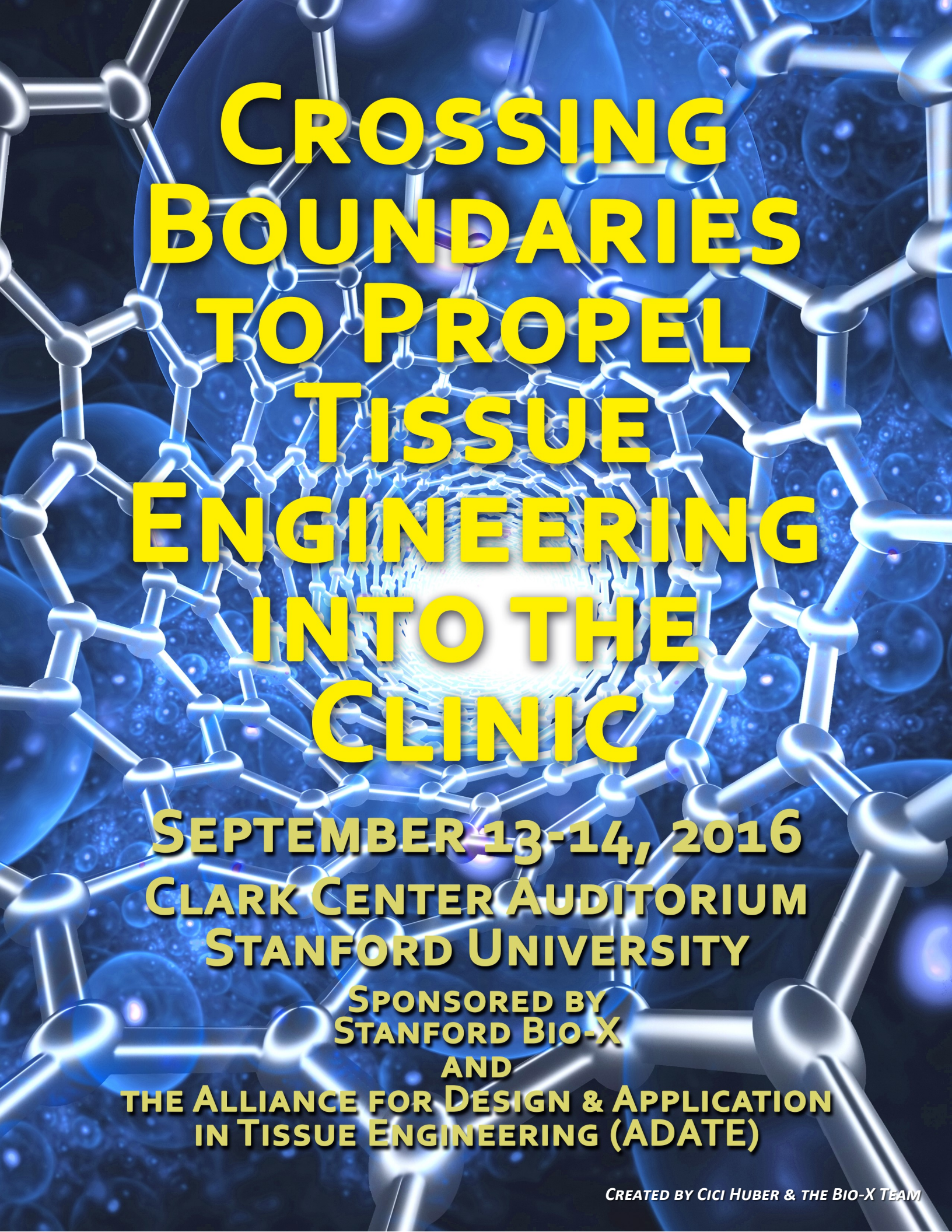

Crossing Boundaries to Propel Tissue Engineering into the Clinic
September 13-14, 2016
Clark Center Auditorium
Stanford University
Sponsored by
Stanford Bio-X
and
the Alliance for Design & Application in Tissue Engineering (ADATE)
Created by Cici Huber & the Bio-X Team

Crossing Boundaries to Propel Tissue Engineering into the Clinic

Tuesday, September 13th

Carla Shatz

9:00 AM

Welcome and Introduction

Carla Shatz, Sapp Family Provostial Professor
Professor of Biology and Neurobiology
David Starr Jordan Director of Stanford Bio-X

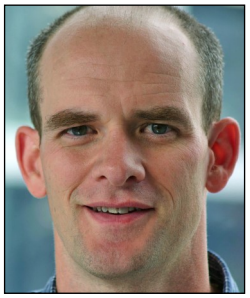
9:10 AM

Transplanted Cells and Viscoelasticity

David Mooney, Robert P. Pinkas Family Professor of Bioengineering, School of Engineering and Applied Sciences and Wyss Institute, Harvard University

Abstract:

There is tremendous interest in the role of substrate stiffness on cell behavior, but most current work ignores that tissues are typically viscoelastic and also has not examined the impact of physical properties on tissue regeneration. We have developed materials that allow changes in mechanical properties to be decoupled from changes in hydrogel architecture, and have found with these materials that both gel stiffness and the rate of relaxation regulate participation of MSCs in bone regeneration in rodents. To exploit the impact of these properties at the single cell level, a microfluidic-based method for encapsulating single cells in an ~5 micron thick layer of hydrogel has been developed.



David Mooney

Zufu Lu

9:40 AM

The Exosomes from Adipose Tissue-derived Mesenchymal Stem Cells: Potential Application for Bone Tissue Regeneration

Zufu Lu, Postdoctoral Fellow, Biomaterials and Tissue Engineering Research Unit, School of Aerospace, Mechanical and Mechatronic Engineering, University of Sydney

Abstract:

Mesenchymal stem cells (MSCs) are a promising cell source for tissue repair and regeneration. However, direct MSCs transplantation to tissue injury sites has its inherent drawbacks such as senescence-induced genetic instability and limited cell survival. The aim of this study was to employ the exosomes produced by MSCs for use in bone tissue regeneration. We showed that adipose tissue-derived MSC (ASCs)-derived exosomes (ASC-EXO) are capable of promoting proliferation, migration, and osteogenic differentiation in osteoblasts, and the effects are further harnessed by TNF-α pre-conditioning through Wnt signaling pathway, suggesting that ASC-derived exosomes might offer a promising approach to replace direct stem cell transplantation for bone repair and regeneration.

Hong-pyo Lee

9:50 AM

Enhanced Stress Relaxation in Hydrogels Promotes Cartilage Matrix Formation by Chondrocytes

Hong-pyo Lee, Graduate Student, Chaudhuri Lab, Stanford University

Abstract:

Cartilage tissue equivalents formed from hydrogels containing chondrocytes could provide a solution for replacing damaged cartilage. However, there has been limited success to date, possibly because the hydrogels typically used are elastic, as elastic stresses would be expected to restrict formation of cartilage matrix. Here we investigated how stress relaxation of viscoelastic hydrogels impacted the ability of chondrocytes to form cartilage matrix. Strikingly, we found that faster stress relaxation led to an increase in cartilage matrix formation by chondrocytes and cell proliferation. These results highlight stress relaxation as an important design parameter in biomaterials used for cartilage tissue engineering.

10:00 AM

TISSUE ENGINEERING FOR OSTEOARTHRITIS – DOES THE DISEASE PHENOTYPE MATTER?

Christopher Little, Director of the Raymond Purves Bone and Joint Research Labs at the Kolling Institute of Medical Research at Royal North Shore Hospital, Australia and Professor of Surgery, University of Sydney

Abstract:

The emerging paradigm is that rather than being a single entity, OA is a collection of disease sub-types with similar end-stage pathology, but distinct underlying molecular pathophysiology. Pre-clinical research in OA is increasingly embracing the study of the joint as an organ and interpreting data in the context of the different OA phenotype that is being modeled. It is hoped this approach will improve the presently poor translation of pre-clinical research to clinical trails and better-targeted treatment strategies for OA. As relevant to tissue engineering as to pharmacological approaches to treat OA, this talk will investigate the pathophysiology and joint-tissue interactions in different OA phenotypes and how this might impact on treatment strategies.

CHRISTOPHER LITTLE

10:30 AM

BREAK

11:00 AM

BUILDING INJECTABLE MICROPOROSITY THROUGH THE ASSEMBLY OF PARTICLE BUILDING BLOCKS

Tatiana Segura, Associate Professor of Chemical and Biomolecular Engineering, University of California, Los Angeles

Abstract:

Injectable materials that can conform to the shape of a desired space are used in a variety of fields including medicine. The ability to fill a tissue defect with an injectable material can be used for example to deliver drugs, augment tissue volume, or promote repair of an injury. This talk will explore the development of injectable materials that are based on assembled particle building blocks, which generate a microporous network. Due to the injecability of this microporous material we have explored its wide applicability to tissue repair applicatins ranging from skin to brain wounds.

TATIANA SEGURA

RACHEL SHPARBERG

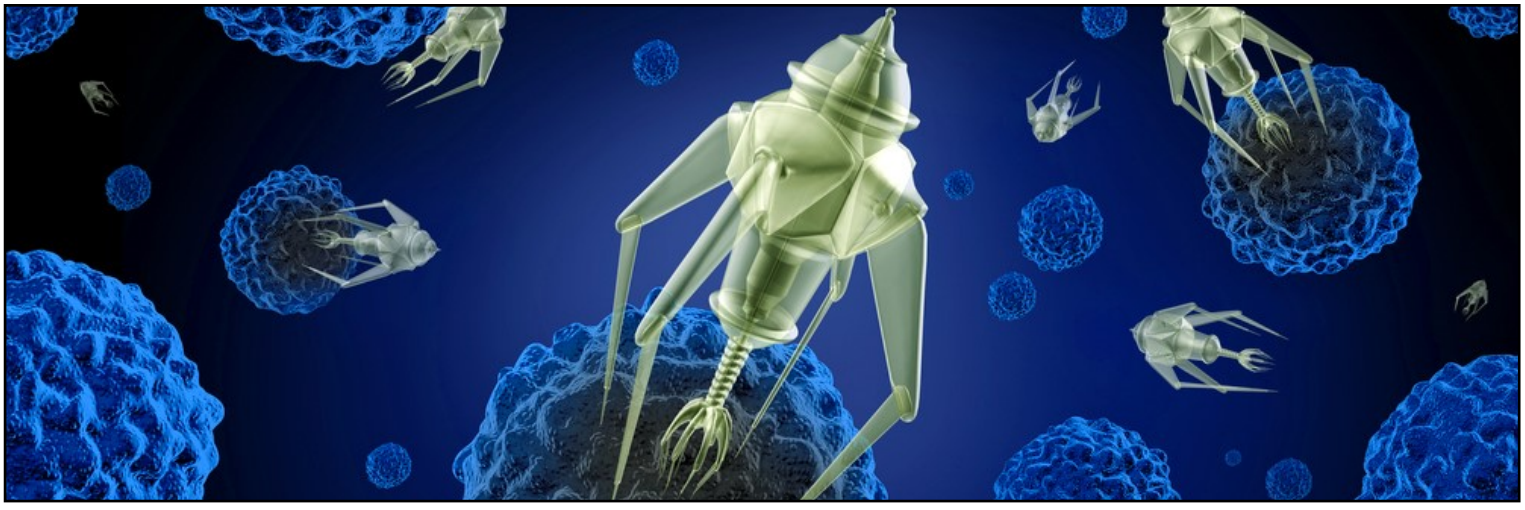
11:30 AM

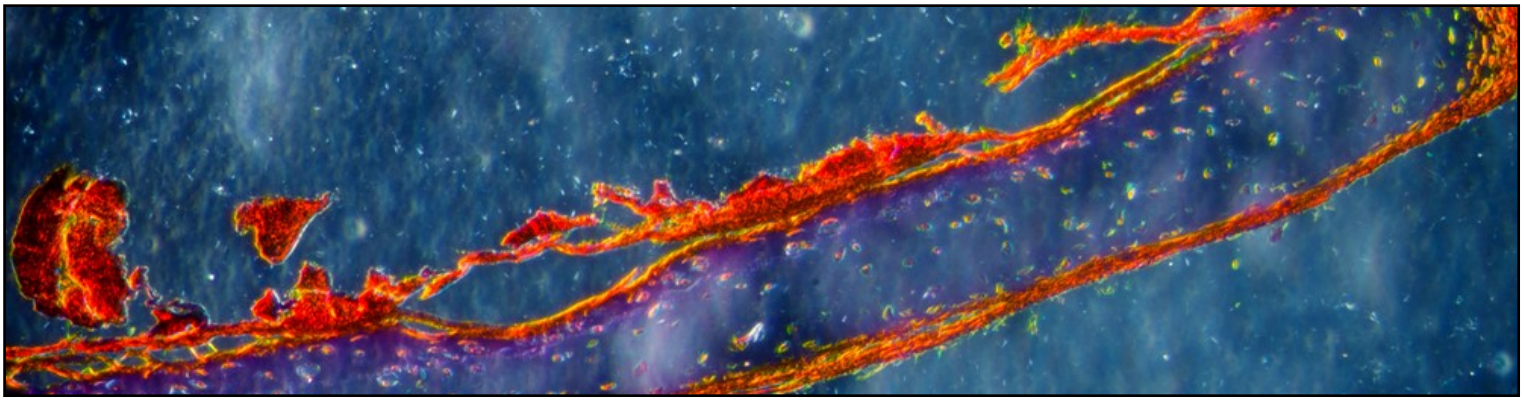
A NOVEL GROWTH FACTOR-LIKE ROLE FOR THE AMINO ACID L-PROLINE IN DRIVING NEURAL LINEAGE COMMITMENT OF MOUSE EMBRYONIC STEM CELLS THROUGH EARLY PRIMITIVE ECTODERM-LIKE CELL, DEFINITIVE ECTODERM-LIKE AND NEURECTODERM POPULATIONS

Rachel Shparberg, Graduate Student, Embryonic Stem Cell Lab, Bosch Institute and Discipline of Physiology, School of Medical Sciences, University of Sydney

Abstract:

To engineer cells that may be useful for regenerative medicine, it is useful to understand the mechanisms that govern how one cell type is transformed (or differentiated) into another cell type. Currently, little is known about the mechanisms that take cells of the very early embryo and turn them into cells of the early nervous system. Using mouse embryonic stem cells (mESCs) as a laboratory tool for studying early embryogenesis, we have developed a protocol that mimics this complex process. This tool has revealed unique processes by which the early nervous system is constructed in the developing embryo.





Christopher Madl

11:40 AM

Maintenance of Neural Progenitor Cell Stemness in 3D Hydrogels Requires Matrix Remodeling

Christopher Madl, Graduate Student, Heilshorn Lab, Stanford University

Abstract:

Neural progenitor cells (NPCs) hold significant therapeutic potential for use in the treatment of nervous system disorders. Delivering these cells in hydrogel material carriers is a promising strategy to enhance cell survival post-transplantation, but the material properties that are required to maintain the proper function of NPCs within such hydrogels have yet to be elucidated. Using two different engineered hydrogel systems, we have identified matrix degradability as a critical material property for maintaining the stem cell phenotype of NPCs, as stemness is best maintained in high degradability gels. Furthermore, we have demonstrated a novel role for the protease ADAM9 in NPC-mediated matrix remodeling. We anticipate that biomaterials that exploit ADAM9-mediated remodeling may increase the regenerative potential of NPC therapies.

Yu-I Hsu

11:50 AM

Surface Modification of Poly(L-lactic acid) Nanofiber Conduits with Oligo(D-lactic acid) Bioactive Peptide Conjugates for Nerve Regeneration Tube

Yu-I Hsu, Postdoctoral Fellow, Department of Biomedical Engineering, National Cerebral and Cardiovascular Center Research Institute, Osaka, Japan

Abstract:

Nerve injuries result in significant nerve gaps leading to the loss of motor and sensory functions. An autologous nerve graft from the patient's own body is used to bridge the injury site. However, it causes the permanent loss of donor function, and size mismatch between the injured nerve and the graft nerves. Recently, artificial nerve conduit is developed for bridging the gap between severed nerve stumps. In this study, we developed a PLLA nanofibrous nerve conduit, modified with a conjugate of oligo(D-lactic acid) (ODLA) and the neurite outgrowth, thereby promoting bioactive peptide IKVAV to improve the nerve regeneration.

12:00 PM

Customized Biomaterials for Stem Cell Biomanufacturing and Human Tissue Assembly

William L. Murphy, Harvey D. Spangler Professor of Biomedical Engineering, Co-Director of Stem Cell and Regenerative Medicine Center, University of Wisconsin, Madison

William Murphy

Abstract:

The need for human, organotypic culture models coupled with the requirements of contemporary drug discovery and toxin screening (i.e. reproducibility, high throughput, transferability of data, clear mechanisms of action) frame an opportunity for a paradigm shift. The next generation of high throughput cell-based assay formats will require a broadly applicable set of tools for human tissue assembly and analysis. Toward that end, we have recently focused on: i) generating patient-derived cells that properly represent the diverse phenotypic characteristics of developing or mature human somatic cells; ii) assembling organotypic cell culture systems that are robust and reproducible; iii) translating organotypic cell culture models to microscale systems for high throughput screening; and iv) combining genomic analyses with bioinformatics to gain insights into organotypic model assembly and the pathways influenced by drugs and toxins. This talk will emphasize recent studies in which we have explored therapeutic cell manufacturing and biologically driven assembly of organotypic vascular and neural tissues. These tissues mimic critical aspects of human tissues, and can be used for disease modeling, drug discovery, and predictive toxicology.

12:30 PM

Lunch

1:40 PM

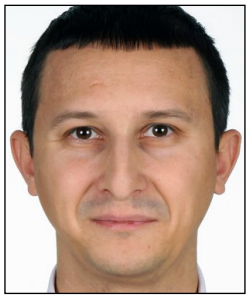
TOOLS FOR ACCELERATED MEDICAL INNOVATION

JEFF KARP

Jeff Karp, Associate Professor of Medicine, Brigham and Women's Hospital & Harvard Medical School

Abstract:

Scientists have something in common with professionals in business, academia, government and beyond. We all need to solve problems, but we're tempted to get comfortable with a limited "toolbox" of techniques and approaches. No matter our field, it can be difficult to break out of our old limitations and achieve something new and different. In this talk, Dr. Jeffrey Karp reveals two of the most powerful "tools" used by his bio-research lab to solve problems. The first tool is bioinspiration—the art and discipline of adapting proven-effective techniques, materials, designs and concepts from nature to provide the foundation for a bold new human-designed solution. For example, creatures like slugs and snails have provided inspiration for a next generation surgical adhesive. The second tool is radical simplicity—the art and discipline of reducing a problem to its essence. Dr. Karp has harnessed this tool to develop prophylaxis technologies for contact dermatitis that were rapidly advanced to the market and are being used in 15 countries and therapeutic strategies to combat inflammatory bowel disease that are advancing to clinical studies. Jeff explains how his team has employed these tools and how they can succeed in any field. This talk opens exciting new paths to the continual innovation that is so important in today's fast-changing world.



GABRIEL NASTASE

2:10 PM

ISOCHORIC CRYOPRESERVATION FOR TISSUE ENGINEERING

Gabriel Nastase, Postdoctoral Fellow, Rubinsky Lab, University of California, Berkeley

Abstract:

An important aspect of tissue engineering is preservation of the tissue or organ between the time it is produced and used. Refrigeration, reduces metabolism and, therefore, is used to preserve biological matter. However, preservation at above freezing temperature is limited to several hours; about 6 hours for a heart. Preservation at below freezing temperatures, introduces a whole array of different biotechnological challenges, and is not successful yet. We have introduced a new concept for sub-zero ºC preservation of biological matter, without freezing – isochoric preservation. Isochoric preservation, employs thermodynamic principles based on a system at constant volume.

PETER NEWMAN

2:20 PM

3D PRINTING MULTIVARIATE HYDROGELS FOR BOTTOM-UP FABRICATION OF CELLULAR ENVIRONMENTS

Peter Newman, Graduate Student, Biomaterials and Tissue Engineering Research Unit, School of Aeronautical Mechanical and Mechatronics Engineering, University of Sydney

Abstract:

This work explores bottom up synthesis of extracellular environments using 3D printing. We combine a small set of modular components to create scaffolds with varying mechanical, biochemical and architectural properties in a manner in that these properties are not intrinsically linked. Using this approach, we create heterogeneous environments and examine the cellular response of mesenchymal stem cells to various permutation of differing mechanical, biochemical and architectural properties.

Specifically, we use direct ink writing of bio inert polyethylene glycol (PEG) hydrogels. Using a custom built micro dispensing system we vary and mix PEG with bioactive peptide sequences. Through combination of these components at various ratios we control the mechanical and biochemical properties of our scaffolds. Finally, using the printer we control the architecture of the final scaffolds. We show human mesenchymal stem cells change their response to the contrasting environments altering cell attachment, mechanotransduction and differentiation.

2:30 PM

ORGANS ON A CHIP: THE FUTURE OF PRECLINICAL RESEARCH AND PERSONALIZED MEDICINE?

KEVIN HEALY

Kevin E. Healy, Jan Fandrianto Distinguished Chair in Engineering, Professor and Chair of Bioengineering, and Professor of Materials Science and Engineering, University of California, Berkeley

Abstract:

Drug discovery is hampered by high failure rates attributed to reliance on non-human animal models that poorly recapitulate human disease states. Exploiting human induced pluripotent stem cells, we have developed in vitro disease specific tissue models for more predictive high content drug screening and patient specific medicine. This presentation will discuss our progress in developing integrated in vitro models of human cardiac and liver tissue based on populations of normal and patient specific hiPS cells differentiated into cardiomyocytes, hepatocytes, or supporting cells. Emphasis will be placed on whether these 'organs on a chip' are the future of preclinical research and patient specific therapy.

3:00 PM

BREAK

3:30 PM

BIOTECH PANEL

MODERATOR:

Widya Mulyasasmita, Manager of New Ventures, Johnson & Johnson California Innovation Center

Bio:

Widya is a Manager of New Ventures at Johnson & Johnson Innovation, supporting deals and collaborations across consumer, medical device and pharmaceutical sectors. Prior to Johnson & Johnson, Widya was a management consultant at McKinsey & Company, worked at GE Ventures Healthcare, and was a co-founder of Lap IQ, a medical device startup. She received her B.S. in Materials Science Engineering and Bioengineering from UC Berkeley and her Ph.D. in Bioengineering from Stanford University.

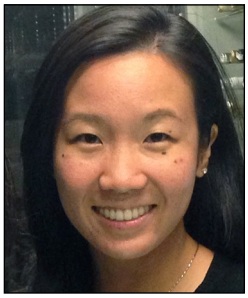
PANELISTS:

JENNIFER COCHRAN

Jennifer Cochran, Associate Professor of Bioengineering and (by courtesy) of Chemical Engineering, Stanford University

Bio:

Dr. Jennifer Cochran is the Hitachi America Faculty Scholar Associate Professor of Bioengineering and (by courtesy) Chemical Engineering at Stanford. Her expertise spans protein-based drug discovery and development for applications in oncology and regenerative medicine, and development of new technology for high-throughput protein analysis and engineering. Dr. Cochran is currently on leave of absence from Stanford to lead technology transfer efforts from academia to the commercial sector in the form of start-up companies and licensing opportunities.



HANWEI LI

Hanwei Li, Industry & Strategic Alliance Manager, Stanford Bio-X

Bio:

Dr. Li manages the Bio-X Corporate Forum Program, in which she has bridged the gap between academia and industry by cultivating and managing 50+ collaborations between 75+ Stanford faculty and 15+ corporations. This has secured $14M+ in external funding to support Stanford research through numerous mechanisms in the past 5 years. Prior to Stanford, Hanwei worked in biotech after obtaining her PhD in Biomedical Engineering from Johns Hopkins University School of Medicine with a focus in tissue engineering, and also a BS in Electrical Engineering from MIT.

HALA ZREIQAT

Hala Zreiqat, Professor of Biomedical Engineering and Head of Tissue Engineering & Biomaterials Research Unit, School of AMME/Faculty of Engineering and IT and Bosch Institute, The University of Sydney

Bio:

Dr. Hala Zreiqat is interested in biomaterials and translational orthopaedic research. She recently developed a novel ceramic biomaterial (Sr-HT Gahnite) for regenerating large bone defects, which led to a global licensing agreement with Allegra Orthopaedics and a $1.6M grant from the NSW Medical Device Fund. In addition, she has established an industry partnership with a German orthopaedic company to take another ceramic material to clinical trial.

JEFF KARP

Jeff Karp , Associate Professor of Medicine, Brigham and Women's Hospital & Harvard Medical School

Bio:

Chemical Engineer Dr. Jeff Karp is a world leader in the fields of drug delivery, stem cell therapeutics, and tissue adhesives. He is an Associate Professor at Brigham and Women's Hospital, Harvard Medical School, has published >100 peer-reviewed papers (with 11,000 citations) and has given 235 national and international invited lectures, and has 65 issued or pending patents. Several technologies developed in his lab have formed the foundation for multiple products on the market and currently under development and for the launch of five companies.

GORDON SAUL

Gordon M. Saul, Executive Director of Biodesign and Adjunct Professor of Bioengineering, Stanford University

Bio:

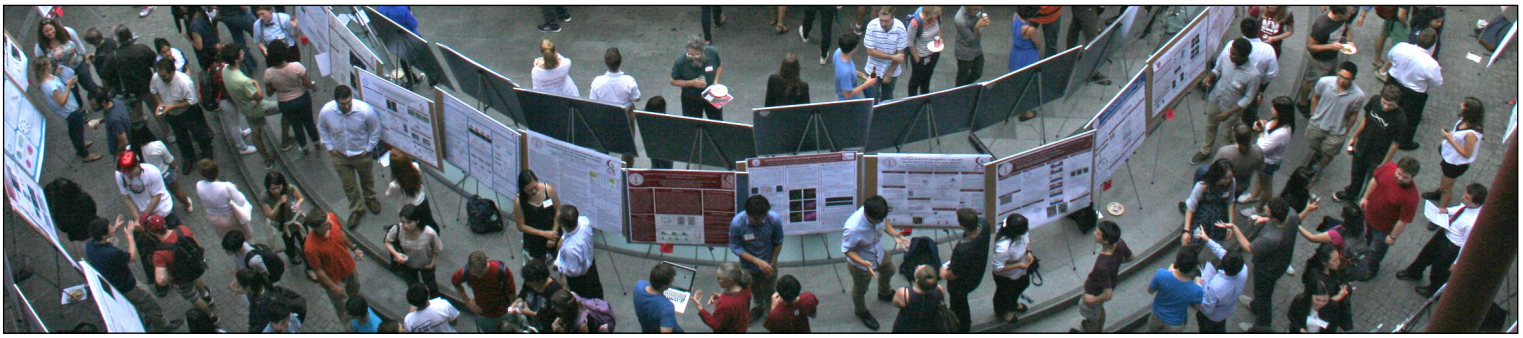
Gordon is the Executive Director of the Byers Center for Biodesign at Stanford, a unit of Bio-X dedicated to advanced training in medical technology innovation. Prior to joining Stanford, Gordon was an Executive-in-Residence at InterWest Partners, a leading Silicon Valley venture capital firm. At InterWest, Gordon served as a founding or interim executive in over a dozen medical device and biopharmaceutical companies. Prior, he was a co-founder, board member and senior vice president of business development and marketing for PowderJect Pharmaceuticals. He held business development roles at ALZA Corporation and Advanced Cardiovascular Systems. He has also worked in Japan in financial services and in management consulting for The Boston Consulting Group. Gordon has an A.B. in engineering sciences from Dartmouth College and an M.B.A. from Stanford.

TOM WEHRMAN

Tom Wehrman, Head of Discovery R&D, Primity Bio

Bio:

Tom Wehrman received his PhD from the Molecular Pharmacology Department at Stanford University in 2004. His thesis centered around drug screening technologies using enzyme complementation. These inventions were subsequently licensed to DiscoveRx where he led the development and commercialization as the Vice President of R&D. In 2012 he co-founded Primity Bio with an ex-Stanford colleague, Peter Krutzik. Primity focuses on applications of flow cytometry in drug discovery using technologies developed internally and licensed from Stanford.



5:00 PM

POSTER SESSION

1. Telomere and Mitochondrial Dysfunction in Duchenne Muscular Dystrophy
2. Engineering Pre-Vascularized Skeletal Muscle with Physiologically-Relevant Cellular Organization for Treatment of Volumetric Muscle Loss
3. Maintenance of Neural Progenitor Cell Stemness in 3D Hydrogels Requires Matrix Remodeling
4. Human Bone Marrow-Derived Mesenchymal Stem Cells Delivery Using Biomimetic Cell-Laden Hydrogels
5. Engineering of Three-Dimensional Microenvironments to Promote Contractile Behavior in Primary Intestinal Organoids
6. Reconstruction of Large Segmental Bone Defects in Sheep Tibiae Using Novel Baghdadite Scaffolds as Bone Graft Substitutes
7. Decreased Osteogenesis in Mesenchymal Stem Cells Derived from the Aged Mouse is Associated with Enhanced NF-κB Activity
8. A Novel Growth Factor-Like Role for the Amino Acid L-proline in Driving Neural Lineage Commitment of Embryonic Stem Cells through Early Primitive Ectoderm-Like Cell, Definitive Ectoderm-Like and Neurectoderm Populations
9. L-Proline Regulates Mouse Embryonic Stem Cell Pluripotency through the mTOR and MAPK Pathways to Initiate Differentiation to Neural Cells
10. Isolation of Undifferentiated iPS Cell Based on Cell Rolling Phenotype in Antibody Immobilized Microfluidic Channel
11. Improving Cell Transplantation Therapies for Spinal Cord Injury using Injectable Hydrogels
12. Spatial Organization of Multiple Peptide Gradients within a Single Scaffold to Guide Osteochondral Interface Regeneration
13. Surface Modification of poly(L-lactic acid) Nanofiber Conduits with oligo(D-lactic acid) Bioactive Peptide Conjugates for Nerve Regeneration Tube
14. Viscoelastic Elastin-like Protein – Hyaluronic Acid (ELP – HA) Hydrogels for Organotypic Cultures
15. Extracellular Matrix Promote Survival and Phenotype of Human iPSC-Derived Endothelial Cell in Hypoxia
16. Physicochemical Characterization of a Novel Bioactive Ion-Doped Calcium Silicate Phosphate Injectable Bone Cement
17. Hydrogel Brain Delivery of Clustered VEGF for Post-Stroke Tissue Regeneration

Wednesday, September 14th

ANUSUYA RAMASUBRAMANIAN

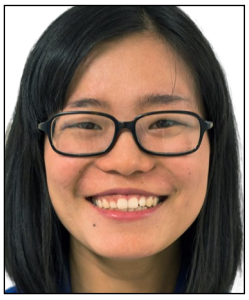
9:30 AM

ENGINEERING NOVEL LAMININ-MIMETIC PEPTIDES FOR HUMAN PLURIPOTENT STEM CELL SELF-RENEWAL AND DIFFERENTIATION

Anusuya Ramasubramanian, Graduate Student, Healy Lab, University of California, Berkeley

Abstract:

Developing synthetic materials for human pluripotent stem cell (hPSC) expansion has been a challenge in regenerative medicine. Here, we used unbiased selection strategies to identify peptide mimetics for laminin-511 – an important component of hPSC extracellular matrices (ECM). Using bacterial display and microculture techniques, we pared massive peptides libraries to identify high-affinity binders of the laminin-511 receptor, α6β1 integrin. Through thiol-mediated chemistries, these peptides were self-assembled into monolayers or functionalized onto thermoreversible biopolymers to generate 2D and 3D hPSC culture systems. Our results, thus, outline a viable synthetic ECM for hPSC self-renewal as well as unbiased strategies to generate novel biomaterials.



SANDY SHUORAN LI

9:40 AM

EFFECTS OF INTEGRIN-SPECIFIC TUNING ON VASCULAR DEVELOPMENT

Sandy (Shuoran) Li, Graduate Student, Segura Lab, University of California, Los Angeles

Abstract:

The development of vasculature is highly dependent on the extracellular matrix (ECM). Integrin binding to natural ECM-mimicking bioengineered hydrogel scaffolds is essential for tissue regrowth and regeneration, yet not all integrin binding can lead to tissue repair. Also, both upregulation and abolishment of integrin activation have shown to be related to pathological angiogenesis. Thus, strategies to effectively and safely promote vascularization at injured or diseased sites based on integrin activation needs careful evaluation. Therefore, we established a platform to precisely control integrin specificity of hydrogel scaffolds and studied the effects of integrin-specific tuning on vascular development.

JIAJO JIAO LI

9:50 AM

RECONSTRUCTION OF LARGE SEGMENTAL BONE DEFECTS IN SHEEP TIBIAE USING NOVEL BAGHDADITE SCAFFOLDS AS BONE GRAFT SUBSTITUTES

Jiao Jiao Li, Postdoctoral Researcher, Biomaterials and Tissue Engineering Research Unit, University of Sydney

Abstract:

The effective treatment of large bone defects, particularly those with segmental bone loss, remains a significant clinical challenge. In this study, novel baghdadite ceramic scaffolds were implanted as bone graft substitutes into critical-sized segmental defects in sheep tibiae for 26 weeks. Radiographic, biomechanical, μ-CT and histological analyses showed that the scaffolds could withstand physiological loads at the defect site and induce substantial bone bridging across the defect, in the absence of supplementation with cells or growth factors. These results support the potential use of baghdadite scaffolds for the treatment of large bone defects while circumventing the drawbacks of bone grafting.

10:00 AM

HIGH PRESSURE ENGINEERING FOR ACELLULAR BLOOD VESSEL PREPARATION AND CANCER THERAPY

Tetsuji Yamaoka, Director of Department of Biomedical Engineering, National Cerebral and Cardiovascular Center Research Institute (NCVC), Japan

Abstract:

High pressure treatment ranging from 150-1000MPa is very useful to decellularize tissues or to inactivate (kill) the cells in the tissue under a much milder condition with less ECM denaturation than the other methods such as heating, lyophilization, or irradiation. One example is the ostrich carotid artery-derived acellular blood vessel with the inner diameter of 2mm and length of 30cm. Very high patency and tunica media regeneration was achieved in porcine and goat transplantation models. In addition, we recently established cancer therapy using high pressure and started clinical trials of autologous transplantable artificial skin tissues for treating giant congenital melanocytic nevi. These two examples will be introduced.

TETSUJI YAMAOKA

10:30 AM

BREAK

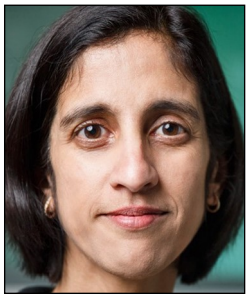
11:00 AM

NANOSTRUCTURED PLATFORMS FOR CELL BASED THERAPY AND TISSUE REGENERATION

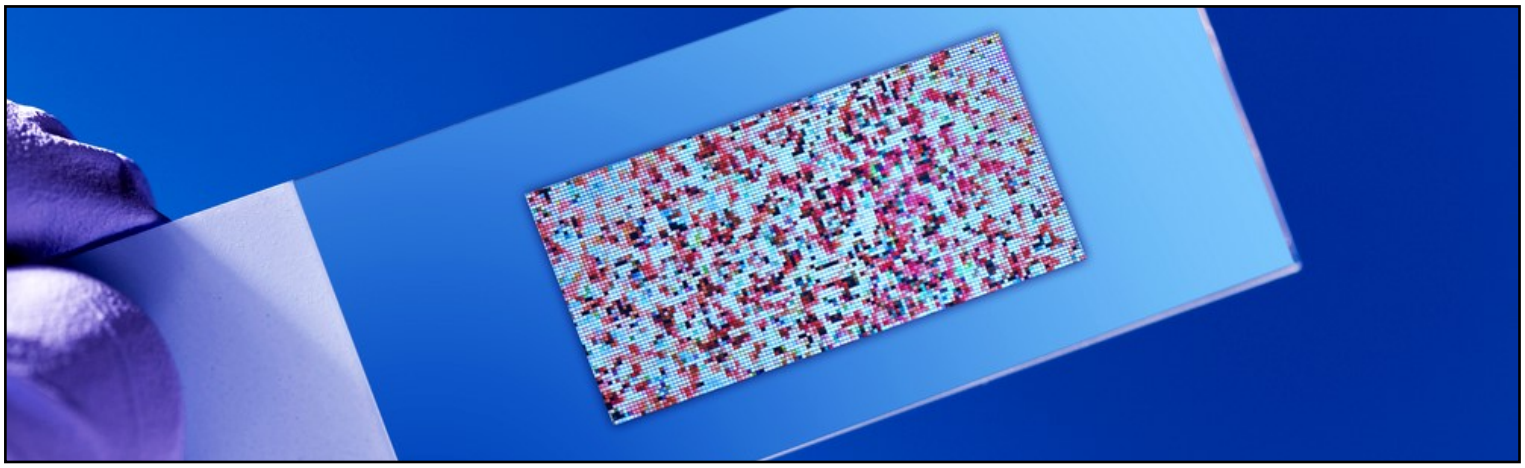
Tejal Desai, Professor and Chair of Bioengineering and Therapeutic Sciences, University of California, San Francisco

Abstract:

The field of nanomedicine offers great potential to revolutionize clinical care, including medical devices, regenerative medicine, and molecular imaging approaches. Recent advancements in nanofabrication applied to biocompatible materials lay the groundwork for creating biomaterials with a high level of control at the molecular scale. These subtle interactions with cell and tissue assemblies can modulate properties such as proliferation, growth factor production, and immune activation. Examples include nanostructured materials for cell-based delivery and immunoprotection as well as microscale materials for the modulation of fibrosis. By gaining a better understanding of how small scale topographies can influence the biological microenvironment, we can design nanostructured platforms for applications in cell based therapy and tissue regeneration.



TEJAL DESAI



Yogambha Ramaswamy

11:30 AM

Effect of Micropatterned Bioceramics on the Growth and Differentiation of Adipose Derived Stem Cells

Yogambha Ramaswamy, NHMRC Early Career Fellow, Biomaterials and Tissue Engineering Research Unit, School of Aerospace, Mechanical and Mechatronic Engineering, University of Sydney

Abstract:

Biomaterial substrates with ordered nano/micro patterns can stimulate cellular responses in terms of adhesion, migration, cytoskeletal organisation, proliferation and differentiation. The aim of this study is to develop a simple cost effective sustainable technique to produce ordered micropatterns on ceramic substrates. The variation in the microtopographic pattern induced marked differences in the cell morphology and osteogenic differentiation of adipose derived stem cells. The cellular responses to the unique patterns developed in this study shows that the topographical changes can affect the cellular activity and may be an important design criteria for enhancing the bioactivity of currently available ceramic implants.

Akihisa Otaka

11:40 AM

Isolation of Undifferentiated iPS Cell Based on Cell Rolling Phenotype in Antibody Immobilized Microfluidic Channel

Akihisa Otaka, Postdoctoral Fellow, Department of Biomedical Engineering, National Cerebral and Cardiovascular Center Research Institute, Osaka, Japan

Abstract:

Immunophenotyping is one of the successful methods to purify homogenous stem cell population. However, labeling cells with antibody is a time-consuming and sometimes results in unintended effects on the purifying cells. We proposed a label-free cell separation device called “cell rolling column” in which cells selectively roll on antibody-immobilized column surfaces. In this study, undifferentiated pluripotent stem cells (iPSCs) were isolated using a microfluidic channel coated with an amphiphilic phospholipid polymer and immobilized with monoclonal antibodies against stage-specific embryonic antigen 1. The moving velocity of iPSCs was significantly decreased with antibody immobilization, and cell rolling column can be a promising tool for iPSC isolation.

Karina Nakayama

11:50 AM

Engineering Pre-Vascularized Skeletal Muscle with Physiologically-Relevant Cellular Organization for Treatment of Volumetric Muscle Loss

Karina Nakayama, Postdoctoral Fellow, Ngan Huang Lab, Stanford University

Abstract:

A successful therapeutic intervention to treat traumatic musculoskeletal injury must restore vasculature, muscle function, and physiological anatomical structure. Towards this goal, we bioengineered parallel-aligned skeletal muscle constructs that mimic the physiological orientation and cellular composition of native muscle tissue. Aligned muscle constructs demonstrated 2-fold greater myotube lengths and nuclei incorporation, and coordinated contraction properties compared to non-aligned constructs. To assess their therapeutic potential, constructs were transplanted into a mouse model of volumetric muscle loss. The region of muscle injury treated with constructs composed of aligned myoblasts and endothelial cells demonstrated significant re-vascularization, improved cell survival, and enhanced muscle regeneration, compared with non-aligned and cell-free constructs. This work demonstrates that pre-vascularized engineered muscle using aligned nanofibrillar scaffolds, mimics the spatial organization of native muscle and has important translational potential as a tissue graft to enhance muscle regeneration.

Bill Keyes

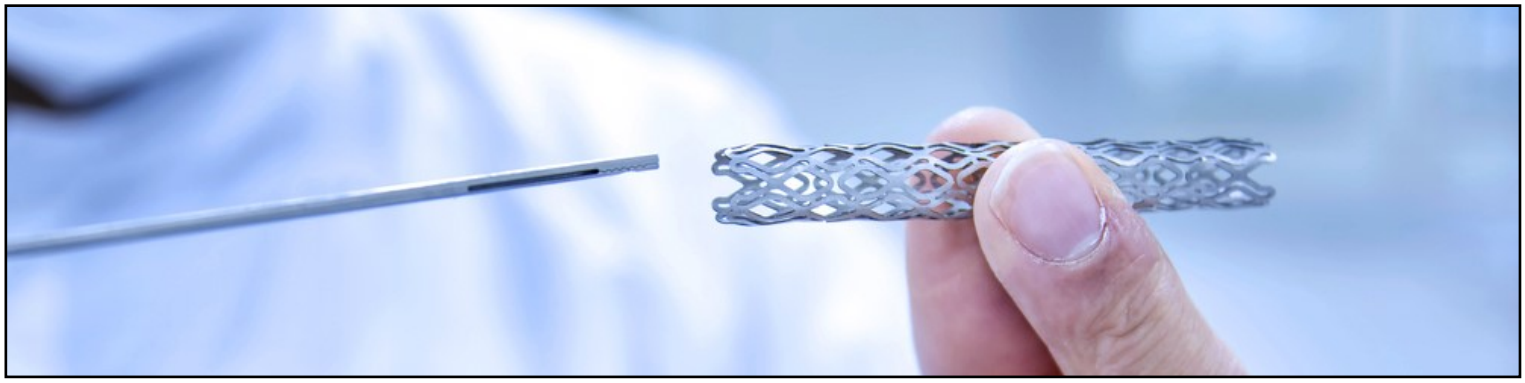
12:00 PM

Senescent Cells Promote Tissue Regeneration Through Their Secretory Component

Bill Keyes, Group Leader, Mechanisms of Cancer and Aging Group, Centre for Genomic Regulation (CRG), Barcelona, Spain

Abstract:

Cellular senescence is a form of cell cycle arrest induced by stress such as DNA-damage and oncogenic signaling. However, even while arrested, senescent cells secrete a variety of proteins collectively known as the senescence-associated secretory phenotype (SASP). This can promote immune cell-mediated clearance, or can reinforce the arrest and induce senescence in a paracrine manner. However, the SASP can also favor tissue growth and repair, such as during embryonic development or wound healing and can even promote tumor growth. These functions suggest more complex physiological roles for senescence and the SASP than currently understood. Here I will discuss our ongoing studies that have uncovered beneficial roles for the SASP in promoting tissue regeneration, a finding that introduces the concept that functional manipulation of senescent cells could be harnessed for regenerative purposes.



12:30 PM

LUNCH

1:45 PM

REPAIRING AND REGENERATING THE INJURED HEART WITH STEM CELLS

James Chong, Cardiologist and Senior Lecturer, University of Sydney School of Medicine and Head of the Cardiac Regeneration Laboratory, Westmead Institute for Medical Research

JAMES CHONG

Abstract:

Stem cell therapies targeting the injured and failing heart could greatly decrease morbidity, mortality and burgeoning health care costs worldwide. These novel therapies can be broadly grouped into two categories: 1) Adult Stem Cells (ASCs) isolated from the heart and other organs 2) Pluripotent Stem Cells (PSCs) including embryonic stem cells and induced pluripotent stem cells. This presentation will detail work using both of these stem cell types. Particular focus will be made on strategies to increase the proliferative and multi-potent capabilities of human cardiac Platelet Derived Growth Factor Receptor-Alpha expressing ASCs and non-human primate experiments demonstrating the feasibility of human PSC derived cardiomyocytes as a means to delivery clinical cardiac regeneration.

MASASHI KAWAMURA

2:15 PM

TRANSPLANT OF SMOOTH MUSCLE CELL-ENDOTHELIAL PROGENITOR CELL BI-LEVEL CELL SHEET ATTENUATED CARDIAC DYSFUNCTION IN DIABETIC CARDIOMYOPATHY

Masashi Kawamura, Postdoctoral Fellow, Woo Lab, Stanford University School of Medicine

Abstract:

Diabetes mellitus (DM) is an independent risk factor for coronary artery disease and negatively impacts outcomes after coronary artery bypass grafting(CABG). Adverse sequelae of DM are largely due to advanced microvascular disease. CABG and PCI are used extensively to treat coronary artery disease in diabetic patients. However, these treatments fail to address the culprit microvascular disease characteristic of DM. Microvascular disease thus remains a significant challenge in managing DM-induced cardiomyopathy(DCM), and effective treatments have yet to be identified. We have developed a smooth muscle cell-endothelial progenitor cell (SMC-EPC) bi-level cell sheet, which stimulates angiogenesis and facilitates mature microvascular formation. This autologous, tissue-engineered therapy represents a novel, translatable approach to improve microvascular disease and prevent heart failure in diabetic patients with coronary artery disease.

RONA CHANDRAWATI

2:25 PM

LOCALIZED AND CONTROLLED DELIVERY OF THERAPEUTICS VIA ENZYME BIOCATALYSIS

Dr. Rona Chandrawati, Lecturer, School of Chemical and Biomolecular Engineering, The University of Sydney

Abstract:

Enzymes play a central role in a spectrum of fundamental physiological processes and can be exploited as a pristine biological trigger to tune material responses and to achieve controlled release of biomolecules at desired sites. This talk highlights our recent development of responsive polymeric materials that are programmed to release therapeutics in response to enzymatic activities. The enzymatic approach increases flexibility in dose, duration, and location of delivered therapeutic agents. We illustrate the fundamental advantages of our approach and their attractive features over conventional strategies to address the challenges of long-term site-specific therapeutic delivery system.

2:35 PM

BREAK

3:15 PM

ENGINEERING 3D MULTICELLULAR ASSEMBLY AND MORPHOGENESIS OF PLURIPOTENT STEM CELLS

Todd McDevitt, Senior Investigator, Gladstone Institutes and Professor of Bioengineering & Therapeutic Sciences, University of California, San Francisco

TODD MCDEVITT

Abstract:

Pluripotent stem cells (PSCs) are uniquely capable of generating virtually any tissue based on their inherent differentiation potential. However, the current inability to robustly and predictably generate functional "organoids" from PSCs severely limits their use for drug discovery and development, modeling of development and disease, and regenerative medicine therapies. We are developing enabling technologies capable of directing the multicellular assembly and subsequent morphogenesis of PSCs in order to better understand fundamental principles of tissue formation. In addition, we are integrating novel cell engineering methods in human PSCs to spatially and temporally control morphogenic processes. We anticipate that these studies will lead to a greater mechanistic understanding of stem cell biology as well as scalable and translatable technologies for manufacturing of PSC-derived products for regenerative medicine.

3:45 PM

BIOMIMETIC SELF-ASSEMBLED SCAFFOLDS FOR MUSCLE REGENERATION

Helen Blau, The Donald E. and Delia B. Baxter Foundation Professor and Director, Baxter Laboratory for Stem Cell Biology, Stanford University

HELEN BLAU

Abstract:

Muscle stem cells are a potent population of myogenic progenitors dedicated to efficacious skeletal muscle regeneration, but their therapeutic utility is currently limited by mode of delivery. We developed biomimetic scaffolds based on peptide amphiphiles (PAs) that assemble to encapsulate cells and growth factors within a muscle-like unidirectionally ordered environment of extremely long nanofibers. PA gel stiffness was found to determine the macroscopic degree of cell alignment within these scaffolds. Furthermore, these PA scaffolds support myogenic progenitor cell survival and proliferation and they can be optimized to induce their differentiation and maturation. We engineered an in vivo delivery system to assemble the scaffolds by injection of a fluid PA solution that enabled co-alignment of scaffold nanofibers with endogenous myofibers. These scaffolds displayed degradation rates matching the time course of tissue regeneration, and they markedly enhanced the engraftment of myogenic progenitors and their repair of damaged muscles in mice.

SARAH HEILSHORN

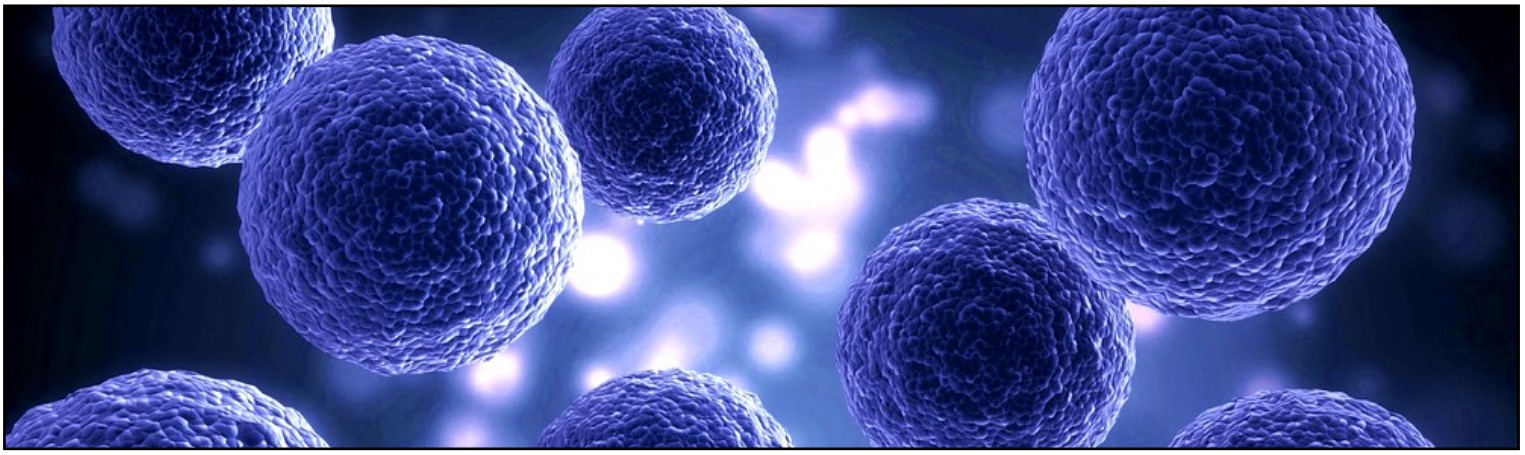
HALA ZREIQAT

4:15 PM

CLOSING COMMENTS AND POSTER AWARDS

Sarah Heilshorn, Associate Professor of Materials Science and Engineering and, by courtesy, of Chemical Engineering and of Bioengineering

Hala Zreiqat, Professor of Biomedical Engineering and Head of Tissue Engineering & Biomaterials Research Unit, School of AMME/Faculty of Engineering and IT and Bosch Institute, The University of Sydney



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