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Temple University School of Medicine
and
College of Engineering

The Second Annual TIME Symposium
Temple University Institute for Regenerative Medicine and Engineering

Wednesday, April 30, 2014
10:00 am – 6:00 pm
Lobby and Luo Auditorium, Medical Education Research Building
3500 North Broad Street, Philadelphia, PA 19140

FINAL PROGRAM AND BIOGRAPHICAL NOTES

The Second Annual TIME Symposium
Temple University Institute for Regenerative Medicine and Engineering

With special thanks also for the support of our sponsors

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PROGRAM

09:00-10:00am	*Poster Setup*
10:00 -11:30 am	*Poster Session I*
11:30 - 12:15pm	*Lunch, Poster Session II*
12:15 -12:30 pm	***Welcome*** ***Arthur M. Feldman, MD, PhD*** *Executive Dean, Temple University School of Medicine* *Chief Academic Officer, Temple University Health System* ***Keyanoush Sadeghipour, PhD*** *Dean, Temple University College of Engineering* *Professor, Mechanical Engineering and Bioengineering*
Session I	***Moderator: Steven R. Houser, PhD, FAHA*** *Chair, Department of Physiology,* *Director, Cardiovascular Research Center* *Senior Associate Dean for Research* *Temple University School of Medicine*

12:30 – 1:00 pm ***David Warburton, OBE, DSc, MD, MMM, FRCP, FRCS, FRCPCH***
Director of Developmental Biology and Regenerative Medicine
Director of the California Institute for Regenerative Medicine Training Program and Stem Cell Shared Laboratory
Professor of Pediatrics, Surgery and Craniofacial Molecular Biology
Keck School of Medicine and Ostrow School of Denistry, University of Southern California
"Lung development and regeneration: solutions for the real world"

1:00 - 1:30pm ***Laura Niklason, MD, PhD***
Professor of Anesthesiology & Biomedical Engineering
School of Engineering & Applied Science
Yale University
"Progress in Lung and Vascular Regeneration"

1:30 –2:00pm ***Sharon Gerecht, PhD***
Associate Professor
Department of Chemical and Biomeolecular Engineering
Johns Hopkins University
"Vascular networks from human pluripotent stem cells"

2:00 –2:15pm **Collin Stabler**.
Department of Bioengineering, Temple University
Enhanced Reseeding of Decellularized Rodent Lung Airway and Vasculature.

2:15 -2:30pm **Mohsin Khan**.
Center for Translational Medicine,
Temple University School of Medicine USM.
Embryonic stem cell derived exosomes revive endogenous repair mechanisms in failing hearts

2:30 –2:45pm **Alexander Krupka**.
Center for Neurobiology and Anatomy, Drexel University.
Neurotrophin Producing Autologous Fibroblast Grafts Promote Locomotor Recovery in Sub-chronic and Chronic Models of Spinal Cord Injury

2:45 – 3:20pm *Coffee Break, Poster Session II*

Session II

Moderator: Walter J. Koch, PhD, FAHA
W.W. Smith Chair in Cardiovascular Medicine
Professor and Chairman, Department of Pharmacology
Director, Center for Translational Medicine

3:20 - 3:50pm ***Walter J. Koch, PhD, FAHA***
W.W. Smith Chair in Cardiovascular Medicine
Professor and Chairman, Department of Pharmacology
Director, Center for Translational Medicine
"GRK Inhibition as an Emerging Target for Heart Failure Treatment and Regeneration"

3:50 – 4 :20pm ***Milica Radisic, PhD***
Assoicate Professor
University of Toronto and Canada Research Chair in Functional Cardiovascular Tissue Engineering
"Engineering Microenvironments for Cardiovascular Regeneration"

4:20 – 4:50pm ***Michael E. Selzer, MD, PhD, FRC,***
Director, Shriners Hospitals Pediatric Research Center
Temple University School of Medicine, Philadelphia, PA
Axon "Regeneration And Collateral Sprouting. What Is The Difference And Why Does It Matter?"

4:50 – 5:00pm ***Michele Masucci, PhD***
Interim Vice Provost for Research
Professor of Geography
Temple University, Philadelphia, PA

5:00-6:00pm ***Reception*** *– Lobby of MERB*

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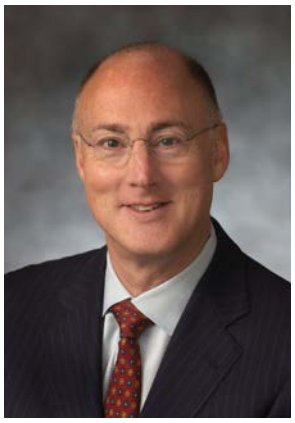


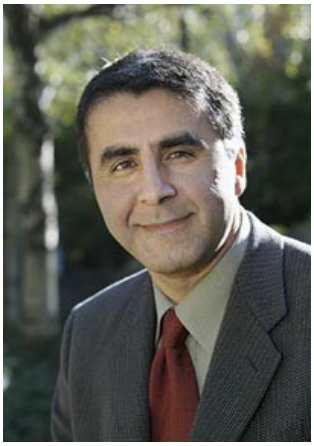
ARTHUR M. FELDMAN, MD, PhD

Executive Dean, Temple University School of Medicine
Chief Academic Officer, Temple University Health System

After receiving his B.A. degree from Gettysburg College, and M.S. and Ph.D. degrees from the University of Maryland, Dr. Feldman served as a post-doctoral fellow in physiology at the Johns Hopkins University School of Medicine. He earned his medical degree from the Louisiana State University School of Medicine and then returned to Johns Hopkins where he served as an intern, resident and cardiology fellow. After joining the faculty in 1985, he was named the Director of the Belfer Laboratory for Molecular Biology of Heart Failure and the Director of the Heart Failure Research Program at The Johns Hopkins University School of Medicine. In 1994, Dr. Feldman joined the faculty at the University of Pittsburgh School of Medicine as the Harry S. Tack Professor of Medicine, Chief of the Division of Cardiology, and Director of the Cardiovascular Institute of the UPMC Health System. In 2002, Dr. Feldman was named the Magee Professor of Medicine and Chairman of the Department of Medicine at Jefferson Medical College. In September, 2011, Dr. Feldman was named the Executive Dean of Temple University School of Medicine and the Chief Academic Officer of Temple University Health System.

Dr. Feldman is a past President of the Heart Failure Society of America and of the Association of Professors of Cardiology. He is the current and founding Editor-in-Chief of *Clinical and Translational Science*. He has received numerous honors including election to Alpha Omega Alpha, the Association of University Cardiologists, the American Society for Clinical Investigation and the Association of American Physicians. In September, 2013, he was awarded the Lifetime Achievement Award by the Heart Failure Society of America and in April, 2014, he was inducted into The Johns Hopkins University Society of Scholars.

His NIH funded research has focused on the molecular pathobiology of heart failure. His lab was the first to recognize the role of G proteins, pro-inflammatory cytokines and vasopressin receptors in the development of the heart failure phenotype. He has translated his basic science work to the clinical arena chairing the steering committees of numerous multi-center clinical trials including PEECH, EMOTE, COMPANION AND WEAR-iT and his research in the molecular biology of heart failure has been published in over 250 peer-reviewed articles. He is the editor of two texts: Heart Failure: Pharmacologic Management and Heart Failure: Device Management. Most recently, he published *Pursuing Excellence in Healthcare: Preserving America's Academic Medical Centers* and *Understanding Health Care Reform – Bridging the Gap between Myth and Reality.* In addition, he was a co-founder and member of the Board of Directors of Cardiokine, Inc., a biotechnology firm.



KEYANOUSH SADEGHIPOUR, PhD

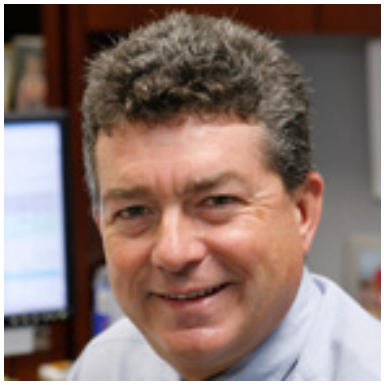
Dean, Temple University College of Engineering
Professor, Mechanical Engineering and Bioengineering *Phone: 215-204-5285*
Email: *keya.sadeghipour@temple.edu*

Keya Sadeghipour graduated from the University of Manchester Institute of Science and Technology (UMIST), Manchester, England, where he obtained his B.Sc. (Honors, 1979), M.S. (1981) and Ph.D. (1984) in mechanical engineering. UMIST is the recipient of the Queen's award in research and the European award in manufacturing. His specialty was in the area of machine tools and manufacturing. After spending three years in the research and industry, he jointed Temple University, Philadelphia, Pennsylvania in 1987, first as an assistant professor and later associate and full professor. He became the chairperson of the Department of Mechanical Engineering in 1996 and acting dean of the College of Engineering in 1998. In 2003, upon the separation of the College of Engineering and the College of Science and Technology, former Temple University President David Adamany appointed Dr. Sadeghipour as the dean of the College of Engineering. In addition to his role as the dean, in 2005 President Adamany and Provost Ira Schwartz asked him to serve as interim dean for the College of Science and Technology while a search for a permanent dean was completed.

The College of Engineering continues to grow very rapidly. In the past five years the undergraduate population has grown by over 70%, from 745 to over 1,277 undergraduates. Research expenditures have doubled in the past three years from $2.3 million to $4.5 million. The College continues to make great strides under the leadership of Dean Sadeghipour.

In addition to his administrative roles, he has guided several research and industrial related projects. He has been involved in receiving over $8 million in funding from various industrial and government sources and has been the principle author of numerous papers in national and international journals and publications. Dr. Sadeghipour is a member and evaluator for the Accreditation Board of Engineering and Technology (ABET) as well as a member of several national and international organizations, such as ASME, IADR and SME. He is also the recipient of the Temple University exceptional research award. Dr. Sadeghipour's current research interests are in the areas of dental materials, bioengineering, and biomechanics systems.

STEVEN R. HOUSER, PhD, FAHA



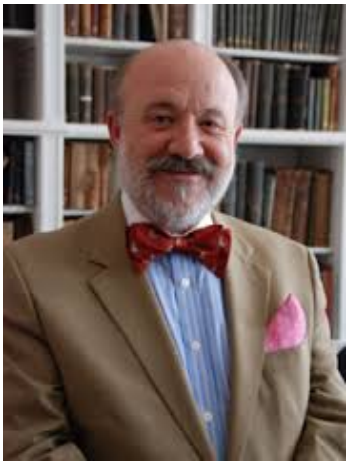
Laura H. Carnell Professor and
Chairperson, Department of Physiology
Director, Cardiovascular Research Center
Senior Associate Dean of Research
Temple University School of Medicine

Steven Houser, Ph.D., FAHA is the Laura H. Carnell Professor of Physiology and Medicine, Director, Cardiovascular Research Center and Chair of Physiology at Temple University School of Medicine. His laboratory has been actively involved in cardiovascular research for over 30 years. His science has focused on the fundamental biology of cardiac myocytes and their response to pathological stress. His research initially focused on the electrical and mechanical properties of the heart and the alterations in these properties that contribute to depressed cardiac performance in heart failure. Dr. Houser was one of the first investigators to develop techniques for isolation of Ca^{2+} tolerant myocytes from large animals. Using these cells, the Houser laboratory defined fundamental aspects of excitation-contraction coupling and Ca^{2+} regulation in the normal heart. The Houser laboratory defined the alterations in myocyte Ca^{2+} regulation that underlie poor contractility and arrhythmias in heart failure. His work has focused on the alterations in myocyte Ca^{2+} regulation that cause depressed contractile reserve in the failing human heart and predispose the heart to arrhythmias.

Dr. Houser's recent research has focused on the idea that heart failure does not result from fundamental defects in myocyte Ca^{2+} regulation, but instead, from Ca^{2+} mediated cell death. Current studies are exploring the idea that the increased Ca^{2+} necessary for the myocytes of the dilated, failing heart to work against increased systolic wall new stress, induces alterations in myocyte Ca^{2+} handling (in an attempt to prevent cellular Ca^{2+} overload) and predisposes the myocyte to apoptosis and necrosis. This new research challenges the dogma that increasing cardiac myocyte Ca^{2+} (and contractility) is a desirable therapeutic strategy. Novel strategies to reduce the excess Ca^{2+} involved in cell death signaling are being studied.

The Houser laboratory is also exploring the idea that heart failure results from a loss of functional cardiac myocytes, and that increasing myocyte number, with cell therapy, can restore more normal function to the failing heart. Approaches that enhance phasic Ca^{2+} entry into cardiac precursor cells are being tested for their cardiogenic potential. The ultimate goal of the work in the Houser laboratory is to develop therapeutic strategies to better treat patients suffering with poor cardiac pump function.

Dr. Houser is an internationally renowned researcher, who has led the way for many important discoveries about the heart disease. His work has been supported consistently by the National Institutes of Health since 1984. Including a grant in 2005 to determine the presence of cardiac stem cells and whether they can be used to fight heart failure. In 2002 he won the University Faculty Award for Research in recognition of his pioneering work. In 2003 he founded the Cardiovascular Research Center. Dr. Houser was named Senior Associate Dean for Research 2003-2007 and was reappointed SADR in 2014. He was selected Chairperson, Department of Physiology in 2006. His research focuses on processes that maintain the electrical and contractile properties of normal heart functions and the defects in these processes that lead to issues such as arrhythmias and congestive heart failure.



DAVID WARBURTON OBE, DSc, MD, MMM, FRCP, FRCS, FRCPCH

Professor of Pediatrics, Surgery and Craniofacial Biology
Director, Developmental Biology and Regenerative Medicine Program
Director, California Institute for Regenerative Medicine Training Program and Shared Laboratory
Saban Research Institute
Children's Hospital Los Angeles
Keck School of Medicine and Ostrow School of Dentistry
University of Southern California

Professor David Warburton is a global thought leader in child health, regenerative medicine and cellular therapeutics. He presently leads the Developmental Biology, Regenerative Medicine and Stem Cell Therapeutics Program at The Saban Research Institute. His personal research program focuses on the lung as the rate limiting step for adaptation of human infants to breathing air. His work and that of his scientific colleagues at TSRI is based on the overarching insight that we all come from one cell and as the information encoded within the genome unfolds, we develop into a multicellular, self-assembling, self-repairing biological machine called a human being. He therefore thinks that developmental studies in children hold the key to inventing future cures for all major diseases that afflict humans over the lifespan. He holds a medical degree as well as a Higher Doctorate of Science from the University of London, is an elected member of numerous Academies and Royal Colleges and has been created an Officer of the Order of the British Empire by Her Majesty, Queen Elizabeth II. He has served on the medical staff of Children's Hospital Los Angeles and the faculty of the University of Southern California for 35 years.

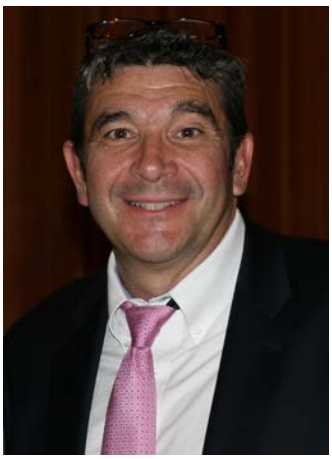
LAURA E. NIKLASON, PhD, MD

Professor of Anesthesiology and of Biomedical Engineering and Residential College Associate Fellow in Faculty of Arts and Sciences
Division Chief, Vice Chair, Research
Yale School of Medicine

Dr. Niklason is a Professor at Yale University in Biomedical Engineering and Anesthesia, where she has been on faculty since 2006. Dr. Niklason's research focuses primarily on regenerative strategies for cardiovascular and lung tissues, and the impact of biomechanical and biochemical signals of tissue differentiation and development. In 2005, Dr. Niklason founded a biotechnology company ("Humacyte, Inc."), which is working to bring engineered tissue replacements to patients. For her work in creating engineered arteries, Dr. Niklason was named one of only 19 "Innovators for the Next Century" by US News and World Report in 2001. Translation of the tissue engineered artery into a clinically applicable therapy was subsequently recognized by the Frost & Sullivan New Product Innovation Award in 2011. She was inducted into the American Institute for Medical and Biological Engineering (AIMBE) in 2008. Dr. Niklason's lab was also the first to describe the engineering of whole lung tissue that could exchange gas in vivo, and this work was cited in 2010 as one of the top 50 most important inventions of the year by Time Magazine.

Dr. Niklason received her PhD in Biophysics from the University of Chicago, and her MD from the University of Michigan. She completed her residency training in anesthesia and intensive care unit medicine at the Massachusetts General Hospital in Boston, and completed post-doctoral scientific training at Massachusetts Institute of Technology. From there she went onto a faculty position at Duke University, where she remained from 1998-2005, before moving to Yale.

WALTER J. KOCH, PhD, FAHA



W.W. Smith Chair in Cardiovascular Medicine
Professor and Chairman, Department of Pharmacology
Director, Center for Translational Medicine

Professor Walter J. Koch (Ph.D., Pharmacology and Cell Biophysics, University of Cincinnati College of Medicine, 1990) is the inaugural holder of the William Wikoff Chair in Cardiovascular Medicine at Temple University School of Medicine. He is the Chairperson of the Department of Pharmacology and Director of the Center for Translational Medicine. Dr. Koch started his career at Duke University Medical Center and Howard Hughes Medical Institute as a postdoctoral fellow (1990-1995) in the lab of Dr. Robert Lefkowitz (Nobel Prize in Chemistry, 2012). He then was recruited to start a molecular cardiovascular biology laboratory in the Department of Surgery at Duke and advanced to tenured Professor in 6 years. In 2003 he was recruited to lead the newly established Center for Translational Medicine and successfully built that Center before moving it to Temple in 2012. The Koch lab studies molecular mechanisms for cardiac injury and repair focusing on G protein-coupled signaling in the heart and also development of novel molecular strategies to repair the heart including gene therapy and stem cell mediated regeneration. His research work has revealed the novel roles G protein-coupled receptor kinases (GRKs) play in cardiac injury and repair. Manipulating these GRKs, and targeting them with therapeutics, could lead to new treatments for heart failure patients. In fact, inhibition of one GRK, GRK2, in the heart has led to the reversal of heart failure. This has been shown to occur by using a gene therapy approach in pre-clinical studies in both small and larger animal models and this methodology is one step away from human clinical trials. Dr. Koch has held at least 4 concurrent NIH R01 grants or their equivalents for over 15 years and currently is the PI of a NIH/NHLBI MERIT Award, and R01, 2 projects on PPG grants and is the PI of another PPG at Temple. This funding has allowed his lab to be leaders in the field of cardiac biology and the lab has over 350 peer-reviewed publications. Numerous awards and honors have recognized Dr. Koch's research over recent years including the International Society for Heart Research 2011 Outstanding Investigator Award, the Jefferson Medical College Inaugural Career Achievement Award in Biomedical Sciences in 2010, the American Heart Association Thomas Smith Memorial Lecture and Award for Cardiovascular Signaling in 2009, and the 10-year MERIT award running through 2019. Dr. Koch naturally is quite active within his field as he has chaired NIH and AHA Study Sections and he is the current Chair of the Basic Cardiovascular Sciences Council of AHA. He also is an Associate Editor of Circulation Research.

SHARON GERECHT, PhD

Associate Professor
Departments of Chemical and Biomolecular Engineering
and Materials Science and Engineering
Johns Hopkins Physical Sciences-Oncology Center
Johns Hopkins University

Dr. Sharon Gerecht is a bioengineer whose research focuses on employing engineering fundamentals to study basic questions in stem cell biology and how to apply them for blood vessel regeneration and repair and the limitation of cancer progression.

Dr. Gerecht earned bachelors and doctoral degrees from the Technion - Israel Institute of Technology. She joined the Johns Hopkins faculty in the in 2007, and is also a lead investigator at the Johns Hopkins Engineering in Oncology Center and a member of the Institute of NanoBioTechnology at Johns Hopkins.

Dr. Gerecht is the recipient of the Allan C. Davis Medal from the Maryland Academy of Sciences (2008), the North America Vascular Biology Organization Junior Investigator Award (2009), the Basil O'Connor Starter Scholar Research Award from the March of Dimes Foundation (2009-2011), the National Scientist Development Award from American Heart Association (2008-2012), the National Science Foundation CAREER award (2011-2016) and W.W. Smith Charitable Trust Heart Research award (2014-2017). She is the author of more than 80 papers and 18 book chapters in her field.

MILICA RADISIC, PhD

Associate Professor
Institute of Biomaterials & Biomedical Engineering
Department of Chemical Engineering and
Applied Chemistry Canada Research Chair (CRC)
Functional Cardiovascular Tissue Engineering
University of Toronto

Dr. Milica Radisic is an Associate Professor at the University of Toronto and Canada Research Chair (Tier 2) in Functional Cardiovascular Tissue Engineering. She obtained B.Eng. in Chemical Engineering from McMaster University in 1999, and Ph.D. in Chemical Engineering from the Massachusetts Institute of Technology in 2004. Before joining University of Toronto in 2005, she was a Postdoctoral Associate at the Harvard-MIT Division of Health Science and Technology. Dr. Radisic has received numerous awards and fellowships, including MIT Technology Review Top 35 Innovators under 35. In 2006, she was featured on the cover of the book *Changing our world: True stories of women engineers*. *Toronto Star* named her one of the people to watch in 2010. She was named "The One to Watch" by the Scientist in June 2010 and she was the recipient of McMaster Arch Award in June 2010. She was a recipient of the Professional Engineers Ontario-Young Engineer Medal in 2011, Engineers Canada Young Engineer Achievement Award in 2012 and Queen Elizabeth II Diamond Jubilee Medal in 2013 and E.W.R Steacie Fellowship in 2014. Dr. Radisic's research is in the field of cardiac tissue engineering and biomaterials. She utilizes heart cells in combination with biomaterial scaffolds and bioreactors to cultivate functional heart tissue in vitro. Her research on electrical field stimulation was featured on the cover of *Toronto Life* in the piece titled *25 Ideas That Are Changing the World* and *Canada AM* in December 2009. Her research interests also include development of injectable biomaterials for cardiac regeneration, microfluidic cell separation and development of in vitro models for cell injection and drug testing. Currently, Dr. Radisic holds research funding from NSERC, CFI, ORF, NIH, CIHR and the Heart and Stroke Foundation. She is a Section Editor-Bioengineering for the International Journal of Artificial Organs and a member of Editorial Board of Tissue Engineering. She serves on CIHR BME panel and TERMIS-AM membership committee. Her research findings were presented in over 100 research papers, reviews and book chapters.

MICHAEL E. SELZER, M.D., Ph.D., FRCP, FAAN, FASNR

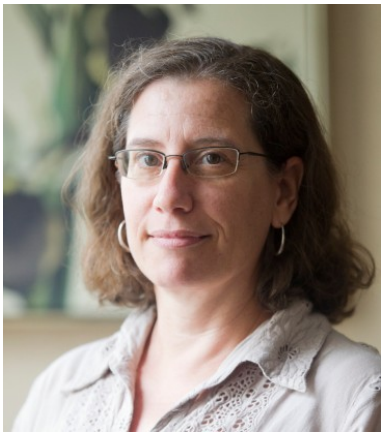
Director, Shriners Hospitals Pediatric Research Center
Temple University School of Medicine, Philadelphia, PA
Professor, Neurology

Dr. Selzer is Professor of Neurology and Director of the Shriners Hospitals Pediatric Research Center at Temple University School of Medicine. He is a leader in the movement to develop a scientific basis for neurorehabilitation, and the immediate past president of the World Federation for NeuroRehabilitation (WFNR). He also served as Director of Rehabilitation Research and Development, Department of Veterans Affairs. After getting an MD and PhD from NYU in 1968, he trained in neurology at the University of Pennsylvania, where he is now Professor Emeritus.

Dr. Selzer's own research focuses on the cellular and molecular mechanisms of axon regeneration after spinal cord injury, using the sea lamprey as an experimental model. He showed that regenerating axons formed functioning synapses selectively with correct neurons across the lesion. More recently, he has emphasized that the mechanisms of regeneration differ from those of early axon development and collateral sprouting. He is the author of more than 100 research articles, reviews and chapters and his two volume Textbook of Neural Repair and Rehabilitation has been influential in defining the scientific basis of this rapidly growing medical field.

Dr. Selzer is a member of the American Neurological Association, and a Fellow of the American Academy of Neurology, the American Society of Neurorehabilitation and the Royal College of Physicians.

MICHELE MASUCCI, PhD



Interim Senior Vice Provost for Research and Graduate Education
Temple University, Philadelphia, PA
Professor and Chair
Dept.of Geography and Urban Studies

Dr. Masucci is a Professor of Geography and Interim Vice Provost for Research at Temple University. She holds a B.S. in Geography and Regional Planning and an M.A. and Ph.D. in Geography from Clark University. Her research expertise is in the areas of Geographic Information systems, Appropriate use of information technologies, water resources management and economic development.

She is the author of two books and over twenty articles and chapters on information, place, and decision making issues, and a large collection of social media works that reflect her role as a public scholar. Her most recent book with Melissa Gilbert is called: Information and Communication Technology Geographies: Strategies for Bridging the Digital Divide. Her work has been supported by over 8 million dollars in federal, state, and foundation grant funding including from the NSF, USDA, USIA, EDA, and Knight Foundation. Her current grant project is called Urban Apps and Maps, a university-wide program and research agenda to investigate the intersection between information technology applications and community economic development.

Her initiatives as the Interim Vice Provost for Research have included developing a policy profile for Temple University with federal funding agencies, a state-wide consortium of research institutions, and the National Academies. These activities aim to amplify the impacts of the large increases in external funding and license revenue that the university has drawn into the research enterprise during the past two years.

PETER I. LELKES, PhD

Fellow, American Institute for Medical & Biological Engineering Laura H. Carnell Professor and Chair, Dept. Bioengineering,
Director, Temple Institute for Regenerative Medicine and Engineering TIME
Professor of Surgery, Temple University Dept. Surgery
Professor of Cancer Biology, Fox Chase Cancer Center
Temple University

Dr. Lelkes joined Temple University in January 2012 as the Laura H. Carnell Professor and Founding Chair of the Department of Bioengineering in the College of Engineering at Temple University. He is also the Inaugural Director of the Institute for Regenerative Medicine and Engineering (TIME) at Temple University's School of Medicine.

Prior to joining Temple University, Dr. Lelkes was from 2000---2011 the Calhoun Chair Professor in the School of Biomedical Engineering, Science and Health Systems at Drexel University in Philadelphia with adjunct appointments in the Departments of Mechanical Engineering and Mechanics (College of Engineering) and Pathology, Biochemistry and Surgery (College of Medicine). Dr. Lelkes was also the Director of the Surgical Engineering Enterprise, one of the major of initiatives of the strategic plan of Drexel University's College of Medicine, the leader for tissue engineering at the Nanotechnology Institute of Southeastern Pennsylvania (NTI), and the Co---Director of PATRIC, the Pennsylvania Advanced Textile Research and Innovation Center, focusing on BioNanoTextiles and Stem Cell Biology.

In his current position, Dr. Lelkes directs an interdisciplinary program in tissue engineering and regenerative medicine, focusing on nanotechnology---based biomaterials and soft tissue engineering, employing developmental biological principles to enhance the tissue---specific differentiation of embryonic and adult stem cells. Dr. Lelkes has organized several Keystone conferences and published more than 175 peer---reviewed papers and 45 book chapters and made more than 400 presentations nationally and internationally.

Dr. Lelkes's basic and translational research has been support by federal (NIH, NSF, NASA, DOE) and state funding agencies, (NTI and Dept. of Commerce, Tobacco Settlement Funds) and private Foundations, including the Coulter Foundation.

Dr. Lelkes has been received numerous honors and awards, nationally and internationally. Amongst them a Forchheimer Visiting Fellowship at the Hebrew University, Jerusalem, Honorary Professorships at The University of Applied Sciences Aachen, Germany and the Changchun Institute of Polymer Chemistry and Physics, Chinese Academy of Sciences, and a Distinguished Visiting Fellowship of the Royal Academy of Engineering at Imperial College, London, UK. In 2011 he was inducted as a Fellow of the AIMBE (American Institute for Medical and Biological Engineering) and received the 2012 Ben Franklin Key Award from IEEE, the Institute of Electrical and Electronics Engineers.

ABSTRACTS OF INVITED TALKS

"Lung development and regeneration: solutions for the real world"

David Warburton, PhD
University of Southern California

The lung develops from a few stem and progenitor cells lying in the floor of the primitive pharynx. Over the course of the first two decades of human life it expands into a gas diffusing organ with an extremely thin yet huge surface area fore diffusion that scales with body size and oxygen demand. This process is controlled by finely coordinated crosstalk between compartments including epithelium, mesenchyme, endothelium, nerves and lymphatics. In this talk we will discuss new ways of looking into the development and involution of alveolar structure as well as genetic and environmental factors that impede this process and which can also accelerate its involution over the subsequent decades of life. We will then turn our attention to possible cell based therapeutic solutions for certain alveolar lung diseases.

"Progress in Lung and Vascular Regeneration"

Laura E Niklason PhD, MD
Yale University

Cardiovascular regenerative medicine has taken many avenues over the past three decades. One approach currently in clinical trials does not require any cells from the patient, and is an engineered tissue that is available "off-the-shelf".

Studies in vascular tissue mechanics showed several decades ago that the bulk of the mechanical properties of arteries derived not from the cellular components, but from the collagen- and elastin-based extracellular matrix. Using this principle, we have utilized banked human vascular smooth muscle cells to engineer implantable arteries. These cells are cultured in a bioreactor under conditions of biomimetic pulsatile strain, and in the presence of multiple growth factors and biochemical supplements that support collagen synthesis. After a 2-month culture period, the engineered arteries are then carefully decellularized, leaving behind an acellular, human collagenous matrix. This matrix has been tested as a 6-mm arterio-venous graft in baboons without any immunosuppression, and has shown excellent function out to 6 months. Based upon these primate data, human studies of the acellular graft conduit in dialysis patients were initiated in December 2012. Early results show mechanical durability and an ability to use the grafts for arteriovenous access in hemodialysis.

The decellularization approach has also allowed us to generate scaffolds to support whole lung regeneration. Repopulation of the acellular lung matrix with mixed populations of neonatal lung epithelial cells results in regio-specific epithelial seeding in correct anatomic locations. Survival and differentiation of lung epithelium is enhanced by culture in a biomimetic bioreactor that is designed to mimic some aspects of the fetal lung environment, including vascular perfusion and liquid ventilation.

"GRK2 Inhibition as an Emerging Target for Heart Failure Treatment and Regeneration"

Walter J. Koch, PhD, FAHA
Temple University School of Medicine

We have spent the last two decades investigating novel molecular targets for correcting ventricular dysfunction in heart failure. We have identified the G protein-coupled receptor (GPCR) kinase-2 (GRK2) as such a target. We have shown that inhibiting the activity of this kinase or genetic deleting this kinase in the heart can prevent and reverse heart failure in mouse models. Moreover, a gene therapy approach with a peptide inhibitor of GRK2 (βARKct) has been used in several small and large animal models to rescue heart failure. This includes a recent study in a pre-clinical pig model of heart failure and βARKct gene delivery reversed ventricular dysfunction and caused reverse remodeling. A clinical trial is being planned and these studies will be presented. Moreover, we have recent unpublished data suggesting that when GRK2 is lower or inhibited in myocytes there is increased new myocyte formation and potential stem cell mediated regeneration. In addition to a gene therapy approach for GRK2 inhibition we are pursuing small molecule pharmacological inhibition and recent studies have shown the FDA approved anti-depressant drug paroxetine is a specific GRK2 target outside its actions to prevent serotonin re-uptake. We now have unpublished results that will be presented at this meeting that paroxetine can reverse heart failure in an animal model and this therapeutic effect is independent to its CNS effects. This paves the way for paroxetine derivatives and other small molecules to target GRK2 for future heart failure therapy.

"Vascular networks from human pluripotent stem cells"

Sharon Gerecht, PhD
Johns Hopkins University

Constructing a functional human vasculature is crucial for the success of tissue regenerative therapies. While endothelial cells, which comprise the vasculature's inner lining, can form nascent networks, these structures regress without the recruitment of perivascular cell that surround the endothelium, stabilize and mature the network. Human pluripotent stem cells offer a unique opportunity to derive vascular cells from a common cell source. We present a step-wise and robust method to guide the derivation of endothelial and perivascular cells. We further define the repertoires of functional phenotypes specific for each of the human vascular cell types. Finally, we engineer three-dimensional human vascular networks in synthetic matrix that survive implantation, integrate with the host vasculature, and establish blood flow. Human PSC-derived vascular cells are useful for the study and use in basic and translational research.

"Engineering microenvironments for cardiovascular regeneration"

Milica Radisic, PhD
University of Toronto

Engineering effective therapies for heart disease will require restoration of beating myocardium as well as revascularization of the injured or impaired area. Since human postnatal cardiomyocytes are terminally differentiated, it is not possible to obtain these cells and expand them from biopsies of primary tissue. Recent advances in stem cell biology and development of directed differentiation protocols enable derivation of cardiomyocytes from human pluripotent stem cells (hPSC). However, hPSC-derived cardiomyocytes are reflective of very early human development, limiting their utility in the generation of in vitro models of mature myocardium suitable for drug or restoration of adult hearts. We developed a new platform that combines three-dimensional cell cultivation in a microfabricated system with electrical stimulation to mature hPSC-derived cardiac tissues. We utilized quantitative structural, molecular and electrophysiological analyses to elucidate the responses of immature human myocardium to electrical stimulation and pacing. We demonstrated that the engineered platform allowed for the generation of 3-dimensional, aligned cardiac tissues (biowires) with frequent striations. Biowires submitted to electrical stimulation markedly increased myofibril ultrastructural organization, displayed elevated conduction velocity and altered both the electrophysiological and calcium handling properties versus non-stimulated controls. These changes were in agreement with cardiomyocytes maturation and were dependent on the stimulation rate. We will also discuss approaches to vascularizing cardiac tissue by control of substrate topography.

"Axon Regeneration and Collateral Sprouting.
What is the Difference and Why Does It Matter?"

Michael Selzer, MD, PhD
Temple University School of Medicine

In response to injury in the central nervous system, severed axons try to regenerate but this is not successful in humans and other mammals. At the same time, spared axons sprout collaterals near the denervated targets to compensate for the loss of the injured axons. Although sprouting can support some functional recovery, it is insufficient to restore normal function, especially when the injury is severe, *e.g.*, after complete spinal cord injuries. Research at the Shriners center suggests that the mechanisms of these two modes of axon growth are different. Many proposed treatments address mechanisms and are based on *in vitro* models that are more relevant to sprouting than regeneration. This could have important consequences for clinical trials currently underway to enhance regeneration after spinal cord injury and other neurological disorders.

ABSTRACTS OF POSTERS

1. Mario Mata. Bioengineering Department. TU

Airbrushing of 3D Scaffolds for Tissue Engineering

Authors: Mario Mata, Yah-el Har-el and Peter I. Lelkes

Affiliations: Dept. Bioengineering, College of Engineering, Temple University Philadelphia, PA 19122

Tissue engineers use nanofibrous scaffolds to emulate the fibrous nanostructure of native extracellular matrix. The most common approach for obtaining nanofibers for tissue engineering scaffolds is electrospinning. However this system is plagued with limited deposition rate, operator hazard, and highly restricted target design. Airbrushing of a polymer solution can avoid most of these issues, while also reducing operating costs and has been proven to yield fibers of similar morphology and dimensions to fibers produced by electrospinning. Airbrushing uses a device with an annulus nozzle, and a process where_ the polymer solution is injected into a stream of flowing air to produce fibers. In this study we explored the versatility and usefulness of airbrushing with the intent to implement this technique for use in engineering three-dimensional scaffolds for tissue engineering applications. In developing a methodology for the airbrushing technique to fabricate fibrous biocompatible scaffolds with similar morphological and mechanical properties to electrospun scaffolds. We sprayed two polymers: polystyrene (PS), and poly (lactic-co-glycolic anhydride) (PLGA) at concentrations from 10-20%w/v utilizing a range of solvents including: Tetrahydrofuran (THF), Dimethylformamide {DMF), and Dichloromethane (DCM). Other optimized parameters included distance between nozzle and target, air pressure, and needle placement. The results demonstrate that not only could nanofibrous scaffolds be airbrushed, but the process is much faster, and more efficient than electrospinning at lower cost initial investment than electrospinning.

2. Kathleen Keefe. Neuroscience/Shriner's Pediatric Research Center. TUSM

The role of mTOR and STAT3 in the intrinsic growth of rubrospinal neurons

Authors: Kathleen M. Keefe, Yingpeng Liu, George Smith

Affiliations: Neuroscience/Shriner's Pediatric Research Center

It is well known that regeneration in the mature central nervous system (CNS) is rare. In order to repair damage with sufficient vigor to re-establish functional connections, the neuronal cell body must be able to turn on genes needed to form new growth cones, produce proteins and growth factors, and elongate and repair damaged axons. Adult CNS neurons are particularly resistant to this type of activation, but there is evidence to show that these 'growth programs' can be stimulated in the right circumstances. In this study, we explore upregulation of growth programs in rubrospinal neurons via stimulation of the mammalian target of rapamycin (mTOR) and signal transducer and activator of transcription 3 (STAT3) pathways. This is accomplished via injection of adeno-associ ated viruses (AAVs) encoding ras homolog enriched in brain (AAV-Rheb), a direct positive regulator of mTOR, and AAV-STAT3, unilaterally into the red nucleus of a rat lesion model. At 5 weeks post-injury, we found that animals injected with AAV-Rheb/AAV-Stat3 showed greater incidences of regrowth such as sprouting, abnormal axon morphology, and growth into the lesion cavity than controls injected with only AAV- GFP. This study highlights the importance of mTOR and STAT3 in axonal growth after injury.

3. Collin Stabler. Department of Bioengineering**.** TU

Enhanced Reseeding of Decellularized Rodent Lung Airway and Vasculature.

Authors: Collin Stabler[1], Shimon Lechtl,Moustafa Barakat[1], Luiz Carlos De Caires Jr.[2], Alexis Rylander[1], Rachel Chiaveremt, Edward Schulman[3], Cezary Marcinkiewicz[1], Peter Lelkes[1]•

Affiliations: [1]Department of Bioengineering, Temple University, Philadelphia, PA. [2]Federal Uniyersity of Juiz de Fora, Brazil. [3]Division of Pulmonary, Critical Care and Sleep Medicine, Drexel University College of Medicine, Philadelphia, PA.

Whole lung engineering with decellularization technology is being explored as an alternative to normal lung transplant. However, repopulation of decellularized lung scaffolds (DLS) is limited due to alterations in the repertoire and ratios of the residual extracellular matrix (ECM) proteins, characterized by e.g., the retention of type I collagen and loss of glycoproteins. We hypothesized that pre-treatment of decellularized matrices with defined ECM proteins, which match the repertoire of integrin receptors expressed by the cells to be seeded (e.g., embryonic stem cells, microvascular endothelial cells) can increase the efficacy of the reseeding process. To test this hypothesis, we first determined the integrin receptors profile of mouse embryonic stem cells (mESCs). Mouse ESCs express a3, a5, a6, a9 and (β1, but not a1,a2 and a4 integrin subunits, as established by Western blotting and adhesion to laminin and fibronectin, but not to collagens type Iand IV. Conversely, the integrin profile of Lung Microvascular Endothelial Cells (LMVECs) allows for attachment to the collagens. Reseeding of DLS with mESCs was inefficient (6.9 ± 0.5%), but was significantly enhanced (2.3 ± 0.1 fold) by pre-treating the scaffolds with media conditioned by A549 human lung adenocarcinoma cells, which we found to contain ~5 μg/ ml laminin. With LMVECs the efficiency of initial attachment was unaffected by coating, but the ability to spread after attachment was enhanced. Furthermore, pre-treatment with A549-conditioned media and optimization of seeding parameters (e.g., volume, flow rate, ventilation) resulted in a significantly more uniform distribution of the seeded mESCs and LMVECs throughout the engineered airways and vasculature respectively as compared to untreated DLS. Our study may advance whole lung engineering by stressing the importance of matching the integrin receptor repertoire of the seeded cells and the cell binding motifs of DLS.

4. Riddhi Gangolli. Department of Bioengineering. TU

Regenerative Endodontics: Tailoring porous degradable biomaterials for guided pulp regeneration

Authors: Riddhi Gangolli[1] BDS MS,Peter Lelkes[1], PhD,Maobin Yang[2],DDS, MS, PhD

Affiliations: [1]Department of Bioengineering, College of Engineering, Temple University
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Background: Regenerative Endodontics (RE) is a biologically based procedure to create new pulp-dentin complex in the root canal system. RE applies all the principles of regenerative medicine and tissue engineering, utilizing a combination of stem cells, three dimensional scaffolds and growth factors. A major challenge of current RE is the lack of a permissive scaffold to spatially control and support dentinogenesis and angiogenesis. The purpose of this study was to use different polymer processing techniques to produce a biodegradable porous scaffold for the regeneration of pulp-dentin complex, evaluate the micro-structures of these scaffolds, and test the cytocompatibility.

Materials and Methods: We used two methods, solvent free melt molding and solvent casting processes, respectively, to develop a PolyQactlc-co-glycolic) acid (PLGA) based scaffold. Different parameters such as polymer/solvent concentration, porogen incorporation and melt molding temperatures were tested. Pore morphology was analyzed by scanning electron microscopy (SEM). To test the cytocompatibility, dental pulp stem cells (DPSC) were loaded on the scaffolds and cultured up to 7 days. SEM and Laser Scanning Confocal Microscopy (LSCM) were used to analyze cell survival and proliferation.

Results: The final scaffolds were 0.15 ± 0.25mm to 15± 0.15mm thick. Compared to the solvent free melt molding method, the solvent casting methods using PLGA/dimethyl sulfoxide (DMSO) provided better cytocompatibilty and better porosity for pulp-dentin regeneration. In addition, the porosity and pore structures can be tailored and controlled by adjusting processing parameters such as polymer/solvent concentration and porogen incorporation.

Conclusion: PLGA/DMSO based scaffold created by solvent casting process provides a very promising scaffold for pulp-dentin complex regeneration.

5. You Song. Department of Bioengineering. TU.

Spectroscopic identification of collagen deposits in kidneys of mice with 0steogenesis Imperfecta

Authors: You Song[1], MugdhaPadakar[1], Josephine Marino[2], Adele Boskey[2], StephenDoyle[2], Cathleen Raggio[2], Nancy Pleshko[1]

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Type I collagen, present in skin, tendon and bone, is heterotrimeric and consists of two ∂1 (I) chains and one ∂2 (I) chain. However defective type I collagen can abnormally accumulate in glomerular mesangium in disease states, and in mice with collagen defects, such as *oim/oim* mice. *Oim/oim* mice modelosteogenesis imperfecta type III as they show severe bone fragility, deformities and frequent fractures. They synthesize only homotrimeric type I collagen, which consists of three ∂1(I) chains, and has been shown to be present during embryogenesis, wound healing, in some cancers and in stressed mesangial cells. Detection and characterization of collagen deposits in kidney is of great interest to researchers and physicians for diagnosis and monitoring of treatments. In the current study we developed a Fourier transform infrared imaging spectroscopy (FT-IRIS) methodology for collagen assessment. This method enables identification of specific molecular species in unstained histological tissue sections. Imagesbased on a 1338 cm-1 infrared absorbance (indicator of collagen content) were compared with the gold standard picrosirius red staining techniques to validate the FT-IRIS method. Our results showed excellent correlation with histology images. W e found that the amount of collagen deposits increases with age of the mice, but that treatment for OI does not affect how much is deposited. In addition, comparison to standard collagen spectra showed that the deposits were likely a combination of type I and type III collagen. Thus, FT-IRIS can be an alternative method to identify glomerular collagen deposition which will also permit evaluation of molecular type in unstained tissue
sections.

6. Maria Cecilia Scimia. Center for Translational Medicine, TUSM.

Limiting GRK2 in the Ischemic Heart can Promote Cardiac Regeneration.

Authors: Maria Cecilia Scimia, Daniel Zuppo, Kate Sydnes, Erhe Gao, Walter J. Koch

The detrimental role of G protein-coupled receptor (GPCR) kinase (GRK2) following cardiac injury /stress has been documented over the last two decades. Importantly, our lab has shown that inhibition or depletion of GRK2 in cardiomyocytes can prevent and also rescue heart failure (HF) phenotypes. Its role in GPCR desensitization including regulation of β-adrenergic receptors (βARs) during HF development has been well characterized. However, recently our lab and others have found that GRK2 can have novel GPCR-Independent effects in the heart that appears to contribute to its pathological effects and thus, inhibition of these actions of GRK2 may contribute to therapeutic effects seen. In this study we explored whether the cardiac repair observed with lower myocardial GRK2 might involve regenerative processes. In cardiac-specific GRK2 knockout (KO) mice and also transgenic mice with cardiac-targeted expression of the βARKct, a peptide inhibitor of GRK2 activation via Gβy sequestration, we induced HF via coronary artery ligation and subsequent myocardial infraction (MI) and measured aspects of cardiac repair including potential regeneration indices. Post-MI mice (GRK2 KO, βARKct mice and wild-type and non- transgenic control mice) were treated with *5-ethynyl*-2'-*deoxy uridine* (EdU) or Bromodeoxy uridne (BrDU) to examine indicated of DNA proliferation in myocytes as well as Ki67 staining. We also

quantitated c-kit+ cells and myocytes in the post-MI hearts to compare how either loss of GRK2 expression or inhibition via its C-terminus altered potential regeneration mechanisms compared to control mice with endogenous GRK2 levels and activity. We found significantly more BrDU positive myocytes in post-MI hearts with lower GRK2 and this correlated with increased myocytes that were also cKit+. Thus, it appears that the myocardial functional improvement seen in the post-MI heart with targeted lowering a GRK2 involves, to at least a certain extent, regenerative mechanisms. This adds novel insight into the therapeutic potential of GRK2 inhibition for HF.

7. Viktorija Grajevskaja. Department of Biology. TU.

Conditional Gene Trap Mutant Reveals a Critical Role of Tbx5a in Cardiac Regeneration

Authors: Viktorija Grajevskaja [1, 2], Diana camerota[1], Jorune Balciuniene[1], Darius Balciunas[1].

Affiliations: [1]Department of Biology, Temple University, Philadelphia, PA, USA, and [2]Department of Zoology, Faculty of Natural Sciences, Vilnius University, Vilnius, Lithuania.

Zebrafish is a vertebrate model system that possesses a great cardiac regenerative capacity (Poss et al2002). Although there are plenty of genetic tools available to study regeneration (reviewed in Gemberling et al.2013), the lack of adult zebrafish conditional mutants still remains an important disadvantage of the system, and complicates the analysis of a function of the developmentally essential genes during regeneration. Our laboratory improves insertional mutagenesis strategies in zebrafish and generates conditional zebrafish mutants. One of the conditional alleles, tpl58, that was isolated from our mutagenesis screen has a null mutation in a developmentally critical gene, Tbx5a. So far, we have shown that tpl58 is fully conditional. Moreover, we have successfully used tpl58 line to study a role of Tbx5a in adult zebrafish heart regeneration.

8. Alexander Krupka. Center of Neurobiology and Anatomy, Drexel.

Neurotrophin Producing Autologous Fibroblast Grafts Promote Locomotor Recovery in Sub-chronic and Chronic Models of Spinal Cord Injury

Authors: Alexander Krupka[1], Jennifer Dashkova[2], and Michel A. Lemay[2]

Affiliations:[1]Neurobiology and Anatomy, Drexel University College of Medicine, Philadelphia, PA, and [2]Bioengineering, Temple University, Philadelphia, PA.

Adult cats show limited locomotor capabilities following spinal transection. With body-weight support training, the animals recover stepping ability with weight-bearing plantar foot placement. We previously found that delivery of neurotrophins via xenografts of genetically modified rats fibroblasts promotes a similar motor recovery even without training. Similar results were obtained in rodents using direct injection of viruses into the cord. Viral delivery raises clinical concerns regarding recombinant genetics, and xeno/allografts require immunosuppression that increase cancer risks. Furthermore, none of these studies has investigated the effects of delayed onset of neurotrophin delivery on recovery. Our study utilized autologous fibroblasts modified to express the neurotrophins BDNF and NT-3 grafted into the spinal cord following a complete transection at T11-T12. Fibroblasts were grafted at the time of injury, 2 weeks after injury, or 6 weeks after injury. Recovery of bipedal stepping on a treadmill was evaluated before and after injury and grafting. Kinematic evaluation indicated that grafting promoted recovery of treadmill stepping in the experimental groups. While control cats could not plantar step with weight-bearing, grafted cats recovered stepping at speed up to O.8m/s. Recovery was seen in many grafted cats as early as 3 weeks after injury, and all but one grafted cat were capable of stepping by 5 weeks after grafting. This recovery remained 12 weeks after grafting. Histological evaluation showed no regeneration through the lesion. We conclude that neurotrophin producing autografts are effective at promoting stepping even when delivered in a chronic spinal cord injury model.

9. Wenjing Cao. Sol Sherry Thrombosis Center. TUSM

A Novel Factor VIII Variant with enhanced Secretion for Gene Therapy of Hemophilia A

Authors: Wenjing Cao[1], Biao Dong[1], Jenni A. Firrman [2], Andrea R. Moore[1], Qizhao Wang[1], Sean A. Roberts[1], Weidong Xiao[1, 2]
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One major limitation of human factor VIII expression with gene therapy strategies is the inefficient secretion of the factor VIII protein. To overcome this hurdle, a systematic screening strategy combining activity-based profiling and DNA recombinant technologies was successfully used to generate a "super'' human B domain-deleted FVIII (BDDFVIII) variant. This new variant, named as BDDFVIII-X5, contains a 5-amino acid change in the A1 domain of the FVIII heavy chain. BDDFVIII-X5 produced a 7- to 8-fold increase in the clotting activity determined by an aPTT assay and about 3- to 4-fold increase in the antigen level determined by ELISA when compare to wild type BDDFVIII *in vitro*. The increased secretion of BDDFVIII-X5 was confirmed by both Western blotting analysis and pulse-chase experimentation. In an immunocompetent *fVIII*$^{-/-}$murine model, intravenous delivery of AAV8-BDDFVIII-XS driven by a liver specific promoter achieved a 25- to 30-fold increase in the clotting activity at a high vector dose and an 8- to 21-fold increase at a low vector dose when compared to AAV8-BDDFVIII. Accordingly, this variant exhibited a 3- to 5- fold increase in the antigen level and a 5- to 6-fold increase in the specific activity compared with the wild type BDDFVIII. Furthermore, this variant shows a 3-fold higher clotting activity than the best bioengineered and codon optimized FVIII variant in the literature. In addition, we did not detect specific neutralizing antibodies against these new amino acids even after extensively screening all IgGs generated against BDDFVIII-X5 in the rat model. We conclude that BDDFVIII-X5 has dramatically enhanced secretion and specific activity and may be further developed as gene- and protein-based therapeutics for patients with hemophilia A.

10. Sean A. Roberts. Thrombosis Research Center. TUSM.

Engineering the human factor VIII signal peptide for enhanced secretion

Authors: Sean A. Roberts[1], Biao Dong[1], Jenni Firrman[1], Weidong Xiao[1]

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Hemophilia A is a bleeding disorder resulting from defects in the factor Vlll protein. Recombinant adeno-associated virus (rAAV) vectors delivering factor VIII have been considered as a promising strategy for the treatment of Hemophilia A. However, this strategy is hindered by the size limitation of the AAV vectors as well as inefficient secretion of the factor Vlll protein. To avoid this size issue, the gene for factor VIII can be divided into two functional fragments. The heavy chain (hHC) and the light chain (hLC) are packaged and delivered by two separate AAV particles. However, the secretion of hHC is far less efficient than the already inefficiently secreted full length factor VIII. To improve full length human factor Vlll or hHC secretion, we have explored using alternative signal peptides for enhancing secretion. The signal peptides for highly secreted plasma proteins such as albumin or alpha-1-antitrpsin failed to improve factor VIII or hHC secretion at all. Interestingly, mutating the endogenous signal peptide of human Factor VIII taking cue from other species was more effective than using signal peptides from other highly secreting plasma proteins. Six of the newly constructed hFVlll-HC molecules exhibited a 2-4 fold increase in activity as measured by an aPTT assay and a 1.5-2 fold increase in antigen levels as measured by ELISA when compared to the native human factor Vlll molecule *in vitro*. In addition, hydrodynamic injection of hemophilia A (HA) mice with engineered ar-hHC exhibited a ~4 fold increase by aPTT and by ELISA. Finally, ar-hHC was packaged into rAAV vectors and delivered into HA mice via intravenous tail vein injection. The combination of ar-hHC+hLC achieved a 2.3 fold higher expression than the wild type hHC+ hLC. This study demonstrated a new strategy to enhance human Factor VIII secretion for rAAV gene therapy for Hemophilia A.

11. Danielle Feather. Shrines Hospital Pediatric Research Center. TUSM.

Therapeutic Interventions as Treatments to Cerebral Palsy

Authors: Danielle Feather, Nikki McCormack, Holly Dykstra, Scott Rawls, Servio Ramirez, and Tanya Ferguson

Cerebral palsy (CP) is a non-progressive motor disorder affecting 1:300 live births annually. However, the exact cause of CP is unknown. Using a neonatal mouse model of CP combining Hypoxia, Ischemia, and inflammation (lipopolysaccharide, LPS) (HIL), we study the underlying cellular causes of CP, as well as a potential diagnostic tool and treatments.

Astrocytes are responsible for removing glutamate from the synapse of neurons, primarily through the glutamate transporter GLT-1. In our CP model, we note significant astrocyte loss 12-18hrs after injury, followed by astrogliosis, beginning around 72hrs. In addition, we find elevated S100β levels, indicating astrocyte cell damage, in HIL blood samples in a time-course matching histological damage. Initially, both GLT-1 protein expression and function are low; however, 1wk after injury, function significantly increases. Neuronal and white matter loss does not occur until 48hrs after injury and then progresses up to 1wk post-injury. This delayed neuronal and white matter loss suggests there may be a treatment window for CP between 0-48hrs after injury. Currently, there is no cure for CP. Our goal is to prevent CP using drug treatment in neonatal mice. We are testing three drugs: clavulanic acid (CA) and two compounds developed by the Moulder Center for Drug Discovery at Temple University, 093 and 031. CA treatment following HIL decreases S100β, the astrocyte cell death biomarker, early after injury. All three compounds (CA, 093, and 031) increase GLT-1 expression in the hippocampus. Short-term visual memory deficits, demonstrated by a novel object recognition test, as well as neonatal and adult motor deficits, determined by a battery of motor tests, are also improved following drug treatment. Thus, in our model of CP, we demonstrate cellular changes and therapeutic interventions for CP.

12. Chris MacDermaid. Institute for Computational Molecular Science. TU.

Advanced modeling of the human skin barrier

Authors: Christopher M. MacDermaid[1], Russell H. DeVane[2], Michael L. Klein[1], Giacomo Fiorin[1]

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The first line of defense of the human body against harmful agents such as toxic chemicals, viruses, and bacteria is the stratum corneum, the skin's outer layer. A simple "brick and mortar" analogy is often used to describe how the lipid matrix (the "mortar") of the stratum corneum holds together keratin-rich and largely impenetrable corneocytes (the "bricks"). Primarily due to uncertainty in the molecular structure of the lipid matrix, the pathways of permeation of toxic chemicals or drugs administered transdermally are not completely understood. We used molecular dynamics simulations of a 30-nm cross-section of the lipid matrix, under varying conditions of acidity and salt concentration. During our simulations, the skin's lipids form spontaneously a multilamellar structure where small pockets of water are separated by regions of partial fusion between the lamellae. In addition to visualizing a key event in the assembly of the largest human organ, our results further clarify the criteria to develop new delivery vehicles for pharmaceutical treatment.

13. Sina Nassiri. School of Biomedical Engineering, Science and Health Systems, Drexel University.

Modeling of Macrophage-Mediated Controlled Release System for the Treatment of Diabetic Wounds

Authors: Sina Nassiri, Kara Spiller

Foot ulcerations occur in about 15 percent of diabetic patients, and lead to over 82,000 lower limb amputations each year in the United States. Normal wound healing involves three stages: inflammation, proliferation, and remodeling. Diabetic wounds are known for being stalled in the inflammatory state. A treatment strategy that facilitates the transition of

macrophages, the main regulatory cells of inflammation, from pro-inflammatory to pro-healing to pro-remodeling phenotypes, and at appropriate times, would restore the natural healing process. Exposure of resting macrophages to interleukin-4 (IL4) and interleukin-10 (IL10) induces a pro-healing (M2A) and pro-remodeling (M2C) phenotype. We have designed a novel hydrogel microsphere-based scaffold that exploits macrophage biology in conjunction with molecular interactions between therapeutic drugs and the hydrogel polymer, to cause sequential delivery of IL4 and IL10. Herein we describe the release profiles of IL4 and IL10 using mechanistic modeling in order to determine the effects of various control parameters on the system.

14. Mohsin Khan. Center for Translational Medicine, TUSM.

Embryonic stem cell derived exosomes revive endogenous repair mechanisms in failing hearts

Authors: Mohsin Khan[1], Srikanth Garikipati[1], Raj Kishore[1]

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Rationale: Embryonic stem cells (ESCs) hold great promise for cardiac regeneration but are susceptible to ethical concerns, lack of autologous donors and teratoma formation. Recently, it has been observed that beneficial effects of stem cells are mediated by exosomes secreted out under various physiological conditions. ESCs have the ability to produce exosomes however their effect in the context of the heart is unknown.
Objective: Determine the effect of ESC derived exosomes for cardiac repair and modulation of CPCs functions in the heart following myocardial infarction.
Methods and Results: Exosomes were isolated from murine ESCs (mES Ex) or embryonic fibroblasts (MEFs) by ultracentrifugation and verified by Flotillin-1 immunoblot analysts. Induction of pluripotent markers, survival and in vitro tube formation was enhanced in target cells receiving ESC exosomes indicating therapeutic potential of mES Ex. mES Ex administration resulted in enhanced neovascularization, cardiomyocyte survival and reduced fibrosis post infarction consistent with resurgence of cardiac proliferative response. Importantly, mES Ex mediated considerable enhancement of cardiac progenitor cell (CPC) survival, proliferation and cardiac commitment concurrent with increased c-kit+ CPCs in vivo 4 weeks after mES Ex transfer. miRNA Array analysis of ESC and MEF exosomes revealed significantly high expression of miR290-295 cluster in the ESC exosomes compared to MEF exosomes. The underlying beneficial effect of mES Ex was tied to delivery of ESC miR-294 to the heart and in particular CPCs thereby promoting CPC survival and proliferation as analyzed by FACS based cell death analysis and CyQuant assay respectively. Interestingly, enhanced G1/S transition was observed in CPCs treated with miR-294 in conjunction with significant reduction of G1 phase.
Conclusion: In conclusion, mES Ex provide a novel cell free system for cardiac regeneration with the ability to modulate both cardiomyocyte and CPC based repair programs in the heart thereby avoiding the risk of teratoma formation associated with ESCs.

15. Charles T. Drinnan, Department of Bioengineering. TU

Response of DPSCs to PEG-Melanie Bydrogels

Authors: C.T. Drinnan. PhD and O.Z. Fisher, PhD.

Affiliations: Department of Bioengineering, Temple University, Philadelphia, PA

Statement of Purpose: Found throughout nature, melanins provide numerous functionalities that could benefit bioengineers. Naturally occurring melanin polymers, however, are heterogeneous, difficult to manipulate, and formulated from cytotoxic precursors. We have developed a PEG-melanic hydi"ogel composed of gallic groups not found in natural melanins, but demonstrate similar melanin-like properties. Recent evidence has highlighted that antioxidant-containing materials could improve both longevity and functionality of adult stem cells. The current goal is to examine the response of DPSCs seeded onto or encapsulated within melanin-like hydrogels synthesized from both gallate and catechol domains.

Methods: PEG-Gallate (Gal) and catechol (Cat) hydrogels were formulated as outlined previously. For 2D studies, hydrogels layers were formed and modified with GRGOSPC (CycRGD). DPSCs were seeded onto hydrogels at 5000 cells/gel. For 3D ecapsulation, DPSCs resuspended in PEG macromers with or without DOPA-GRGOS. Cell viability was verified with MTS and Live/Dead® assays following standard protocols.

Results: DPSCs were. seeded onto hydrogels formed from PEG-Gal and Cat macromers at *5* Wl⁄o and modified with varying concentrations of CycRGD. By day 3, DPSCs had fully attached to PEG-Cat hydrogels without RGD dependency. This was in contrast to PEG-Gal hydrogels which demonstrated dependency to RGD inclusion. Viability of DPSCs encapsulated within 3D PEG-Gal hydrogels was not dependent on RGD prescence indicating that hydrogels synthesized from PEG-Gal macromers could maintian viability without cell attachment domains.

Conclusions: Melanin-like hydrogels were synthesized from PEG-Gal and Cat of various molecular weights. Hydrogels were modified with different concentrations of CycRGD to facilitate cell attachment. DPSCs demonstrated RGD dependency when seeded onto hydrogels synthesized from PEG-Gal macromers but not· PEG-Cat macromers.· DPSCs encapsulated Within 30 PEG-Gal gels demonstrated high viability with the presence of RGD indicating that 30 networks were sufficient for DPSC viability. Future work will examine the phenotype of DPSCs when embedded within 3D, PEG-melanic hydrogels.

16. Seda Karamil. Department of Bioengineering. TU

Modulation of Pulmonary Differentiation of Murine Embryonic Stem Cells using Physical Cues

Authors: Seda Karamil, Camilla Manso Musso, Peter Lelkes

Affiliations: Temple University, Bioengineering Department.

COPD, disease of chronic airflow obstruction, represent some of the major pathologies that threaten human life. Currently, treatment approaches are constricted in aiming to control symptoms and reduce the risk of complications. Lung transplant is an option for certain patients and can improve ability of breathe but it is less available due to shortage of donors and might lead to possibility of rejection and the need for lifelong immune-suppressing therapy. Therefore, current studies focus on creating functioning alveolar units from reliable cell sources to assist lung function, repair and regeneration. This work presents a novel approach for creating functioning alveolar units from mouse embryonic stem cells (mESC) by employing micro-environmental cues for developmental biology based, directed differentiation. In general, embryonic stem cells are pluripotent cells with complex micro-environmental requirements. During embryonic development, inner cell mass cell are exposed to series of tightly regulated micro-environmental signals. But when we take the cells in vitro, we destroy the very complex micro-environmental signaling; and in the tissue culture dish, much of the complex expression patterns and orientation of the signaling can be lost. Hence, one of the most important elements of micro-environmental cues is to provide right physicochem ical signals at the right time during the embryonic development; I aimed to explore one of the important elements of physico- environment, the effects of matrix stiffness on cell fate decisions in mESC. Using polyacrylamide (PA) gels to mimic the physiologic range of soft tissues, bio-activated PA gels was produced with varying elastic modulus and cross- linked with the optimal choice of adhesive extracellular matrix (ECM) protein, fibronectin for stem cells to attach on. In-vitro studies showed that, PA gels with low elastic modulus have significant impact on modulating definitive endodermal differentiation in comparison to stiffer gels and tissue culture plastic (GPa).
Developmental biology based differentiation of mESC into distal alveolar cells is a two-step process, in which the cells are first differentiated into definitive endoderm by exposure to Activin A followed by differentiation into alveolar epithelial cells in the presence of very complex soluble growth factors including FGF2. As I present the matrix stiffness effect on ESCs definitive endoderm commitment; subsequently Ipropose to further test the ability of definitive endoderm derived ESCs differentiation into pulmonary cells, specifically, into distal lung epithelial (AEII) cells. This study demonstrates for the first time the feasibility of utilizing developmental and physiological physicochemical cues as matrix stiffness to enhance pulmonary mESC differentiation. Impact of the results will be relevant for optimizing cell-based lung therapies and for

effectively engineering lung and other endoderm-derived organs.

17. Huaitzung A. Cheng. Department of Bioengineering. TU

Bioinspired Tannin Complexes for Novel Biomaterials

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Introduction: Tannins are naturally occurring macromolCcular polyphenols capable of complexing with various biomolecules, and they exhibit anti-inflammatory, anti-oxidative, and anti-microbial properties. Of particular interest are the interpolymer complexes (IPCs) that they form with poly(ethylene glycol) (PEG). However, IPC studies are limited by purity of plant extracts available. Dextran based polyphenols have been synthesized and engineered to mimic the functionalities of natural tannins and these pseudotannins form nano-scale colloids with PEGs of various molecular weights. In this work, the pseudotannins were complexed with PEG to make a redox responsive particle system. This system was shown to disintegrate upon exposure to oxidative stress. The synthetic tannins were also shown to crosslink gelatin to form leather inspired biomaterials.

Experimental Methods: Synthetic tannins were produced using a two-step process as described previously. First, dextrans were substituted with benzyl protected hydroxybenzoic acids, followed by a palladium catalyzed deprotection under hydrogen gas. IPCs were formed using pseudotannins and commercially available PEGs. Disintegration of IPCs in response to superoxide was determined using a xantbine oxidase (XOD) assay. The antioxidant power of particle formulations was quantified using the Folin-Ciocalteu method. Gelatin hydrogels were formed by dissolving type-B gelatin in water with and without tannins. This was followed by cooling at 4°C overnight

Results and Discussion: The stability of colloidal IPCs was determined by visual inspection, turbidity assays and dynamic light scattering (DLS). The stability was a function of polymer molecular weight, PEG branching, and PEG terminal groups. All colloid formulations demonstrated a range of antioxidant power, but only polygallol derived IPCs showed redox decomplexation (Figure-I). Gelatin gels crosslinked with synthetic tannins did not dissolve after 24 hours of immersion in phosphate buffer, but dissolution of gelatin gels without tannins was observed under the same conditions. All hydrogel formulations were degraded inthe presence of trypsin.

Conclusion: These bioinspired tannins and the biomaterials described in this work demonstrate a wide range of functionalities and warrant further investigation. This platform is shown to scavenge superoxide, potentially limiting the effect of inflammatory responses. The colloidal pseudotannin system may be a central component in therapies for various inflammatory and autoimmune related biomedical applications. The versatility of these pseudotannins to complex with gelatin shows a potential for gel-based antioxidant biomaterials.

18. Farzad Yousefi Gharebaghi. Bioengineering Department. TU

"Detection of metastases in lymph nodes by infrared spectral imaging".

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Histopathology is currently considered to be the gold standard for disease identification in surgical specimens. However, there are morphological similarities between different entities that limit its utility. Techniques such as immunohistochemistry, in-situ hybridization and other molecular methods have attempted to highlight biochemical or genetic differences that might not be apparent at the light microscopic level; however they too have their limitations. Infrared spectral imaging is a new modality which can be applied to the histopathology field. This method is based upon molecular vibrations and enables researchers to image the biochemical changes between normal and diseased tissues at a spatial resolution of ~ 6 microns. The analysis provides objective information from many different tissue components from one single thin tissue section. Absorbances in the infrared spectral regions from proteins, lipids, DNA, RNA, and mineral can be detected, and used to identify pathologic changes. In the current study, we assessed whether metastases in lymph node tissues could be detected with infrared spectral imaging. We collected imaging data from 5 μm thick lymph node sections placed on silicon wafers at 50 microns spatial resolution followed by extended multiplicative signal correction to eliminate the scattering artifacts, and second derivative data pre-processing to resolve the overlapped absorbance peaks. Hematoxylin and eosin (H&E) staining of adjacent sections was also done. Preliminary results show that infrared images created based on the frequency of 964 cm-1, which is assigned to phosphate symmetric stretch in DNA and deoxyribose-phosphate skeletal motions, are very similar to features in the H&E stained sections. This preliminary data supports the possibility implementation of this method to detect tumor metastases in lymph nodes.

19. Jonathan Gerstenhaber, Bioengineering Department. TU

Delta-Style Robot for Electrospinning 3D mats

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Electrospun nanofibrous mats and scaffolds are increasingly used for diverse applications, such as for water filtration or tissue engineering. Common laboratory scale electrospinning setups can be built inexpensively with merely a syringe pump, a high voltage supply, and an aluminum foil target. These systems are typically limited to the creation of flat mats up to several centimeters across as spinneret-target distance must remain constant during the spinning assay. They also require human calibration for each run, and frequent maintenance during spinning. A possible remedy for these drawbacks is to construct a system driven by a robot capable of moving in three dimensions. The design of such a device is complicated by the fact that all grounded sources present in the electrospinning chamber can become targets for the fibers and inhibit the experimenter's ability to customize the electric field. Finally, an ideal system could be environmentally isolated, not only to protect researchers from toxic fumes, but also to control environmental variables such as temperature and humidity. Here we present a 3D delta-style electrospinning robot constructed mostly from plastic parts generated in a simple 3D printer.

20. Mugdha Padalkar, Bioengineering Department. TU

Wavelength-dependent penetration depth of near infrared spectra into cartilage

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The pathology of osteoarthritis (OA) is characterized by a damaged collagen network, loss of proteoglycan, and an increase in water content, often resulting in fibrillation and thinning of articular cartilage. Near infrared (NIR) spectroscopy, a technique based on interaction of light with tissue, has been emerging as a nondestructive modality for cartilage evaluation. However, studies of the depth of penetration of NIR radiation are lacking. The average thickness of human cartilage is about 2.4mm, and it becomes even thinner as OA progresses. In order to ensure that the spectral data collected is restricted to the tissue of interest i.e. cartilage in this case and not from the underlying subchondral bone, it is necessary to determine the depth of penetration of NIR in different wavelength (frequency) regions. In the current study we establish how the depth of penetration varies throughout the NIR frequency range (4000-9000 cm-1). NIR spectra were collected from cartilage samples of different thickness (l mm to 5mm) with and without polystyrene placed underneath. A separate NIR spectrum of polystyrene was collected as a reference. The NIR. frequency range was divided into three sub-regions, 4000-5100 cm-1, 5100-7000 cm-1 and 7000-9000 cm-1• Raw spectra as well as second derivatives were used to determine the depth of penetration of NIR radiation based on whether a polymer absorbance peak can be still seen when a cartilage sample was placed on the top of it. It was found that the depth of penetration varied from ~l.25mm in the 4000-5100 cm-1·range, to ~2.5mm in the 5100- 7000 cm-1·range, and to ~5 mm in 7000-9000 cm-1 frequency range. These findings suggest that the best NIR region to evaluate cartilage only with no subchondral bone contribution is between 4000-7000 cm-1.

21. Gerald Pawlish. Bioengineering Department. TU

pH-Res ponsive Nanogels for Intracellular Delivery

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Delivery of therapeutics in a targeted manner can optimize their effectiveness and decrease potential side effects. Macromolecular therapeutic delivery has become sufficiently more viable through the use of macroscale hydrogels. Our laboratory is currently investigating novel hydrogel-based nanoscale drug delivery methods with the use of "smart polymers, polymeric systems responsive to environmental changes in ways which can be exploited for biomedical purposes. Examples of these stimuli include changes in temperature, light or pH, leading to a broad range of applications. Polybasic nanogels are pH-responsive nanocarriers 50-200 nm in size, small enough to be endocytosed by mammalian cells in a targeted manner (1,2). These nanogels are composed of a poly(methacrylate)-based network decorated with basic amine groups, allowing them to swell in acidic endosomes (2,3). This transition allows for macromolecular loading (e.g., DNA or RNA) and their release into the cytosol upon endosomal escape. This delivery method combines both the pH-dependent endosomal escape of typical polymeric transfection reagents with the scale and delivery properties of conventional nanocarriers (4). Previous macromolecular loading and delivery includes albumin, insulin and colloidal gold, examples of the wide range of molecules which can be incorporated into the polymeric network (2, 3). The properties of the nanogels can be easily tailored through changes in core hydrophobicity, cross-linking schemes and cell uptake ligand decoration to -load various types of anionic macromolecules, such as the current research into gene delivery for potential uses in various types of cancers (2, 3).

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22. Ruchi Malik. Cancer Biology. Fox Chase Cancer Center

Dissecting the extrinsic stimuli parameters of human pancreatic stromal ECM on progressive epithelial tumorigenesis

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Pancreatic cancer is one of the most lethal cancers of our time; while other cancers have been declining due to early detection and better treatments pancreatic adenocarcinomas are in the rise. Unfortunately, current treatments have not le d to much clinical benefit. In pancreatic cancer, an unusually intense desmoplastic stroma reaction contributes to poor prognosis. However the mechanisms behind the tumorigenic effects imparted by desmoplastic stroma remain unclear. The goal of this study is to better understand mechanisms Imparted by human pancreatic stromal ECMs, and how they synergize with epithelial intrinsic mutational cues to enhance progression of pancreatic cancer. We utilize a unique multidisciplinary approach consisting of physiological in vitro 3D extracellular matrix (ECMs) obtained from patient matched (normal and desmoplastic) tissues as well as bioengineered microenvironmental derivatives. The influences of these systems were tested on human isogenic pancreatic cancer cell series (PDECs) exhibiting varying aggressive features.

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