University at Buffalo
The State University of New York

3rd Annual
Stem Cells in Regenerative Medicine Symposium
(SCiRM)

PRESENTED BY :
THE SCRIM TRAINING PROGRAM

NYSTEM NEW YORK STATE STEM CELL SCIENCE

Jacobs School of Medicine and Biomedical Sciences,

University at Buffalo

June 21st, 2019

8:00 A.M.- 5:00 P.M.

CONTENTS

WELCOME FROM THE DIRECTOR

The Stem Cells in Regenerative Medicine (SCiRM) Training Program was launched in Fall of 2016 with $1.85M in funding from the New York State Stem Cell Science Board (NYSTEM). The UB School of Engineering and Applied Sciences, the UB Jacobs School of Medicine and Biomedical Sciences and Roswell Park Cancer Institute (RPCI) Graduate Division joined forces to develop an interdisciplinary program aiming at fostering stem cell science and engineering to accelerate clinical translation of stem cell research and to train the future leaders in stem cell science and engineering.

Our faculty are involved in research with various types of stem cells including embryonic and induced pluripotent stem cells, as well as adult stem cells including mesenchymal, cardiac, skeletal, hematopoietic, neural and neural crest stem cells among others. Our research ranges from basic aspects of stem cell maintenance and differentiation to translational work that aims at using stem cells for treatment of cardiovascular, neurologic or metabolic disorders. SCiRM fellows are co-advised by faculty from Medicine and Engineering, thereby promoting multidisciplinary collaborations and interdisciplinary approaches to research and education. Excellent facilities are available for cutting-edge research including the Western New York Stem Cell Culture and Analysis Center (also funded by NYSTEM), the Next-Generation Sequencing and Expression, Proteomics/Mass Spectrometry, Confocal Microscopy & Flow Cytometry, Cleanroom, Materials Characterization Laboratory and Digital Manufacturing Laboratory among others.

The SCiRM training program is greatly facilitated and enriched by numerous biomedical research and education institutions in the newly built Buffalo-Niagara Medical Campus. These include the new Jacobs School of Medicine and Biomedical Sciences, the new John R. Oishei Children's Hospital, the Clinical and Translational Research Center, the Center of Bioinformatics and Life Sciences, the Hauptman-Woodward Medical Research Institute and the new RPCI Clinical Research Center.
This rich, interdisciplinary environment fosters the integration of scientific discoveries and engineering breakthroughs with the ultimate goal to develop stem cell therapies that can be translated into clinical practice. The combination of a highly trained science and engineering workforce, and the potential for clinical translation and commercialization of research findings, are expected to have significant economic impact in Western New York, as well as throughout NY State.
We look forward to the coming years in the program.

Thank you for your interest.

Stelios Andreadis
Director

Stem Cell in Regenerative Medicine Faculty

Stelios Andreadis, SUNY Distinguished Professor and Department Chair, Chemical Engineering, UB

Ph.D., University of Michigan Chemical Engineering

Research Interests: Stem cells for vascular tissue engineering; signaling pathways in cell-cell adhesion and wound healing; lentiviral vectors and lentiviral microarrays for high-throughput gene expression analysis and gene discovery

John Canty Jr., SUNY Distinguished Professor and Chief, Division of Cardiovascular Medicine UB

MD, University at Buffalo

Research Interests: Apoptosis and cell death; Cardiac pharmacology; Cardiology; Cardiovascular Disease; Gene therapy; Genomics and proteomics; Molecular Basis of Disease; Stem Cells

Thomas Cimato, Associate Professor, Medicine, UB

MD, Ph.D., University at Buffalo

Research Interests: Cardiology; Critical Care Medicine

Jian Feng, Professor, Physiology and Biophysics, UB

Ph.D., University of Tennessee

Research Interests: Apoptosis and cell death; Cytoskeleton and cell motility; Gene Expression; Molecular and Cellular Biology; Molecular genetics; Neurobiology; Neurodegenerative disorders; Neurology; Pathophysiology; Protein Folding; Signal Transduction; Toxicology and Xenobiotics; Transcription and Translation

David Goodrich, Professor Oncology, Roswell Park Comprehensive cancer Center

Ph.D., University of California, Berkeley

Research Interests: Understanding molecular mechanisms underlying tumor suppression mediated by the RB1 and TP53 genes. Identifying genes involved in prostate cancer metastasis. Discerning how transcriptionally formed R-loops contribute to cancer initiation and progression.

Gen Suzuki, Associate Professor, Medicine, UB

M.D., Ph.D., Akita University School of Medicine

Research Interests: Apoptosis and cell death; Cardiology; Cardiovascular Disease; Cell Cycle; Cell growth, differentiation and development; Gene therapy; Internal Medicine; Stem Cells

Stem Cell in Regenerative Medicine Faculty

Richard Gronostajski, Professor Biochemistry, UB; Director, Genetics, Genomics & Bioinformatics Program

Director, Western NY Stem Culture & Analysis Center (WNYSTEM)

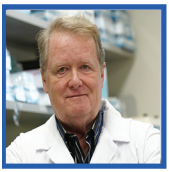
Ph.D., Harvard University

Research Interests: Bioinformatics; Cell growth, differentiation and development; Gene Expression; Genomics and proteomics; Molecular and Cellular Biology; Molecular Basis of Disease; Molecular genetics; Neurobiology; Stem Cells; Transgenic organisms

Kenneth Gross, Emeritus Faculty, Molecular & Cellular Biology, Roswell Park Comprehensive Cancer Center

Ph.D., M.I.T., Cambridge

Research Interests: The Renin-expressing Cell and Development of the Renal Vasculature



Michael Higgins, Associate Professor, Molecular & Cellular Biology, Roswell Park Comprehensive Cancer Center

Ph.D., Queen's University

Research Interests: Molecular genetics of Beckwith-Wiedemann syndrome (BWS); epigenetic imprinting and cancer.

Te-Chung Lee, Associate Professor, Biochemistry, UB

Ph.D., Virginia Commonwealth University

Research Interests: Cardiology

Jonathan Lovell, Assistant Professor, Biomedical Engineering, UB

Ph.D., University of Toronto

Research Interests: Nanomedicine and Phototherapy

Stem Cell in Regenerative Medicine Faculty

Sriram Neelamegham, Professor, Chemical & Biological, Biomedical Engineering, UB

Ph.D., Rice University

Research Interests: Biomedical Engineering; cell biomechanics; vascular engineering

Michael Nemeth, Assistant Member, Medicine, Roswell Park Comprehensive Cancer Center

Ph.D., Dartmouth College

Research Interests: Identifying the mechanisms that regulate the development and maintenance of adult stem cells. Developing therapeutic strategies that can target the cancer stem cell population.

Natesh Parashurama, Assistant Professor, Chemical & Biological Engineering, UB

MD, Ph.D., Rutgers University

Research Interests: Liver stem cell biology; differentiation; cell therapy; organogenesis; disease modeling; tissue engineering; multimodality molecular imaging; monitoring molecular events in living subjects

Steven Pruitt, Professor, Oncology, Molecular & Cellular Biology, Roswell Park Comprehensive Cancer Center

Ph.D., University of Virginia

Research Interests: Understanding the mechanism by which somatic stem cells maintain tissue homeostasis and the consequences of dysfunction in these mechanisms for age related disease.

Fraser Sim, Associate Professor, Pharmacology & Toxicology, UB

Ph.D., University of Cambridge

Research Interests: Genomics and proteomics; Neurobiology; Neurodegenerative disorders

Satrajit Sinha, Associate Professor, Biochemistry, UB

Ph.D., University of Texas Health Science Center

Research Interests: Gene Expression; Genomics and proteomics; Molecular and Cellular Biology

Daniel Swartz, CEO, Angiograft LLC

AGENDA

Friday, June 21st

8:00 - 8:55 a.m.	Continental Breakfast and Registration | M&T Auditorium, 2120B
8:55 a.m.	Welcome | M&T Auditorium, 2120B Dr. Stelios Andreadis, SCiRM Director and SUNY Distinguished Professor, University at Buffalo
9:00 - 9:45 a.m.	Robert Krauss, PhD, Icahn School of Medicine at Mount Sinai "Niche Regulation of Muscle stem cells" | M&T Auditorium, 2120B
9:45 - 10:30 a.m.	Laura Niklason, MD, PhD, Yale University "Functional Regeneration of Tissues and Organs" | M&T Auditorium, 2120B
10:30 - 10:45 a.m.	Coffee Break
10:45 - 11:30 a.m.	Rose-Anne Romano, PhD, University at Buffalo "Delineating the p63-drive network that directs stem and progenitor cell fate decisions in the mouse salvinary gland" | M&T Auditorium, 2120B
11:30 a.m.- 1:30 p.m.	Lunch and Poster Session | Active Learning, 1220
1:30 - 2:15 p.m.	Martin Pera, PhD, The Jackson Laboratory "Human Pluripotent Stem Cells & the Human Embryo" | M&T Adutirorium, 2120B

2:15 - 3:00 p.m.	Laura Feltri, MD, PhD, University at Buffalo "In Vivo Studies of the Lysosomal Storage Disease Krabbe Leukodystrophy" | M&T Auditorium, 2120B
3:00 - 3:15 p.m.	Coffee Break
3:15 - 4:00 p.m.	George Techiryan, PhD/MD-Candidate, University at Buffalo "Translating Postconditioning Cardioprotective Strategies After Acute Myocardial Infraction in Swine" | M&T Auditorium, 2120B
4:00 - 4:45 p.m.	Joseph Wu, MD, PhD, Stanford School of Medicine "Genomics and Stem Cells for Cardiovascular Precision Medicine" | M&T Auditorium, 2120B
4:45 - 5:00 p.m.	Closing remarks and poster winners announced | M&T Auditorium, 2120B ** Students must be present in order to receive an award.

DISTINGUISHED SPEAKERS

Robert Krauss, PhD

Professor, Department of Cell, Development & Regenerative Biology and Department of Oncology Sciences, Icahn School of Medicine at Mount Sinai.

Robert Krauss received a Ph.D. from the University of North Carolina at Chapel Hill and postdoctoral training at Columbia University Medical Center. He has been on the faculty at Mount Sinai since 1992, where he is Professor of Cell, Developmental, and Regenerative Biology and a member of the Mindich Child Health and Development Institute and Black Family Stem Cell Institute. He has been a Career Scientist of the Irma T. Hirschl Trust, an Established Investigator of the American Heart Association, and President of the Society for Muscle Biology. He is on the Editorial Boards of The Journal of Cell Science, Molecular and Cellular Biology, and Skeletal Muscle. In addition to his research program, he maintains a strong commitment to education and mentoring trainees and junior faculty. He is Co-director of the Development, Regeneration, and Stem Cells training area for graduate students and Chair of the Graduate School Steering Committee, and has won awards for teaching graduate and medical students.

Laura Niklason, MD, PhD

Professor, Department of Anesthesia and Biomedical Engineering, Yale University.

Dr. Niklason is the Nicholas M. Greene Professor at Yale University in Anesthesia and Biomedical Engineering, where she has been on faculty since 2006. Dr. Niklason's research focuses primarily on regenerative strategies for cardiovascular and lung tissues. She was inducted into the National Academy of Inventors in 2014, and was elected to the National Academy of Medicine in 2015. She was also named (along with Bill Gates and Joe Biden) as one of 34 leaders who are changing healthcare by Fortune Magazine in 2017. Niklason received her PhD from the University of Chicago in Biophysics in 1988, and received her MD from the University of Michigan in 1991. Dr. Niklason completed her medical training in anesthesiology and critical care medicine at the Massachusetts General Hospital in 1996.

Rose-Anne Romano, PhD

Professor, Department of Dentistry, University at Buffalo

Rose-Anne Romano received a BS from the University of Pittsburgh and a Ph.D. and postdoctoral training from the University at Buffalo. She has been on the faculty at the University at Buffalo since 2011, where she is Professor in Department of Oral Biology and a member of the Society for Investigative Dermatology, American Association for Dental Research, and International Association for Dental Research and the treasurer for the American Association for Dental Research, Buffalo Section. She has been awarded several University Professions Awards and Fellowships.

Her research interests are broadly centered on studying the transcriptional regulatory mechanisms governing the development and differentiation of epithelial rich tissues including those of the skin and oral cavity. My laboratory focuses on the lineage-specific master transcription factor, p63, which is a member of the p53 family of proteins.

Martin Pera, PhD

Professor, The Jackson Laboratory

Martin Pera received his BA from the College of William and Mary, and his PhD from George Washington University, and undertook postdoctoral training in the UK at the Institute of Cancer Research and the Imperial Cancer Research Fund.

He held independent research positions at the Institute of Cancer Research and the Department of Zoology at Oxford University before joining Monash University in 1996. In 2006 he moved to Los Angeles as the Founding Director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at the University of Southern California. He returned to Melbourne in 2011 to become Professor of Stem Cell Sciences at the University of Melbourne and Program Leader for Stem Cells Australia, the Australian Research Council Special Research Initiative in Stem Cell Sciences. He joined the Jackson Laboratory in 2017.

Pera's research focus is the cell biology of human pluripotent stem cells. His laboratory at Monash University was the second in the world to isolate embryonic stem cells from the human blastocyst, and the first to describe their differentiation into somatic cells in vitro. Currently his lab studies the regulation of self-renewal and pluripotency and neural specification of pluripotent stem cells. His early work on neural differentiation of human pluripotent stem cells helped lead to the development of a new treatment for macular degeneration, a common form of blindness, which is now entering clinical trial in Israel and California. At the Jackson Laboratory, he is using human stem cells and mouse models to study the genetic basis of individual differences in the response of the central nervous system to injury.

Laura Feltri, M.D., Ph.D.

Professor, Department of Biochemistry and Neurology, Jacobs School of Medicine and Biomedical Sciences, State University of New York at Buffalo.

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Dr. Feltri is Acting Director of the Hunter James KellyDr. Feltri is Acting Director of the Hunter James Kelly Research Institute and Professor of Biochemistry andResearch Institute and Professor of Biochemistry and Neurology at the Jacobs School of Medicine and BiomedicalNeurology at the Jacobs School of Medicine and Biomedical Sciences at Sciences at University at BuffaloDr. Feltri received her medical degree from the University of Milano, Italy. She completed her internship in Medicine and Residency in Neurology in the San Raffaele Hospital, University of Milano, Italy. She was a Neuroscience post-doctoral fellow at Thomas Jefferson University and at the University of Pennsylvania. Dr. Feltri worked from 1993 to 2011 at the San Raffaele Scientific Institute of Milano, Italy, where she was the Head of the Unit of Neuro-Glia. Dr. Feltri's scientific interest is on myelin and myelin diseases. Together, with the laboratory of Lawrence Wrabetz, she developed the first Cre transgene that targets specifically Schwann cells, and pioneered conditional transgenesis to understand the role of extracellular matrix components and their receptors in developing and pathological peripheral nerves. Her laboratory has identified the diverse roles and many of the downstream signals for laminin receptors in nerve development. The NIH, National Multiple Sclerosis Society, Hunter Hope Foundation, Charcot-Marie-tooth Association, Telethon Italy and the European Community have funded her research and she has authored more than 100 peer-reviewed publications.

Dr. Feltri has mentored many graduate and MD-PhD students with several of them achieving independent faculty and other leadership positions, and has served the clinical and scientific community on the Board of the Peripheral Nerve Society, the medical board of the Charcot-Marie-Tooth Association, as Member of the Cellular and Molecular Biology of Glia NIH and National Multiple Sclerosis Study Sessions and as Editorial member of the Journal of Neuroscience, Glia and Experimental Neurology. At UB, Dr. Feltri was awarded an Exceptional Scholar Award for Sustained Achievements and the Distinguished Post-doc Mentor Award.

George Techiryan, Ph.D.

M.D./Ph.D.-Candidate, Department of Toxicology & Pharmacology, University at Buffalo

Juliane Nguyen, Ph.D., is an assistant professor of Pharmaceutical Sciences at the University at Buffalo. The Nguyen Lab is developing novel protein-, RNA-, and lipid-based biochemical and delivery platforms for treating myocardial

infarction and cancer. One of her research foci is the development of biomaterials equipped with molecular zip codes for the subcellular delivery of macromolecules. Dr. Nguyen's research has received recognition through the Biomedical Breakthrough Award, the UB Exceptional Scholar Young Investigator Award, and the NSF CAREER Award. Dr. Nguyen received her Ph.D. in Pharmaceutical Sciences from the Philipps-University of Marburg (Germany). She then trained at UCSF under Dr. Frank

Joseph Wu, M.D., Ph.D.

Professor, Department of Medicine and Radiology, Stanford School of Medicine, Stanford University.

Joseph C. Wu, MD, PhD is Director of the Stanford Cardiovascular Institute and Simon H. Stertzer, MD, Professor of Medicine and Radiology at the Stanford School of Medicine.

Dr. Wu received his MD from Yale University School of Medicine. He trained in internal medicine and cardiology at UCLA followed by a PhD in the Dept of Molecular Pharmacology.

Dr. Wu has published >350 manuscripts. His lab works on biological mechanisms of patient-specific and disease-specific induced pluripotent stem cells (iPSCs). The main goals are to (i) understand basic cardiovascular disease mechanisms, (ii) accelerate drug discovery and screening, (iii) develop "clinical trial in a dish" concept, and (iv) implement precision cardiovascular medicine for prevention and treatment of patients.

Dr. Wu has received numerous awards, including National Institutes of Health (NIH) Director's New Innovator Award (2008), NIH Roadmap Transformative Award (2009), American Heart Association (AHA) Innovative Research Award (2009), Presidential Early Career Award for Scientists and Engineers given out by President Obama (2010), AHA Established Investigator Award (2012), Burroughs Wellcome Foundation Innovation in Regulatory Science Award (2015), AHA Merit Award (2017), and AHA Distinguished Scientist Award (2018).

He also received the inaugural AHA Joseph A. Vita Award (2015) which is given to an investigator whose body of work published in the last 5 years has had transformative impact on basic, translational, or clinical cardiovascular research. Dr. Wu currently serves on the Scientific Advisory Board for the Keystone Symposia (2014-2020), FDA Cellular, Tissue, and Gene Therapies Advisory Committee (2017-2020), AHA National Board of Directors (2017-2021), Chair of the AHA Basic Cardiovascular Science Counci
(2018-2020), and Chair of the AHA National Research Committee (2017-2021).

SPEAKER ABSTRACTS

Niche regulation of skeletal muscle stem cells

Robert S. Krauss, Ph.D.
Icahn School of Medicine at Mount Sinai
New York, NY

Satellite cells (SCs) are skeletal muscle stem cells responsible for the remarkable regenerative properties of this tissue. During normal skeletal muscle homeostasis, SCs are largely quiescent. Quiescence is maintained by a combination of cell-autonomous and niche-derived signals and is thought to be required for SC maintenance, as non-injury-related breaks in quiescence generally lead to depletion of SCs. The myofiber is a major constituent of the SC niche, and it provides signals that promote quiescence of associated SCs. We have identified the cell-cell adhesion molecules N-cadherin (Ncad) and M-cadherin (Mcad) as quiescence-promoting factors of the SC niche in mice (Goel et al. 2017). Conditional genetic removal of these cadherins led to an unusual phenotype: long-term expansion of a regeneration-proficient SC pool, with SCs displaying a state between quiescence and full activation. Ncad/Mcad-deficient SCs remained in the niche and were normally polarized along the apical-basal axis. This phenotype is likely attributable to partial disruption of cadherin-based junctions due to the presence of multiple additional cadherins. These studies have led us to address several additional questions. First, what would happen to SCs if cadherin-based junctions were fully disrupted? We have genetically removed various catenins from SCs to address this point. Second, how does the myofiber construct and maintain a niche for SCs? Myofibers are very large large, multinucleated, non-polarized cells, whereas SCs are small, mononucleated, highly polarized cells that are in contact with a very small proportion of the myofiber cell surface. We have developed a combined single-molecule FISH/immunofluorescence protocol for use on whole-mount, ex vivo myofiber-muscle stem cell preparations to acquire spatial and quantitative information about niche components. Our recent studies on these questions will be presented.

Functional Regeneration of Tissues and Organs

Laura Niklason, M.D., Ph.D.
Yale University
New Haven, CT

The journey of taking a new idea from its initial inception, through to clinical trials with good efficacy, is exciting, surprising, and oftentimes fraught. In developing any new therapeutic tissue, critical attention must be paid to target tissue composition, mechanics, remodeling capacity, and immunogenicity. Through the development process for the tissue product, paying careful attention to where prior technologies have failed, and to the real-life medical realities of the disease under treatment, are paramount. This talk with focus on current challenges to the fields of connective tissue and whole organ regeneration, with foci on arteries and lungs, and on methodological developments that will move tissue engineering forward.

Cardiovascular regenerative medicine has taken many avenues. 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". Our approach to vascular engineering involves seeding allogeneic vascular cells onto a degradable substrate to culture vascular tissues in a biomimetic bioreactor. After a period of 8-10 weeks, engineered tissues are then decellularized to produce an engineered extracellular matrix-based graft. The advantage of using allogeneic cells for graft production is that no biopsy need be harvested from the patient, and no patient-specific culture time is required. These grafts are currently being tested in a Phase III clinical trial in Europe and in the US. Early experience supports the potential utility of this novel tissue engineered vascular graft to provide vascular access for hemodialysis.

The decellularization approach has also allowed us to generate scaffolds to support whole lung regeneration. Using rat, porcine and human sources of organs, lungs have been subjected to a range of decellularization procedures, with the goal of removing a maximal amount of cellular material while retaining matrix constituents. Next-generation proteomics approaches have shown that gentle decellularization protocols result in near-native retention of key matrix molecules involved in cell adhesion, including proteoglycans and glycoproteins. 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. Current challenges involve the production of a uniformly recellularized scaffold within the vasculature, in order to shield blood elements from the collagenous matrix which can stimulate clot formation. In addition, we have developed methods to quantify barrier function of acellular and repopulated matrix, in order to predict functional gas exchange in vivo.

Delineating the p63-driven network that directs stem and progenitor cell fate decisions in the mouse salivary gland

Rose-Anne Romano, Ph.D.
University at Buffalo
Buffalo, NY

The transcription factor ΔNp63 is highly expressed in the stem and progenitor cell populations of epithelial rich tissues including the salivary gland (SG), where it plays critical roles in lineage commitment and cell fate decisions. The importance of ΔNp63 in the SG is highlighted by the dramatic phenotype of ΔNp63 null-mice, which display a complete block in gland morphogenesis and die shortly after birth due to global agenesis of stratified and glandular tissues. Although the role of ΔNp63 in SG development has been reported, our current knowledge regarding the function of ΔNp63 in commitment, maintenance, and differentiation of the stem/progenitor cell population in adult glands, is limited. Using scRNA-seq and in vivo genetic lineage tracing analyses, we have generated a detailed map of the cell fate trajectories of the p63+ve stem/progenitor cells of the mouse submandibular gland. Our studies show that p63+ve cells give rise to and maintain all the epithelial cell lineages of the SG. To obtain a better understanding of the function of p63 in directing cell fate choices, we have conditionally ablated p63 in adult mice and assessed for alterations in stem/progenitor cell differentiation and function. In parallel we have performed a comprehensive transcriptomic (RNA-seq), and epigenomic (ChIP-seq) characterization of the ΔNp63-driven global circuitry in the SG. Moreover, we have performed scRNA-seq of ΔNp63-null salivary glands to interrogate the cellular identities and cell states that are dependent on ΔNp63. Our studies reveal that ablation of ΔNp63 results in dramatic skewing in SG epithelial cell differentiation programs that are accompanied by a demonstrable loss of the stem/progenitor cell population. Interestingly, integrated analysis of our transcriptomic data with ChIP-seq studies, have unearthed key mediators of the ΔNp63-driven molecular network that converge on key facets of stem and progenitor cell function. In particular, our findings suggest that ΔNp63 may serve as an upstream master regulator of the TGF-β signaling pathway governing the proliferative and differentiation programs in the SG. Taken together, our multipronged biochemical and genetic approach has revealed novel and high-resolution mechanistic insights into the ΔNp63 target gene regulatory networks important in SG stem cell hierarchy, and offers new avenues for the development of regenerative therapies following SG injury, damage or during diseased states.

Human Pluripotent Stem Cells and the Human Embryo

Martin Pera, Ph.D.
The Jackson Laboratory
Bar Harbor, ME

Pluripotent stem cells have opened up a previously inaccessible phase of the human life cycle to experimental study. However, in order to exploit stem cells in the study of human development, it is critical to have a clear understanding of what embryonic stage and cell type the cultured cells equate to. In the mouse, two different types of pluripotent stem cell lines have been established, one representing the pre-implantation epiblast (naïve or ground state stem cells) and another representing a later post-implantation stage (primed or epiblast stem cells). It is widely held that conventional (archetypal) human pluripotent stem cells (hPSC) are most similar to mouse cells in the primed state. Heterogeneity within hPSC cultures complicates this interspecies comparison. A subpopulation of archetypal hPSC enriched for high self-renewal capacity (ESR) has distinct properties relative to the bulk of the population, including a cell cycle with a very low G1 fraction and a metabolomic profile that reflects a combination of oxidative phosphorylation and glycolysis. Global DNA methylation levels in the ESR subpopulation are lower than those in mouse epiblast stem cells. Chromatin accessibility analysis revealed a unique set of open chromatin sites in ESR cells. RNA-seq at the subpopulation and single cell levels shows that, unlike mouse epiblast stem cells, the ESR subset of hPSC displays no lineage priming, and that it can be clearly distinguished from gastrulating cell populations in the primate embryo. ESR hPSC correspond to an earlier stage of post-implantation development than mouse epiblast stem cells. These findings will help us to build high fidelity models of the early human embryo for the study of normal development and its disorders.

In vivo studies of the Lysosomal Storage Disease Krabbe Leukodystrophy

Laura Feltri, M.D., Ph.D.
University at Buffalo
Buffalo, NY

Lysosomal storage disorders (LSDs) are inherited metabolic diseases caused by enzyme deficiencies 1. Therapy for LSDs relies on cross-correction of lysosomal enzymes between cells 2,3. In globoid cell leukodystrophy (GLD), mutations in the galactosylceramidase gene (GALC) cause toxic accumulation of a minor GALC-substrate, psychosine, that may directly induce demyelination, a neuroinflammatory "globoid" cell reaction and neurodegeneration. The cellular origin of psychosine, the role of the GALC major substrate galactosylceramide and the efficiency of GALC transfer in vivo are poorly understood 4 5,6. Using a novel GLD model we show that cross-correction does not occur in vivo in the peripheral nervous system and that GALC-deficient Schwann cells are the source of psychosine, which causes demyelination, but not formation of globoid cells. Infiltrating neural macrophages require GALC for myelin degradation, as ablating GALC in Schwann cells and macrophages produce a GLD-like phenotype. GALC-deficient macrophages are induced to globoid cells by galactosylceramide, suggesting a role for this major GALC substrate. Finally, nerves from GLD patients treated with hematopoietic stem cell transplantation have fewer globoid cells than untreated patients, suggesting that the major effect of therapy is immunomodulatory. These data reveal that GLD pathogenesis may consist of two intertwined mechanisms: psychosine-induced demyelination and secondary neuroinflammation from galactosylceramide storage in macrophages.

1 Eisenstein, M. Myriad maladies. Nature 537, S146-147, doi:10.1038/537S146a (2016).

2 Sands, M. S. & Davidson, B. L. Gene therapy for lysosomal storage diseases. Molecular Therapy 13, 839-849 (2006).

3 Solomon, M. & Muro, S. Lysosomal enzyme replacement therapies: Historical development, clinical outcomes, and future perspectives. Advanced drug delivery reviews 118, 109-134 (2017).

4 Suzuki, K. Evolving perspective of the pathogenesis of globoid cell leukodystrophy (Krabbe disease). Proc. Japan. Acad. 79 (2003).

5 Spassieva, S. & Bieberich, E. Lysosphingolipids and sphingolipidoses: Psychosine in Krabbe's disease. J Neurosci Res 94, 974-981, doi:10.1002/jnr.23888 (2016).

6 Wenger, D. A., Rafi, M. A. & Luzi, P. Krabbe disease: One Hundred years from the bedside to the bench to the bedside. J Neurosci Res 94, 982-989, doi:10.1002/jnr.23743 (2016).

Translating Postconditioning Cardioprotective Strategies After Acute Myocardial Infarction in Swine

George Techiryan, M.D., Ph.D. - Candidate
University at Buffalo
Buffalo, NY

Ischemic heart disease persists as a significant cause of morbidity and mortality around the world. With the advances in infrastructure and technology, we can achieve rapid reperfusion therapy, which dramatically reduces the burden from acute myocardial infarction. Nevertheless, preclinical research studies suggests there is an opportunity to further reduce the acute infarction and remodeling, preventing the impairment of cardiac structure and function which precipitates the slow progressive decline towards eventual heart failure. This approach, broadly called cardioprotection, has repeatedly failed at clinical testing despite significant research investment over the past several decades.

To address this, we developed and investigated two promising cardioprotective approaches in a clinically relevant and translational porcine model of acute myocardial infarction. The first therapy is a pharmacologic approach utilizing an acute administration of metformin, an anti-diabetic drug, with a specific focus on infarction, function, and remodeling. The second therapy is a biologic approach utilizing allogeneic cardiosphere derived stem cells with the additional intention of regenerating heart tissue. Both agents were investigated with rigorous methodology, utilizing extensive blinding and randomization, and clinically relevant techniques.

In spite of an abundance of pre-clinical support for both therapies, we were unable to demonstrate any benefits on infarct size, cardiac function, or remodeling with either therapy in our translational model of acute myocardial infarction. This underscores the need for rigorous testing and development of potential therapies in preclinical translational research prior to attempting expensive and futile clinical trials.

Genomics and Stem Cells for Cardiovascular Precision Medicine

Joseph Wu, M.D., Ph.D.
Stanford University
Stanford, CA

Heart disease is the most significant cause of morbidity and mortality in the industrialized world, accounting for nearly 25% of all deaths in the United States alone. While the use of human induced pluripotent stem cell (iPSCs) in regenerative medicine is a long-term goal, a growing body of studies has shown promising results in the fields of drug discovery, development, and toxicity screening. Specifically, recent technological advancement has enabled the generation of patient-specific and disease-specific human induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) in vitro. These iPSC-CMs carry all the genetic information from the individuals from whom they are derived. Here I will discuss recent advances in this technology and how it may be used for elucidating mechanisms of rare inherited cardiovascular diseases, for drug discovery, and for precision medicine.

POSTER ABSTRACTS

1. Developing Cell Adhesion Engineering (CAE) Technology to Improve Stem Cell Delivery Following Myocardial Ischemia-Reperfusion Injury.

Arezoo Momeni [1,2], Sriram Neelamegham[1,2]

[1] Department of Chemical and Biological Engineering, University at Buffalo, SUNY
[2] Division of Cardiovascular Medicine, Clinical Translational Research Center, University at Buffalo, SUNY

[3] VA Western New York Health Care System, Buffalo

2. Engagement of Cadherin-11 Promotes Cell Growth in Cooperation with Platelet Derived Growth Factor Receptor (PDGFR) via AKT Pathway

Yayu Liu[a], Sindhu Row[b], Pedro Lei[b] , Stelios T. Andreadis[a,b]

[a] Biomedical Engineering, University at Buffalo, Buffalo NY
[b] Chemical and Biological Engineering, University at Buffalo, Buffalo NY

3. NANOG Expression Ameliorates the Hallmarks of Aging in Skeletal Muscle Progenitors

Aref Shahini[1], Nika Rajabian[1], Debanik Choudhury[1], Kalyan Vydiam[2], Thy Nguyen[2], Tyler Santarelli[2], Izuagie Ikapolah[1],Yali Zhang[3], Song Liu[3], Hannah Pletts[4], Aimee Stablewski[4], Ramkumar Thiyagarajan[5], Yonas Redae[5], Kenneth Seldeen[5], Bruce R. Troen[5], Pedro Lei[1], Stelios T. Andreadis[1,2,6]

[1] Bioengineering Laboratory, Department of Chemical and Biological Engineering, University at Buffalo

[2] Department of Biomedical Engineering, University at Buffalo
[3]Department of Biostatistics and Bioinformatics, Roswell Park Cancer Institute
[4] Gene Targeting and Transgenic Shared Resource, Roswell Park Cancer Institute
[5] Department of Medicine, Jacobs School of Medicine & Biomedical Sciences
[6] Center of Excellence in Bioinformatics and Life Sciences

4.Store-Operated Calcium Signaling Regulates Human Oligodendrocyte Progenitor Stem Cell Fate

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5. Genome Editing of Primary Neutrophils Derived from CD34+ Human Hematopoietic Stem Cells: CD44 is a Physiological Human Neutrophil E-selectin Ligand

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6. Transforming human skin cells to functional peripheral neurons

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7. Exosomes secreted by cardiosphere-derived cells induce an Arginase 1-dependent phenotype in diverse macrophage polarization states that promotes angiogenesis

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8.Multipotency of Neural Crest Stem Cells from Human Epidermis of Aged Donors in Vitro and in Vivo

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9. Spatial Delivery of FGF-7 and FGF-10 via Laminin-111 Peptide Conjugated Fibrin Hydrogels Controls the Branching Phenotype in Parotid Gland Cell Clusters

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10. Bioengineered senescent muscle tissue model for assessing therapeutic compounds.

Nika Rajabian[1], Aref Shanini[1], Mohammadnabi Asmani[2], Kalyan Vydiam[2], Debanik Choudhury[1], Thy Nguyen[2], Pedro Lei[1], Ruogang Zhao[2], Stelios T. Andreadis[1,2,3]

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11. 6-O Sulfation Modulates Cell-Fate Signaling in Oligodendrocyte Progenitor Cells

Jessie J. Polanco[1], Hani J. Shayya[2], Suyog U. Pol[2], R. Ross Welliver[2], Melanie A. O'Bara[2], Toin H. van Kuppervelt[3], Joanna J. Phillips[4,5], Fraser J. Sim[1,2]

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12. NANOG Restores Collagen Type III Production in Aged Stem Cells

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13. CDC-exosomes influence regulation of the orphan nuclear receptor-Nr4a1 in macrophages and potentiate immunosuppressive effects on downstream inflammatory genes

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14. Off-the-shelf Vascular Grafts in a Growing Animal Model

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15. The Role of Monocytes in Endothelium Regeneration

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16. From Skin to Nervous System: Epidermis Derived Neural Crest Stem Cells, Road to Cell Therapy

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17. NFIA and NFIB are Jointly Required for Mouse Neural Stem Cell Self-renewal and Differentiation

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18. Metabolic Mechanisms Underlying NANOG-Induced Reversal of Aging

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19. An in vitro, three-dimensional model of liver development from human pluripotent stem cells

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20. The effects of organoid formation on hPSC-derived pancreatic progenitor maturation

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21. Improved Action Potential Recordings in Stem Cell Derived Cardiomyocytes with Leak Current Correction via Dynamic Clamp

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22. Establishing Stable, Physiological IKr Expression Levels in Human-Derived Stem Cell Cardiomyocytes for Improved Cardiotoxicity Drug Screening

Ronique Fletcher[1], Christine Hickey[3], Mark W. Nowak[3], Brian K. Panama[1,3], Leigh Korbel[3], Zhengfeng Zhou[2], Randall L. Rasmusson[1,3], Glenna CL. Bett[1,3]

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23. Improving Action Potential Recording in Human Stem Cell Derived Neurons by Utilization of a Neuronal Dynamic Clamp System

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24. MODELING TRAPPING BLOCK OF HERG FOR CIPA: DOES THE BASAL HERG MODE MATTER?

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25. Pharmacological inhibition of IFN-γ signaling by heparin mimetic PI-88 encourages a favorable environment for remyelination in demyelinating lesions

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