The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Board on Health Sciences Policy
Forum on Regenerative Medicine

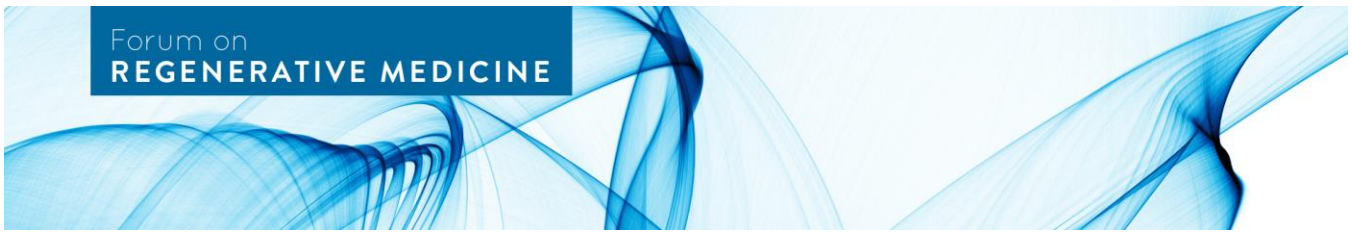
Exploring Sources of Variability Related to the Clinical Translation of Regenerative Engineering Products – A Workshop

October 18, 2018

National Academy of Sciences Building
Lecture Room
2101 Constitution Avenue NW
Washington, DC 20418

Statement of Task:

The emerging and multidisciplinary field of regenerative engineering aims to repair, regenerate, or replace damaged tissues in the body using a combination of principles and technologies from advanced materials science, developmental/stem cell biology, and immunology. The term "regenerative engineering," used here to encompass regenerative medicine and tissue engineering, reflects the growing number of research and product development efforts that incorporate elements from both fields. Because regenerative engineered therapies rely on live cells and/or scaffolds, there are inherent challenges in quality control associated with variability in source and final products. Each patient recipient, tissue donor, and product application is unique and therefore the field faces complexities in the development of safe and effective new products and therapies that are not faced by developers of more conventional therapies. To further explore the various factors that contribute to successful regenerative engineering products, an ad hoc committee will plan a one-day public workshop in Washington, DC. Invited speakers and participants may discuss factors and sources of variability in the development and clinical application of regenerative engineering products, characteristics of high-quality products, and how different clinical needs, models, and contexts can inform the development of a product. Speakers may also discuss ways to reduce variability and ensure consistent, high-quality products and improve patient outcomes, share lessons learned, and highlight opportunities for collaboration. A broad array of stakeholders may take part in the workshop, including academic and industry experts, regulators, clinicians, patients, and patient advocates. The ad hoc committee will develop the workshop agenda, select and invite speakers and discussants, and may moderate the discussions. Proceedings of the workshop will be prepared by a designated rapporteur in accordance with institutional policy and procedures.



Regenerative Engineering – The convergence of advanced materials sciences, stem cell science, physics, developmental biology and clinical translation for the regeneration of complex tissues and organ systems (source: Regenerative Engineering Society).

AGENDA

8:30 a.m. **Opening Remarks**

JAY SIEGEL, *Forum Co-Chair*
Scientific Advisor
Tycho Therapeutics, Inc.

SHARON TERRY, *Forum Co-Chair*
Chief Executive Officer
Genetic Alliance

8:35 a.m. **Charge to Workshop Speakers and Participants**

MARTHA LUNDBERG, *Workshop Co-Chair*
Program Director, Division of Cardiovascular Sciences
Advanced Technologies and Surgery Branch
National Heart, Lung, and Blood Institute
National Institutes of Health

KATHY TSOKAS, *Workshop Co-Chair*
Regulatory Head of Regenerative Medicine & Advanced Therapy
Johnson & Johnson

8:45 a.m. **Stage Setting – The Impact of Variability on Regenerative Engineering Products**

GUILLERMO AMEER
Daniel Hale Williams Professor of Biomedical Engineering and Surgery
Director, Center for Advanced Regenerative Engineering
Northwestern University

SESSION I: USING CASE STUDIES TO IDENTIFY THE SOURCES OF VARIABILITY ASSOCIATED WITH REGENERATIVE THERAPIES

Session Objective:

- To gain a better understanding of the sources of variability associated with regenerative engineering products through a series of case studies.

Session Moderator: Cato Laurencin, University Professor, Director, Institute for Regenerative Engineering, University of Connecticut

9:05 a.m. **CASE STUDY 1:** VARIABILITY IN THE USE OF MESENCHYMAL STEM CELLS FOR TREATING CARDIOMYOPATHY
IVONNE HERNANDEZ SCHULMAN
Professor of Clinical Medicine
University of Miami Miller School of Medicine

9:20 a.m. **CASE STUDY 2:** SOURCES OF VARIABILITY IN PRECLINICAL AND CLINICAL RESEARCH ON STEM CELL THERAPIES FOR ALS
CLIVE SVENDSEN
Kerry and Simone Vickar Family Foundation Distinguished Chair in Regenerative Medicine
Cedars-Sinai Medical Center

9:35 a.m. **CASE STUDY 3:** VARIABILITY IN THE DEVELOPMENT OF CELLULAR THERAPIES
DAVID STRONCEK
Chief, Cell Processing Section
Department of Transfusion Medicine
NIH Clinical Center

9:50 a.m. **Panel Discussion with Speakers and Workshop Participants**

10:20 a.m. **Break**

SESSION II: CONSIDERING THE FACTORS THAT CONTRIBUTE TO PATIENT VARIABILITY AND APPROACHES TO ADDRESSING THOSE DIFFERENCES

Session Objectives:

- Discuss factors that contribute to patient variability such as a patient's genetics, the severity of their condition, past treatments, the placebo effect, and the patient's built environment/geography.
- Examine the feasibility of a precision medicine approach that would target the right patient with the right regenerative engineering therapy.

Session Moderator: Brian Fiske, Senior Vice President, Research Programs, Michael J. Fox Foundation

10:35 a.m. JENNIFER ELISSEEFF
Morton Goldberg Professor
Wilmer Eye Institute and Biomedical Engineering, Translational Tissue Engineering Center
Johns Hopkins University

10:50 a.m. JOSEPH WU
Director, Stanford Cardiovascular Institute
Simon H. Stertzer, MD, Professor of Cardiovascular Medicine & Radiology
Stanford University School of Medicine

11:05 a.m. STEVE BADYLAK
Professor of Surgery
McGowan Institute for Regenerative Medicine
University of Pittsburgh

11:20 a.m. FLAGG FLANAGAN
Chief Executive Officer & Chairman of the Board
Discgenics

11:35 a.m. **Panel Discussion with Speakers and Audience Members**

12:05 p.m. **Working Lunch**

SESSION III: THE IMPORTANCE OF ADDRESSING VARIABILITY IN DONOR TISSUES AND CELLS

Session Objectives:

- Consider the sources of variability among donor tissues and cells such as the source (e.g., bone marrow, adipose, cord blood), the dose, route of administration, and culture conditions, among other factors.
- Discuss methods to address the variability among source tissues and cells so that patients receive a consistent and effective product.

Session Moderator: Martha Lundberg, Program Director, Division of Cardiovascular Sciences, Advanced Technologies and Surgery Branch, NHLBI

1:00 p.m. ANDREW FESNAK
Assistant Professor of Clinical Pathology and Laboratory Medicine
University of Pennsylvania Perelman School of Medicine

1:15 p.m. GEORGE MUSCHLER
Staff Member, Department of Biomedical Engineering
Cleveland Clinic

1:30 p.m. ALLISON HUBEL
Professor of Mechanical Engineering
University of Minnesota

1:45 p.m. **Panel Discussion with Speakers and Audience Members**

2:15 p.m. **Break**

SESSION IV: THE IMPORTANCE OF ADDRESSING VARIABILITY AND MEETING QUALITY EXPECTATIONS IN THE MANUFACTURING SETTING

Session Objectives:

- Explore the translational research priorities for the maturing of the fields of tissue science and regenerative engineering.
- Describe advances in preservation technologies needed to sustain fragile cells and tissues under biologically optimized conditions for storage, shipment and handling.
- Discuss metrics for reproducibility, robustness, and user-friendliness that will enable the broad distribution of products.

Session Moderator: Krish Roy, Robert A. Milton Endowed Chair and Director, Center for ImmunoEngineering, Georgia Tech

2:30 p.m. CARL BURKE
BioTherapeutics Development
Johnson & Johnson

2:45 p.m. MICHELE MYERS
Senior Director, Cell Process Development
Cell and Gene Therapy Platform
GSK

3:00 p.m. ERIK FINGER
Assistant Professor, Department of Surgery
University of Minnesota

3:15 p.m. **Panel Discussion with Speakers and Workshop Participants**

SESSION V: EXPLORING OBJECTIVE METRICS AND OUTCOMES FOR CLINICAL TRIALS AND THE REGULATORY APPROVAL PATHWAY

Session Objectives:

- Discuss ideas for objective metrics and reliable approaches to interpreting the outcomes of clinical trials of regenerative engineering therapies.
- Explore how variability in regenerative engineering products can affect the regulatory approval pathway.

Session Moderator: Kathy Tsokas, Regulatory Head of Regenerative Medicine & Advanced Therapy, Johnson & Johnson

3:45 p.m. KAREN CHRISTMAN
Scientific Co-Founder
Ventrix

4:00 p.m. PETER MARKS
Director
Center for Biologics Evaluation and Research
U.S. Food & Drug Administration

4:15 p.m. **Panel Discussion with Speakers and Workshop Participants**

4:35 p.m. **Final Panel Discussion**

CARL BURKE
KAREN CHRISTMAN
ALLISON HUBEL
PETER MARKS
CLIVE SVENDSEN

5:00 p.m. **Final Remarks from Workshop Co-chairs**

MARTHA LUNDBERG, *Workshop Co-Chair*
Program Director, Division of Cardiovascular Sciences
Advanced Technologies and Surgery Branch
National Heart, Lung, and Blood Institute
National Institutes of Health

KATHY TSOKAS, *Workshop Co-Chair*
Regulatory Head of Regenerative Medicine & Advanced Therapy
Johnson & Johnson

5:10 p.m. **Adjourn**