Regenerative Medicine at UNMC

The Holland Regenerative Medicine Program was established at the 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.

“A necessary component for the success of the Regenerative Medicine Program is clinical translation. It’s a delicate balance that requires a multidisciplinary approach” states Nora Sarvetnick, Ph.D., professor in the transplant section of the UNMC Department of Surgery and Director of the Regenerative Medicine Program. Without the help of involved/collaborative clinicians here at UNMC we cannot bring our current research into the clinic. We would like to encourage those interested in Regenerative Medicine to contact us with their thoughts and suggestions. Our goal is to foster collaborations between scientists and clinicians to drive new, innovative techniques that are currently absent in the field.

Dr. Sarvetnick has been working with the Regenerative Medicine Advisory Committee and Faculty to establish directions for the Regenerative Medicine Program as well as recruit potential candidates to fill available faculty positions. “We hope to grow the field of Regenerative Medicine at UNMC, but also give both junior and senior investigators the chance to participate in research and therapy development.”

The Regenerative Medicine Program seeks to establish approaches that generate new therapies for disease. The types of activities undertaken utilize:

- Cellular Therapies, involving both adult and embryonic stem cells
- Translational Research leading to clinical trials
- Restoration with synthetic and cellular components
- Collaboration with Bioengineering Facility at UNL
- Stem Cell Differentiation
- Biotech collaborations
- Induced Pluripotent Stem Cells
Table of Contents

Letter from the Director ..............................................................1
Dedication to Richard Holland ....................................................2
Faculty ..........................................................................................3
Administration Team ...................................................................5
Focus: Mission and Values .........................................................6
Goals 2015-2016 ..........................................................................7
Goals 2016-2017 ..........................................................................8
Research Successes 2016-2017 ................................................9
Development Successes 2016-2017 ..........................................13
  Grants ..........................................................................................13
  Awards .....................................................................................15
  New Additions .........................................................................15
Spotlight: Distinguished Visitors ..............................................16
Appendix A: New Grants .........................................................17
Appendix B: Publications ..........................................................18
Appendix C: Staff and Student Recognitions .........................24

Mary and Dick Holland Regenerative Medicine
2017 Annual Report
Dear Friends,

It is a privilege to serve as the Director of the Holland Regenerative Medicine Program at the University of Nebraska Medical Center. I write to you in this annual report to share some of the program’s successes and our vision for the coming year.

The past year has seen some interesting challenges and also some great successes. The Holland Regenerative Medicine Program continues to become locally significant, but also global in scope and impact. Among our most distinctive and important characteristics is that we are unusually collaborative with numerous program activities, including, weekly seminars, research update talks, incoming speakers, annual retreats, and symposia, which foster a sense of community and provide a foundation for our shared research interests. This last year has seen some fantastic visiting and local speakers in particular, who continue to inspire further collaborative efforts and research directions.

Our mission has always been 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. The last year has seen the introduction of five new regenerative medicine initiatives, which are being given seed funding from the program to foster collaborations and development of these novel research areas. We look forward to further evolving and adding new faculty, initiatives, and collaborations in the coming year with the introduction of new faculty who focus on exciting up-and-coming research, such as organ-on-a-chip technology.

In the next year we are also looking at expanding our resources for graduate students. Our program is uniquely broad and yet intimate. Our more than 40 faculty over the University of Nebraska campuses investigate a diverse range of problems from basic mechanisms in cell biology to translational applications of stem cell biology. We have the infrastructure to maintain a close-knit and supportive learning environment and plan to make this a larger part of our mission. In order to achieve this, in part, we are developing two regenerative medicine courses to be included in the new UNMC umbrella degree granting program, the Interdisciplinary Graduate Program in Biomedical Sciences (IGPBS).

We are also excited to announce the successful launch of our new Bioprinting core. The Bioprinting Core provides 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 I look forward to seeing where this technology and research can take us.

Support continues to be a valuable tool of which we are profoundly thankful. We look forward to continuing to share our research with yourselves and the scientific and educational communities.

Regards

Nora Sarvetnick, PhD, Director of Regenerative Medicine
On August 11th 2016, one of our biggest and longest standing supporters, Richard ‘Dick’ Holland, died following a short illness at the age of 95.

His gifts allowed for the creation of the Mary and Dick Holland Regenerative Medicine Program and words cannot express how much his ongoing support has meant to the success of the program. He always expressed great interest not only in the activities of the program, but the well-being of its members.

He was a champion for science and progress and will be greatly missed. Our condolences go out to his family and friends.
Key Faculty

Nora Sarvetnick, Ph.D., Professor

Sung-Ho Huh, Ph.D., Assistant Professor

Bin Duan, Ph.D., Assistant Professor

Haitao Wen, Ph.D., Assistant Professor

Andrew Dudley, Ph.D., Associate Professor

Jingwei Xie, Ph.D., Assistant Professor
Faculty

University of Nebraska Medical Center
Iqbal Ahmad, Ph.D., Professor, Ophthalmology & Visual Sciences
Hamid Band, M.D., Ph.D., Professor, Eppley Institute
Vimla Band, Ph.D., Professor, Genetics, Cell Biology & Anatomy
Hesham Basma, Ph.D., Instructor, Internal Medicine, Cardiology
Surinder Batra, Ph.D., Professor, Biochemistry & Molecular Biology
B. Timothy Baxter, M.D., Professor, Surgery
Jennifer Black, Ph.D., Professor, Eppley Institute
Brian Boerner, M.D., Assistant Professor, Internal Medicine
Shannon Buckley, Ph.D., Assistant Professor, Genetics, Cell Biology & Anatomy
Keely Buesing, M.D., F.A.C.S., Assistant Professor, Surgery
Mark Carlson, M.D., Professor, Surgery
Howard Fox, M.D., Ph.D., Professor, Pharmacology & Experimental Neuroscience
Hani Haider, Ph.D., Professor, Orthopaedic Surgery
James Hammel, M.D., Assistant Professor, Surgery
Peng Jiang, Ph.D., Assistant Professor, Munroe-Meyer Institute
Peter Kador, Ph.D., Professor, Pharmaceutical Sciences
Anne Kessinger, M.D., Professor, Internal Medicine, Oncology
Brian Lowes, M.D., Ph.D., Professor, Internal Medicine, Cardiology
David Mercer, M.D., Ph.D., Professor, Surgery
Ted Mikuls, M.D., Professor, Internal Medicine, Rheumatology
Ali Nawshad, Ph.D., Associate Professor, Dentistry
Tara Gries Nordgren, Ph.D., Instructor, Internal Medicine - Pulmonary
Jeffrey Payne, D.D.S., Professor, Dentistry
Iraklis Pipinos, M.D., Ph.D., Professor, Surgery
Ruben Quiros, M.D., Professor, Pediatrics Gastroenterology
Richard Reinhardt, D.D.S., Ph.D., Professor, Dentistry
Angie Rizzino, Ph.D., Professor, Eppley Institute
Graham Sharp, Ph.D., Professor, Genetics, Cell Biology & Anatomy
Rakesh Singh, Ph.D., Professor, Pathology and Microbiology
Geoffrey Thiele, Ph.D., Professor, Internal Medicine
Dong Wang, Ph.D., Professor, Pharmaceutical Sciences
Wanfen Xiong, Ph.D., Associate Professor, Surgery
Jialin Zheng, M.D., Ph.D., Professor, Pharmacology & Experimental Neuroscience

University of Nebraska – Lincoln
Nicole Iverson, Ph.D., Assistant Professor, Biological Systems Engineering
Srivatsan Kidambi, Ph.D., Assistant Professor, Chemical & Biomolecular Engineering
Yuguo Lei, Ph.D., Assistant Professor, Chemical & Biomolecular Engineering
Jung Yul Lim, Ph.D., Associate Professor, Mechanical & Materials Engineering
Angela Pannier, Ph.D., Associate Professor, Biological Systems Engineering
William Velander, Ph.D., Professor, Chemical & Biomolecular Engineering
Rebecca Wachs, Ph.D., Assistant Professor, Biological Systems Engineering
Timothy Wei, Ph.D., Professor, Mechanical & Materials Engineering

University of Nebraska at Omaha
Mukul Mukherjee, Ph.D., Assistant Professor, Biomechanics
Sara Myers, Ph.D., Associate Professor, Biomechanics
Nicholas Stergiou, Ph.D., Professor, Biomechanics
Kota Takahashi, Ph.D., Assistant Professor, Biomechanics
Jenna Yentes, Ph.D., Assistant Professor, Biomechanics
Administration Staff

Jenni Irving, Ph.D., Administrative Project Associate

Heather Jensen Smith, Ph.D., Research Coordinator

Neha Woods, Ph.D., Research Administration Specialist
Focus: Mission and Values

Mission
Driven by the needs of patients who seek treatment for their incurable diseases, The University of Nebraska Medical Center has established the 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.

Vision
Envision a world with no donor organ shortage, where patients with diabetes are cured, damaged hearts are repaired, and gastrointestinal birth defects are corrected. Regenerative medicine may make these dreams a reality. The potential outcomes of Regenerative medicine are endless.

Our vision will see that the research and therapies stemming from this project can be taken directly into the clinic to treat those patients who may have no other hope. Therapies being developed today will offer a faster, more complete recovery with significantly fewer side effects or risk of complications.

Focus
Regenerative medicine brings together several different disciplines of science including bioengineering, biology, chemistry, computer science, genetics, medicine, robotics, and many other fields. The regenerative medicine program is focused on uniting these areas as one force to battle disease head on. We look forward to the outcomes this project will create both for patients and UNMC as a center of scientific and clinical excellence.
Goals 2015-2016

• Write a collaborative bioengineering T32 with UNL and UNO
• Develop a bioprinting facility
• Hold two brainstorming sessions that lead to collaborative projects
• Hold an Annual Regenerative Medicine Symposium

Progress

The last year has been a productive and busy one for the Regenerative Medicine Program. We aimed to build our program by establishing new collaborations and facilities, starting work towards a training program for graduate students in translational and regenerative medicine, and holding bigger more integrative events such as the second Regenerative Medicine Symposium.

We have been largely successful in these ventures. In the past year, six new collaborative projects were started with faculty from UNMC, UNL, and the VAMC. These include:

• SOX2 levels determine the quality of pluripotent stem cells; PI: Angie Rizzino
• Regenerative approaches for glaucomatous neuropathy; PI: Iqbal Ahmad
• Small intestine tissue engineering collaborative; PI: Jingwei Xie
• Genetic dissection of the role of CBL; PI: Vimla Band
• Mechanisms of cartilage growth; PI: Andrew Dudley
• Cartilage tissue engineering project; PI: Bin Duan

Additionally we acquired the Bioprinter for the establishment of the Bioprinting Facility, which is headed up by Bin Duan. We successfully obtained an NRI grant for expenses and also hired a technologist specifically for the facility. Collaborations have been started with the Biomechanics Department at UNO, UNL faculty and Children’s Hospital and UNMC staff and faculty are already benefitting from the facility.

In May 2016 we submitted a collaborative bioengineering T32 grant with Howard Fox as PI. This grant is a collaborative venture with UNO and UNL faculty to provide translational opportunities for graduate students related to regenerative medicine. The grant was reviewed in November and received favourable reviews but requires revision. We will be working on resubmission, using the opportunity to incorporate newer faculty and to design a regenerative medicine course as part of the in the Interdisciplinary Graduate Training Program in Biomedical Sciences umbrella.

The second annual Regenerative Medicine Symposium was held in April 2016 at Mahoney State Park and was very successful. One hundred and ten people attended including faculty, staff, students, postdoctoral fellows and members of the public. Thirty posters were presented by students, postdoctoral fellows and collaborators and the annual report for the previous year was published and distributed. We hope to continue this venture in 2017.

The Regenerative Medicine Program has a major focus on cutting-edge research. The Summer Regenerative Medicine Research Program represents a chance for science and engineering undergraduate and/or graduate students to work in the specialty areas of regenerative medicine. These summer opportunities for students allow them to become members of research teams and discover first-hand the spectrum of research activities occurring in the field of regenerative medicine. This year we have had students in many of our labs in the Durham Research Center II.
Goals 2016-2017

• Continue developing a bioengineering training grant
• Develop a regenerative medicine course
• Develop a regenerative medicine conference

We are actively looking for new faculty members to increase the capabilities and research interests of the Regenerative Medicine Program. Specifically, at this time, we are looking for faculty with expertise in the Biomimetic Microsystems platform. We seek faculty applicants to join our interdisciplinary team of biologists and engineers with expertise in the development of these novel “organ-on-a-chip” microsystems technologies. Organ-on-a-chip is a tissue system used to test stem cell therapies and in drug testing. It is a microfluidic cell culture device created with microchip manufacturing methods that contains continuously perfused chambers inhabited by living cells arranged to simulate tissue- and organ-level physiology.

In 2017 we will be instituting a Fall Regenerative Medicine Annual Meeting. This will be aimed at the newer faculty, giving them the opportunity to invite peers, potential collaborators, and reviewers to review their research and present their own.
Research Successes 2016-2017

Study Shows Avenue for Treating Brain Injuries
by John Keenan, UNMC public relations | May 26, 2016

Peng Jiang, Ph.D., assistant professor in the division of Developmental Neuroscience at the Munroe-Meyer Institute, has had a manuscript published in the journal Cell Reports. The study documents the efforts of Dr. Jiang and his co-authors to identify a new treatment for white matter injury in the brain.

While most people are familiar with the term “gray matter,” white matter is an important part of brain function. White matter mainly contains nerve fibers and a substance called myelin, which wraps around nerve fibers to facilitate transmission of nerve impulses. The well-known examples of myelin-loss disorders include multiple sclerosis and neonatal hypoxic ischemic brain injury, which is a leading cause of cerebral palsy.

“Our brain has a very limited regenerative capacity. So in these cells, damage is permanent,” Dr. Jiang said. “But we are developing a new strategy to promote myelin regeneration.”

Dr. Jiang’s study shows that a type of star-shaped brain cell called astrocytes, which can be derived by human-induced pluripotent stem cells (hiPSCs), can act on oligodendrocytes, the myelin-producing cells, to promote their proliferation. This is a process called oligodendrogenesis and results in the generation of new myelin, suggesting that white-matter injuries can possibly be healed.

The “stem cells” Dr. Jiang is using for the work are generated from the skin cells of patients. “Stem cells provide new hope to treat this disease, because stem cells are capable of differentiating into brain cells, and we can use these cells to replace the damaged cells and rebuild the myelin.”

In early cell culture studies, Dr. Jiang’s work compared the effects of hiPSC-derived immature and mature astrocytes on oligodendrocytes, and found that much better than the mature astrocytes, the immature astrocytes promoted proliferation and the maturation of oligodendrocytes, which promote myelination.

“Normally, there are very few maturing oligodendrocytes in the culture,” he said. “After we add the immature astrocytes, a large number of proliferating and maturing oligodendrocytes show up.”

With animal models of white matter damage, they observed that animals who had received the immature astrocyte transplant showed a higher density of myelin and better learning and memory recovery in tests conducted for the study, compared to the control group of animals without transplanted immature astrocytes.

Going forward, Dr. Jiang and his team want to apply this new strategy to different diseases.

“Now we’re testing a neonatal hypoxic ischemic injury model, and we’re also interested in other myelin-loss disorders such as multiple sclerosis and white matter stroke,” he said. “We are also hopeful that this strategy can be applied to other neurodegenerative disorders that involve white matter injury.”
UNMC will Lead Endovascular Training Course
by Tessa Bowen, The National Strategic Research Institute | November 10, 2016

The National Strategic Research Institute (NSRI) at the University of Nebraska recently received a contract funding research for the U.S. Army Medical Research and Materiel Command (USAMRMC).

The NSRI, a University Affiliated Research Center (UARC), is one of 13 established UARCs across the nation, delivering relevant and timely research solutions directly impacting Department of Defense (DoD) operations and national security.

The USAMRMC research contract requests a team from UNMC to further improve a DoD training course designed for medical professionals on an endovascular surgical procedure to control severe bleeding.

The procedure involves passing a balloon catheter from a peripheral artery in the thigh up into the aorta, the largest blood vessel in the body deep in the chest and abdomen. Upon inflation of the balloon intra-abdominal bleeding can be temporarily controlled, maintaining blood flow to the heart and brain until the patient can receive definitive repair of the injury.

“Hemorrhage is a leading cause of potentially preventable death in civilian and military trauma victims,” said Jason MacTaggart, M.D., associate professor, UNMC Department of Surgery. “Control of hemorrhage in the chest and abdomen has traditionally been done only through surgery, with large incisions, in hospital settings. Recently, significant experience has been gained with new, minimally invasive endovascular techniques that allow for rapid control of bleeding with far less physical insult to the patient than standard surgical methods. Most importantly, many of these endovascular techniques have the potential to be applied outside the hospital, in harsh environments such as battlefields, rural and wilderness settings.”

“Currently the endovascular skills to perform these hemorrhage control techniques are possessed primarily by vascular surgeons, radiologists, and other cardiovascular interventionalists,” he said. “However, these providers are not typically on the front lines caring for critically injured, unstable patients in hemorrhagic shock. The goals of the work under this contract are to help disseminate the knowledge and technical skills to perform aortic balloon occlusion to frontline trauma providers, and to study the optimal methods of teaching and practicing the technique.

“The curriculum we are developing at UNMC will help to better prepare trauma providers to save lives, whether on the battlefield or potentially in response to a Weapons of Mass Destruction (WMD) event.”
A UNMC M.D., Ph.D. student was the lead author of a study which found that restoring blood flow to the legs of patients with peripheral artery disease (PAD) may stop the progression of scarring in their leg muscles.

Results of the preliminary research were presented on May 5 at the American Heart Association’s Arteriosclerosis, Thrombosis and Vascular Biology/Peripheral Vascular Disease 2016 Scientific Sessions in Nashville, Tenn.

PAD causes pain and fatigue while walking due to poor blood circulation in arteries that supply blood to the limbs. The decreased blood flow can lead to substantial scarring and damage in leg muscles. There are currently no available treatments once the scarring has occurred. Supervised exercise therapy and revascularization procedures (which reopen or bypass blockages in the blood vessels) may help PAD patients walk further and longer, but it is not known if these treatments affect the scarring process.

Duy Ha, a doctoral candidate in cellular and integrative physiology, was the lead author on the study. Co-authors on the study from UNMC included George Casale, Ph.D., associate professor, surgery-general surgery, and Iraklis Pipinos, M.D., professor, surgery-general surgery.

The study is funded by the National Heart Lung and Blood Institute, National Institute of Aging, and the Charles and Mary Heider Fund for Excellence in Vascular Surgery. The VA Nebraska and Western Iowa Health Care System provided additional support.

“Duy Ha has been an outstanding and highly productive graduate student,” said Irving Zucker, Ph.D., professor and chair of the UNMC Department of Cellular and Integrative Physiology. “His research was a blend of clinical and basic science and shows the value of clinical and basic science departments co-mentoring graduate students.”

Ha won travel awards from the Society for Vascular Surgery and the Atherosclerosis Thrombosis and Vascular Biology Council of the American Heart Association to allow him to share this work at the conference. He was one of only six researchers who were selected to give a moderated poster presentation in which he gave an oral presentation on the poster in front of a crowd of researchers.
New UNMC Partnership

Regenerative Medicine Program collaborators, Keely Buesing M.D., assistant professor of Surgery at UNMC, and Benjamin Terry, Ph.D., assistant professor of mechanical and material engineering at UNL, will be part of a partnership on a new contract. The Office of the Air Force Surgeon General has awarded a contract, valued at $1.3 million, to the National Strategic Research Institute (NSRI) at the University of Nebraska, and UNMC will be a collaborator in the project.

The aim of the contract is to advance the new medical treatment process using microbubble oxygenation, an emerging technology to provide oxygen to patients whose lungs cannot function efficiently due to trauma. Microbubble technology provides rapid oxygen delivery and could provide the levels of blood oxygen needed to survive during emergency patient transport from remote environments far from hospitals.

Mark Borden, Ph.D., associate professor of mechanical engineering at the University of Colorado Boulder and inventor of the oxygen microbubbles, will create a process and system capable of large scale manufacturing. Benjamin Terry, Ph.D., assistant professor of mechanical and materials engineering at the University of Nebraska-Lincoln (UNL) will design and develop a medical device that delivers the oxygen microbubbles to patients. Keely Buesing, M.D., assistant professor of surgery at UNMC, will develop injury models for testing the new technique.

Drs. Terry and Borden invented the new way of administering oxygen to patients who cannot breathe.
Development Successes 2016-2017

New Grants Spotlight

Andrew Dudley, Ph.D.
Associate Professor, Genetics, Cell Biology & Anatomy

Received an NIH R01, 07/01/2016 – 06/30/2021
Title: Cell Biological Mechanisms that Regulate Development of Cartilage Architecture
Our bones grow longer and we grow taller because of specialized cartilage near the ends of our bones known as growth plate cartilage. Although the signaling molecules (hormones and growth factors) that regulate growth have been known for many years, therapeutic interventions are available for only a small number of growth disorders. The goal of our research is to understand how these signaling molecules act on cells in cartilage to promote growth. Unlike most tissues that grow by increasing the number of cells, cartilage grows primarily via depositing a highly structured matrix composed of specific proteins and sugars. The structure of this matrix, in turn, depends on the rotation of pairs of cells to form columns aligned with the direction of growth. Previously we showed that rotation occurs when cells exert force on their environment through cell adhesion and activation of motor proteins. The funded research will determine how signaling molecules regulate cell adhesion and motor protein activity to control the forces that promote column formation. The information obtained from these studies will provide new tools to engineer cartilage that displays appropriate growth and mechanical properties to replace defective tissue in the treatment of growth disorders.

Haitao Wen, Ph.D.
Assistant Professor, Pathology and Microbiology

Received an LB606 Stem Cell Grant
Title: O-GLcNAc Signaling in Intestinal Stem Cell Mediated Epithelial Regeneration
Dr. Haitao Wen has been awarded a Stem Cell Project Award by the Nebraska Stem Cell Research Advisory Committee for his project entitled “O-GLcNAc Signaling in Intestinal Stem Cell Mediated Epithelial Regeneration.” His proposal will investigate the role of a novel post-translational modification of O-Linked N-Acetylglucosamine addition to serine/threonine residues – on STAT3 – to counter activating effects of phosphorylation of STAT3 during intestinal stem cell regeneration using a sepsis model.

Received NIH R01
Title: Immunometabolism in Microbial Sepsis
Dramatic increase in glucose metabolism occurs in immune cells during microbial sepsis. This Proposal aims to study the role and mechanism of two glucose metabolism pathways, the pentose phosphate pathway and the hexosamine biosynthesis pathway, in the innate immune function during microbial sepsis. Understanding the consequence of immunometabolic changes in septic inflammation will be instrumental for the generation of new strategies targeting the prevention and/or treatment of this complex syndrome.
Wanfen Xiong, M.D., Ph.D.  
Associate Professor, Surgery

Received NIH R01  
Title: Role of Early SMC Phenotypic Switch in the Aortic Pathology of Marfan Syndrome

Thoracic aortic aneurysm and dissection (TAAD) are the most deadly manifestation of the inherited connective tissue disorder, Marfan syndrome (MFS). MFS is caused by mutations in the fibrillin-1 gene (FBN-1). Although the molecular and cellular mechanisms driving TAAD remain unclear, transforming growth factor-beta (TGF-ß) has become a major target. However, the most recent data from the largest randomized clinical trial showed that targeting TGF-ß signaling by losartan was not effective in controlling aortic dilatation. We hypothesize: 1) TAAD in MFS results primarily from KLF4 down-regulation and abnormal aortic SMC phenotypic switching from ED14 to PD14 in the mouse; 2) Similar SMC phenotypic changes occur normally in humans over a longer time span; 3) that increasing KLF4 levels during early aortic development will attenuate morphologic changes and prevent aneurysm formation in MFS. Our long-term goal is to identify the role of premature differentiation of aortic SMCs in MFS, to further understand the pathogenesis of other syndromic causes of thoracic aneurysms, and eventually to develop rational therapeutic strategies to prevent and treat TAA.

Nora Sarvetnick, Ph.D.  
Professor, Surgery

Received NIH U01  
Title: Uncovering Pathogenic Anti-bacterial Defense Mechanisms to Identify Novel Targets for Prevention of T1D

While contemporary research has shown Type 1 diabetes (T1D) is associated with intestinal dysbacteriosis and leakage, it is not known whether these factors cause the disease. Establishing a causative link between the onset and progression of T1D and dysbacteriosis is critical for developing effective prevention strategies. The overarching hypothesis of this application is that T1D is preceded by pancreatic bacterial exposure, which promotes an anti-bacterial response, pancreatic inflammation, insulitis, and autoimmunity. This hypothesis was formulated based on our preliminary data demonstrating: 1) heightened anti-bacterial responses in juvenile T1D; 2) pathologic responses by islets to bacteria overrepresented in the T1D microbiome; 3) pancreatic inflammation and insulitis in a mouse model of experimental leakage of bacteria into the pancreas; and 4) blockade of the anti-bacterial response protects islets from insulitis. In aim 1 we will determine whether human T1D development is preceded by a cellular and humoral anti-bacterial response and establish an association with the duodenal microbiome. In aim 2 we will ascertain whether pancreatic exposure to bacteria leads to immune activation, insulitis, and hyperglycemia. To accomplish this task, we have established a novel mouse animal of intestinal dysbiosis and leakage to test therapeutic interventions.

Jingwei Xie, Ph.D.  
Assistant Professor, Surgery

Received NIH R01  
Title: Nanofiber-based Delivery of Combined Immune-modulating Compounds to Minimize Infection and Enhance Wound Healing

Surgical site infections (SSIs) within 30 days of an operation contribute substantially to surgical morbidity and mortality each year. The majority of these infections involve antibiotic-resistant ESKAPE pathogens. These bacteria thrive in healthcare settings and traditional antibiotics cannot kill them as they are either multi-drug or extremely drug resistant. The increasing frequency of these pathogens underscores the priority for developing novel approaches to supplement the current antimicrobial regimens used in the prevention of surgical site and wound infections. To address this research priority, we seek to develop technologies that prevent infections associated with SSIs or traumatic injuries by local sustained co-delivery of vitamin D3 and other immune-boosting compounds for endogenous antimicrobial peptide induction. We expect successful completion of this proposed study to lay the foundation for developing therapeutic anti-infective wound dressings with a new mechanism of action that could greatly speed healing, reduce rates of SSIs in patients post-surgery and possibly decrease development of antibiotic resistance.
Faculty / Staff Awards

New Investigator Award
New Investigator Awards go to outstanding UNMC scientists who in the past year have secured their first independent funding from the National Institutes of Health, the Department of Defense or other national sources. New Investigators also had to demonstrate scholarly activity such as publishing their research and/or presenting their findings at national conventions.

Research Leadership Award
The Research Leadership Award is intended to honor scientists previously recognized as Distinguished Scientists who have a longstanding research funding history, and also serve as research leaders and mentors on campus.

UNL Parents Association for Contributions to Students Award
The awards, presented during a Jan. 29 ceremony, are earned through nominations made from parents of UNL students. Presented annually, the honors provide positive feedback to faculty and staff about their work with students. They also encourage good student and faculty relationships and provide recognition in an area often overlooked in the formal rewards system.

New Additions
Postdoctoral Fellows
Jehan Alam, Ph.D. – Sarvetnick Lab
Prathapan Ayyappan, Ph.D. – Sarvetnick Lab
Michael Ebeld, Ph.D. – Huh Lab
Lina Fu, Ph.D. – Xie Lab
B.Sunil Kumar, Ph.D. – Xie Lab
Oluwatobi Ogun, M.D. – Buesing Lab
Shaohua Wu, Ph.D. – Duan Lab
Erin Wuebben, Ph.D. – Rizzino Lab

PhDs
Sophie Walsh – Iverson Lab
Spotlight: Distinguished Visitors

Adrian Gombart, Ph.D.

May 2016

Principal Investigator at the Linus Pauling Institute and Associate Professor in the Department of Biochemistry and Biophysics at Oregon State University. Dr. Gombart presented on his research on “Nutritional Regulation of Cathelicidin Antimicrobial Peptide Gene Expression.”

Song Li, Ph.D.

September, 2016

Chancellor Professor and Department Head in the Department of Bioengineering at the University of California. Dr. Li presented on his research on the “Mechanobiology of Cell Reprogramming.”

David Ornitz, M.D., Ph.D.

December, 2016

Alumni Endowed Professor in the Department of Developmental Biology at Washington University in St. Louis. Dr. Ornitz presented on his research on “Fibroblast Growth Factors: Critical Regulators of Osteogenic and Chondrogenic Growth Programs.”
During 2016 we were fortunate enough to host the following speakers:

**Nicholas Stergiou, Ph.D.**
Harnessing Movement Variability to Treat and Prevent Motor Related Disorders

**Andrew Dudley, Ph.D.**
Perspectives on Cartilage Engineering

**Jason Johanning, M.D.**
Frail Explorations: Research, QI, Implementation

**Brian Lindegaard Pedersen, M.D. Ph.D.**
Muscle Function in Patients with PAD and Diabetes Type 2 – Implications in Treatment

**Shane Farritor, Ph.D.**
Miniature Surgical Robotics Research at the University of Nebraska

**Aaron Mohs, Ph.D.**
Nanoparticle Formulations of near Infrared Dyes for Image-guided Surgery

**Peng Jiang, Ph.D.**
Pluripotent Stem Cells for Regenerative Medicine and Disease Modeling

**Matthew Zimmerman, Ph.D.**
Role of Redox Signaling Antioxidants in the Brain in the Pathogenesis of Hypertension

**David Oupicky, Ph.D.**
Development of Pharmacologically Active Polymers

**John Ikonomidis, M.D. Ph.D.**
The Role of Membrane Type 1 Matrix Metalloproteinase and Cellular Phenotype Change in the Pathogenesis of Thoracic Aortic Aneurysm

**Alberto Figueroa, Ph.D.**
Surgical Planning in Congenital Heart Disease using Computational Techniques: Procedure Optimization and Clinical Validation

**Aimin Peng, Ph.D.**
Phosphatase 1 Nuclear Targeting Subunit in Cell Cycle Regulation and DNA Repair

**Hernan Hernandez, M.D.**
Improved Physician Ergonomics and Reduced Radiation Exposure with the use the Attachable Radiation Reduction Extension Support Sheath (ARRRESS) for Endovascular Procedures

**Carrie Vyhlidal, Ph.D.**
Drug Metabolism and Precision Medicine: Lessons from CYP3A Enzymes

**Santhi Gorantla, Ph.D.**
Humanized Mice for Regenerative Medicine

**Jenny Wang, Ph.D.**
LGR5 Suppresses Colon Cancer Metastasis

**Melanie Simpson, Ph.D.**
Targeting Steroid Elimination in Prostate Cancer

**Jennifer Keshwani, Ph.D.**
Biomedical Engineering as a Vehicle for Science Literacy

**Aleem Siddique, M.B.B.S.**
Developing a Database, Tissue Bank and Other Projects

**Nick Woods, Ph.D.**
Domainomics Reveals Novel Role of CTDP1 in ICL Repair

**Kishor Bhakat, Ph.D.**
Regulatory Functions of APE1 Acetylation in Cancer

**Bernadette McCrory, Ph.D.**
Protecting Healthcare Workers using Human Factors Engineering

**Bin Duan, Ph.D.**
3D Bioprinting for Tissue Engineering Applications

**HelenMari Merritt-Genore, D.O.**
No Heparin, No Problem? Re-exploring Anticoagulation on ECMO

**Mark Carlson, M.D.**
Disease Modeling With Pigs

**Tara Nordgren, Ph.D.**
Activation and Regulation of Lung-resident Mesenchymal Stem/ Stromal Cells by Organic Dusts

**Mukul Mukherjee, Ph.D.**
The Effects of Sensory Stimulation on Learning Gait Coordination in Health and After Stroke

**Shree Singh, Ph.D.**
Lipolysis Pathway Regulates Survival of Normal and Transformed Stem Cells

**David Ornitz, M.D., Ph.D.**
Fibroblast Growth Factors: Critical Regulators of Osteogenic and Chondrogenic Growth Programs

**Yu Shrike Zhang, Ph.D.**
Integrated Multi-Organ-on-a-Chip Platform

The audience is a mix of Ph.D. 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.
Opportunities

Conferences, Meetings, and Workshops

MAY
International Society for Cell Therapy
Annual Meeting
May 3-6, 2017
London, United Kingdom

Musculoskeletal Regenerative Medicine
and Biology: From Development to
Regeneration
May 4-6, 2017
Washington University in St. Louis,
St. Louis, Missouri

World Advanced Therapies &
Regenerative Medicine Congress
May 17-19, 2017
London, United Kingdom

Advances in Stem Cells and
Regenerative Medicine, EMBL Meeting
May 23-26, 2017
Heidelberg, Germany

JUNE
Bioprocessing of Advanced Tissue
Repair & Regeneration, Gordon
Research Conferences
June 4-9, 2017
New London, New Hampshire

CSHL Mouse Development, Stem Cells,
& Cancer featuring 35th Anniversary
Symposium
June 7-26, 2017
Cold Spring Harbor, New York

ISSCR Annual Meeting 2017
June 14-17, 2017
Boston, Massachusetts

18th Congress of ISDB
June 18-22, 2017
Singapore

Developmental Biology, Gordon
Research Conferences
June 25-30, 2017
South Hadley, Massachusetts

JULY
4th Annual Congress on Drug Discovery
& Designing
July 3-5, 2017
Bangkok, Thailand

AUGUST
6th International Conference on Tissue
Engineering and Regenerative Medicine
August 23-24, 2017
San Francisco, California

CSHL Stem Cell Biology
September 25-29, 2017
Cold Spring Harbor, New York

SEPTEMBER
9th Annual Conference on Stem Cell and
Regenerative Medicine
Sep 25-26, 2017
Berlin, Germany

OCTOBER
7th International Conference on Tissue
Engineering & Regenerative Medicine
October 2-4, 2017
Barcelona, Spain

10th World Congress on Stem Cell and
Biobanking
October 23-24, 2017
Osaka, Japan
Appendix A: New Active Grants

Hamid Band
26-6236-0102-002
University of Nebraska – Lincoln
04/15/2016 – 04/30/2018
Targeting CBL-family Ubiquitin ligases to reverse diet-induced obesity and insulin resistance

Surinder Batra
0047829(127913-1)
University of Pittsburgh
05/17/2016 – 03/31/2017
Validation of Biomarkers for Early Diagnosis and Risk Prediction of Pancreatic Neoplasms

Nicole Iverson
UNL’s Research Council
Faculty Seed Grant

Alexey Kamenskiy
W81XWH-16-2-0034 U.S.Amy
09/30/2016 – 09/29/2019
Rapid acute endovascular management of non-compressible truncal and junctional haemorrhage and long-term analysis of stent-grant durability in young military trauma populations

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26-6236-0102-002
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Angie Rizzino
2017-53 NE DHHS LB506
07/01/2016 – 06/30/2017
Roles of SOX2-High tumor cells in pancreatic ductal adenocarcinoma

Nora Sarvetnick
2-SRA-2016-288-S-B JDRF
09/01/2016 – 08/31/2018
Anti-bacterial factors as biomarkers for predicting T1D in at-risk population

Rakesh Singh
1 R41 TR001902-01A1
Actorius Pharmaceuticals, LLC
09/15/2016 – 08/31/2017
Development of Chol-DsiRNA polyplexes to improve the treatment of breast cancer

Geoffrey Thiele
Bristol-Myers Squibb Company
12/19/2016 – 12/18/2017
Malondialdehyde-acetaldehyde (MAA) antibodies in abatacept treatment response in rheumatoid arthritis (RA)

Dong Wang
1 R01 AI 119090-01A1 NIH NIAID
05/26/2016 – 04/30/2021
Nanomedicine development for systemic lupus erythematosus

Haitao Wen
32675-Y3 NE DHHS – LB606
07/01/2016 – 06/30/2017
O-GlcNAc signalling in intestinal stem cell-mediated epithelial regeneration LB606

Wanfen Xiong
5 R01 HL1 30623-02 NIH NHLBI
01/01/2016 – 12/31/2019
Role of early SMC phenotypic switch in the aortic pathology of Marfan syndrome

Jialin Zheng
1 R01 NS097195-01 NIH NINDS
09/30/2016 – 05/31/2020
Glutaminase and its neurotoxic link to HAND
Appendix B: Publications

Iqbal Ahmad


Hamid Band


Hesham Basma

Surinder Batra


B. Timothy Baxter

**Mark Carlson**


**James Hammel**

**Nico Iverson**

**Peng Jiang**

**Peter Kador**

**Alexey Kamenskiy**


**Anne Kessinger**


**Srivatsan Kidambi**


**Yujuo Lei**

**Jung Yul Lim**

Appendix B: Publications


Brian Lowes


Jason MacTaggart


David F. Mercer

Ted Mikuls


Ali Nawshad

Angie Pannier

Angie Rizzino


Angela Pannier

Jeffrey Payne


Iraklis Pipinos


Richard Reinhardt

Appendix C: Staff and Student Recognition

**Staff**

Jenni Irving, Ph.D.
Administrative Project Associate, Regenerative Medicine
Jenni graduated with her Ph.D. in Medical History from Macquarie University in Sydney, Australia and both a Certificate and Advanced Certificate in Medical Writing and Editing from the University of Chicago. She also completed the 2016 Foundations for Success Series and the 2016-2017 Management Series.

**Students**

Taylor Laughlin, M.S.
Taylor graduated with a Masters from Angela Pannier’s lab in August 2016. She was offered and accepted a position after graduation as a process engineer at Desmet Ballestra North America in Atlanta.

Krishna Sarma, B.S.
Krishna Sarma received first place in the Department of Genetics, Cell Biology and Anatomy for his oral presentation at the MSBRF conference in March 2016. He also received first place in the Department for his poster presentation at the American Physician Scientist Association Regional Meeting in November 2016.

Erin Wuebben, Ph.D.
Erin Wuebben graduated from Angie Rizzino’s laboratory with a Ph.D. in November 2016. She has now joined the Rizzino lab as a Postdoctoral Fellow.
Contact

Mary and Dick Holland
Regenerative Medicine Program

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Omaha, NE 68198-5965
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Fax: 402-559-7521

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Professor, Surgery-Transplant, College of Medicine
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Jenni Irving, Ph.D.
Administrative Project Associate, Surgery-Transplant
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Heather Jensen Smith, Ph.D.
Research Coordinator, Surgery-Transplant
402-559-9379 | heather.smith@unmc.edu

Neha Woods, Ph.D.
Research Administrator Specialist, Surgery-Research
402-559-5540 | neha.woods@unmc.edu

Greg Prorok, M.S.
Research Manager
402-559-6759 | gprorok@unmc.edu
A very special thank you to our donors

The Holland Family &
The Durham Family

Save the Date

Musculoskeletal Regeneration Research Conference

Monday, September 18, 2017

Mary and Dick Holland Regenerative Medicine Program
University of Nebraska Medical Center