

*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.

Forum on  
**REGENERATIVE MEDICINE**



**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**

<b>SESSION II: CONSIDERING THE FACTORS THAT CONTRIBUTE TO PATIENT VARIABILITY AND APPROACHES TO ADDRESSING THOSE DIFFERENCES</b>
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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**

<b>SESSION III: THE IMPORTANCE OF ADDRESSING VARIABILITY IN DONOR TISSUES AND CELLS</b>
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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**

<b>SESSION IV: THE IMPORTANCE OF ADDRESSING VARIABILITY AND MEETING QUALITY EXPECTATIONS IN THE MANUFACTURING SETTING</b>
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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**

<b>SESSION V: EXPLORING OBJECTIVE METRICS AND OUTCOMES FOR CLINICAL TRIALS AND THE REGULATORY APPROVAL PATHWAY</b>
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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**