GCC REGENERATIVE MEDICINE INTERACTIVE CONFERENCE

PRACTICAL ASPECTS OF DELIVERING REGENERATIVE MEDICINE THERAPIES TO THE CLINIC

OCTOBER 12, 2022

BIOSCIENCE RESEARCH COLLABORATIVE

HOUSTON, TEXAS

REGENERATIVE MEDICINE CONSORTIUM

Gulf Coast Consortia
QUANTITATIVE BIOMEDICAL SCIENCES

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QUANTITATIVE BIOMEDICAL SCIENCES

The Gulf Coast Consortia (GCC), located in Houston, Texas, is a dynamic, multi-institution collaboration of basic and translational scientists, researchers, clinicians, and students in the quantitative biomedical sciences, who benefit from joint training programs, topic-focused research consortia, shared facilities and equipment, and exchange of scientific knowledge. Working together, GCC member institutions provide a cutting-edge collaborative training environment and research infrastructure beyond the capability of any single institution. GCC research consortia gather interested faculty around research foci within the quantitative biomedical sciences, and currently include Regenerative Medicine, Antimicrobial Resistance, Cellular and Molecular Biophysics, Innovative Drug Discovery and Development, Immunology, Mental Health Research, Single Cell Omics, Theoretical and Computational Neuroscience, and Translational Pain Research. GCC training programs currently focus on Biomedical Informatics, Computational Cancer Biology, Molecular Biophysics, Pharmacological Sciences, Precision Environmental Health Sciences, and Antimicrobial Resistance. Current members include Baylor College of Medicine, Rice University, University of Houston, The University of Texas Health Science Center at Houston, The University of Texas Medical Branch at Galveston, The University of Texas M. D. Anderson Cancer Center, The Institute of Biosciences and Technology of Texas A&M Health Science Center and Houston Methodist Research Institute.

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Gulf Coast Consortia - Research

October 12

8:30 Welcome and Opening Remarks, Suzanne Tomlinson, Gulf Coast Consortia

Co-Chairs: Phil Horner, HMRI, and George Eisenhoffer, MDACC

Session 1: *Practical Aspects of Moving Investigator-Initiated Cell Therapies and Reg Med Products/Devices to Trials*

Moderators: Jason Sakamoto, BioDesign

8:40 **Julie Allickson**, Mayo Clinic

8:55 **Matt Murphy**, Murphy Technology Consulting

9:10 **Rob Whitman**, Forward Science

9:25 **Carl Gregory**, TAMU

9:40 Panel Q&A

10:10 Vendor Session and Break

Session 2: *University GMP Manufacturing: When to Outsource?*

Moderators: Doris Taylor, Regenmedix, and Kevin McHugh, Rice Univ.

10:45 **Adrian Gee**, CAGT, BCM/TCH

11:00 **Fabio Triolo**, UTHealth

11:15 **Frank Bugg**, Lonza

11:30 Panel Q&A

12:00 Rapid Fire presentations
Daniel Harrington, Univ. of Texas Health Science Center Houston
Matthew Hogan, Houston Methodist Research Institute
Andie Caroline Dorn, Univ. of Texas Health Science Center Houston
Candice Haase, Univ. of Texas Health Science Center Houston
Amber Lee Royal, Houston Methodist Research Institute
Francesca Taraballi, Houston Methodist Research Institute

12:30 ***Lunch and Poster Session***

12:30 Lunch

1:15 Poster session

Session 3: *Business Strategies: Academic Licensing or NewCo?*

Moderators: Dan Harrington, UTHeatlh and Will Clifton, Polyvascular

2:30 **Stan Watowich**, Ridgeline Therapeutics

2:40 **Doris Taylor**, Organamet Bio Technologies

2:50 **Donna Chang**, Hope Biosciences

3:00 Panel Q&A

3:30 Break

Session 4: *University Perspectives on Tech Management and Tech Transfer: Mistakes Faculty Make and How to Prevent Them*

Moderators: Ann Tanabe, BioHouston and Ross Poché, BCM

4:00 **Asha Rajagopal**, Rice Univ.

4:05 **Michael Dilling**, BCM

4:10 **John Schultz**, HMRI

4:15 **Papia Ghosh**, MDA

4:20 **Sundeep Mattamana**, UTMB

4:25 **Rick Silva**, TAMU

4:30 Panel Q&A

5:00 *Ion. Accelerating Innovation. Connecting Communities*

Jan Odegard, The Ion

5:20 Reception

Presenters in alphabetical order

Julie G. Allickson, PhD

Michael S. and Mary Sue Shannon Director of Mayo Clinic's Center for Regenerative Medicine and the Otto Bremer Trust director, Biomanufacturing and Product Development, Center for Regenerative Medicine and Associate Professor of Regenerative Medicine

Julie Allickson, Ph.D., is the Michael S. and Mary Sue Shannon director of Mayo Clinic's Center for Regenerative Medicine and the Otto Bremer Trust director, Biomanufacturing and Product Development, Center for Regenerative Medicine and Associate Professor of Regenerative Medicine. Dr. Allickson recently joined Mayo Clinic from Wake Forest Institute for Regenerative Medicine at Wake Forest School of Medicine, where she was the chief manufacturing development center officer. Dr. Allickson is leading the next phase of development of the Center for Regenerative Medicine as it delivers on innovations that Cure, Connect and Transform patient care in alignment with Mayo Clinic's 2030 vision. She directs the enterprise-wide biomanufacturing strategy that aspires to introduce new regenerative therapeutics into the practice and establish Mayo Clinic as a category of one in regenerative medicine for rare and complex conditions. Dr. Allickson provides strategic leadership for all center activities and operations across Mayo Clinic. The Center for Regenerative Medicine has over 200 clinical trials and projects underway and has filed more than 150 regenerative patents. The center performs over 100,000 regenerative procedures annually. With more than 25 years of experience in clinical translation of cellular therapies and regenerative medicine products, Dr. Allickson has expertise in business management, regulatory affairs, strategic planning, project management and team-building. She has served as an executive officer of a publicly traded company that builds services for cellular banking, including licensure of technology with international affiliates.

Frank Bugg, MBA
Vice President
Site Head, Houston
Lonza Cell & Gene

Frank Bugg has over 15 years of pharmaceutical experience in many different roles including operations, manufacturing, quality control, quality assurance, manufacturing science and technology, validation, sales, and business development. For the past 5 years he has worked for Lonza, a large contract development and manufacturing organization. Most recently he is the site head for Lonza's largest cell and gene manufacturing facility that offers development, clinical, and commercial manufacturing for viral vectors, autologous and allogenic cell therapies. He has spent time in multiple pharmaceutical modalities including radiopharmaceuticals, solid oral dosage, biologics, and cell and gene. As well as worked for many industry leaders such as Lonza, Novartis, and Cardinal Health. His passion has always centered around problem solving and challenging the status quo. His undergrad is in biology from the Ohio State University and masters is in business administration from the University of Phoenix.

Donna Chang, MS
President and CEO
Hope Biosciences

As the President and CEO of Hope Biosciences, Donna Chang is on a mission to revolutionize the field of cell therapy. She has over 15 years of experience in biotechnology business development, including business expansion and strategic partnering. Donna started her career in economic development in life sciences. She later transitioned into industry, focused entirely on cellular therapeutics. Her passion in this subject is the leading motivation to find solutions to the current limitations in cell therapy and deliver approved therapies to the market - quickly. Donna started Hope Biosciences in 2016 with a goal to develop and deliver adult stem cell therapeutics that are safe, effective and affordable. Hope Bio's groundbreaking patented core cell culture technology has been utilized in over 30 FDA authorized protocols in the United States. The company anticipates to bring these therapies to market in the very near future. Donna graduated from the University of Toronto with a degree in Bioethics and Human Biology. She received her Masters (M.S.) in Biotechnology with a concentration in Enterprise Development from Johns Hopkins University.

Michael B. Dilling, PhD, CLP
Executive Director Commercialization,
Technology Management
Certified Licensing Professional
Baylor College of Medicine Ventures

Michael Dilling is the Executive Director, Commercialization & Technology Management with BCM Ventures, Baylor College of Medicine's integrated commercialization team. Baylor College of Medicine is a leading biomedical research institution and the only private medical school in the Southwestern United States. BCM leads all Texas-based institutions in research funding from the National Institutes of Health and is home to a number of nationally-ranked departments. The BCM Ventures team is responsible for managing relationships between the college and commercial partners. These commercial relationships lead to the development of new products and services that benefit patients and maximize the impact of college's research, clinical and educational missions. Without commercial relationships, much of the promising research conducted by college faculty will never have the opportunity to impact and improve healthcare. BMCV is here to catalyze those relationships and make them happen. Our technology management team has a strong pragmatic, principled focus on finding common ground to get deals closed and executed. Academic technology commercialization is a team effort: Over the past five fiscal years we have executed over 250 licensing transactions, and we have negotiated industry sponsored research and services contracts that have brought over $95 million in revenue to the college.

Dilling is responsible for directing the activities of a team of six technology management professionals and a compliance professional. He has 20 over years of academic technology commercialization experience. He spearheaded the development and launch of an online disclosure application to simply the disclosure submission process for our faculty, which has resulted in a 30% increase in invention disclosure submissions. He led the authorship and production of a Faculty Guide to Commercialization at BCM to provide a comprehensive resource to our faculty on the commercialization process. Dilling is an active member of the Association of University Technology Managers (AUTM), where he most recently chaired the organization's Mentorship Committee, and was responsible for the development of new tools to support growth of mentorship efforts in the association.

Dilling has a Ph.D. in Genetics from Texas A&M University (1993) and an MBA from the University of Memphis (1999). He did postdoctoral work at St. Jude Children's Research Hospital in Memphis, TN. He joined Baylor College of Medicine in January of 2000.

Adrian Gee, PhD
Director, GMP Facilities
Baylor College of Medicine Center for Cell and Gene Therapy

Dr. Gee received his PhD in immunology from the University of Edinburgh, Scotland. After post-doctoral positions at the National Cancer Institute and the Universities of Toronto and Florida he joined Baxter Healthcare, where he helped develop devices for immunomagnetic removal of tumor cells from autologous bone marrow and enrichment of stem cells from apheresis collections. He directed GMP cell manufacturing facilities at the University of South Carolina and M.D. Anderson Cancer Center at the University of Texas. For the last 22 years he has been the Director of the GMP Facilities at Baylor College of Medicine Center for Cell and Gene Therapy, where he oversees preparation of plasmids, vectors and a wide range of cell therapy products. He was co-founder of the International Society of Cell and Gene Therapy (ISCT) and its associated accreditation organization, the Foundation for the Accreditation of Cell Therapy. He has sat on numerous regional, national and international committees on development of regulations for the field. He has authored more than 200 peer-reviewed publications, numerous book chapters and two textbooks on cellular therapies. He is the recipient of the 2017 Career Achievement Award from ISCT.

Papia Ghosh, PhD
Associate Director
Office of Technology Commercialization
MD Anderson Cancer Center

Papia is Associate Director in the Office of Technology Commercialization at MD Anderson Cancer Center and is involved in all aspects of commercialization including assessing the technology/opportunity, identifying the right partner and establishing the relationship with chosen partner. Papia previously worked as a Consultant at LEK Consulting in both their Boston and London offices. There she advised large biotech and pharma on various aspects of strategy, from market assessment, acquisition screening, portfolio management, due diligence, other. Prior to LEK, Papia was a post-doctoral fellow at Dana-Farber Cancer Institute and received her PhD at Yale University, and in both positions her research was in oncology.

Carl Gregory, PhD
Associate Professor and Associate Department Head of the Department of and Molecular and Cellular Medicine
Texas A&M School of Medicine

Carl Gregory is currently Associate Professor and Associate Department Head of the Department of and Molecular and Cellular Medicine at Texas A&M School of Medicine with an adjunct appointment in the Department of Biomedical Engineering. He graduated with a PhD in Biochemistry from Manchester, United Kingdom (UK) with postdoctoral training in academia and industry in the UK, followed by postdoctoral training with Darwin Prockop at Tulane University, New Orleans.

The Gregory laboratory specializes is development of stem cell-derived materials for bone healing and immune-related disorders, and the laboratory also has program developing therapies for bone related cancers. The Gregory laboratory currently collaborates with faculty in the Texas A&M School of Medicine and the College of Engineering to develop technology platforms for the generation of clinically relevant yields of stem-cell, extracellular vesicle, and extracellular matrix-based products. Recent work has focused on the manufacture of chemically and physically customizable microcarriers by scalable microfluidic approaches. The microcarriers facilitate vesicle, matrix, and cell harvest in scalable vertical wheel bioreactors. Superior optical properties facilitate non-invasive, label-free 3D imaging of cell laden microcarriers using elastic light scattering modalities and light-sheet microscopy. Artificial intelligence-based algorithms have been developed to rapidly evaluate morphology. These approaches suggest the feasibility of an automated, in-line, continuously monitored system for therapeutic cell expansion and biomass recovery.

Relevant publications:

Rogers et al. (2021) A scalable system for generation of mesenchymal stem cells derived from induced pluripotent cells employing bioreactors and degradable microcarriers. Stem Cells Transl Med. 2021 Dec;10(12):1650-1665. doi: 10.1002/sctm.21-0151. PMID: 34505405.

McNeill et al. (2020) Characterization of a pluripotent stem cell-derived matrix with powerful osteoregenerative capabilities. Nat Commun. 2020 Jun 15;11(1):3025. doi: 10.1038/s41467-020-16646-2. PMID: 32541821.

Mota et al. Automated mesenchymal stem cell segmentation and machine learning-based phenotype classification using morphometric and textural analysis. J Med Imaging. 2021 Jan;8(1):014503. doi: 10.1117/1.JMI.8.1.014503. PMID: 33542945.

Sundeep Mattamana, PhD, MBA
Executive Director
Technology Transfer
University of Texas Medical Branch
Galveston

Sundeep Mattamana, Executive Director for Technology Transfer joined the Office of Technology Transfer at UTMB in 2004. He is responsible for evaluating Invention disclosures, marketing and negotiating license agreements and assisting in the formation of startups. Prior to joining OTT, he worked as the Chief Market Research Analyst for Sucampo Pharmaceuticals, a biotechnology company in Bethesda, MD. His main role was conducting primary and secondary marketing research on products in the pipeline and providing support to licensing and business development activities. Sundeep holds a PhD in Chemistry from the University of Maryland, College Park and an MBA in Marketing and Information Technology from the University of Delaware.

Matt Murphy, PhD
Murphy Technology Consulting

Matt Murphy Ph.D. is a Houston native who earned his bachelors of science in chemical engineering from the University of Texas at Austin and his doctorate in bioengineering at Rice University. His PhD and postdoctoral research at UT-Houston HSC focused on orthopedic regenerative medicine and tissue engineering utilizing biomaterials and adult stem cells. He served as Director of R&D and Product Development for Celling Biosciences in Austin, TX from 2011-2017, where he released several best-in-class devices for harvesting and concentrating autologous cells and proteins for regenerative applications. He currently consults for several human and veterinary regenerative medicine companies for product development, regulatory clearance, and post market support. He is an annual speaker on the topic of regenerative medicine at clinical conferences for orthopedic surgery, sports medicine, and pain management. He has co-authored several clinical studies using autologous biologics in orthopedics and spine, including the first to establish a correlation between mesenchymal stem cell concentration and improvements in degenerative disc disease.

Jan E. Odegard, PhD
Executive Director
Ion
Ion. Accelerating Innovation. Connecting Communities

Dr. Odegard is the Executive Director at the Ion. The Ion is the epicenter for Houston's innovation ecosystem and currently anchors the 16-acre Ion District that is being developed by the Rice Management Company. The Ion serves as a hub focusing on quality collaborations between entrepreneurs, incubators, accelerators, corporations, academics, and the broader Houston community. The Ion's mission is to create opportunities to advance and sustain economic growth in Houston and to foster innovation in energy, healthcare, space, transportation, manufacturing, and other industries. It is home to event space hosting daily programs, Common Desk coworking, the Ion Investor Studio, the Ion Prototyping Lab powered by TXRX, and tenants such as Microsoft, Chevron Technology Ventures, ARA Partners, Rice University, and OpenStax, with more to be announced.

Odegard has over 25 years of leadership experience supporting innovators and enabling research and life-long learning engagements in computing, data science, and information technology.

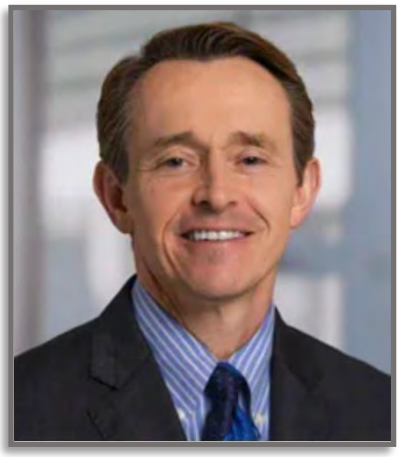
Prior to joining Ion, Odegard served as the Executive Director of the Ken Kennedy Institute at Rice University, where he focused on building strategic partnerships to serve as catalysts for research, education, and external engagements in data and computing. During his tenure at Rice, Odegard also served as the Associate VP for Research Computing from 2015 until he joined the Ion. While at Rice, Odegard worked with colleagues in the industry to launch the Oil & Gas High-Performance Computing Conference series in spring 2008 and then to launch the Ken Kennedy Institute Data Science Conference series in fall 2017.

Odegard was an associate professor in the Department of Electrical and Computer Engineering at the University of Stavanger, Norway, (1999-2001), and served as department chair (2000-2001). From 1996 to 1997, he was the founding executive director of the Computational Mathematics Laboratory and research associate in Electrical and Computer Engineering at Rice. From 1997 to 1999, he served as the founding executive director of the Rice Center for Multimedia Communication. Odegard received the Michael Pearlman Memorial Service Award from Rice University in 2009 and was elected Senior Member of IEEE in 2002.

Odegard received his Ph.D. in electrical and computer engineering from Rice University in 1996, earned a Bachelor of Science degree (1987) and a Master of Science degree (1990), both from Texas A&M University in electrical engineering and holds an associate degree (1986) in electrical engineering from Telemark College of Engineering, Porsgrunn, Norway.

Asha Rajagopal, PhD
Executive Director
Office of Technology Transfer
Rice University

Dr. Asha Rajagopal was appointed executive director of the Office of Technology Transfer at Rice University in 2016. She is a seasoned expert in the commercialization of university innovations. Dr. Rajagopal holds a bachelor's degree and two master's degrees from the University of Texas at Austin. She has also earned a PhD in cell and molecular biology from Rockefeller University.



John A. Schultz, MBA, CLP
Director for the Office of Technology Transfer
Houston Methodist Hospital and Research Institute

John A. Schultz, MBA, CLP, is currently the Director for the Office of Technology Transfer at Houston Methodist Hospital and Research Institute. Previously, he was Acting Vice President of Business Development at Pharmozyme Inc., an engineered enzyme platform company. Prior to that he was Vice President of Corporate Development at Intrexon Corporation (now Precigen) where he led all corporate development activities supporting a portfolio of synthetic biology assets in the healthcare, food and industrial biotech sectors. He was also formerly the Director of Business Development at Roche Tissue Diagnostics and the Senior Vice President of Licensing and Strategic Development at Clinical Data Inc. a drug development (vilazodone) and laboratory services provider of patient testing and contract DNA sequencing services for pharma, which was acquired by Forest Laboratories. Mr. Schultz has also worked in various general management, sales and marketing positions for Serono / BioChem Pharma (lamivudine) and Sigma-Aldrich Chemical Asia-Pacific. He began his career as the Sales and Marketing Manager – Asia Pacific for Mallinckrodt.

Rick Silva, PhD
Executive Director
Clinical | Translational | Industry Collaborations
Office of Research
Texas A&M University Health

Dr. Silva joined the Texas A&M in 2019 to develop an external-facing collaborations program to augment the clinical and economic impact of the research enterprise at the Texas A&M Health Sciences Center. He has successfully led over 300 transactions with academic, nonprofit, and commercial organizations in the US, Europe, and Asia, ranging from start-ups to Fortune 500® companies including the creation of 60 biomedical startup companies. Prior to Texas A&M, he spent 5 years at University of Arizona's academic medical center in a similar role spanning the implementation of Banner Health's academic affiliation with University of Arizona and assuming operation of their hospitals and practice plan. Previously, in 15 years at the University of Colorado, he had diverse experience in developing and leading a variety of collaborations including licensing transactions, technology development partnerships, public-private partnerships, multiparty collaborations, clinical trials, biomarker validation projects, supply and distribution agreements, strategic alliances, and a major emphasis on new venture development. He holds an academic appointment in Texas A&M's Institute for Biosciences and Technology in the Texas Medical Center and publishes and speaks on emergent collaboration models at the academic industry interface. Dr. Silva is passionate about strategies for achieving organizational effectiveness at the academic medical center- industry interface.

He received a Bachelor of Science degree in Agriculture from New Mexico State University, a Doctor of Philosophy in Physiology from Colorado State University, and a Master of Business Administration emphasizing Entrepreneurship and Finance from the University of Colorado-Boulder Leeds School of Business and is Certified Licensing Professional.

Doris A. Taylor, PhD
Chief Executive Officer
Organamet Bio Technologies

Dr. Taylor is a dynamic innovator, scientist and entrepreneur and a global thought leader and speaker in regenerative medicine. She has published over 180 papers, holds over 30 patents, and is the founder of multiple companies.

She has trained hundreds of undergraduate, graduate, and post-graduate fellows worldwide in her laboratories in the U.S. and Europe. Although she has held academic positions for over 20 years, she recently founded RegenMedix Consulting LLC to enable academic and commercial enterprises in the regenerative medicine space. In 2021she founded a new biotech Organamet Bio Inc. to bioengineer personalized replacement hearts on demand.

Taylor is credited with the first functional scientific repair of injured heart with stem cells in 1998. Her group further transformed the field of organ transplantation science in 2008 by developing a unique cell removal (decellularization) method that makes un-transplantable organs into usable scaffold frameworks for building new organs with stem cells. This was so revolutionary it was recognized as one of the "Top 10 Research Advances" by the American Heart Association and Taylor was nominated as one of "100 most influential people in the world" by Time magazine. Next she turned to disease prevention and has begun to develop "cellular signatures" of heart disease and aging that appear to differ by sex race and ethnicity.

Dr. Taylor frequently appears as an expert on cell therapy, women's health, cardiac repair and organ transplantation in the public media. Her work has been recognized and featured by 60 Minutes, CNN, The New York Times, The Wall Street Journal, Forbes, Natonal Geographic, BBC Horizon, BBC News Health, ABC, NBC and CBS News, Associated Press, Good Morning America, , the Oprah Winfrey Show, NOVA Science Now, PBS NOVA Transplanting Hope, Discovery Channel's Through the Worm Hole with Morgan Freeman, Science Channel's Stem Cell Universe with Stephen Hawking, NPR's On Being with Krista Tippet and most other worldwide media outlets.

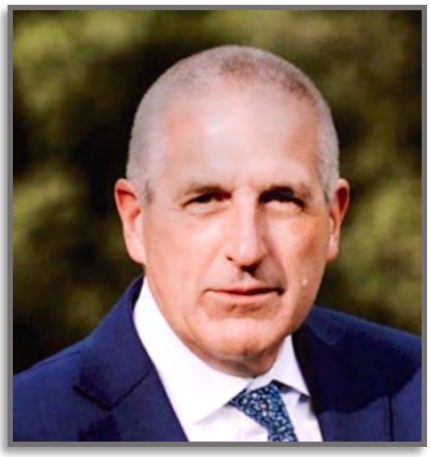
Taylor sits on numerous think tanks and international scientific committees including for the NIH, the FDA, the American Association of Blood Banks, and the Alliance for Regenerative Medicine. She is a member of the Leadership Advisory Committee for the Alliance for Regenerative Manufacturing Institute (ARMI) and sat on the international jury for the Institut de France LeFoulon-Delalande Foundation Grand Prix which is awarded annually to individuals making worldwide contributions to cardiovascular medicine.

Dr. Taylor earned a B.S. from Mississippi University for Women (MUW) and a Ph.D. from UT Southwestern Medical Center. She is appointed as a Fellow of the American Heart Association, American College of Cardiology, and European Society for Cardiology. She was awarded an honorary Doctor of Science degree by MUW and the national Distinguished Alumnus Award by the American Association of State Colleges and Universities. In 2019 she was elected as a Senior member of the National Academy of Inventors and in 2020, was elected as a fellow to the American Institute for Medical and Biological Engineering.

Her motto is, “Build the Future of Medicine Today.”

Fabio Triolo, DdR, MPhil, PhD
The Clare A. Glassell Distinguished Chair
Director, Cellular Therapy Core
Professor, Pediatric Surgery
Professor, Clinical and Translational Sciences

Dr. Triolo has a broad background in clinical-grade cell-based, tissue-based and combination product manufacturing for regenerative medicine applications, and extensive experience in compliance with American and European current Good Manufacturing Practices (cGMPs). He has 15 years of experience establishing and directing Investigational New Drug (IND)-dedicated cell production facilities compliant to European and American cGMPs in Europe and in the US and has supported >20 cellular therapy clinical trials aimed at adult and pediatric patients and conducted in Europe and in the US based on various cell-based products (e.g., fetal liver progenitor cells, pancreatic islets, bone marrow and umbilical cord derived mononuclear cells, adipose tissue, umbilical cord tissue and bone marrow derived mesenchymal stromal cells, regulatory T cells, genetically modified T cells). In collaboration with Biostage, Inc., his team produced a FDA-compliant adipose tissue derived MSC-seeded esophageal implant that was the first tissue engineered esophagus ever implanted in man, and he was the first to publish specific risk analysis approaches and procedures applicable to cell therapy manufacturing and to provide a specific model for guidance of cell transplantation centers and cell processing facilities, especially if approaching risk management for the first time. He directs the Cellular Therapy Core at UTHealth, and functions as a bridge between scientists and clinicians, enabling the translation, scale-up, and validation of promising new therapeutic technologies developed by scientists at a preclinical level, into clinical-grade processes that can be used to manufacture cell-based and/or tissue engineered and/or combination products for clinical applications. He also ensures that such processes are designed/translated in compliance with national and/or international regulations according to the nature of the trial. For the last decade, he has been manufacturing cell-based products at UTHealth to support multiple single- and multi-center clinical trials aimed at developing cell-based therapies to improve neurological conditions, such as anoxic brain injury at birth, cerebral palsy, traumatic brain injury, stroke, amyotrophic lateral sclerosis (in collaboration with Dr Stan Appel of Houston Methodist), and treatment-resistant bipolar disorder, all of which are still unmet medical needs.



Stan Watowich, PhD
Associate Professor
Biochemistry & Molecular Biology
University of Texas Medical Branch

Dr. Watowich is an Associate Professor of Biochemistry & Molecular Biology at the University of Texas Medical Branch. He is also Founder & CEO of Ridgeline Therapeutics, a Houston-based biotechnology company developing transformative drugs that enable adults to age stronger and live healthier. He is an accomplished entrepreneur, inventor, educator, researcher, and developer of world-class innovative resources, including the global “DiscoveryingDengueDrugs-Together” project with IBM and the DrugDiscovery@TACC supercomputer-based drug screening portal. Among his prime interests is developing accessible drugs to treat chronic global health problems, including age-linked muscle degeneration and obesity. Dr. Watowich graduated from Carleton College, received his Ph.D. in Physical Chemistry from the University of Chicago, and was a research fellow at Harvard University before migrating to Texas.

Robert J. Whitman, MSE
Chief Executive Officer
Forward Science

Robert J. Whitman is a biomedical engineer with a passion for science and a focus on people. After receiving his bachelor's and master's degrees in biomedical engineering from Tulane University, Robert began his career as a Clinical Engineer at M.D. Anderson Cancer Center, where he developed a passion for early cancer diagnostics. Robert is currently the CEO of Forward Science, a vertically integrated MedTech company focused on R&D and commercializing advanced technologies. Robert co-founded Forward Science over a decade ago with the goal to innovate current technologies into more cost-effective solutions to change more lives. With Robert's lead, Forward Science has successfully launched multiple products through the FDA process and is entering their second decade of business.

In addition to his role as Chief Executive Officer of Forward Science, Robert also serves as an adviser to startup medical technology companies on product development strategies at the Texas Medical Center and speaks nationally on topics including oral cancer and diagnostics, MedTech startups and Entrepreneurship. On a personal note, Robert is married to his high school sweetheart, Kristi, living in West University Place, TX and raising (or learning how to raise) three boys – Beckett (7), Bennet (4) and Briggs (2). [Advice always welcome].

Rapid Fire Presenters

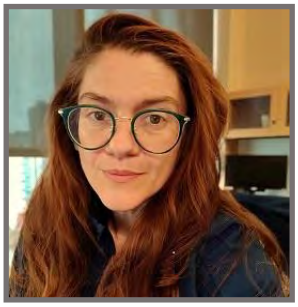
Daniel Harrington, Univ. of Texas Health Science Center
Bringing Hydrogel-Based Craniofacial Therapies to the Clinic
Poster 9

Matthew Hogan, Houston Methodist Research Institute
Clinical Epidural Electrodes to Assess Physiological Impacts of Spinal Electrode Location in a Large Animal Model
Poster 10

Andie Caroline Dorn, Univ. of Texas Health Science Center Houston
The Enteric Nervous System Improves Mesenchymal Development in Transplanted Human Intestinal Organoids
Poster 7

Candice Haase, Univ. of Texas Health Science Center Houston
Testing a Potency Approach for Clinical Grade MSC Manufacturing from UC-MSC
Poster 8

Amber Lee Royal, Houston Methodist Research Institute
Use of Bioengineered Scaffold to Retain Nanotherapeutics in Cardiac Tissue
Poster 12



Francesca Taraballi, Houston Methodist Research Institute
Biomaterials Design for Translational Orthobiologics
Poster 15

Poster Presenters
in alphabetical order

First Name	Last Name	Institution	Title	Poster #
Caitlynn	Barrows	Univ. of Texas Health Science Center Houston	Tissue Engineering Strategies to Promote Neural Innervation of Salivary Stem Progenitor Cells	1
Yareli	Carcamo-Bahena	Houston Methodist Research Institute	Nanochannel Delivery Of Osteogenic Growth Peptide For Bone Regeneration In	4
Maximilien	DeLeon	Rice Univ.	Bone Analog Models to Understand Role of Mechanotransduction in	5
Rocio	Diaz Escarcega	Univ. of Texas Health Science Center Houston	Chemotherapy as a Risk Factor for Alzheimer's Disease	6
Andie Caroline	Dorn	Univ. of Texas Health Science Center Houston	The Enteric Nervous System Improves Mesenchymal Development in Transplanted Human Intestinal Organoids	7
Candice	Haase	Univ. of Texas Health Science Center Houston	Testing a Potency Approach for Clinical Grade MSC Manufacturing from UC-MSC	8
Dan	Harrington	Univ. of Texas Health Science Center Houston	Bringing Hydrogel-Based Craniofacial Therapies to the Clinic	9
Matthew	Hogan	Houston Methodist Research Institute	Clinical Epidural Electrodes to Assess Physiological Impacts of Spinal Electrode Location in a Large Animal Model	10
Jeonghoon	Oh	Houston Methodist Research Institute	Targeted Recruitment of Upper-limb Motoneurons Using Transcutaneous Electrical Stimulation of Cervical Spinal Cord	11
Amber Lee	Royal	Houston Methodist Research Institute	Use of Bioengineered Scaffold to Retain Nanotherapeutics in Cardiac Tissue	12
Antonio	Soares	Univ. of Texas Health Science Center Houston	cAMP Signaling and CREB-activated Transcription Coordinate Muscle Satellite Cell Proliferation During Regeneration	13

Poster Presenters
in alphabetical order

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Francesca	Taraballi	Houston Methodist Research Institute	Biomaterials Design for Translational Orthobiologics	15
Danielle	Wu	Univ. of Texas Health Science Center Houston	Bioengineered Salivary Tissue (3D-ST) in Immunosuppressed Miniswine	16
Yu	Yin	Rice Univ. / Univ. of Texas Health Science Center Houston	Microfluidics-Based Coaxial 3D Bioprinting of Hydrogels for Salivary Tissue Engineering	17

Poster 1

Tissue Engineering Strategies to Promote Neural Innervation of Salivary Stem Progenitor Cells

Barrows C, Wu D, Smith Callahan L, Young S, Farach-Carson MC

Introduction. Salivary glands are branched networks consisting of acinar and ductal cells. During salivary gland development, the nervous system plays an integral role in branching morphogenesis and ductal elongation process and therefore may be important in developing a tissue engineered salivary replacement tissue. Previous work has shown a 3D salivary tissue construct (3D-ST) was successfully implanted into an irradiated miniswine model and remained viable for up to 14 weeks. We aim to generate a 3D innervated salivary gland model to better understand the role the nervous system plays on branching morphogenesis and to inform the hydrogel modifications needed to promote biointegration and neural innervation in the next preclinical model. We hypothesize that innervation along with the addition of growth factors FGF7 and FGF10 will promote salivary cell assembly and polarization.

Methods. Patient derived salivary stem/progenitor cells (hS/PCs) are co-encapsulated with murine embryonic neural precursor cells (NPCs) in a functionalized migration permissive hyaluronic acid and laminin-based hydrogel. NPCs are differentiated through the addition of retinoic acid for seven days. After which different combinations of FGF7 and FGF10 were added to identify the right sequence to promote the polarization of salivary cells. Salivary cell maturity and polarity was assessed through MUC1, junctional proteins, and aquaporin 5. Functional salivary maturation was assessed by α-amylase and neural maturation was assessed through βIII-tubulin expression.

Results. Co-encapsulation of NPCs and hS/PCs showed neural extensions migrating and wrapping around salivary hS/PC clusters. Neurally innervated salivary clusters were larger than controls lacking NPCs. Lumen-like features were showing in some groups with α-amylase expression localized towards the center of some clusters. Our system was shown to support and differentiate NPCs and hS/PCs and maintain their viability.

Conclusion. Neural progenitor cells were successfully matured in our 3D HA/Laminin based hydrogels and assist in the formation of salivary gland avatars. Ongoing work seeks to understand the role of growth factors on the maturation process. To further assist in biointegration we are examining the role of neurturin in promoting salivary cell assembly.

Poster 4

Nanochannel Delivery of Osteogenic Growth Peptide for Bone Regeneration in a Rabbit Model

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Background

With about 80% of the population experiencing back pain and Americans spending an ~$50B/year towards treatment, there is a need for alternative, low cost methods to help those dealing with chronic pain. Biologic adjuvants such as cell-based therapies, growth factors, osteoconductive matrices, and anabolic agents are available clinically to enhance bone repair and remodeling. With respect to spinal fusion, osteobiologics have been increasing in popularity. One example is bone morphogenic protein, which has been in use since 2002, but is associated with complications, such as cancer. Osteogenic growth peptide (OGP) is another osteobiologic found endogenously and when administered daily systemically, it was shown to promote osteogenesis. Despite its lack of severe side effects, it is susceptible to proteolysis as a 14-residue peptide.

Hypothesis/Goals

We hypothesize sustained and constant delivery of OGP from a novel nanofluidic implant will result in new bone growth. We analyzed OGP release through a nanofluidic membrane and assessed *in vivo* bone growth induction with cone-beam computed tomography (CT) by comparing peptide-releasing implants to vehicle-releasing implants in a large animal (rabbit) model of spinal arthrodesis (spinal fusion).

Methods

Release studies of OGP from 3.5nm membranes (n=4) showed sustained and constant release over two months, targeting ~30mg of peptide demonstrated using a custom robotic UV-Vis apparatus.[2,3] *In vivo* studies were conducted in female 14-week-old New Zealand White Rabbits. Briefly, decortication occurred along the lamina of the vertebrae and PEEK devices containing two reservoirs, each mounting a nanochannel membrane were fabricated and assembled, loaded with either PBS or OGP (200 ng/kg body weight, n=4/group) surgically implanted between L4-L6 vertebrae without external fixation. X-ray images and cone-beam CT scans were obtained pre- and post-implantation (days 7, 28, 42, and 56) to assess implant placement and *de novo* bone mass. Histology was performed on the fibrotic capsule surrounding the implant as well as the spine itself to assess implant tolerability and efficacy.

Results

The implants were well tolerated by the rabbits in both groups for the study duration. Volumetric quantifications of L4-L6 vertebrae were performed in both groups for each timepoint. Local release of OGP from the nanofluidic device resulted in new bone growth along the base of the transverse processes after 42 ($p<0.005$) and 56 ($p<0.005$) days post-implant. Histology revealed robust endochondral ossification and unilateral bony spicules close to the drug releasing ports.

Conclusions

Sustained release nanofluidic implants could eliminate the need for repeated injections and help improve patient compliance and outcomes. This work successfully demonstrates use of an implantable system capable of releasing a bioactive molecule (OGP) in a continuous, sustained manner in a rabbit model which can overcome the problems associated with high systemic dosing, such as off target effects.

Acknowledgements

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Poster 5

Bone Analog Models to Understand Role of Mechanotransduction in Bone Marrow

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Background: Bone remodeling process is a continuous process that shifts balance between bone deposition and bone resorption. Age and physical exercise are two major factors that determine the balance of this remodeling process. In older humans, bone resorption occurs at a faster rate than bone deposition. Both elderly individuals and astronauts in microgravity experience a net bone loss even with interventions. Bone marrow stromal cells (BMSCs) are responsive to mechanical loading and contribute to the anabolic response in bone. To study this relationship, a 3D bone marrow analog system was created. Scaffolds were architecturally inspired from computerized topography (CT) scans of trabecular bone of young and old mice and scaffolds were printed using extrusion 3D printer, 25% (young) and 13% (aged) (%: bone volume/total volume). The scaffold contained BMSC-laden hydrogels that would be exposed to low-intensity vibrations (LIV) (1g, 100 Hz) daily. We hypothesize that higher trabecular bone volume and LIV increases bone anabolism and BMSC differentiation.

Objective: To discover an intervention useful to prevent or slow bone loss in the elderly or those subjected to prolonged microgravity.

Methods: Bone analogs are made of three components: a polylactic acid (PLA) scaffold, a tunable hyaluronic acid (HA)-based hydrogel, and BMSCs. The PLA scaffold was extrusion printed based on mice CT trabecular bone scans. The HA-based hydrogel contained matrix metalloproteinase (MMP)-cleavable peptides and pendant integrin-binding motifs to create a cell-modifiable hydrogel. BMSCs were seeded at a density of 1 million cells per mL. The control group (0%: no scaffold) was compared to 25% and 13% bone analog systems with and without LIV (+/- LIV). LIV regimen was performed for one hour every day for 14 days at room temperature. Type I collagen, nuclei, vinculin, YAP, Ki67 and mineralized nodules were examined using quantitative image analysis from confocal micrographs.

Results: In our 3D bone marrow analogs, exposure to LIV led to a significant increase in type I collagen production between both young bone and old bone models. Additionally, there was more type I collagen expression seen in the 25% bone analog when compared to the 13%. Although it was expected to see an increase in cellularity between LIV positive and negative groups, only an increase was observed in the young (25%) bone analog group.

Conclusions: Increased type I collagen production was observed in young bone marrow and in loaded bone marrow analogs when compared to their unloaded counterparts. Bone marrow analogs provide a highly tunable platform to study the role of mechanical stresses on bone anabolism. Identification of interventions capable of slowing bone loss will benefit the elderly, individuals subjected to prolonged inactivity or microgravity, and patients with an increased risk for skeletal-related events.

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Poster 6

Chemotherapy as a Risk Factor for Alzheimer's Disease

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Abstract

Background
Cognitive impairments may occur in cancer patients and survivors during or after chemotherapy. Cognitive deficits associated with neurotoxicity (chemobrain) can be subtle or disabling and frequently include disturbances in memory, attention, executive function, and processing speed. Cognitive impairments may go away soon after chemotherapy is over or may persist for years and yet, there is a paucity of effective treatments. Research has shown that chemotherapy drugs such as doxorubicin promote neurotoxicity and cognitive disturbances. Critically, some studies demonstrated that dementia occurs more commonly in cancer patients who had chemotherapy treatment compared to individuals never exposed to chemotherapy. Understanding whether and how chemotherapy may promote dementia later in life is needed.

Methods
To establish new insights into chemotherapy-induced cognitive impairments, we use wild-type and Tg2576 mice (a model of Alzheimer's disease (AD)) treated with Doxil, a liposomal form of doxorubicin. Mice are injected intraperitoneally with saline or Doxil for six weeks. These conditions recapitulate a dosing schedule used in human patients and are the same as those used in similar studies in mice. Mice are then tested with cognitive and behavior assays, and their brains are analyzed for aging and AD phenotypes.

Results
In our studies, we discovered that Doxil promotes cognitive impairment in wild-type mice. We also found that the brains of young mice exposed to Doxil contain lipofuscin—a mixture of oxidized proteins and lipids that is usually found only in the aged or diseased brains. DNA damage occurred with Doxil treatment in mice, confirming Doxil accelerated features of brain aging. Critically, Doxil enhances the deposition of amyloid in Tg2576 mice.

Conclusion
Our study demonstrates evidence of accelerated brain aging in wild-type mice and amyloid deposition in AD mice due to Doxil treatment. Our data provide a foundation for investigating chemotherapy as a potential risk factor for AD that warrants further study. This research is being pursued in our laboratory.

Poster 8

Nanochannel Delivery of Osteogenic Growth Peptide for Bone Regeneration in a Rabbit Model

Abstract

Cells isolated from umbilical cord through explant cultures are plastic adherent, self-renew, and are multipotent in vitro. UC-MSCs possess immunomodulatory properties that could be utilized to treat inflammatory conditions. We aim to use in vitro potency to indicate efficacy via immunomodulation. We utilize a potency profile created through a standard set of assays. First, the effect on secretion of TNFα or IFNɣ with coculture of UC-MSCs with lipopolysaccharide or concanavalin A stimulated rat splenocytes was assessed. Second, UC-MSCs were assessed for their ability to suppress human T cell proliferation. Third, the expression of key markers of immunomodulation (IDO1, PTGS2, TNFAIP6, and IL1rn) in response to TNFα or IFNɣ was determined by quantitative reverse transcription-polymerase chain reaction. Fourth, UC-MSC secretion of potential anti-inflammatory mediator prostaglandin E2 (PGE2) in response to TNFα or IFNɣ was evaluated with enzyme-linked immunosorbent assay. Together, these assays measure UC-MSCs immunoregulatory properties. UC-MSCs are an attractive candidate for allogeneic cell therapies in treating a variety of immune-mediated diseases, and our approach to measuring this is practical for cGMP production.

Poster 10

Clinical Epidural Electrodes to Assess Physiological Impacts of Spinal Electrode Location in a Large Animal Model

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Background: Recent advances in electrical stimulation of the spinal cord suggest it may be a potential therapy for neuromotor disorders. Clinically, electrodes are routinely placed in the dorsal epidural space after spinal cord injury. While the effects of electrode location and position on the dorsal surface have been explored in the clinic, no data is available regarding the potential benefits of ventral placement.

Hypothesis: Ventrally placed clinical electrodes will access unique circuitry from those on the dorsal surface, producing distinct and potentially clinically relevant physiological output in a pig.

Methods: A functional neurosurgeon placed spinal electrodes in the epidural space of two pigs using a computed tomography arm to guide electrode placement (Fig 1). Electrodes were implanted bilaterally in the cervical, thoracic, and lumbar dorsal space to target proximal and distal muscles of the fore- and hind-limb. Further, a single electrode was positioned in the lateral ventral compartment in the cervical spine to compare the physiological output of the proximal and distal muscles of a single fore-limb with changing stimulation frequencies. Bipolar needle electrodes were placed into proximal and distal muscles of each limb to measure the evoked potential. Stimulation was provided via dual Digitimer SP-8 stimulators and muscle outputs were gathered separately using Tucker-Davis Technologies and A-D Instruments physiology systems. Compound spinal potentials were measured via a BrainVis amplifier and data were synchronized and analyzed post-hoc using Matlab scripts.

Results: Ventral spinal stimulation (VSS) resulted in stable muscle responses with increasing frequencies; in contrast, dorsal spinal stimulation (DSS) resulted in modulated evoked responses with increasing frequencies.

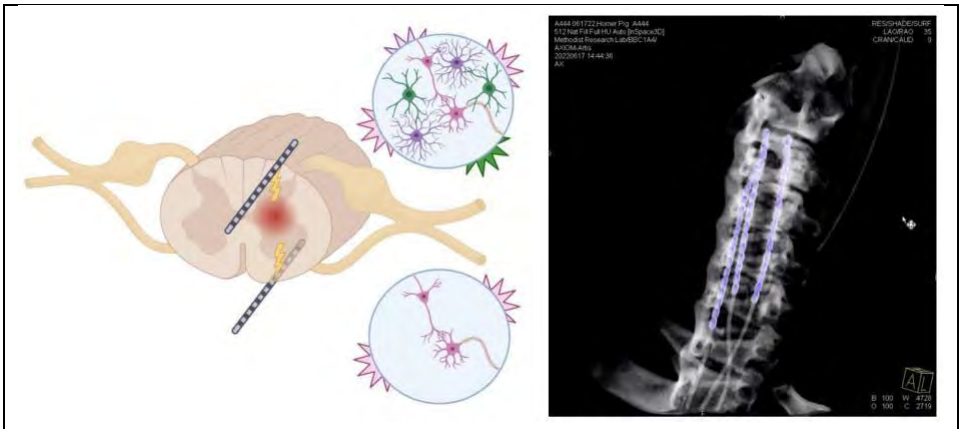

Figure 1: VSS activated unique circuitry compared with DSS.

Conclusions: The results indicate VSS is more involved with direct or monosynaptic activation of motor circuitry due to the stable output with changing frequencies. Alternatively, the modulating outputs of DSS imply polysynaptic sensorimotor involvement. Given each modality targets unique spinal circuitry, there is an opportunity to explore comparisons and combinations of each in order to achieve greater clinical benefit.

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Poster 11

Targeted Recruitment of Upper-limb Motoneurons Using Transcutaneous Electrical Stimulation of Cervical Spinal Cord

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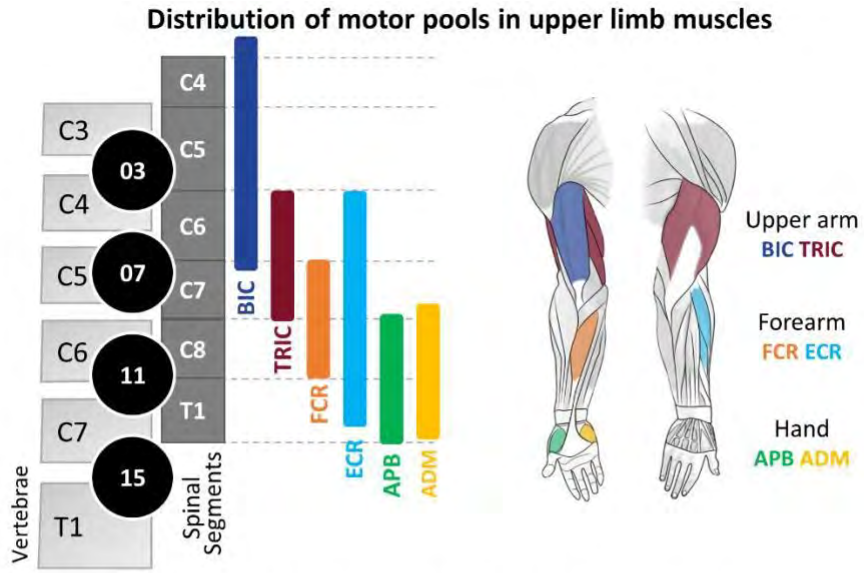
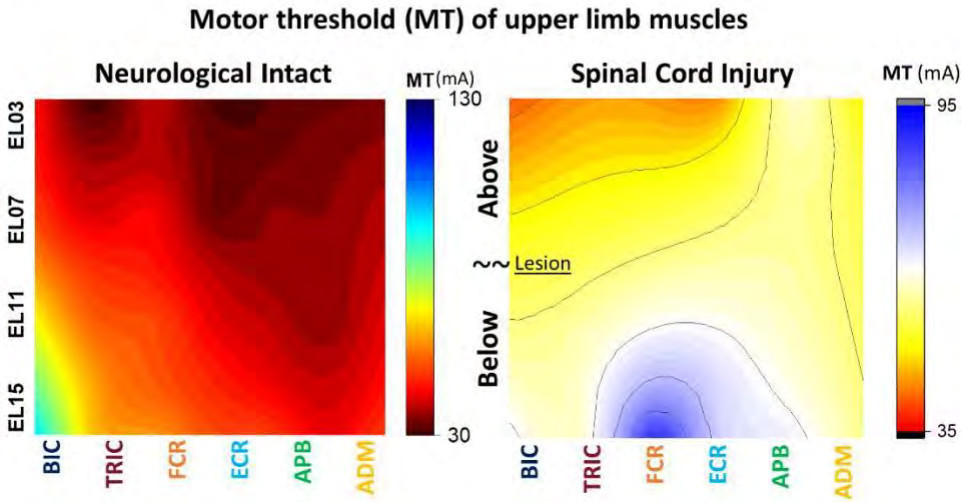
Background: Spinal cord injury (SCI) affects approximately 18,000 individuals every year in the United States, with over half of the cases resulting in upper-limb (UL) impairment. Regaining hand function is of the utmost importance for many individuals with SCI. Non-invasive, transcutaneous spinal cord stimulation (TSS) is a novel electrical neuromodulation strategy that has the potential to increase the excitability of spinal circuits and facilitate functional recovery after SCI. **Hypothesis:** We hypothesized that the individual UL motor pools can be selectively recruited by using specific stimulation locations during cervical TSS, as revealed by motor threshold intensity, maximum amplitude, and the amount of post-activation depression in neurologically intact subjects (NIS). We then implemented this approach in individuals with SCI to examine how the level and severity of injury affects the response of activated motor pools. **Methods:** Eleven NIS and five SCI participants were recruited in this study. We delivered TSS to the cervical spinal cord via a multi-electrode array using a pair of monophasic pulses of 500 μs duration, with inter-stimuli interval of 30 ms. TSS was delivered over the rostral and caudal spinal cord as well as its midline and lateral aspects. **Results/Discussion:** We demonstrated that TSS delivered over the cervical spinal cord in NIS can preferentially activate proximal and distal muscles along the rostrocaudal axis, as well as ipsilateral UL muscles along the mediolateral axis. While rostral stimulation resulted in activation of all tested muscles, caudal stimulation produced a larger magnitude of response at distal muscles. Midline stimulation resulted in a higher probability of activation at proximal muscles, and stimulation at lateral sites resulted in a higher probability of activation at distal muscles. In SCI, the response of activated motor pools obtained from evoked potentials TSS delivered above and below the lesion showed the different motor pools' recruitment along the rostrocaudal and mediolateral axes compared to NIS. **Conclusion:** Our findings provide a baseline for future large clinical trials for people with neurological injuries, including people with severe cervical SCI, for mapping motor pool function with the goal of restoring UL motor function. **Acknowledgements:** This work was in part supported by the NeuroSpark Seed Funding Program (20130009) and Craig H. Neilsen Foundation (733278).

Poster 11


Distribution of motor pools in upper limb muscles
C3
C4
C5
C6
C7
T1
03
07
11
15
Vertebrae
C4
C5
C6
C7
C8
T1
Spinal Segments
BIC
TRIC
FCR
ECR
APB
ADM
Upper arm
BIC TRIC
Forearm
FCR ECR
Hand
APB ADM


Motor threshold (MT) of upper limb muscles
Neurological Intact
MT(mA)
130
30
EL03
EL07
EL11
EL15
BIC
TRIC
FCR
ECR
APB
ADM
Spinal Cord Injury
MT (mA)
95
35
Above
Lesion
Below
BIC
TRIC
FCR
ECR
APB
ADM

Poster 12

Use of Bioengineered Scaffold to Retain Nanotherapeutics in Cardiac Tissue

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Background:

Regenerative medicine has broad applications in the heart as novel therapies are needed to address disorders such as heart disease, which affects an estimated 15.5 million people in the United States alone. Repairing a damaged myocardium requires treatment with therapeutics that can enter an injured area and remain there, such that their properties can be exploited. These therapeutics can range from cells to drugs to nanoparticles. In this work we demonstrate use of a bioengineered scaffold to deliver and retain gold-shell silica-core nanoparticles (GNS) in the myocardium. As gold is inherently radiopaque, these nanoparticles demonstrate strong X-ray attenuation and are easily visualized with computed tomography (CT) imaging. As opposed to delivery via traditional routes, such as intravenous or intracoronary infusion, which often lead to coronary washout, administration in the bioengineered scaffold allows for localization and retention directly in the myocardial tissue.

Hypothesis/Goals:

We hypothesize that injection of GNS in a bioengineered scaffold will allow for concentrated particle accumulation with improved retention and distribution into the myocardium. We examined the signal strength, scaffold volume, and longevity of scaffold after administration in porcine cardiac tissue.

Methods:

Concentrated GNS were delivered in a bioengineered scaffold into porcine left ventricle tissue at different injection volumes. Tissues were serially imaged every 10 minutes over the course of an hour via a Siemens SOMATOM Definition Edge Scanner. The scaffolds were visualized and quantified within the target tissues via 3D Slicer. Inductively coupled plasma - optical emission spectrometry (ICP-OES) was performed using an Agilent 700 series instrument to determine gold content within the tissue. GraphPad Prism 9 was utilized for statistical analyses. Comparison of scaffold signals and volumes as well as gold content were analyzed via unpaired t-test.

Results:

As injection volumes increased (1 to 2 mL), a significant increase in scaffold volume inside the cardiac tissue (65.8 ± 15.2 to 235.9 ± 35.0 mm^3, $p<0.0001$) was observed via CT imaging followed by analysis with 3D Slicer. Signal attenuation of the scaffold also increased (286.8 ± 8.0 to 378.0 ± 43.4 HU, $p<0.0001$) with an increase in injection volume. Notably, the signal and volumes in the tissue were stable across the hour-long serial imaging sessions. ICP-OES analysis demonstrated a significant increase in gold content within the tissue from 245 ± 12 to 548 ± 119 Au (μg)/ tissue (g) ($p=0.0139$) when injection volumes doubled from 1 to 2 mL, respectively.

Conclusions:

Encapsulating nanotherapeutics with strong X-ray attenuation within a bioengineered scaffold allowed for quantitative measurements in their retention within the target tissue. Overall, our GNS scaffold was able to maintain its signal attenuation, position, and volume over an hour-long imaging session within myocardial tissue, overcoming the rapid dissipation expected with traditional systemic delivery.

Acknowledgments:

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Poster 13

cAmp Signaling and CREB-Activated Transcription Coordinate Muscle Satellite Cell Proliferation During Regeneration

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Background: Adult skeletal muscle regeneration requires proliferation and differentiation of quiescent progenitor cells referred as satellite cells. The number and activity of satellite cells decrease during aging, after traumatic injury and in advanced muscular dystrophy. Therefore, detailed molecular understanding of signaling pathways controlling these cells could lead to therapeutic strategies to promote muscle regeneration and function. **Goal:** Although it is known that cAMP and the cAMP response element binding protein CREB can stimulate for muscle satellite cell proliferation, it is unknown whether CREB regulated transcriptional co-activators (CRTC) contribute to regeneration and which key CREB transcriptional targets are crucial to muscle satellite cell proliferation. **Methods:** Using genetically modified mice to over-express a synthetic Gs-coupled GPCR (Gs-DREADD) or to knock-out CREB co-activators (Crtc2 and Crtc3). **Results:** We found that stimulating cAMP signaling by clozapine-N-oxide, Gs-DREADD activator, extends the duration of satellite cell proliferation in vivo. Deletion of Crtc3, but not Crtc2, in satellite cells reduced the proliferative response and impaired myogenic regeneration, particularly in aged mice. As next steps, we will interrogate the CREB/CRTC3 targeted transcriptome in muscle satellite cells during the proliferative phase of regeneration using next gen mRNA sequencing technology. **Conclusions:** Our results indicate that promotion of CRTC3 activity by chemical or genetic means could lead to improved muscle mass, particularly in people suffering from satellite cell depletion or as a method to increase satellite cell number for stem cell transplantation therapy.
Funding source: NIH/NIAMS R01AR072368-02 for Rebecca Berdeaux.

Poster 14

Modulation of Neuroinflammation via Nanoparticles Loaded with MK2 Inhibitor to Target Activated Microglia/Macrophages after Spinal Cord Injury

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Background

After spinal cord injury (SCI), inflammatory responses lead to extensive tissue damaging that contribute to the amplification of neural and glial cell loss, and to function impairment. Up-regulation of pro-inflammatory cytokines TNF-α and IL-1β, secretion of vasoactive substance by glia and leukocytes, and production of MMP-9 by neutrophils, contribute to create a detrimental pro-inflammatory microenvironment. Despite the damaging inflammatory response, neutrophils and microglia do exert neuroprotection and regeneration, and provide trophic support to neurons and glia. Standard immunosuppressant therapies are unfitted to address inflammation after CNS injuries, and yet were discontinued for inefficacy and unfavorable side effects.

Hypothesis/Goals

Immune cells are necessary for tissue repair, thus a tailored therapy aiming the modulation of the immune response toward a pro-regenerative one could represent a more effective strategy to maximize repair and reduce function loss. We focused on the potential of pharmacologically targeting MAPK-activated protein kinase 2 (MK2) to modulate the response of microglia/macrophages after injury.

Methods

We propose to delivery of MK2 inhibitor to macrophages/microglia via polymeric nanoparticles (NPs). MK2 is a key kinase in the pro-inflammatory cascade, but not in the pro-inflammatory response. NPs are administrated in CSF and the accumulation at the injury site is facilitated by magnetic targeting. Macrophages and microglia, highly phagocytic cells at the injury, uptake the NPs becoming the preferred targets of the therapy.

Results

NPs are homogeneous and spherical with a diameter around 100 nm. The NPs core encases iron oxides and drug PF3644022. In vitro tests with microglia and macrophages cell lines, have demonstrated high phagocytosis rate and no toxicity. In addition, NPs loaded with drug (PF-NPs) significantly reduced TNF-α after LPS stimulation compared to control NPs. In vivo when injected in CSF, NPs were specially accumulated at the site of injured cord. Co-staining of microglia/macrophages, astrocytes, and neurons have demonstrated the preferential uptake of NPs by the immune cells. NPs were able to deliver the drug and efficiently reduce the MK2 phosphorylation after injury. Furthermore, NPs loaded with MK2 inhibitor had a significant effect on microglia/macrophage trafficking; quantification study has showed a reduced accumulation of inflammatory cells around the injury. Precisely, active phagocytic cells were reduced compared to the resting ramified cells at the injury epicenter. Finally, after NPs treatment anti-inflammatory IL-10 was increased, while pro-inflammatory IL-6 was reduced at the injury.

Conclusion

Our platform exhibits therapeutic efficiency and specificity for local, pharmacologic manipulation of activated microglia/macrophages. Following MK2 inhibition mediated by nanoparticles treatment, immune cells accumulation was reduced, and potential reprogramming of the immune cells was induced for the creation of a more permissive anti-inflammatory microenvironment.

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Poster 15

Biomaterials Design for Translational Orthobiologics

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Endogenous mechanisms of tissue healing after trauma are present in the whole animal kingdom. Although the outcome of healing process is so diverse between species, the aim is still common: wound repair to reestablish homeostasis and tissue remodeling to restore form and function of the damaged tissue. In adult mammals the healing process is often incomplete and results in scar formation. Despite this primary function, scars prevent the process of functional tissue recovery. On the contrary, most of the processes of functional healing are scar-free. Understanding these processes would allow the development of new therapeutic strategies based on the driving molecular mechanisms that improve the regenerative process. Creating biomaterials for tissue healing has been a daunting challenge in the past twenty years. During this time frame, many efforts for developing new devices to support different clinical practices failed to complete the translational steps from "bench to bedside". Successful treatments will require advances in areas ranging from basic cell biology to material synthesis. One of the main reasons why the biomaterials field did not capitalize on the past promising advances is due to the lack of a complete investigation of the physiological and molecular mechanisms involved in the biomaterial/tissue interactions. This justification should not be considered an oversight but rather a new perspective on facing the biomaterial development in order to accelerate the process of clinical translation. We currently work on a variety of material-based platforms with a translational approach, from biodegradable polymers for wound healing to nanoparticle treatments for angiogenesis and inflammation. We will present an overview of our past and present working areas focusing on the important steps of biomaterials design toward the FDA approval and the final translation in clinical practice.

Poster 16

Bioengineered Salivary Tissue (3D-ST) in Immunosuppressed Miniswine

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Background: An urgent need exists to develop large animal models for preclinical testing of new cell therapies designed to replace lost or damaged tissues. Patients receiving irradiation for treatment of head and neck cancers frequently develop xerostomia/dry mouth, a condition that could one day be treated by cell therapy to repopulate functional saliva-producing cells. Using immunosuppression protocols developed for patients receiving whole face transplants, we successfully used immunosuppressed miniswine as a suitable host animal to evaluate the long-term stability, biocompatibility, and fate of matrix-modified hyaluronate (HA) hydrogel/bioscaffold materials containing encapsulated salivary human stem/progenitor cells (hS/PCs).

Objectives: We developed a large, immunosuppressed animal model to test preclinical cell therapies. Host integration in irradiated parotid tissue of Bioengineered Salivary Tissue (3D-ST) is evaluated in this study.

Experimental Methods: Immunosuppressed Minipigs (10-20 kg) received 3D-ST implants, containing human primary stem/progenitor cells (hS/PCs) infected with lentivirus expressing Gaussia Luciferase (GLuc), in an irradiated parotid gland for up to 12 weeks. GLuc reporter expression and human AMY1 was quantified in saliva collections from host. Tissue resections containing 3D-STs in irradiated glands and control tissue from non-irradiated glands were embedded in OCT, frozen, and sectioned for immunohistochemistry. Images were acquired using confocal microscopy and analyzed. Live/Dead assays were also performed on resected tissue and in vitro controls.

Results: All 3D-STs were well tolerated with no local tissue reactions. They remained viable (Live/Dead) and functional co-expressing human nuclear antigen (NHA^+) and α-amylase after implantation in the parotid gland. Clusters of HNA^+ /α-$amylase^+$ cells were identified in resected parotid gland tissue with matched clustered distribution and size to those of in vitro controls. $CD31^+$ and β_3-$tubulin^+$ structures were adjacent to hS/PC microstructures. GLuc and human α-amylase quantification in saliva collections is measured to determine functional host-3D-ST integration.

Conclusion: The immunosuppression regimen was effective and viable human salivary cells secreting salivary proteins were maintained in the target minipig tissue. This continued work is critical for developing an autologous human salivary stem/progenitor (hS/PC) cell line for salivary gland restoration therapies.

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Poster 17

Microfluidics-Based Coaxial 3D Bioprinting of Hydrogels for Salivary Tissue Engineering

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Background: Regeneration therapy for the salivary gland (SG) remains as an unmet clinical need and the complex branched organ structure has presented challenges to tissue engineering approaches. Xerostomia ("dry mouth") due to hyposalivation can result from injury or disease to the salivary gland, such as salivary acinar death caused by radiation therapy (RT) for head and neck cancer. Currently only palliative treatments exist for xerostomia, and many patients endure deteriorated oral health and poor quality of life. Tissue engineering could offer a permanent solution for salivary gland replacement by isolating healthy SG tissues prior to RT, expanding its cells in vitro, and recreating a functional SG neogland for implantation post-RT. We have shown that 3D hydrogel-based encapsulation of primary human salivary stem/progenitor cells (hS/PCs) promotes self-assembly into organized acini-like spheroids with coordinated, functional response. 3D bioprinting methods potentiate spatial cell deposition into defined architectures, but extremely thin structures (<100 μm), mimicking epithelial layers, are challenging to produce.
Goals: Our goal is to bioengineer thin salivary epithelium with complex structure and functional responses using a microfluidics-based 3D bioprinter and customized hydrogels.
Methods: 3D structures were designed using computer-aided design software, imported as .STL files into Aspect Studio software to optimize printing pathways, and printed using a RX1 microfluidic bioprinter. Printing employed either a DUO printhead (to generate thin, solid fibers) or a CENTRA printhead (to generate hollow tubes with thin wall). On-printhead crosslinking of hydrogel was realized by 1.5% w/v sodium alginate as the hydrogel precursor solution, crosslinked using 20 mM $CaCl_2$ as the exterior crosslinker sheath. 6% w/v poly(vinyl alcohol) (PVA) served as the interior sacrificial core for printing hollow hydrogel tubes. Tube wall thickness was visualized by FITC-dextran using confocal imaging and measured by ImageJ. Primary hS/PCs were mixed in sterile hydrogel to investigate the effect of initial cell density on the printed cell viability and behaviors. Encapsulated cell structures were cultured in humanized salivary media after bioprinting. Cell viability was assessed by live/dead assays. Cell proliferation was characterized by Ki67 immunocytochemistry.
Results: Adjusting absolute and relative pressures for the alginate and crosslinker solutions enabled fine control over solid fiber diameters, down to <100μm. Similarly, tube wall thickness ranging from 45-80 μm could be printed by matching the pressures of the hydrogel shell, the crosslinker and the core solution. Cell-laden, self-adherent hydrogel tubes could be printed within minutes and stacked in honeycomb-like patterns to mimic open salivary ducts. Bioprinted structures preserved the designed characteristics and maintained structural integrity throughout culture. hS/PCs remained viable and proliferation after bioprinting over several days.
Conclusions: Leveraging a microfluidics-based bioprinter with coaxial polymer and crosslinker streams, we established biocompatible printing strategies suitable to hydrogel biomaterials and innovative bioprinting structure designs, and fabricated thin, reproducible, and biocompatible hydrogel features that recapitulate characteristics of SG. Our results demonstrated that microfluidics-based 3D bioprinting using hydrogel biomaterials can generate ultra-thin solid fibers or open tubes with high hS/PC viability. This promising method to create salivary epithelium-mimicking structures ~~that~~ represents potential for future engineered salivary therapeutics that can restore salivary function.

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