



*International Technology Research Institute
World Technology (WTEC) Division*



NIST



WTEC Workshop on

TISSUE ENGINEERING RESEARCH IN THE UNITED STATES

June 5-6, 2000

PROCEEDINGS



International Technology Research Institute
R.D. Shelton, Director
Geoffrey M. Holdridge, WTEC Division Director and Series Editor

**4501 North Charles Street
Baltimore, Maryland 21210-2699**

WTEC Panel on Tissue Engineering Research

Sponsored by the National Science Foundation, the Defense Advanced Research Projects Agency, the National Institute of Standards and Technology, the National Aeronautics and Space Administration, the National Institutes of Health, and the Food and Drug Administration of the U.S. government

Larry V. McIntire
E.D. Butcher Professor and Chair
Institute of Biosciences and Bioengineering
Rice University
MS 144, 6100 Main Street
Houston, TX 77005-1892

Peter C. Johnson
President and Chief Executive Officer
TissueInformatics, Inc.
711 Bingham St., Suite 202
Pittsburgh, PA 15203

Nancy L. Parenteau
Senior Vice President and Chief
Scientific Officer
Organogenesis, Inc.
150 Dan Road
Canton, MA 02021

Howard Greisler
Department of Cell Biology, Neurobiology, and
Anatomy
Loyola University Medical Center
Building 102, 5th Floor
2160 South First Avenue
Maywood, IL 60153

David J. Mooney
Department of Chemical Engineering
Department of Biologic & Materials Sciences
University of Michigan
2300 Hayward St.
Room 3074 H.H. Dow Bldg.
Ann Arbor, MI 48109-2136

David Smith
General Counsel
TissueInformatics, Inc.
711 Bingham St., Suite 202
Pittsburgh, PA 15203

Linda Griffith
Chemical Engineering Department and Division
of Bioengineering and Environmental Health
MIT
Cambridge, MA 02139-4307

Milan Mrksich
Dept of Chemistry
SCL-463
University of Chicago
5801 S. Ellis Ave.
Chicago, IL 60637

INTERNATIONAL TECHNOLOGY RESEARCH INSTITUTE World Technology (WTEC) Division

WTEC at Loyola College (previously known as the Japanese Technology Evaluation Center, JTEC) provides assessments of foreign research and development in selected technologies under a cooperative agreement with the National Science Foundation (NSF). Loyola's International Technology Research Institute (ITRI), R.D. Shelton, Director, is the umbrella organization for WTEC. Elbert Marsh, Deputy Assistant Director for Engineering at NSF's Engineering Directorate, is NSF Program Director for WTEC. Several other U.S. government agencies provide support for the program through NSF.

WTEC's mission is to inform U.S. scientists, engineers, and policymakers of global trends in science and technology. WTEC assessments cover basic research, advanced development, and applications. Panels of typically six technical experts conduct WTEC assessments. Panelists are leading authorities in their field, technically active, and knowledgeable about U.S. and foreign research programs. As part of the assessment process, panels visit and carry out extensive discussions with foreign scientists and engineers in their labs.

The ITRI staff at Loyola College help select topics, recruit expert panelists, arrange study visits to foreign laboratories, organize workshop presentations, and finally, edit and disseminate the final reports.

Dr. R.D. Shelton
ITRI Director
Loyola College
Baltimore, MD 21210

Mr. Geoff Holdridge
WTEC Division Director
Loyola College
Baltimore, MD 21210

Dr. George Gamota
ITRI Associate Director
17 Solomon Pierce Road
Lexington, MA 02173

WTEC Study on

TISSUE ENGINEERING RESEARCH

PROCEEDINGS OF THE JUNE 5-6 2000 U.S. REVIEW WORKSHOP

March 2001

This document was sponsored by the National Science Foundation (NSF) and other agencies of the U.S. government under NSF Cooperative Agreement ENG-9707092, awarded to the International Technology Research Institute at Loyola College in Maryland. The government has certain rights in this material. Any opinions, findings, and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the United States government, the authors' parent institutions, or Loyola College.

PREFACE

The National Science Foundation and other agencies of the U.S. Government have asked the World Technology (WTEC) Division of the International Technology Research Institute to perform an assessment of status and trends in tissue engineering research and applications around the world in comparison to that in the United States. The purpose of this study is to assess the U.S. tissue engineering R&D effort in comparison to activities abroad, provide the scientific/engineering community with a critical view of the field and identify the most promising areas for future research and industrial development, stimulate the development of an inter-disciplinary and international community of tissue engineering researchers, and identify opportunities for international collaboration in the field. WTEC has recruited a panel of U.S. experts in the various related fields to perform this assessment (see inside cover). The panel is charged with analyzing and comparing research in the United States with that being pursued abroad. This panel has now visited relevant R&D facilities in Japan and Western Europe during the summer of 2000. Prior to these visits the panel first needed to develop an understanding of the state-of-the art in these technologies in the United States.

Towards this end, WTEC invited leading U.S. tissue engineering researchers to a workshop held at NIH in Bethesda, MD on June 5 and 6, 2000. This volume is a collection of papers presented at the workshop. Paper authors were asked to provide a broad description of all related U.S. work in their respective fields (i.e., not necessarily just the activities in their own laboratories). Authors were chosen to be representative of cutting edge U.S. research in each of the topic areas. This edition also includes overviews of each session prepared by the respective WTEC panelists, as well as some revised contributions.

Thanks to all the participants for their contributions to this volume and the workshop, and to our sponsors for supporting this activity.

Sincerely,

Geoff Holdridge, WTEC Division Director
International Technology Research Institute

International Technology Research Institute (ITRI)

R. D. Shelton, Principal Investigator, ITRI Director

World Technology (WTEC) Division

(Staff working on this study)

Geoffrey M. Holdridge, WTEC Division Director

Bobby A. Williams, Financial Officer

Roan E. Horning, Head of Information Technologies

Aminah Grefer, Global Support Inc., Europe Advance Contractor

Gerald Whitman, ENSTEC, Inc. Japan Advance Contractor

Hiroshi Morishita, WTEC Japan Representative

Copyrights reserved by individual authors except as noted herein. Reproduced by permission. This work relates to NSF Cooperative Agreement ENG-9707092. The U.S. government retains a nonexclusive and nontransferable license to exercise all exclusive rights provided by copyright. The final report from this study will be distributed by the National Technical Information Service (NTIS) of the U.S. Department of Commerce. A list of available WTEC reports and information on ordering them from NTIS is included on the inside back cover of this report.

TABLE OF CONTENTS

Introduction: “Overview of the U.S. tissue engineering enterprise” (Michael Lysaght, PhD, Director, Center for Biomedical Engineering, Brown University)	1
1. Biomaterials.....	27
Overview (Linda Griffith, MIT)	27
“Ceramics!” (Ali Tofighi, PhD, ETEX Corp.)	29
“Biomechanical and structural properties of native and biologically-derived soft tissues” (Michael S. Sacks, PhD, University of Pittsburgh)	41
“Biodegradable, synthetic polymers” (Kathryn E. Uhrich, PhD, Associate Professor, Rutgers University).....	62
“Progress and outlook in biomimetic materials” (Jeffrey A. Hubbell, PhD, Professor of Biomedical Engineering, Swiss Federal Institute of Technology and University of Zurich)	72
“Biomaterials opportunities and challenges” (Buddy Ratner, PhD, Professor and Director, University of Washington Engineered Biomaterials Center)	77
2. Cells.....	79
Overview (Nancy Parenteau, Organogenesis)	79
“Hematopoietic cell transplantation and tolerance induction to allografts and xenografts” (David K.C. Cooper, PhD, Associate Professor of Surgery, Harvard Medical School & Immunologist, Transplantation Biology Research Center, Massachusetts General Hospital).....	82
“Human mesenchymal stem cells for regenerative medicine” (Daniel R. Marshak, PhD, Johns Hopkins University School of Medicine & Executive Scientific Advisor, Osiris Therapeutics, Inc.)	84
“Quality and manufacturing considerations for autologous chondrocyte implantation” (Gary C. du Moulin, PhD, MPH, Senior Director, Quality Systems, Genzyme Tissue Repair)	86
“The use of allogeneic cells in tissue engineering” (Jan Hardin-Young, PhD, Organogenesis)	89
“Enabling culture systems for homogeneous, multiplex, and composite tissue engineering with clonal expansion of differentiated, primary adult human cells” (Geoffrey D. Block, MD, MSc, MPH, University of Pittsburgh).....	92
3. Biomolecules	95
Overview (Howard Greisler, Loyola University Medical Center).....	95
“Gene therapy” (Jeff Bonadio, PhD, Selective Genetics, Inc.).....	98
“Angiogenic growth factors” (Michael Simons, MD, Associate Professor of Medicine’ Harvard Medical School; Director, Angiogenesis Research Center, Beth Israel Deaconess Medical Center).....	105
“Use of rhBMP-2 in tissue engineering” (Elizabeth Morris, DVM, Genetics Institute).....	122
4. Cell-based Sensors, Other Non-Medical Applications	133
Overview (Milan Mrksich, University of Chicago).....	133
“Cell-based sensors – Electrical transduction” (Joseph J. Pancrazio, PhD, Naval Research Laboratory).....	135
“Restoration of vision in blind individuals using a multiple-unit artificial retina chipset (MARC) system” (Mark S. Humayun, MD, PhD, Johns Hopkins University)	146
“High content screening and the CellChip™ system” (Ravi Kapur, PhD, Director, CellChip Program, Cellomics, Inc.).....	148

5. Engineering Design Aspects	151
Overview (David Mooney, University of Michigan)	151
“Bioreactor design considerations in cell therapies and tissue engineering” (William M. Miller, PhD, Professor, Chemical Engineering Department, Northwestern University).....	154
“Mass transfer issues in tissue engineering” (Clark K. Colton, PhD, MIT).....	166
“The engineering of vascular substitutes and the role of biomechanics” (Robert Nerem, PhD, Institute Professor, Parker H. Petit Distinguished Chair for Engineering in Medicine, and Director, Parker H. Petit Institute for Bioengineering and Bioscience, Georgia Tech.).....	171
“Functional tissue engineering of articular cartilage: The role of biomechanics” (Farshid Guilak, Ph.D., Director of Research, Division of Orthopaedic Surgery, Duke Univ. Medical Center).....	175
“Long-term storage of engineered tissues and living systems” (Mehmet Toner, Associate Professor, Massachusetts General Hospital, Harvard Medical School)	180
6. Informatics	195
Overview (Peter C. Johnson, Tissue Informatics).....	195
“New technology for 3D microscopy of tissue and materials” (Russel Kerschmann, PhD, RSC)	198
“Spectral imaging alternatives for the life sciences” (Jeremy Lerner, PhD, LightForms, Inc.)	200
“Computational biological modeling in tissue engineering” (Donna Rounds, PhD, VP External Affairs & Intellectual Property’ Physiome Sciences, Inc.....	221
7. Legal and Regulatory Issues.....	225
Overview (David Smith, Tissue Informatics).....	225
“Access to human biological materials” (Michael Malinowski, JD, Associate Professor of Law, Widener University).....	229
“Current issues in U.S. patent law” (Patrea Pabst, AGG, LLP)	236
“An industry perspective on regulatory oversight of cell and tissue based products” (Alison Lawton, Senior Vice President, Regulatory Affairs’ Genzyme Corporation).....	239
“Commercialization of a tissue engineered product: challenges and the role of government” (Patrick Bilbo, Director, Commercial Development, Organogenesis Inc.).....	243
8. Review of U.S. Government Activities and Interests.....	255
Overview (Fred G. Heineken, National Science Foundation).....	255
“MATES and U.S. Government tissue engineering initiative: an overview” (Kiki B. Hellman, PhD, U.S. Food and Drug Administration).....	256
9. Addenda	
“Tissue engineering medical products standards” (Grace Lee Picciolo, U.S. Food and Drug Administration).....	269
“International Technology Research Institute (ITRI), WTEC Division (R.D. Shelton, ITRI/Loyola)....	274
List of Contributors	279