Realizing the Promise of Regenerative Medicine and Upholding Public Trust: The Need for Rigorous Science and Data Sharing

NIH PERSPECTIVE

Congressional Briefing on Regenerative Medicine Cell Therapies

September 19, 2019
12:00 PM – 1:30 PM
902 Hart Senate Office Building
NIH: Mission, Roles, Principles

▪ Mission:
  – To seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to enhance health, lengthen life, and reduce illness and disability

▪ Roles:
  – Fund and conduct research
  – Stimulate and lead avenues of scientific inquiry
  – Serve as responsible stewards through peer review and oversight

▪ Principles:
  – Scientific rigor and reproducibility
  – Scientific integrity in conduct and reporting of research
  – Sharing of research data, materials, and other resources
  – Transparency and accountability
  – Engagement of the research community, patients, and other public sectors
Regenerative Medicine

- Aims to repair or replace cells and tissues damaged by injury, disease, or aging
- Includes a wide range of technologies such as engineered biomaterials and tissues as well as gene editing or replacement/addition

The Promise:
- Delivery of therapeutic cells that restore normal structure and function
- Leverage and enhance the body’s own innate healing capacity
Promise of Regenerative Medicine: Example

Still Many Challenges

In-depth Cell Characterization
Preclinical Studies
Clinical Trials
Data Sharing

Cardiomyocytes derived from Human iPSC contract in vitro (Cell Applications Inc.)

Proof Pending: Safety and Efficacy
In-depth Cell Characterization

Levels of Cell Product Characterization

- Total Cell Characteristics
  - Deep Fingerprinting
  - Critical Qualify Attributes
  - Specifications

Cell Purity/Identity

- Cell Surface Marker Analysis

Cell Reprogramming Factors

- Genomic Stability

Critical Quality Attributes

- Specifications

Pluripotency

- Morphology

Biochemical Attributes

- Metabolomics
- System biology
- Integrative physiology
- System medicine
- System pharmacology
- Regenerative medicine
- Integrated biomarkers
- Human disease
  - Prediction
  - Diagnosis
  - Treatment efficacy

Biophysical Attributes

- Function
National and International Expert Consensus

- State of the science and clinical applications of RM:
  - While cell therapies offer potential promise, much must be learned about cell function and product manufacturing before safe and effective products can be administered in the clinic
Upholding Public Trust

Importance of rigorous science and avoidance of “hype”

- Considerable hype in marketing; untested and unapproved RM products advertised
  - A number of trials are not under IND
  - “Pay-to-participate” clinical trials

- Harms to individuals from using such products have occurred; may lead to loss of public trust in:
  - The field of RM
  - Biomedical research in general
21st Century Cures Act: Regenerative Medicine

- RM provisions applicable to NIH, FDA, and NIST

- Themes:
  - Accelerating progress
  - Scientific rigor
  - Appropriate regulatory oversight and standards
  - Stimulating innovation and partnership

- Established RM Innovation Project (RMIP)
  - NIH, working in coordination with FDA, to support research to advance the field of regenerative medicine using adult stem cells
  - Funding authorized 2017-2020
To significantly accelerate the field of RM through:

- Funding late-stage pre-clinical and IND/IDE-enabling studies as well as carefully selected clinical trials that exemplify:
  - Rigorous science
  - Optimal regulatory compliance
  - Enhanced data sharing

- Providing resources necessary for investigators to address critical challenges identified through broad consultation

- Developing an innovative model for the support and conduct of RM research

Current RMIP Portfolio: Clinical Indications

- Autologous stem cell therapy for Type 1 Diabetes
- Restoring cardiac functions for ischemic CVD and MI
- Erythropoietin-producing cell-based therapy for anemia of CKD
- Generating functional alveolar epithelial cells & IPF treatment using iPSC
- Vascular tissue engineering for PAD & congenital heart surgery
- Therapeutic skin revascularization by endothelial cell transplantation / Epidermolysis Bullosa therapy using iPSC
- Generating RPE to treat Macular Degeneration (e.g. AMD) / Corneal engineering through LSC therapy
- Manufacturing cells expressing FVIII to treat Hemophilia A / Engineered platelet production and optimization of RBC transfusions
Understanding Scientific Challenges in RM

NIH-FDA co-hosted a multi-sector workshop to identify and discuss solutions to major scientific barriers in RM

- Several universal challenges emerged:
  - Need for regulatory support to enable development of robust IND/IDE applications
  - Transitioning from laboratory- to clinical-grade manufacturing of cell products
  - Limited understanding of the identity and nature of RM cell products used in the clinic
  - Limited availability of standardized data for analysis across studies hampers advancement of the field
Accelerating Innovation: Addressing Challenges

Regenerative Medicine Innovation Catalyst (RMIC)

- NIH-FDA-NIST collaboration, in consultation with RM community
- Network of academic and private sector entities being launched to:
  - Provide manufacturing support and regulatory “coaching”
  - Apply advanced technologies for in-depth cell characterization
  - Develop data standards and common data elements
  - Promote collection and sharing of standardized cell product and clinical outcomes data

➢ A pilot for a new model for support and conduct of RM clinical research
Consultative Approach to Advancing RM Clinical Research

Strategic and Tactical Framework for Advancing RM Clinical Research

Requests for Information

Further Expert Multi-Sector Scientific Input

Advisory Groups

Workshops
Accelerating the Development of Safe and Effective Cell-based Treatments

- Promote and support rigorous science and regulatory compliance
- Assist investigators in developing clinical-grade cell products
- Standardize and collect in-depth cell characterization data and individual level participant data
- Use common vocabularies and provide a cloud-based platform for sharing, integration, and analysis of product and clinical data
- Advances the field, promotes public trust
- Optimizes ability to manufacture cells that will produce the intended clinical effects
- Enables deeper understanding of the composition and function of stem cell products and correlation of cell characteristics with clinical outcomes
- Enables analyses across studies
Realizing the promise of Regenerative Medicine and upholding public trust

- Rigorous science
- Attention to safety
- Accountability
  - Stewardship and oversight
- Transparency
  - Broad sharing of both cell product and clinical outcomes data