking in vivo micro-flows is designed to test fluid flow effects on bone cells. Stem cell rescue of damaged cells is examined via assessing stem cell migration in a microfluidic channel containing healthy and damaged cells.

### Nanoscale Biomaterials for Stem Cell Osteogenesis and FAK Signaling

MSCs are induced to differentiate into osteogenic fate by culturing on advanced nanostructured biomaterials and the role of focal adhesion signaling (FAK) in this induction is investigated with MSCs displaying FAK-shRNA or overexpression.

### Mechanical Control of Bone and Stem Cell Fate and ROCK Signaling

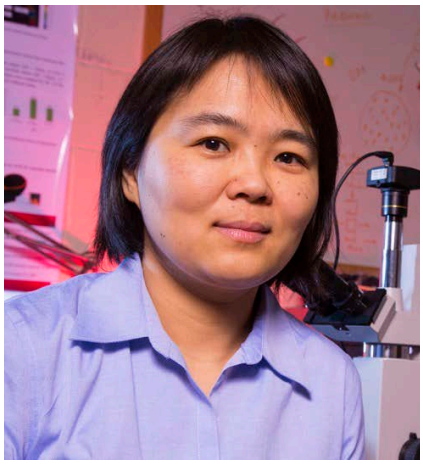
Osteoblastic and stem cells are molecularly manipulated to express altered cell tension signaling, e.g., ROCK, and exposed to fluid flow-induced shear stress and mechanical cell stretch to reveal the role of tension signaling in mechanotransduction during skeletal differentiation.

**Recent Publications:**


Akankshya Shradhanjali,* Brandon D. Riehl,* Il Keun Kwon, **Jung Yul Lim**. Cardiomyocyte stretching for regenerative medicine and hypertrophy study. *Tissue Eng. Regen. Med.* 2015;12:398-409.

Brandon D. Riehl, Jeong Soon Lee, Ligyeom Ha, **Jung Yul Lim**. Fluid-flow-induced mesenchymal stem cell migration: Role of focal adhesion kinase and RhoA kinase sensors. J. R. *Soc. Interface* 2015;12:20141351.

Hillary Stoll, Frederick G. Hamel, Jeong Soon Lee, Ligyeom Ha, **Jung Yul Lim**. Mechanical control of mesenchymal stem cell adipogenesis. *Endocrinol. Metab. Synd.* 2015;4:152.

Linxia Gu, PhD

## Trauma Mechanics Research Initiative

**Linxia Gu, PhD**

Linxia Gu, associate professor of mechanical and materials engineering at UNL, is lead author in a study that examines how improvised explosive devices impact blood vessel networks and can lead to traumatic brain injury. The researchers have authored a study examining, for the first time, how blood vessel networks affect the potential incidence of traumatic brain injury from improvised explosive devices that blanket combat zones throughout the Middle East. The team simulated the force of IEDs by using a "shock tube" to propel 900-mile-per-hour blasts of air at two models of the human head — one featuring blood vessels, the other without. Sensors then recorded levels of strain, or how much these blasts deformed the brain in each model. They specifically measured principal strain — the maximum compression of a material at a specific point — and shear strain — the angular shift of an object's shape. The model embedded with blood vessels suffered almost three times as much principal strain and more than six times as much shear strain in the brain stem. Its corpus callosum, which facilitates communication between the left and right hemispheres of the brain, experienced almost twice the principal strain and nearly 2.5 times the shear strain of its counterpart in the control model. Similarly, the study showed that both types of strain rose in tandem with the density and diameter of blood vessels.


# New Initiatives

## SOX2 Levels Determine the Quality of Pluripotent Stem Cells

**PI: Angie Rizzino, PhD**

**Problem:** There is a pressing need to understand how levels of the stem cell transcription factor SOX2 regulates the behavior of stem cell self-renewal and developmental potential. Recent studies have shown that lowering the levels of the stem cell transcription factor OCT4 in pluripotent stem cells (PSC) promotes self-renewal and eliminates heterogeneity within the stem cell population, but blocks differentiation. Our studies strongly argue that this is also true for SOX2.

**Hypothesis:** The levels of SOX2 in PSC are optimized to support self-renewal without sacrificing their ability to differentiate into a vast array of cells. Lowering the SOX2 levels in PSC will enhance the self-renewal and homogeneity of the stem cell population. When SOX2 levels are allowed to rise, PSC will be primed to differentiate.

**Impact:** The use of PSC in regenerative medicine requires the maintenance of homogeneous populations of stem cells, but also our ability to differentiate PSC into differentiated cells that can be used in replacement therapies in the clinic. Support for our hypothesis will improve the quality of PSC by developing conditions that improve the maintenance of PSC in a homogeneous PSC state.

**Overall objective:** To determine whether lowering the levels of SOX2 eliminates the heterogeneity present in pluripotent stem cells

**Aims:** 1) Determine whether lowering the levels of SOX2 in mouse embryonic stem cells (mESC) reduces heterogeneity in the population by limiting the spontaneous differentiation observed in PSC populations. Initially, this will be achieved by using SOX2 shRNA under the control of an inducible transgene. Going forward, SOX2 siRNA will also be evaluated. 2) Monitor the levels of other key stem cell genes as SOX2 is lowered (e.g. OCT4, Nanog, Essrb, etc.). 3) Determine whether lowering SOX2 in mESC over prolonged periods in culture alters their pluripotency after levels of SOX2 are allowed to return to their original levels. In these pilot studies, we will examine the pluripotency of the cells by monitoring their differentiation when cultured as embryoid bodies.

**Anticipated outcome:** We anticipate that lowering the levels of SOX2 in mESC will reduce the cellular heterogeneity observed in cultured PSC without altering their pluripotency. Importantly, collection of critical preliminary will provide support for competitive NIH grant proposal that will extend our work to human induced pluripotent stem cells.

# New Initiatives

## Regenerative Approaches for Glaucomatous Neuropathy

**PI: Iqbal Ahmad, PhD**

**Problem:** Selective degeneration of optic nerve cells in glaucomatous neuropathy leading to irreversible blindness

**Hypothesis:** Muller glia with stem cell properties can directly differentiate into degenerated neurons.

**Impact:** Muller glia mediated therapeutic regeneration represents a viable and non-invasive alternative to ex-vivo stem cell approach to treat blindness due to glaucoma.

**Overall objective:** To understand the mechanism underlying neurogliogenesis, which will be targeted for activating neurogenic potential in the Muller glial in adult retina.

**Aims of the project:** 1) Examine the role of lin28 and proneural miRNAs in the neurogliogenic decision in the developing retina 2) Examine the role of Lin28 and miRNAs in the directed differentiation of Muller glia into optic nerve cells.

**Anticipated outcome:** Identification of approaches for facile activation of Muller glia along the neuronal lineages.

## Small Intestine Tissue Engineering

**PIs: Jingwei Xie, PhD, Mark Carlson, MD, Bin Duan, PhD, Haitao Wen, PhD, Andrew Dudley, PhD, Jennifer Black, PhD, Jenni Wang, PhD**

**Problem:** Short bowel syndrome (SBS) affects neonates and children and has mortality rates up to 10-30%.

**Hypothesis:** The most promising treatment for SBS remains intestinal transplant, however, overall worldwide survival for isolated small bowel transplantation is around 50% at 5 years.

**Impact:** There is a critical need for engineering small intestine due to a desperate shortage of donors and donor-to-recipient size mismatch.

**Overall objective:** The objective of the projects in this proposal is to understand the mechanism of small intestine regeneration and engineer functional small intestine tissues.

**Aims of the project:** 1) Identify, validate and characterize biomarkers/signaling pathways for small intestine regeneration; and, 2) To engineer functional small intestine tissues for treatment of SBS in the animal model.

**Anticipated outcome:** We anticipate that the identification of biomarkers and mechanisms of small intestine regeneration will lead to more effective ways for engineering functional small intestine tissues for SBS treatment.

## Genetic Dissection of the Role of CBL-family Ubiquitin Ligases in Muscle Atrophy

**PIs: Vimla Band, PhD, and Hamid Band, MD, PhD**

**Problem:** Muscle atrophy (excessive loss of muscle mass) affects millions of patients with chronic disease, worsening treatment outcomes, and as part of aging, contributing to falls and fractures in the elderly. Effective treatments are lacking.

**Hypothesis:** CBL and CBL-B are key mediators of signals that promote loss of muscle mass. Genetic deletion of CBL and CBL-B in muscle tissue will lead to resistance to induction of muscle atrophy by exaggerating signals that help retain and build muscle mass.

**Impact:** Genetic proof for an important role of CBL and CBL-B in muscle atrophy will provide the needed rationale to embark on development of drugs against these enzymes as a therapy for muscle atrophy.

**Overall objective:** Use genetic mouse models established by the investigators to provide evidence that CBL and CBL-gene are needed for induction of muscle atrophy. Show that CBL and CBL-B gene deletion will make muscles resistant to atrophy.

**Aims of the project:** 1) Use isolated human muscle cells and those from our mouse models to show the importance of CBL and CBL-B in muscle atrophy. 2) Engineer a new mouse model in which CBL and CBL-B are only deleted selectively in muscle cells and show that such mice are resistant to muscle atrophy.

**Anticipated outcome:** This study will provide proof of our hypothesis that CBL and CBL-B contribute to muscle atrophy. Our studies will form the basis for future drug screens to identify new drugs to prevent and treat muscle atrophy.

## Engineering Growth Plate Cartilage using Layered Alginate Hydrogel 3-D Matrices

**PIs: Andrew Dudley, PhD, UNMC and Angela K. Pannier, PhD, UNL**

**Problem:** Growth plate cartilage is crucial to skeletal development. Defects in growth plate function due to genetics, metabolic disease radiation and chemotherapy, and high-impact fractures affect skeletal growth lead to deformities, growth arrest, or instability of developing long bones. However, an incomplete understanding of the molecular and cellular processes that produce growth has resulted in few clinical options to treat growth disorders.

**Hypothesis:** Growth plate cartilage is a dynamic, multi-zone, ordered cell array in which disorganized progenitor cells (resting chondrocytes) mature into columnar (proliferative) chondrocytes and then into terminally differentiated, prehypertrophic and hypertrophic chondrocytes.

**Impact:** This project uses a layered alginate hydrogel structure [methodological innovation] to generate a tunable environment in which interaction of signaling pathways and matrix properties on growth plate development can be rigorously interrogated [intellectual innovation].

**Overall Objective:** The objective of this proposal is to use tissue-engineering principles to develop an in vitro model of growth plate cartilage to investigate molecular and cellular mechanisms of growth and growth disorders. We will use the innovative layered alginate gel system that was developed by our laboratories to analyze the effects of gradients of signaling and/or mechanical factors on the spatial organization of gene expression, cell shape and cell organization through the following aims:

**Aims of the project:** 1) To recapitulate the PTHrP-IHH feedback loop within layered alginate beads. We will test the hypothesis that activation of the PTHrP-IHH feedback loop is sufficient to induce zones of maturation in alginate cultures of growth plate chondrocytes, using a novel layered hydrogel scaffold that enables the formation of defined concentration gradients of soluble factors. 2) Investigate interactions between planar cell polarity and matrix properties in chondrocyte arrangement in vitro. We will test the hypothesis that cell adhesion and mechanical properties of the extracellular matrix influence cell morphology and clonal growth of growth plate chondrocytes, by assessing the roles of cell-matrix adhesivity and matrix stiffness on growth plate architecture through analysis of cell morphology and column size/shape.

# New Programs

## Establishment of Bioprinting Core:

The Bioprinting Core will provide access to advanced imaging technologies enabling precise placement of cells, biomaterials, and biomolecules for regenerative medicine-related research. Current tissue engineering and regenerative medicine (TERM) approaches have inherent limitations in producing constructs with accurate anatomical shape and geometry and in precisely controlling microarchitecture and cell/matrix components. 3D bioprinting technology has emerged as a versatile and powerful tool for fabricating 3D tissue and organ analogs.

This core will be run by one of our new faculty member, Dr. Bin Duan, who comes to UNMC from Cornell University, where he has been an American Heart Association Postdoctoral Fellow for the past 2 years. His background is in mechanical engineering and materials science, and he has more than 8 years' research experience. Additionally, he has 29 peer-reviewed publications and is the co-inventor on 2 patents. He has been performing bioprinting for 8 years and will establish and run a core service at UNMC using this equipment.

This technology is combined with computer aided design and manufacturing (CAD/CAM) and advanced imaging technologies and enables precise placement of cells, biomaterials, and biomolecules in spatially predesigned locations in a layer-by-layer manner to form 3D constructs. 3D bioprinted constructs are being developed not only for tissue and organ regeneration and transplantation but also as disease or cancer models for drug discovery and basic research. In addition, the 3D bioprinting technique is promising for the generation of customized implants based on a patients' own medical images. The acquisition of the 3D bioprinter and bioprinting technology will enhance the collaborations between science, engineering, and health disciplines, increase our competitiveness for federal grants, and improve basic, translational, and clinical research in Nebraska.

The bioprinter and bioprinting techniques enable collaborations between investigators in the fields of engineering, regenerative medicine, surgery, cancer, and pharmaceutical science. At the beginning stage, we will focus on four research projects:

1. Osteochondral Regeneration
2. Cardiac Valve Replacement
3. Pancreas Regeneration
4. Cancer Metastasis Model

Many other related projects, like craniofacial and periodontal regeneration, peripheral nerve, and spinal cord regeneration will also be explored using bioprinting techniques.

Four categories of research will be assisted by biomedical applications of 3D bioprinting:

1. 3D bioprinting of tissue engineered constructs
2. 3D bioprinting of functional organs
3. 3D bioprinting of living constructs as disease or cancer models
4. Customized implants

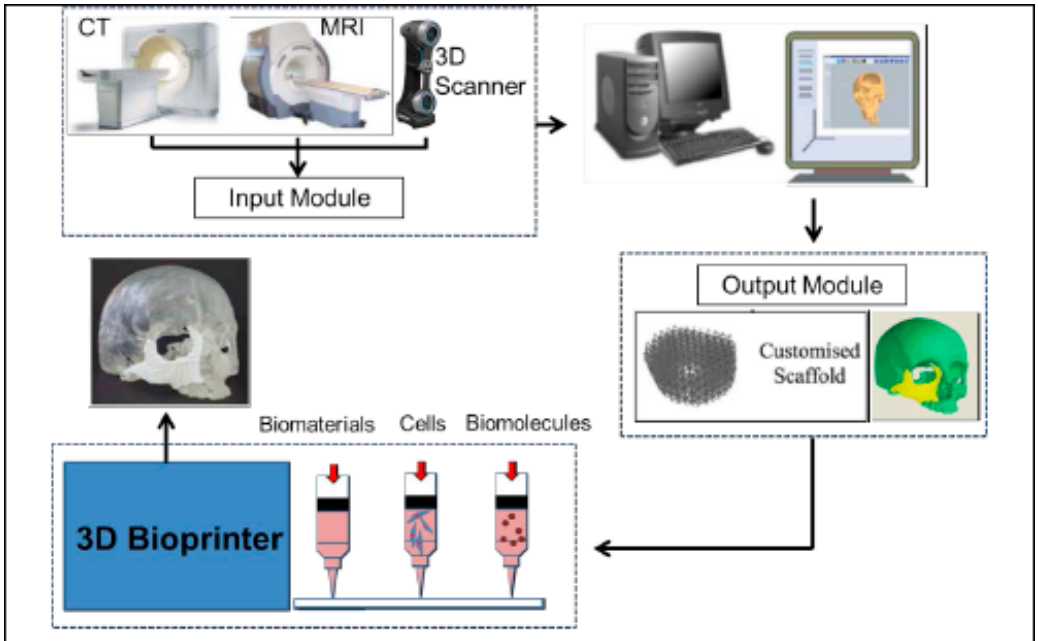



**Figure 1:** Schematic of 3D bioprinting.

# Highlights

## New Post-Doctoral Fellows and Research Coordinators

**Shruthi Aravind, MD**
Joined Mark Carlson's Lab

**Hernan Hernandez, MD**
Joined Iraklis Pipinos' Lab

**Heather Jensen-Smith, PhD**
Joined Nora Sarvetnick's Lab
as Research Coordinator

## Awards

**Devendra Agrawal, PhD**
Harpal Buttar Award for Excellence in Cardiovascular Sciences (2015)

Distinguished Leadership Award, Heart Academy (2015)

**Jennifer Black, PhD**
Distinguished Scientist Award, UNMC (2016)

**Andrea Cupp, PhD**
Irvin T and Wanda R Omtvedt Professor of Animal Science, and also Gamma Sigma Delta (Ag Honorary Society) Excellence in Research Award (2015)

**Hani Haider, PhD**
Leroy Wyman Award by the American Society for Testing and Materials (ASTM International) (2015)

**Philip Hexley, PhD**
ABRF Outstanding Scientist/ Technologist Travel Award (2015)

**Alexey Kamenskiy, PhD**
New Investigator Award, UNMC (2016)

**Srivatsan Kidambi, PhD**
Emerging Innovator Award, UNL Technology Transfer Office (2015)

Trainee Travel Award, 18th International Symposium on Cells of the Hepatic Sinusoid (2015)

President's Choice Presentation, International Symposium on "Cells on the Hepatic Sinusoid" (2015)


Jung Yul Lim (right), associate professor of mechanical and materials engineering, was awarded the Berton Rahn Research Fund Prize by the AO Foundation at a trustees meeting on June 19.

**Jung Yul Lim, PhD**
NSF CAREER Award for the research "CAREER: Adipocytic Mechanotransduction for Obesity" (2015)

Berton Rahn Research Fund Prize, AO Foundation (2015)

**Jason MacTaggart, MD**
Gilmore Award, UNMC (2016)

**David F. Mercer, MD, PhD**
Distinguished Scientist Award, UNMC (2016)

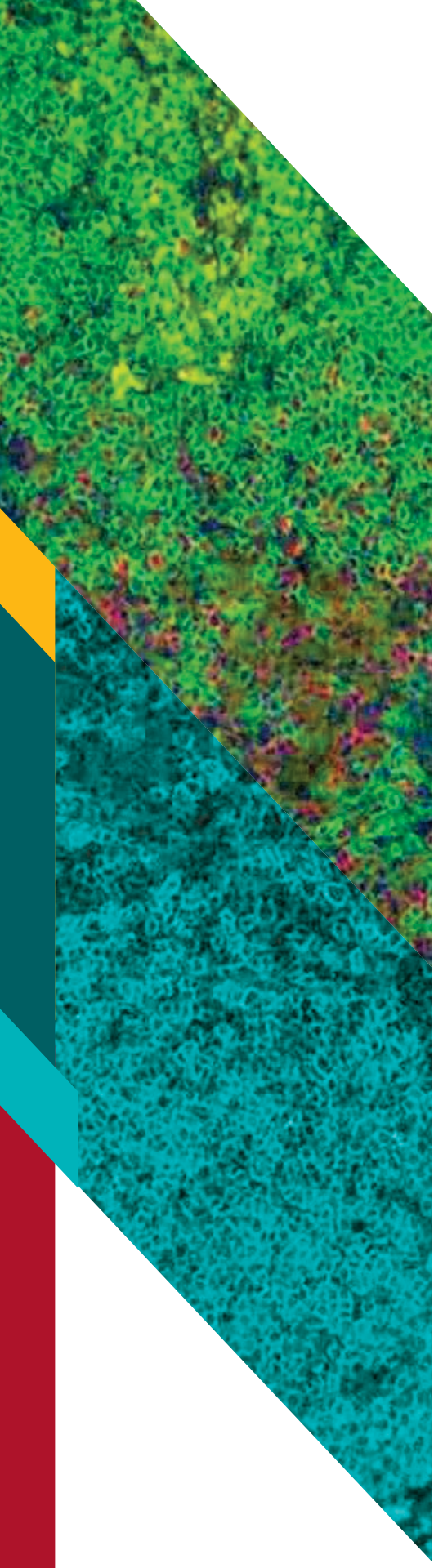
Nebraska Coalition for Lifesaving Cures, Chancellor Emeritus Harold M. Maurer, M.D. and Beverly Maurer Scientific Achievement Award (2015)

**Angie Rizzino, PhD**
Faculty Mentor of Graduate Students Award, UNMC (2015)

**Sarah Romereim, PhD**
(Postdoctoral Fellow of Andrea Cupp) received the Best Postdoctoral Research Poster at the Gil Greenwald Reproductive and Regenerative Medicine Symposia (2015) at the University of Kansas Medical Center, which is a regional reproductive and regenerative medicine meeting.

**Kevin Sargent**
(Graduate Student of Andrea Cupp) Gamma Sigma Delta Outstanding Graduate Student Award (2015), Also Midwest American Society of Animal Science Young Scholar Award (2016) Kevin Sargent's project is the Stem Cell Regenerative Medicine Project on Spermatogonial Stem cells.

**Jingwei Xie, PhD**
New Investigator Award, UNMC (2016)



# New Grants

## Jennifer Black, PhD

NIH T32
Cancer Biology
Training Program
$217,106
July 1, 2015 - June 30, 2020

NIH R21
Evaluating the PKC
Enzyme System in
Human Colon Cancer
$130,500
July 16, 2015 - June 30, 2017

## Andrea Cupp, PhD

Nebraska Department
of Health and Human
Services grant
Mechanisms of VEGFA
Isoforms on germ stem cells
$87,000
July 1, 2015 - June 30, 2016

## Howard Fox, MD PhD

NIH R21
Elucidating the Role of
Exosomal miR-21 in SIV/HIV
Neurological Dysfunction
$125,000
January 1, 2016 -
December 31, 2016

## Hani Haider, PhD

Amedica Corporation
Comparative Testing of
Ceramic Femoral Heads
for Total Hip Arthroplasty
(Amedica Phase I)
$126,246
July 6, 2015 - May 31, 2016

## Sung-Ho Huh, PhD

NIH R00
Mechanisms Regulating
Cochlear Development
$195,575
January 5, 2016 -
December 31, 2016

## Iraklis Pipinos, MD, & George Casale, PhD (Co-PIs)

NIH R01
Ramipril Treatment of
Claudication: Oxidative
Damage and Muscle Fibrosis
$649,599
August 1, 2015 -
March 31, 2020

## Angie Rizzino, PhD

NE DHHS
Cancer Stem Cells
of Pancreatic Ductal
Adenocarcinoma
$87,400
July 1, 2015 - June 30, 2016

NE DHHS
Pancreatic Tumor Cells:
SOX2 and MEK Inhibitors
$50,000
July 1, 2015 - June 30, 2016

## Nora Sarvetnick, PhD

Benaroya Research Institute
at Virginia Mason
Bactericidal Proteins
and Autoimmunity
$118,258
May 1, 2015 - April 30, 2016

Helmsley Charitable Trust
Mechanistic Insights
into the Pathogenesis of
Autoantibody Negative T1D
$163,686
February 1, 2016 -
January 31, 2017

GlaxoSmithKline
Factors Responsible for
Inflammasome Act
$150,000
April 1, 2015 - June 19, 2016

## Haitao Wen, PhD

NIH K01
Role & Mechanism of
NLRX1-mediated Cell
Stress Response in
Insulin Resistance
$117,475
October 21, 2015 -
May 31, 2016

## Jingwei Xie, PhD

Otis Glebe Foundation
Local Sustained Co-
delivery of Vitamin D3 and
Other Immune Boosting
Compounds for Minimizing
Surgical Site Infection
$90,000
February 1, 2016 -
January 31, 2017

## Wanfen Xiong, PhD

NIH R01
Role of early SMC
Phenotypic Switch in
the Aortic Pathology of
Marfan Syndrome
$250,000
January 1, 2016 -
December 31, 2019

## Jialin Zheng, MD

NIH R56
Glutaminase and its
Neurotoxic Link to HAND
$250,000
August 1, 2015 - July 31, 2016

NE DHHS
Estrogen Regulation
of Glutaminase in
Pulmonary LAM
$50,000
July 1, 2015 - May 30, 2016

# Publications

Xia, Xiaohuan, and **Iqbal Ahmad**. "let-7 microRNA regulates neurogliogenesis in the mammalian retina through Hmga2." *Developmental biology* (2015).

**Ahmad, Iqbal**, Xing Zhao, Sowmya Parameswaran, Christopher J. Destache, Jorge Rodriguez-Sierra, Wallace B. Thoreson, Hiba Ahmad, John Sorrentino, and Sudha Balasubramanian. "Direct Differentiation of Adult Ocular Progenitors into Striatal Dopaminergic Neurons." *International journal of stem cells* 8, no. 1 (2015): 106.

Parameswaran, Sowmya, Shashank Manohar Dravid, Pooja Teotia, Raghu R. Krishnamoorthy, Fang Qiu, Carol Toris, John Morrison, and **Iqbal Ahmad**. "Continuous Non-Cell Autonomous Reprogramming to Generate Retinal Ganglion Cells for Glaucomatous Neuropathy." *Stem Cells* 33, no. 6 (2015): 1743-1758.

Shukla, Ashima, Karan Rai, Vipul Shukla, Nagendra K. Chaturvedi, R. Gregory Bociek, Samuel J. Pirruccello, **Hamid Band**, Runqing Lu, and Shantaram S. Joshi. "Sprouty 2: a novel attenuator of B-cell receptor and MAPK-Erk signaling in CLL." *Blood* (2016): blood-2015.

Arya, Priyanka, Mark A. Rainey, Sohinee Bhattacharyya, Bhopal C. Mohapatra, Manju George, Murali R. Kuracha, Matthew D. Storck, Vimla Band, Venkatesh Govindarajan, and **Hamid Band**. "The endocytic recycling regulatory protein EHD1 Is required for ocular lens development." *Developmental biology* 408, no. 1 (2015): 41-55.

William, Basem M., Wei An, Dan Feng, Scott Nadeau, Bhopal C. Mohapatra, Matthew A. Storck, Vimla Band, and **Hamid Band**. "Fasudil, a clinically safe ROCK inhibitor, decreases disease burden in a Cbl/Cbl-b deficiency-driven murine model of myeloproliferative disorders." *Hematology* (2015).

Kumar, Virender, Goutam Mondal, Paige Slavik, Satyanarayna Rachagani, **Surinder K. Batra**, and Ram I. Mahato. "Codelivery of small molecule hedgehog inhibitor and miRNA for treating pancreatic cancer." *Molecular pharmaceutics* 12, no. 4 (2015): 1289-1298.

Yanala, Ujwal R., Roger D. Reidelberger, Jon S. Thompson, Valerie K. Shostrom, and **Mark A. Carlson**. "Effect of proximal versus distal 50% enterectomy on nutritional parameters in rats preconditioned with a high-fat diet or regular chow." *Scientific reports* 5 (2015).

Haverland, Nicole A., Lance M. Villeneuve, Pawel Ciborowski, and **Howard S. Fox**. "The Proteomic Characterization of Plasma or Serum from HIV-Infected Patients." *HIV Protocols* (2016): 293-310.

Villeneuve, Lance M., Phillip R. Purnell, Michael D. Boska, and **Howard S. Fox**. "Early Expression of Parkinson's Disease-Related Mitochondrial Abnormalities in PINK1 Knockout Rats." *Molecular neurobiology* 53, no. 1 (2016): 171-186.

Pendyala, Gurudutt, Palsamy Periyasamy, Shannon Callen, **Howard S. Fox**, Steven J. Lisco, and Shilpa J. Buch. "Chronic SIV and morphine treatment increases heat shock protein 5 expression at the synapse." *Journal of neurovirology* 21, no. 5 (2015): 592-598.

Stauch, Kelly L., Phillip R. Purnell, Lance M. Villeneuve, and **Howard S. Fox**. "Data for mitochondrial proteomic alterations in the aging mouse brain." *Data in brief* 4 (2015): 127-129.

Cserhati, Matyas F., Sanjit Pandey, James J. Beaudoin, Lorena Baccaglini, Chittibabu Guda, and **Howard S. Fox**. "The National NeuroAIDS Tissue Consortium (NNTC) Database: an integrated database for HIV-related studies." *Database* 2015 (2015): bav074.

**Kamenskiy, Alexey V.**, **Iraklis I. Pipinos**, Yuris A. Dzenis, Carol S. Lomneth, Syed A. Jaffar Kazmi, Nicholas Y. Phillips, and **Jason N. MacTaggart**. "Passive biaxial mechanical properties and in vivo axial pre-stretch of the diseased human femoropopliteal and tibial arteries." *Acta biomaterialia* 10, no. 3 (2014): 1301-1313.

Hayward, Stephen L., David M. Francis, Matthew J. Sis, and **Srivatsan Kidambi**. "Ionic Driven Embedment of Hyaluronic Acid Coated Liposomes in Polyelectrolyte Multilayer Films for Local Therapeutic Delivery." *Scientific reports* 5 (2015).

Wilson, Christina L., Vaishaali Natarajan, Stephen L. Hayward, Oleh Khalimonchuk, and **Srivatsan Kidambi**. "Mitochondrial dysfunction and loss of glutamate uptake in primary astrocytes exposed to titanium dioxide nanoparticles." *Nanoscale* 7, no. 44 (2015): 18477-18488.

Daverey, Amita, Allison P. Drain, and **Srivatsan Kidambi.** "Physical Intimacy of Breast Cancer Cells with Mesenchymal Stem Cells Elicits Trastuzumab Resistance through Src Activation." *Scientific reports* 5 (2015).

Shradhanjali, Akankshya, Brandon D. Riehl, Il Keun Kwon, and **Jung Yul Lim**. "Cardiomyocyte stretching for regenerative medicine and hypertrophy study." *Tissue Engineering and Regenerative Medicine* 12, no. 6 (2015): 398-409.

Lee, Jeong Soon, Alexey Lipatov, Ligyeom Ha, Mikhail Shekhirev, Mohammad Nahid Andalib, Alexander Sinitskii, and **Jung Yul Lim**. "Graphene substrate for inducing neurite outgrowth." *Biochemical and biophysical research communications* 460, no. 2 (2015): 267-273.

Riehl, Brandon D., Jeong Soon Lee, Ligyeom Ha, and **Jung Yul Lim**. "Fluid-flow-induced

# Publications

mesenchymal stem cell migration: role of focal adhesion kinase and RhoA kinase sensors." *Journal of The Royal Society Interface* 12, no. 104 (2015): 20141351.

Stoll, H., F. G. Hamel, J. S. Lee, H. A. Ligyeom, and **J. Y. Lim**. "Mechanical Control of Mesenchymal Stem Cell Adipogenesis." *Endocrinol Metab Synd* 4, no. 152 (2015): 2161-1017.

Lee, Jeong Soon, **Jung Yul Lim**, and Jinu Kim. "Mechanical stretch induces angiotensinogen expression through PARP1 activation in kidney proximal tubular cells." *In Vitro Cellular & Developmental Biology-Animal* 51, no. 1 (2015): 72-78.

Zhao, Shijia, Alex Stamm, Jeong Soon Lee, Alexei Gruverman, **Jung Yul Lim**, and **Linxia Gu**. "Elasticity of Differentiated and Undifferentiated Human Neuroblastoma Cells Characterized by Atomic Force Microscopy." *Journal of Mechanics in Medicine and Biology* 15, no. 05 (2015): 1550069.


**Kamenskiy, Alexey**, Andreas Seas, Grant Bowen, Paul Deegan, Anastasia Desyatova, Nick Bohlim, William Poulson, and **Jason MacTaggart**. "In situ longitudinal pre-stretch in the human femoropopliteal artery." *Acta biomaterialia* (2016).

Burton, Mary Jane, Jeffrey R. Curtis, Shuo Yang, Lang Chen, Jasvinder A. Singh, **Ted R. Mikuls**, Kevin L. Winthrop, and John W. Baddley. "Safety of biologic and nonbiologic disease-modifying antirheumatic drug therapy in veterans with rheumatoid arthritis and hepatitis B virus infection: a retrospective cohort study." *Arthritis research & therapy* 17, no. 1 (2015): 136.

Kasputis, Tadas, Alex Pieper, Keith B. Rodenhausen, Daniel Schmidt, Derek Sekora, Charles Rice, Eva Schubert, Mathias Schubert, and **Angela K. Pannier**. "Use of precisely sculptured thin film (STF) substrates with generalized ellipsometry to determine spatial distribution of adsorbed fibronectin to nanostructured columnar topographies and effect on cell adhesion." *Acta biomaterialia* 18 (2015): 88-99.

Martin, Timothy M., Beata J. Wysocki, Tadeusz A. Wysocki, and **Angela K. Pannier**. "Identifying Intracellular pDNA Losses From a Model of Nonviral Gene Delivery." *NanoBioscience, IEEE Transactions on* 14, no. 4 (2015): 455-464.

Martin, Timothy M., Sarah A. Plautz, and **Angela K. Pannier**. "Temporal endogenous gene expression profiles in response to lipid-mediated transfection." *The journal of gene medicine* 17, no. 1-2 (2015): 14-32.

Myers, Sara A., Neil B. Huben, Jennifer M. Yentes, John D. McCamley, Elizabeth R. Lyden, **Iraklis I. Pipinos**, and Jason M. Johanning. "Spatiotemporal Changes Posttreatment in Peripheral Arterial Disease." *Rehabilitation research and practice* 2015 (2015).

George, Nicholas M., Brian P. Boerner, Shakeel UR Mir, Zachary Guinn, and **Nora E. Sarvetnick**. "Exploiting Expression of Hippo Effector, Yap, for Expansion of Functional Islet Mass." *Molecular Endocrinology* 29, no. 11 (2015): 1594-1607.

Harms, Robert Z., Danielle N. Yarde, Zachary Guinn, Kristina M. Lorenzo-Arteaga, Kevin P. Corley, Monina S. Cabrera, and **Nora E. Sarvetnick**. "Increased expression of IL-18 in the serum and islets of type 1 diabetics." *Molecular immunology* 64, no. 2 (2015): 306-312.

Nandi, Shyam Sundar, Michael J. Duryee, Hamid R. Shahshahan, **Geoffrey M. Thiele**, Daniel R. Anderson, and Paras K. Mishra. "Induction of autophagy markers is associated with attenuation of miR-133a in diabetic heart failure patients undergoing mechanical unloading." *American journal of translational research* 7, no. 4 (2015): 683.

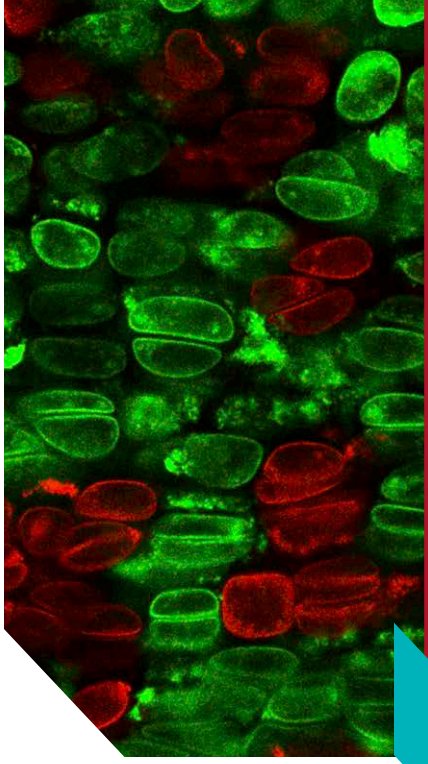
Payne, Jeffrey B., Lorne M. Golub, **Geoffrey M. Thiele**, and **Ted R. Mikuls**. "The link between periodontitis and rheumatoid arthritis: a Periodontist's perspective." *Current oral health reports* 2, no. 1 (2015): 20-29.

Ren, Ke, Hongjiang Yuan, Yijia Zhang, Xin Wei, and **Dong Wang**. "Macromolecular glucocorticoid prodrug improves the treatment of dextran sulfate sodium-induced mice ulcerative colitis." *Clinical Immunology* 160, no. 1 (2015): 71-81.

Zhang, Min, Aihong Song, Siqiang Lai, Lisha Qiu, Yunlong Huang, Qiang Chen, Bing Zhu, Dongsheng Xu, and **Jialin C. Zheng**. "Living cell imaging and Rac1-GTP levels of CXCL12-treated migrating neural progenitor cells in stripe assay." *Data in brief* 5 (2015): 712-716.

Zhang, Min, Aihong Song, Siqiang Lai, Lisha Qiu, Yunlong Huang, Qiang Chen, Bing Zhu, Dongsheng Xu, and **Jialin C. Zheng**. "Applications of stripe assay in the study of CXCL12-mediated neural progenitor cell migration and polarization." *Biomaterials* 72 (2015): 163-171.

# Seminar Series



Each year we invite specialists to present, from within UNMC and from universities nationwide, to increase our knowledge of the field and encourage collaboration and networking. Speakers can give an overview of their research, or if they would like to go over any Aims/Research Strategy for an upcoming grant proposal or any reviews received that is welcomed as well. Our director, Nora Sarvetnick, provides a supportive audience to provide feedback on grant submissions and/or summary statements.

## During 2015 we were fortunate enough to host the following speakers:

**Angie Rizzino, PhD**
Professor, UNMC
*The Dark Side of SOX2: Cancer*

**Wanfen Xiong, MD, PhD**
Assistant Professor, UNMC
*Abnormal Phenotypic Switch of Smooth Muscle Cells in the Aorta of Marfan Syndrome*

**Scott Berceli, MD, PhD**
Professor, University of Florida
*Systems Biology and its Application to Understanding Vein Graft Failure*

**Chris Rogers, PhD**
Chief Scientific Officer, Exemplar Genetics
*Gene-Targeted Pigs: Improved Models for Translational Research*

**Ram Mahato, PhD**
Professor, UNMC
*Polymeric Nanomedicines of Small Molecules and miRNA for treating Liver Fibrosis*

**Angela Pannier, PhD**
Associate Professor, UNL
*Biomaterials for in Vitro Models of Development and Nonviral Gene Delivery*

**Ali Nawshad, PhD**
Associate Professor, UNMC
*Building the Roof of mouth: TGFß3 Signaling in Palate Development*

**Sri Kidambi, PhD**
Assistant Professor, UNL
*What does the Stromal Cells say (to the Tumor Cells)? One Sound That No One Knows...*

**Quan Ly, MD**
Assistant Professor, UNMC
*Novel Therapies for Pancreatic Cancer*

**Melissa Collins, PhD**
Post-Doctoral fellow, University of Missouri
*A Structurally Based Investigation of Vein Graft Remodeling in Mouse Models*

**Mark Carlson, MD, FACS**
Professor, UNMC
*Biomedical Porcine Models at the Omaha VAMC*

**Timothy Wei, PhD**
Professor, UNL
Building Bridges to UNMC
*Endothelial Cell Mechanotransduction and Biofilm Growth through the Eyes of an Aerospace Engineer*

**Andrea Cupp, PhD**
Professor, UNL
*Novel avascular roles for Vascular Endothelial Growth Factor A (VEGFA) Isoforms in Spermatogonial Stem Cell Maintenance in the Testis*

**Sasha Shillcutt, MD, FASE**
Associate Professor, UNMC
*Echocardiography-Guided Hemodynamic Management Strategy to Improve Clinical Outcomes for Elderly Patients with Left Ventricular Diastolic Dysfunction Undergoing Noncardiac Surgery*

**Linxia Gu, PhD**
Associate Professor, UNL
*Mechanics of Arterial Remodeling and Clinical Implications*

**Irving Zucker, PhD**
Professor, UNMC
*Cardiac Sympathetic Afferent Denervation Attenuates Cardiac Remodeling and Improves Cardiovascular Dysfunction in Rats with Heart Failure*

**Stephen Neeley, DSc**
Director, Boys Town
*Measurement and Modeling of Auditory Signal Processing*

**Iraklis Pipinos, MD, PhD**
Professor, UNMC
*Pathogenesis of the Limb Manifestations and Functional Limitations in Peripheral Artery Disease*

**Jingwei Xie, PhD**
Assistant Professor, UNMC
*Co-delivery of Vitamin D3 and Other Immune Boosting Agents for Combating Infection*

**Kota Takahashi, PhD**
Assistant Professor, UNO
*Paradoxical Foot and Ankle Biomechanics During Human Locomotion*

**Jenna Yentes, PhD**
Assistant Professor, UNO
*Locomotor-Respiratory Coupling as a Clinical Tool*

**Gilbert Upchurch, MD**
Professor, University of Virginia
*Gender Differences in Aortic Aaneurysms*

**Michael Moulton, MD**
Professor, UNMC
*Heart Ffailure with a Preserved Ejection Fraction (HFpEF): Pathophysiologic Mechanisms and How Mathematical Modeling Might Shed Some Light*

**Jung Yul Lim, PhD**
Associate Professor, UNL
*Mechanotransduction Approaches Applied to Cells Traditionally Not-Highlighted as Mechanosensitive*

**Robert Norgren, PhD**
Professor, UNMC
*The Production of Large Animal Models of Human Disease with Next Generation Sequencing and Directed Breeding*

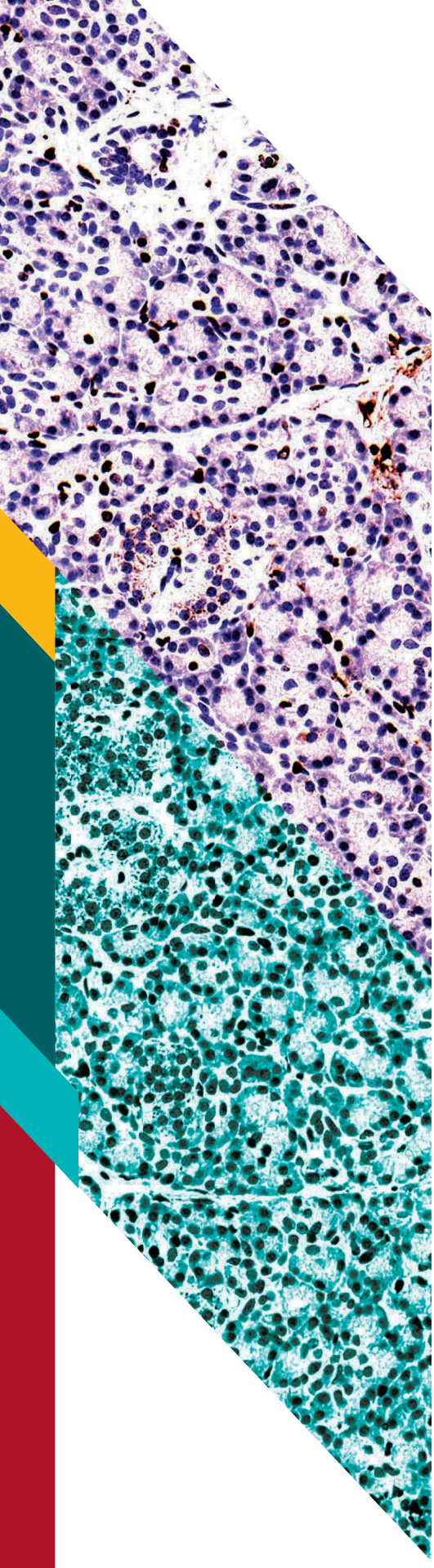
**Haitao Wen, PhD**
Assistant Professor, UNMC
*Metabolic Regulation of the Innate Immunity in Gastrointestinal Inflammation*

**Jennifer Black, PhD**
Professor, UNMC
*The PKC Enzyme System in Epithelial Renewal and Cancer*

**Ben Terry, PhD**
Assistant Professor, UNL
*Using the Gastrointestinal Tract to Implement Disappearable Cyber Physical System Sensors and Actuators*

The audience is a mix of PhD students, post docs, technologists, clinicians, and faculty.

If you are interested in coming to speak or have someone you would like to invite to speak, please contact us.



# Regenerative Medicine Speakers

Bringing in guest speakers who offer new and innovative ideas in regenerative medicine research is an integral part of the program. Guest presentations are made possible with the help of contributions from the Durham Fund.

## The following speakers are presenting in 2016:

### JANUARY 2016

"Molecular Imaging and Engineering of Stem Cells
for Regenerative Medicine"

Zhe Wang, PhD

*Research Fellow, National Institute of Biomedical Imaging and Bioengineering,*
*National Institutes of Health*

Dr. Wang's research looks at the application of molecular engineering methods to generate polypeptides/proteins for 1) nanomedicine, especially in cancer and regenerative medicine and 2) molecular imaging of cellular functions and metabolism. He also studies the integration of chemistry, biology, pharmaceutical science, material science and nanotechnology to design, synthesize and characterize polymeric biomaterials for diagnosis and treatment of human diseases. Additionally, Dr. Wang has been looking at stem cells in relation to traumatic brain injury using animal models.

### FEBRUARY 2016

"Unraveling Endogenous
Cardiac Regeneration"

Johannes (Jop) van Berlo, MD, PhD

*Assistant Professor, Cardiovascular Division,*
*Department of Medicine, University of Minnesota*

Dr. van Berlo's lab studies the mechanisms that drive cardiac regeneration. The ultimate goal of his research is to identify novel therapeutic strategies to enhance cardiac regeneration in patients. They mainly use animal models to study cardiac regeneration and have developed targeted mouse models to perform genetic lineage tracing of cardiac progenitor cells. Broadly, his lab has two independent lines of research, one aimed at studying the role of endogenous cardiac progenitor cells and one aimed at understanding cardiomyocyte proliferation.

## MARCH 2016

"Guiding Cardiomyocytes to a Regenerative State"

Caitlyn O'Meara, PhD

*Post-Doctoral Fellow, Harvard Medical School, Brigham and Women's Hospital, Department of Medicine, Division of Cardiology, Brigham Regenerative Medicine Center*

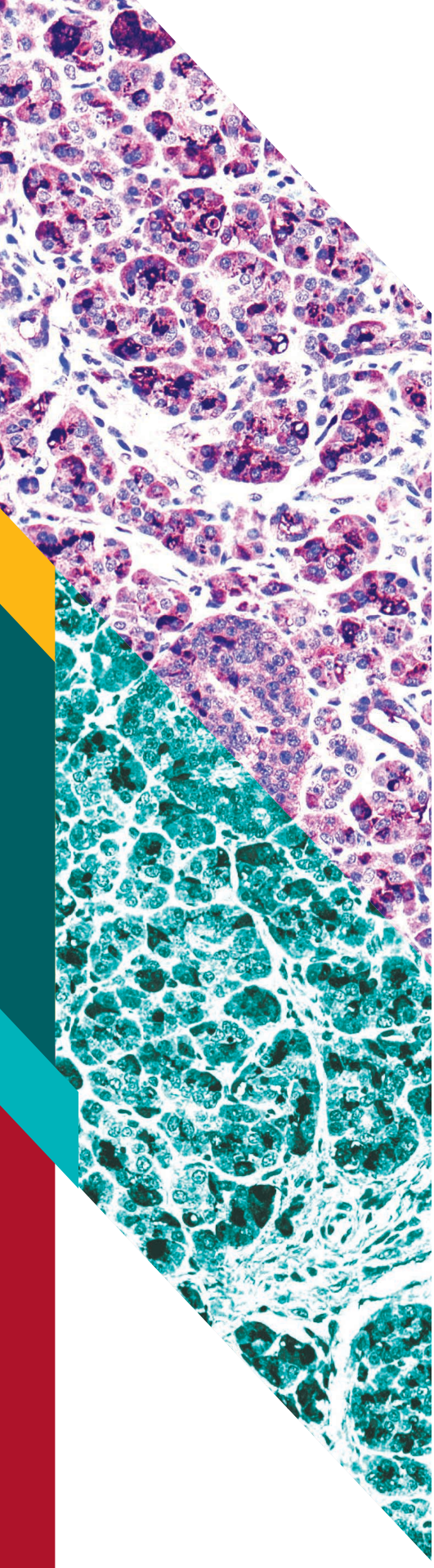
As an independent investigator, Dr. O'Meara's long-term plan is to implement the genetic mapping strategies that she acquired during her graduate school training to identify and validate factors that control mammalian regeneration. For her initial goal, she will employ genetically inbred strains and transcriptional profiling approaches to dissecting differences in mouse and rat heart regenerative potential. The candidate factors identified using these tools will then be validated in vitro and in vivo. Similar techniques have been successfully used to dissect mammalian complex phenotypes such as hypertension, heart failure, cancer, and kidney disease among many others, yet genetic mapping techniques have for the most part not been applied to mammalian regeneration. As she establishes her lab she plans to broaden the scope of mapping projects with new collaborations to use the powerful potential of genetics in the field of regenerative medicine.

## APRIL 2016

Amir Hirsa, PhD

*Professor, Department of Mechanical, Aerospace & Nuclear Engineering, Rensselaer Polytechnic Institute,* New York

Amir H. Hirsa received his B.S. degree in aeronautics from San Jose State University in 1983, and M.S.E. and Ph.D. degrees in aerospace engineering from University of Michigan in 1986 and 1990, respectively. He joined the RPI faculty in 1990. His current research interests are in the area of interfacial hydrodynamics, including monolayer hydrodynamics (such as measurements and modeling of intrinsic interfacial viscosities for lung surfactant applications), and other surface tension effects such as capillarity (e.g. capillary instability and its applications to liquid lenses). His work in the area of bio-fluids also includes studies of protein structure in the presence of flow, especially at the air/water interface. He has made advances to experimental techniques including particle image velocimetry, nonlinear optical technique of second-harmonic generation, as well as Brewster angle microscopy for flowing systems. His lab also works in the area of microfluidics, especially in relation to free surface effects. His research has received funding from the Office of Naval Research (ONR), Defense Advanced Research Projects Agency (DARPA), National Science Foundation (NSF), and National Aeronautics and Space Administration (NASA).



# Regenerative Medicine Speakers

## MAY 2016

### Adrian Gombart, PhD

*Principal Investigator, Linus Pauling Institute*
*Associate Professor, Department of Biochemistry and Biophysics, Oregon State University*

Dr. Gombart's research is focused on understanding the regulation of antimicrobial peptide expression by the vitamin D pathway. When immune cells called macrophages encounter a pathogen and become activated, the vitamin D pathway is turned on, leading to the induction of the cathelicidin antimicrobial peptide if serum levels of vitamin D are sufficient. His lab has developed a transgenic mouse that carries the human cathelicidin gene. Using this model, they are testing the ability of vitamin D to protect against infection by influenza, Salmonella, and Mycobacterium tuberculosis. Vitamin D has been used to treat tuberculosis, and its deficiency is associated with increased risk of tuberculosis. This model will allow them to test the role of vitamin D and cathelicidin during initial infection, latency, and reactivation.

## SEPTEMBER 2016

### Song Li, PhD

*Chancellor Professor, UCLA Biomedical Engineering Program*

Dr. Li's research interests include vascular cell and tissue engineering, stem cell engineering, mechano-chemical signal transduction, biomimetic matrix and molecules, bioinformatic applications in tissue engineering, and molecular dynamics. Professor Li is actively involved in expanding the curriculum and promoting graduate/undergraduate research activities in the area of cell and tissue engineering. Professor Li has introduced a new course on Cell and Tissue Engineering, which is offered in spring semester.

# Opportunities

## Conferences, Meetings, and Workshops

### MAY

**NYSTEM 2016**
May 10-11, 2016
Rockefeller University, NY, NY
Annual meeting of the New York State Stem Cell Science program, featuring keynote Sean Morrison

**10th World Biomaterials Congress**
May 17-22, 2016
Quebec, Canada

11th Annual World Stem Cells Regenerative Medicine Congress
May 18-20, 2016
London, UK

**The Stem Cell Niche–Development & Disease**
May 22-26, 2016,
Hillerød, Denmark

**2016 TERMIS-AP Conference**
May 23-28, 2016
Tamsui Town of New Taipei City

**International Society for Cellular Therapy**
May 25-28 2016
Singapore

### JUNE

**Bioprocessing of Advanced Cellular Therapies**
June 2-3, 2016
London, UK

**Bioinspired Materials Gordon Research Conference**
June 5-10, 2016
Girona, Spain

**EMBL Hematopoietic Stem Cells: From the Embryo to the Aging Organism**
June 3-5
Heidelberg, Germany

**Mouse Development, Stem Cells, & Cancer CSHL**
June 8-28, 2016
Cold Spring Harbor, NY USA

**Germline Stem Cells Conference, Abcam meeting before ISSCR**
June 19-21, 2016
San Francisco, California, USA

**ISSCR 14th Annual Meeting**
June 22-25 , 2016
San Francisco, California, USA

### JULY

**TERMIS-EU Conference**
June 28- July 1, 2016
Uppsala, Sweden

**International Conference on Next Generation Sequencing**
July 21-22, 2016
Berlin, Germany

**Notch Signaling in Development, Regeneration & Disease**
**Gordon Research Conference**
July 31-August 5, 2016
Lewiston, ME, USA

### AUGUST

**Tissue Niches & Resident Stem Cells in Adult Epithelia Gordon Research Conference, Regulation of Tissue Homeostasis by Signaling in the Stem Cell Niche**
August 7-12
Hong Kong, China

**KLF and Sp Transcription Factors in Disease and Regenerative Medicine**
August 7-12, 2016
Snowmass, USA

**Biotechnology World Convention**
August 15-17, 2016
Sao Paulo, Brazil.

### SEPTEMBER

**TERMIS-AM Conference**
September 3-6, 2016
San Diego, USA

**2nd International Conference & Exhibition on Tissue preservation and Bio-banking**
September 12-13, 2016
Philadelphia, USA

**Tissue Science and Regenerative Medicine**
September 12-14, 2016
Berlin, Germany

**11th World Congress on Biotechnology**
September 19-21, 2016
New Delhi, India

**10 Years of IPSCs, Cell Symposia**
September 25-27, 2016
Berkeley, CA, USA

**The Company of Biologists Workshops: From Stem Cells to Human Development**
September 25-28, 2016
Southbridge, MA, USA

**2nd International Conference and Exhibition on Molecular Medicine and Diagnostics**
September 26-28, 2016
Orlando, Florida, USA

### OCTOBER

**International Conference on Cardiovascular Medicine**
October 10-11, 2016
Manchester, UK

**Changing the face of modern medicine: Stem Cells & Gene Therapy**
October 18-21, 2016
Florence, Italy

**Till & McCulloch Meetings 2016**
October 24-26, 2016
Whistler, BC, Canada

**International Conference on Restorative Medicine**
October 24-26, 2016
Chicago, USA

**Cellular Therapies Manufacturing & Clinical Trials**
October 27-28, 2016
Whistler, BC, Canada

### NOVEMBER

**World Congress on Human Genetics**
October 31- November 02, 2016
Valencia, Spain

**12th Biotechnology Congress**
November 28-30, 2016
San Francisco, CA, USA

### DECEMBER

**ASH Annual Meeting**
December 3-6, 2017
San Diego, CA, USA

**International Conference on Histocompatibility and Immunogenetics**
December 5-6, 2016
San Antonia, USA

**2016 World Stem Cell Summit**
December 6-8, 2016
West Palm Beach, FL, USA

# Opportunities–RFAs

NIH NIDDK PA-16-062

***Ancillary Studies in the NIDDK Intestinal Stem Cell Consortium (R01)***

Expiration Date: January 8, 2019

This funding opportunity invites investigator-initiated research project applications for ancillary studies to a major ongoing study, the Intestinal Stem Cell Consortium (ISCC), supported by the NIDDK and NIAID. Research projects should be designed to capitalize on or contribute to the already established ISCC infrastructure and ongoing research to enhance the scientific output of the proposed project and/or the ISCC.

NIH PA-16-040

***Exploratory/Development Bioengineering Research Grants (R21)***

Expiration Date: January 8, 2019

The purpose of this FOA is to encourage submission of EBRG applications which establish the feasibility of technologies, techniques or methods that: 1) explore a unique multidisciplinary approach to a biomedical challenge; 2) are high-risk but have high impact; and 3) develop data which can lead to significant future research. In addition, NIAMS would also like to use the R21 mechanism to stimulate and promote research in building complex 3-dimensional in vitro musculoskeletal and skin tissue models to study developmental biology, physiology, and disease pathogenesis as well as for drug discovery and toxicity studies.

NSF PD 15-1491

***Biotechnology and Biochemical Engineering***

Full Proposal Window: October 1-20, 2016

A quantitative treatment of biological and engineering problems of biological processes is considered vital to successful research projects in the BBE program. The program encourages highly innovative and potentially transformative engineering research leading to novel bioprocessing and manufacturing approaches, and proposals that address emerging research areas and technologies that effectively integrate knowledge and practices from different disciplines which incorporating ongoing research into educational activities.

NIH NIDDK RFA-DK-16-004

***Development of New Technologies and Bioengineering Solutions for the Advancement of Cell Replacement Therapies for Type 1 Diabetes (R43/R44)***

Expiration Date: June 29, 2016

It is necessary to investigate methods to use different cell sources including human progenitor cells and induced pluripotent stem cells as a valid option for cell replacement therapy. Also, further research on the potential use of xenogeneic cells/islets is needed. This RFA encourages the development of techniques to maintain and expand human physiologically responsive insulin-producing cells derived from stem/progenitor cells to make them suitable for cell replacement and disease modeling.

NIH NICHD PAR-13-094 & PAR-13-095

***Differentiation and Integration of Stem Cells (Embryonic and Induced-Pluripotent) Into Developing or Damaged Tissues (R01 and R21)***

Expiration Date: September 8, 2016

The primary focus of this FOA is to promote in vivo studies of stem cells in animal models and in humans (if applicable) to better understand how stem cells function within developing or damaged tissues. The purpose is to gain in-depth knowledge of the mechanisms involved in: progressive differentiation of Embryonic Stem Cells (ESCs) into embryonic lineages, progenitor cells and specialized cell types; adult stem cells/progenitor cells during tissue regeneration and wound healing; and Induced Pluripotent Stem Cells (iPSCs) at the site of injury during stem cell therapy.

NIH NIAAA PA-14-124 & PA-14-125

***Alcohol-Induced Effects on Tissue Injury and Repair (R01 and R21)***

Expiration Date: May 8, 2017

NIAAA is especially interested in integrative research that elucidates alcohol's effects on complex mechanisms of injury and repair that are either common or specific to each organ system. This FOA encourages the study of alcohol's effect on stem cells, embryonic development, and regeneration. Also encouraged are studies on molecular and cellular actions of moderate alcohol consumption. A better understanding of these underlying mechanisms may provide new avenues for developing more effective and novel approaches for prognosis, diagnosis, intervention, and treatment of alcohol-induced organ damage.

NSF PD 14-7479

***Biomechanics and Mechanobiology***

Full Proposal Window: September 1-15, 2016; February 1-15, 2017

This program supports fundamental research in biomechanics and mechanobiology. An emphasis is placed on multiscale mechanics approaches in the study of organisms that integrate across molecular, cell, tissue, and organ domains. The influence of in vivo mechanical forces on cell and matric biology in the histomorphogenesis, maintenance, regeneration, and aging of tissues is an important concern. In addition, the relationships between mechanical behavior and extracellular matrix composition and organization are of interest.

NSF PD 15-5345

***Biomedical Engineering***

Full Proposal Window: Annually, October 1-20, 2016

Projects should include methods, models and enabling tools of understanding and controlling living systems; fundamental improvements in deriving information from cells, tissues, organs, and organ systems; new approaches to the design of structures and materials for eventual medical use in the long-term; and novel methods for reducing health care costs through new technologies.

NSF PD 06-7623

***Biomaterials***

Full Proposal Window: Annually, September 1-October 31, 2016

This program supports fundamental materials research related to (1) biological materials, (2) biomimetic, bioinspired, and bioenabled materials, (3) synthetic materials intended for applications in contact with biological systems, and (4) the processes through which nature produces biological materials. Projects involving in vitro demonstration of biological compatibility and efficacy are appropriate, but the program can support only limited in vivo studies. Tissue engineering and drug/gene delivery projects must have a specific focus on fundamental materials development and characterization.

# Contact

## Mary and Dick Holland
## Regenerative Medicine Program


University of Nebraska Medicial Center
Regenerative Medicine
985965 Nebraska Medical Center
Omaha, NE 68198-5965

402-559-7584 | Fax: 402-559-7521

**Nora Sarvetnick, PhD**
*Director, Regenerative Medicine Program*
*Professor, Surgery-Transplant, College of Medicine*

402-559-6735 | noras@unmc.edu

**Jan Martin, MA**
*Administrator, Regenerative Medicine*

402-559-3803 | jan.martin@unmc.edu

**Jenni Irving, PhD**
*Administrative Project Associate, Surgery-Transplant*

402-559-7584 | jenni.irving@unmc.edu

**Heather Jensen Smith, PhD**
*Research Coordinator, Surgery-Transplant*

402-559-9379 | heather.smith@unmc.edu

**Neha Woods, PhD**
*Research Administrator Specialist, Surgery-Research*

402-559-5540 | neha.woods@unmc.edu

Mary and Dick Holland

University of Nebraska Medical Center