Tissue Engineering/Regenerative Medicine Meeting Summary

Introduction

Tissue engineering/Regenerative medicine (TE/RM) involves the engineering of functional tissues and organs *in vitro* for implantation *in vivo*, and the remodeling and regeneration of tissue *in vivo* for the purpose of repairing, replacing, maintaining, or enhancing tissue and organ function. It requires a complex approach combining living and biologically derived components such as cells and proteins with synthetic components such as organic polymers and inorganic materials. Some of the challenges in TE/RM include understanding and controlling cellular responses and developing scaffolding materials appropriate as an extracellular matrix environment. Additionally, new measurement tools, engineering methods, and design principles are essential.

As part of an ongoing effort to get input from the scientific community on this research area, the NIBIB staff met with thirteen investigators with a broad range of expertise in TE/RM, in conjunction with the Regenerate 2005 Conference in Atlanta, Georgia, to discuss future opportunities in the field. The names and affiliations of the participants are attached at the end of this summary. Prior to the meeting, the participants were provided with a list of currently funded NIBIB TE grants, a description of the NIBIB TE Program, the NIBIB mission statement, and the draft NIBIB strategic plan. In addition, the participants were asked to discuss the research opportunities in this area with their colleagues for additional advice in advance of the meeting. The NIBIB welcomes additional input from the community on this research area. Please send any comments to Dr. Fei Wang at wangf@mail.nih.gov.

Summary of Discussion

TE/RM requires the integration of the engineering and life science disciplines. The workshop participants suggested that the NIBIB TE program should promote such integration as well as focus on the engineering approaches to move the field forward. The major suggestions for specific NIBIB TE Program focus areas include the following:

1. Promote the Development of Enabling Technologies for TE/RM including: (1) strategies to move from 2D to 3D tissue cultures; (2) tools for non-invasive and quantitative monitoring of structure, composition and function of tissues in real time (during cultivation, following implantation); (3) predictive models of native and engineered tissues; (4) microfabrication technologies for tissues-on-a-chip; (5) novel bioreactors to precisely control the chemical and mechanical environment for 3D tissue growth; (6) novel tissue regeneration strategies, that avoid the limitations of current scaffolds, and include biomimetic and bioinspired scaffolds, potentially combined with bioactive molecules, to “instruct” cells to differentiate in a desired direction; and (7) cross-cutting technologies required for manufacturing of tissue engineered products such as preservation, sterilization, and packaging.

2. Develop Engineered 3D Tissues as Model Systems including; (1) tissue engineered constructs as models for diseases, systems biology, complex tissue interactions, inflammatory, pharmacological and toxicological modeling and metabolism *in vitro*; (2) 3-D tissue constructs for drug discovery and development; and (3) tissue engineered phantoms for imaging and drug delivery.

3. Develop Effective Strategies for Tissue Vascularization and Innervation including (1) scaffolds that support complex microvascularization and innervation; (2) strategies to direct spatial/temporal control of neovascularization and neurogenesis; (3) methods that enable perfusion of blood immediately following implantation; and (4) methods to evaluate functional vasculogenesis and neurogenesis.

4. Develop Engineering Technologies for Translational Stem Cell Research including (1) advanced bioreactors to rapidly expand stem cells; (2) methods for controllable stem cell purification/separation (without batch-to-batch variability and cell exposure to materials of animal origin); and (3) control of stem cell differentiation *in vivo* such as induced differentiation by a device.

To best accomplish the above, participants suggested that the Institute work together with other federal agencies and public or private organizations to (1) encourage collaborations among biologists, clinicians and engineers; (2) promote critical mass, bench-to-bedside multidisciplinary centers for TE/RM; (3) hold workshops to identify core problems and facilitate cooperation along problem-centric areas; and (4) move basic research more rapidly to clinical application by focusing on unmet clinical needs and collaborating with other NIH disease-specific Institutes to achieve clinical milestones for progress.

Additional suggestions for the future research opportunities included:

- Better understand tissue development to instruct engineered tissue, with emphasis on the relationships between evolving material/mechanical properties and evolving composition, architecture, and structure, at the molecular and macroscopic levels.

- Improve the understanding of, and ability to locally control, host immune response to implanted tissue engineered constructs, and their importance in determining healing in the context of re-establishing implant site homeostasis, device integration, and the functional fate of the implant in the host.

- Standardize functional assessment criteria, benchmarking methods and assays, and protocols for TE/RM testing and functional assessments *in vitro* and *in vivo*.

- Develop well-characterized cell sources, including 1) repositories for cells frequently employed in TE/RM to facilitate sharing and comparison, 2) adult and embryonic stem cells and standardization of cell isolation, 3) phenotypic markers important to functional performance and comparisons with secondary and normal primary human cell lines.

- Support standardized polymer/scaffold bank for TE/RM.

- Develop animal models for testing tissue engineered constructs and study general problems such as neovascularization or immune response.

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