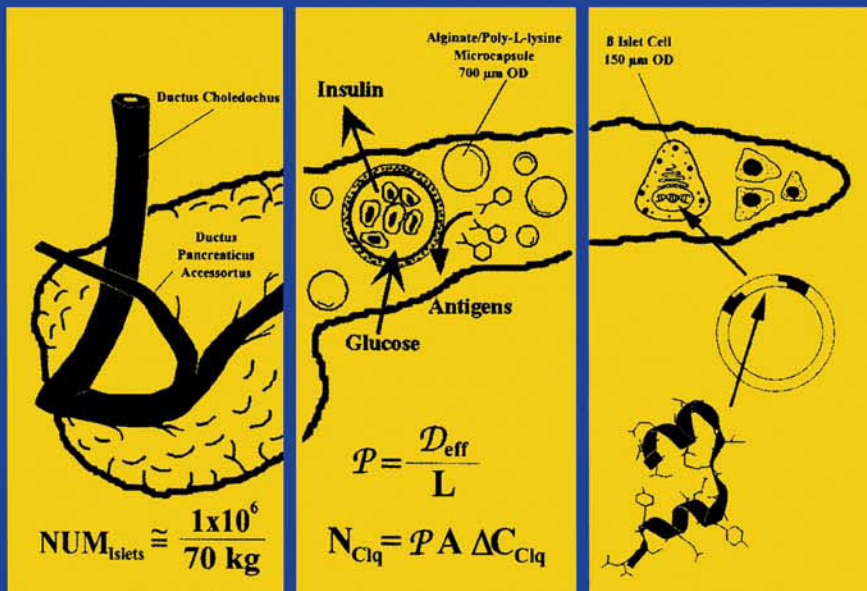


# FRONTIERS IN TISSUE ENGINEERING



**Edited by**  
**Charles W. Patrick Jr, Antonios G. Mikos**  
**and Larry V. McIntire**

**PERGAMON**

# FRONTIERS IN TISSUE ENGINEERING

This Page Intentionally Left Blank

# FRONTIERS IN TISSUE ENGINEERING

Edited by

**CHARLES W. PATRICK JR.**

Laboratory of Reparative Biology and Bioengineering  
Department of Plastic Surgery, M.D. Anderson Cancer Center  
Houston, Texas, USA

**ANTONIOS G. MIKOS**

*and*

**LARRY V. MCINTIRE**

Institute of Biosciences and Bioengineering  
Rice University, Houston, Texas, USA



PERGAMON

U.K.	Elsevier Science Ltd. The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, U.K.
U.S.A.	Elsevier Science Inc., 655 Avenue of the Americas, New York NY 10010, U.S.A.
JAPAN	Elsevier Science Japan, Higashi Azabu 1-chome Building 4F, 1-9-15, Higashi Azabu, Minato-ku, Tokyo 106, Japan

---

Copyright © 1998 Elsevier Science Ltd

*All Rights Reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means: electronic, electrostatic, magnetic tape, mechanical, photocopying, recording or otherwise, without permission in writing from the publishers.*

First edition 1998

**Library of Congress Cataloging in Publication Data**

A catalog record for this book is available from the Library of Congress

**British Library Cataloguing in Publication Data**

A catalogue record for this book is available from the British Library

ISBN 0 08 042689 1

*Printed in Great Britain by Redwood Books Ltd.*

**Cover Illustration:** Tissue engineering involves a synergistic coupling of the disparate fields of engineering, life science, and clinical science. The illustration depicts a pancreas viewed from each field's vantage point in the following order, left to right: clinical science (anatomy and transplantation of pancreas), engineering (encapsulated islets releasing insulin), and life science (upregulation of insulin secretion via genetic engineering). Illustration by C.W. Patrick Jr.

# Contents

<i>Contributors</i>	ix
<i>Preface</i>	xv
<i>Section I Prospectus of Tissue Engineering</i>	
I Prospectus of Tissue Engineering <i>Charles W. Patrick Jr., Antonios G. Mikos and Larry V. McIntire</i>	3
<i>Section II Fundamentals and Methods of Tissue Engineering</i>	
II.1 Cell–Extracellular Matrix Interactions <i>Julia M. Ross</i>	15
II.2. Cell–Cell Interactions <i>Sharad Kukreti, Konstantinos Konstantopoulos and Larry V. McIntire</i>	28
II.3 Mechanical Forces and Growth Factors <i>Keith J. Gooch, Torsten Blunk, Christopher J. Tennant, Gordana Vunjak-Novakovic, Robert Langer and Lisa E. Freed</i>	61
II.4 Polymer Synthesis <i>Amarpreet S. Sawhney and Paul D. Drumheller</i>	83
II.5 Fabrication of Biodegradable Polymer Scaffolds <i>Markus S. Widmer and Antonios G. Mikos</i>	107
II.6 Cell–Synthetic Surface Interactions <i>Nina M. Lamba, Jennifer A. Baumgartner and Stuart L. Cooper</i>	121
II.7 Wound Healing <i>Jennifer West</i>	138
II.8 Biocompatibility of Tissue Engineered Implants <i>James M. Anderson</i>	152
II.9 Tissue Engineered Construct Design Principles <i>Gregory P. Reece and Charles W. Patrick Jr.</i>	166

II.10	Orthopedic Surgical Applications <i>Michael J. Yaszemski and Alan W. Yasko</i>	197
II.11	Tissue Engineering and Plastic Surgery <i>Michael J. Miller and Gregory R.D. Evans</i>	213
II.12	Tissue Engineering and Visceral Surgery <i>Rosa S. Choi and Joseph P. Vacanti</i>	233
II.13	Immunoisolation <i>Michael V. Sefton, Julia E. Babensee and Michael H. May</i>	248
II.14	Drug Delivery <i>You Han Bae and Sung Wan Kim</i>	261
II.15	Gene Therapy in Tissue Engineering <i>Jeffrey R. Morgan and Martin L. Yarmush</i>	278
II.16	Ethical Considerations of Tissue Engineering on Society <i>Timothy W. King and Charles W. Patrick Jr.</i>	311
II.17	Product Applications and Regulatory Issues <i>Kiki B. Hellman, Emma Knight and Charles Durfor</i>	341
<i>Section III Tissue Engineering Applied to Specialized Tissues</i>		
III.1	Adipose Tissue Engineering <i>Charles W. Patrick Jr., Priscilla B. Chauvin and Geoffrey L. Robb</i>	369
III.2	Options for Engineering Bone <i>Elisa A. Burgess and Jeffrey O. Hollinger</i>	383
III.3	Tissue Engineering of Cartilage <i>Angela M. Rodriguez and Charles A. Vacanti</i>	400
III.4	Tissue Engineered Tendon <i>L. Louie, I.V. Yannas and M. Spector</i>	412
III.5	Dental Tissue Engineering <i>Lonnie D. Shea, Isaac C. Yue and David J. Mooney</i>	443
III.6	Hematopoietic Cells <i>Bernhard Palsson</i>	460

III.7	The Regeneration of Skeletal Tissues <i>Arnold I. Caplan, David J. Fink, Scott P. Bruder and Randell G. Young</i>	471
III.8	Hemoglobin-Based Blood Substitutes <i>Alan S. Rudolph</i>	481
III.9	Muscle Tissue Engineering <i>Patricia Petrosko, Tahsin O. Acarturk, Paul A. Dimilla and Peter C. Johnson</i>	495
III.10	Tissue Engineering of the Peripheral Nervous System <i>Elizabeth J. Furnish and Christine E. Schmidt</i>	514
III.11	CNS Disorders: Site-specific Treatment of CNS Disorders using Encapsulated Cells <i>Frank T. Gentile and Dwaine F. Emerich</i>	536
<i>Section IV Tissue Engineering Applied to Organs</i>		
IV.1	Tissue Engineering and the Cardiovascular System <i>Robert M. Nerem, Linda G. Braddon and Dror Seliktar</i>	561
IV.2	Tissue Engineering Applied to the Heart <i>Christine L. Tock and Timothy Scott-Burden</i>	580
IV.3	Tissue Engineering Esophagus <i>Yoshito Ikada</i>	598
IV.4	Engineering Small Intestine <i>James J. Cunningham, Gregory M. Organ and David J. Mooney</i>	610
IV.5	Tissue Engineered Kidney for Renal Replacement <i>H. David Humes, Derek C. Blakeney and Won-Kyoung Lee</i>	632
IV.6	Tissue Engineering in Urology <i>Anthony Atala</i>	649
IV.7	Tissue Engineered Skin <i>J. Teumer, J. Hardin-Young and N.L. Parenteau</i>	664
IV.8	Engineering a Bioartificial Liver Support <i>Julie R. Friend and Wei-Shou Hu</i>	678
Author index		696
Subject index		697



This Page Intentionally Left Blank

## Contributors

### **Tahsin Oguz Acarturk**

Division of Plastic and  
Maxillofacial Reconstructive  
Surgery,  
University of Pittsburgh Medical  
Center,  
676 Scaife Hall,  
3550 Terrace Street,  
Pittsburgh, Pennsylvania 15261, USA

### **James M. Anderson**

Institute of Pathology,  
Case Western Reserve University,  
Cleveland, Ohio 44106, USA

### **Anthony Atala**

Department of Urology,  
Children's Hospital and  
Harvard Medical School,  
300 Longwood Ave.,  
Boston, Maryland 02115, USA

### **Julia E. Babensee**

Department of Chemical Engineering  
and Applied Chemistry  
and Centre for Biomaterials,  
University of Toronto,  
Toronto, Ontario, M5S, 3E5, Canada

### **You Han Bae**

Department of Materials Science and  
Engineering,  
Kwangju Institute of Science and  
Technology,  
Kwangju, 506-303, Korea

### **Jennifer A. Baumgartner**

Department of Chemical Engineering,  
University of Delaware,  
Newark, Delaware, 19716, USA

### **Derek C. Blakeney**

Department of Internal Medicine  
and Department of Biomedical  
Engineering,  
The University of Michigan Medical  
Center,

Veterans Administration Medical  
Center and  
The University of Michigan at Ann  
Arbor,  
Ann Arbor, Michigan 48105, USA

### **Torsten Blunk**

Department of Chemical Engineering,  
Massachusetts Institute of  
Technology,  
77 Massachusetts Ave.,  
Cambridge, Massachusetts 02139,  
USA

### **Linda G. Braddon**

Parker H. Petit Institute for  
Bioengineering and Bioscience,  
Georgia Institute of Technology,  
Atlanta, Georgia 30332-0363, USA

### **Scott P. Bruder**

Osiris Therapeutics, Inc.,  
2001 Aliceanna Street,  
Baltimore, Maryland 21231, USA

### **Elisa A. Burgess**

Oregon Health Sciences University,  
Department of Surgery,  
3181 SW Sam Jackson Park Rd L352A,  
Portland, Oregon 97201-3098, USA

### **Arnold I. Caplan**

Skeletal Research Center,  
Biology Department,  
Case Western Reserve University,  
2080 Adelbert Road,  
Cleveland, Ohio 44106, USA

### **Rosa S. Choi**

Department of Surgery,  
Harvard Medical School,  
Children's Hospital  
300 Longwood Ave.,  
Boston, Massachusetts 02115, USA

### **Priscilla B. Chauvin**

Laboratory of Reparative Biology and  
Bioengineering,

Department of Plastic Surgery,  
The University of Texas M.D. Ander-  
son Cancer Center  
1515 Holcombe Blvd., Box 62,  
Houston, Texas 77030, USA

**Stuart L. Cooper**

Department of Chemical Engineering,  
University of Delaware,  
Newark, Delaware 19716, USA

**James J. Cunningham**

Department of Chemical Engineering,  
The University of Michigan,  
Ann Arbor, Michigan 48109, USA

**Paul Dimilla**

Pittsburgh Tissue Engineering  
Initiative, Inc.,  
Center for Biotechnology and  
Bioengineering,  
300 Telephone Drive,  
Pittsburgh, Pennsylvania 15219, USA

**Paul D. Drumheller**

Gore Hybrid Technologies, Inc.,  
Flagstaff, Arizona 86003, USA

**Charles Durfor**

Center for Devices and Radiological  
Health,  
United States Food and Drug  
Administration,  
5600 Fishers Lane,  
Rockville, Maryland 20857, USA

**Dwaine F. Emerich**

Cyto Therapeutics, Inc.,  
2 Richmond Square,  
Providence, Rhode Island 02906, USA

**Gregory R. D. Evans**

Laboratory of Reporative Biology and  
Bioengineering,  
Department of Plastic Surgery,  
The University of Texas M.D.  
Anderson Cancer Center,  
1515 Holcombe Blvd, Box 62  
Houston, Texas 77030, USA

**David J. Fink**

Osiris Therapeutics, Inc.,

2001 Aliceanna Street,  
Baltimore, Maryland 21231, USA

**Lisa E. Freed**

Department of Chemical Engineering,  
Massachusetts Institute of  
Technology,  
77 Massachusetts Ave.,  
Cambridge, Massachusetts 02139,  
USA

**Julie R. Friend**

Department of Chemical Engineering  
and Materials Science,  
University of Minnesota,  
421 Washington Ave. SE,  
Minneapolis, Minnesota 55455-0132,  
USA

**Elizabeth J. Furnish**

Department of Chemical Engineering,  
The University of Texas-Austin,  
Austin, Texas 78712, USA

**Frank T. Gentile**

Cyto Therapeutics, Inc.,  
2 Richmond Square,  
Providence, Rhode Island 02906, USA

**Keith J. Gouch**

Department of Chemical Engineering  
and Division of Health Sciences and  
Technology,  
Massachusetts Institue of Technology,  
77 Massachusetts Ave.,  
Cambridge, Massachusetts 02139,  
USA

**J. Hardin-Young**

Organogenesis Inc.,  
150 Dan Road,  
Canton, Massachusetts 02021, USA

**Kiki B. Hellman**

Center for Devices and Radiological  
Health,  
United States Food and Drug  
Administration,  
5600 Fishers Lane,  
Rockville, Maryland 20857, USA

**Jeffrey O. Hollinger**

Oregon Health Sciences University,  
Department of Surgery,  
3181 SW Sam Jackson Park Rd L352A,  
Portland, Oregon 97201-3098, USA

**Wei-Shou Hu**

Department of Chemical Engineering  
and Materials Science,  
University of Minnesota,  
421 Washington Ave. SE,  
Minneapolis, Minnesota 55455-0132,  
USA

**H. David Humes**

Department of Internal Medicine and  
Department of Biomedical  
Engineering,  
The University of Michigan Medical  
Center,  
Veterans Administration Medical  
Center and  
The University of Michigan at Ann  
Arbor,  
Ann Arbor, Michigan 48105, USA

**Yoshito Ikada**

Research Center for Biomedical  
Engineering,  
Kyoto University,  
53 Kawahara-cho, Shogoin, Sakyo-ku,  
Kyoto 606, Japan

**Peter C. Johnson**

Division of Plastic and Maxillofacial  
Reconstructive Surgery,  
University of Pittsburgh Medical  
Center, 676 Scaife Hall,  
3550 Terrace Street,  
Pittsburgh, Pennsylvania 15261, USA  
and Pittsburgh Tissue Engineering  
Initiative, Inc.,  
Center for Biotechnology and  
Bioengineering,  
300 Technology Drive,  
Pittsburgh, Pennsylvania 15219, USA

**Sung Wan Kim**

Center for Controlled Chemical  
Delivery,

University of Utah,  
Salt Lake City, Utah 84112, USA

**Timothy W. King**

Laboratory of Reparative Biology and  
Bioengineering,  
Department of Plastic Surgery,  
The University of Texas M.D. Ander-  
son Cancer Center,  
1515 Holcombe Blvd., Box 62,  
Houston, Texas 77030, USA

**Emma Knight**

Center for Biologics Evaluation and  
Research,  
United States Food and Drug Admin-  
istration,  
1401 Rockville Pike,  
Rockville, Maryland 20852, USA

**Konstantinos Konstantopoulos**

Cox Laboratory for Biomedical  
Engineering,  
Institute of Biosciences and  
Bioengineering,  
Rice University  
6100 S. Main  
Houston, Texas 77005, USA

**Sharad Kukreti**

Cox Laboratory for Biomedical  
Engineering,  
Institute of Biosciences and  
Bioengineering,  
Rice University  
6100 S. Main  
Houston, Texas 77005, USA

**Nina M. K. Lamba**

Department of Chemical Engineering,  
University of Delaware,  
Newark, Delaware, 19716, USA

**Robert Langer**

Department of Chemical Engineering,  
Massachusetts Institute of  
Technology,  
77 Massachusetts Ave.,  
Cambridge, Massachusetts 02139,  
USA

**Won-Kyoung Lee**

Department of Internal Medicine and  
Department of Biomedical Engineering,  
The University of Michigan Medical  
Center,  
Veterans Administrations Medical  
Center and  
The University of Michigan at Ann  
Arbor,  
Ann Arbor, Michigan 48105, USA

**L. Louie**

Department of Materials Science and  
Engineering,  
Massachusetts Institute of  
Technology,  
Cambridge, Massachusetts 02139,  
USA

**Michael H. May**

Department of Chemical Engineering  
and Applied Chemistry  
and Center for Biomedicals,  
University of Toronto,  
Toronto, Ontario, M5S, 3E5, Canada

**Larry V. McIntire**

Institute of Biosciences and  
Bioengineering,  
Rice University,  
6100 S. Main,  
Houston, Texas 77005, USA

**Antonios G. Mikos**

Institute of Biosciences and  
Bioengineering,  
Rice University,  
6100 S. Main,  
Houston, Texas 77005, USA

**Michael J. Miller**

Laboratory of Reparative Biology and  
Bioengineering,  
Department of Plastic Surgery,  
The University of Texas M.D.  
Anderson Cancer Center,  
1515 Holcombe Blvd, Box 62  
Houston, Texas 77030, USA

**David J. Mooney**

Department of Biologic and Materials  
Science,  
The University of Michigan,  
Ann Arbor, Michigan 48109, USA  
and  
Department of Chemical Engineering,  
The University of Michigan,  
Ann Arbor, Michigan 48109, USA

**Jeffrey R. Morgan**

Center for Engineering in Medicine,  
Massachusetts General Hospital,  
Shriners Burns Institute and  
Harvard Medical School,  
Boston, Massachusetts 02115, USA

**Robert M. Nerem**

Parker H. Petit Institute for  
Bioengineering and Bioscience,  
Georgia Institute of Technology,  
Atlanta, Georgia 30332-0363, USA

**Janeta Nikolovski**

Department of Internal Medicine  
and Department of Biomedical  
Engineering,  
The University of Michigan Medical  
Center, Veterans Administration  
Medical Center and  
The University of Michigan at Ann  
Arbor,  
Ann Arbor, Michigan 48105, USA

**Gregory M. Organ**

Columbia Michael Reese Hospital,  
Medical Center,  
Chicago, Illinois 60680, USA

**Bernhard Palsson**

Department of Bioengineering,  
University of California–San Diego,  
La Jolla, California 92093-0412, USA

**N.L. Parenteau**

Organogenesis Inc.,  
150 Dan Road,  
Canton, Massachusetts 02021, USA

**Charles W. Patrick Jr.**

Laboratory of Reparative Biology and

Bioengineering,  
Department of Plastic Surgery,  
The University of Texas M.D. Ander-  
son Cancer Center,  
1515 Holcombe Blvd., Box 62  
Houston, Texas 77030, USA

**Patricia Petrosko**  
Division of Plastic and Maxillofacial  
Reconstructive Surgery,  
University of Pittsburgh Medical  
Center,  
676 Scaife Hall,  
3550 Terrace Street,  
Pittsburgh, Pennsylvania 15261, USA

**Gregory P. Reece**  
Laboratory of Reparative Biology and  
Bioengineering,  
Department of Plastic Surgery,  
The University of Texas M.D. Ander-  
son Cancer Center,  
1515 Holcombe Blvd., Box 62  
Houston, Texas 77030, USA

**Geoffrey L. Robb**  
Laboratory of Reparative Biology and  
Bioengineering,  
Department of Plastic Surgery,  
The University of Texas M.D. Ander-  
son Cancer Center,  
1515 Holcombe Blvd., Box 62,  
Houston, Texas 77030, USA

**Angela M. Rodriguez**  
University of Massachusetts Medical  
Center,  
S-2, Room 751, 55 Lake Avenue North,  
Worcester, Massachusetts 01655, USA

**Julia M. Ross**  
Department of Chemical and  
Biochemical Engineering,  
University of Maryland-Baltimore  
Maryland,  
Baltimore, Maryland 21250, USA

**Alan S. Rudolph**  
Center for Biomolecular Science and  
Engineering,

Naval Research Laboratory,  
Washington DC 20375, USA

**Amarpreet S. Sawhney**  
Focal, Inc.,  
Lexington, Massachusetts 02173, USA

**Christine E. Schmidt**  
Department of Chemical Engineering,  
The University of Texas-Austin,  
Austin, Texas 78712, USA

**Timothy Scott-Burden**  
Vascular Cell Biology Laboratory,  
Texas Heart Institute,  
Houston, Texas 77030, USA

**Michael V. Sefton**  
Department of Chemical Engineering  
and Applied Chemistry  
and Center for Biomaterials,  
University of Toronto,  
Toronto, Ontario, M5S 3E5, Canada

**Dror Seliktar**  
Parker H. Petit Institute for Bioengi-  
neering and Bioscience,  
Georgia Institute of Technology,  
Atlanta, Georgia 30332-0363, USA

**Lonnie D. Shea**  
Department of Chemical Engineering,  
The University of Michigan,  
Ann Arbor, Michigan 48109, USA

**M. Spector**  
Department of Orthopedic Surgery,  
Brigham and Women's Hospital,  
Harvard Medical School,  
Boston, Massachusetts 02115, USA  
and  
Rehabilitation Engineering Research  
and Development,  
Brockton/West Roxbury VA Medical  
Center,  
West Roxbury, Massachusetts 02115,  
USA

**Christopher J. Tennant**  
University of Maryland-College Park  
Baltimore, Maryland, USA

**J. Teumer**

Organogenesis Inc.,  
150 Dan Road,  
Canton, Massachusetts 02021, USA

**Christine L. Tock**

Vascular Cell Biology Laboratory,  
Texas Heart Institute,  
Houston, Texas 77030, USA

**Charles A. Vacanti**

University of Massachusetts Medical  
Center,  
S-2, Room 751, 55 Lake Avenue North,  
Worcester, Massachusetts 01655, USA

**Joseph P. Vacanti**

Department of Surgery,  
Harvard Medical School,  
Children's Hospital  
300 Longwood Ave.,  
Boston, Massachusetts 02115, USA

**Gordana Vunjak-Novakovic**

Department of Chemical Engineering,  
Massachusetts Institute of  
Technology,  
77 Massachusetts Ave.,  
Cambridge, Massachusetts 02139,  
USA

**Jennifer L. West**

Department of Bioengineering,  
Rice University,  
Houston, Texas 77005, USA

**Markus S. Widmer**

Institute of Biosciences and  
Bioengineering,  
Rice University,  
6100 Main Street,  
Houston, Texas 77005, USA

**I.V. Yannas**

Department of Mechanical  
Engineering,  
Massachusetts Institute of  
Technology,  
Cambridge, Massachusetts 02139,  
USA

**Martin L. Yarmush**

Center for Engineering in Medicine,  
Massachusetts General Hospital,  
Shriners Burns Institute and  
Harvard Medical School,  
Boston, Massachusetts 02115, USA

**Alan W. Yasko**

Orthopaedic Surgical Oncology,  
The University of Texas M.D. Ander-  
son Cancer Center,  
1515 Holcombe Blvd.,  
Houston, Texas 77030, USA

**Michael J. Yaszemski**

Orthopaedic Surgery,  
Adult Reconstruction and Spine  
Surgery,  
Mayo Clinic,  
200 First Street SW,  
Rochester, Minnesota 55905, USA

**Isaac C. Yue**

Department of Chemical Engineering,  
The University of Michigan,  
Ann Arbor, Michigan 48109, USA

**Randell G. Young**

Osiris Therapeutics, Inc.,  
2001 Aliceanna Street,  
Baltimore, Maryland 21231, USA

## Preface

The beauty of the human form has been the subject of countless artistic masterpieces through the ages, the focus of exquisite poetry and central to every art form. However, it can also be considered the most elegant and sophisticated of machines. As with all machines, wear and tear occurs with aging and accidents can happen. With living machines, disease processes can also occur which can lead to destruction of tissues. It is the role of reconstructive surgeons to help patients who are afflicted with disease, trauma, or malfunction due to aging. Reconstructive surgical procedures have been developed over the last century to replace human tissues and organs so that people can return to a good quality of life or, in the case of many operations, to save life. Current reconstructive strategies include replacement of defective body parts with totally prosthetic devices, transfer of one tissue to another site or transplantation of organs and tissue from one individual to another when that becomes necessary. These techniques have improved and saved countless lives. However, all have limitations.

The fundamental roadblock to future improvements is the lack of sufficient tissue for ideal structural replacement to produce functional normalcy. It has been estimated that in the United States alone, the care of patients with tissue malfunction and loss can exceed one-half of a trillion dollars annually. It is this need that has driven the emergence of the field of Tissue Engineering. The concept of the rational design and fabrication of living tissues and organs for repair and replacement is relatively new, emerging within the last quarter of this century. The field has brought together diverse scientific and clinical areas. Clinical physicians and surgeons are working hand-in-hand with basic scientists in the fields of molecular and cell biology, biochemistry and the engineering fields of chemical engineering and materials science. This unique grouping has produced dramatic experimental examples that are shedding knowledge in the areas of new tissue fabrication, implantation and function. From its inception, the field has also brought the business community in contact with the academic community. As well, the regulatory agencies have been involved with the rigorous design and safe implementation of clinical trials. This broad representation of the medical, scientific, industrial and regulatory community is detailed in this book. The book is divided into three parts including the fundamentals and the methods of tissue engineering, tissue engineering applied to specialized tissues and tissue engineering applied to organs. The book has taken on an enormous task of providing a comprehensive overview of this emerging field and communicating the excitement felt by its many participants. No one can predict the future of any new scientific endeavor at its early stages, but if enthusiasm were an



important component, then this field promises to bring hope to many people who are afflicted with serious disease or injury.

*J.P. VACANTI,*  
Department of Surgery, Children's Hospital,  
300 Longwood Ave., Boston, MA 02115, USA

*R.S. LANGER,*  
Department of Chemical Engineering, Massachusetts Institute of  
Technology, 77 Massachusetts Ave., Boston, MA 02139, USA

*SECTION I*

**PROSPECTUS OF TISSUE  
ENGINEERING**

This Page Intentionally Left Blank

## CHAPTER I

# Prospectus of Tissue Engineering

**CHARLES W. PATRICK JR.**

*Laboratory of Reparative Biology and Bioengineering,  
Department of Plastic Surgery,  
M.D. Anderson Cancer Center,  
1515 Holcombe Blvd., Box 62,  
Houston, Texas 77030, USA*

**ANTONIOS G. MIKOS**

*Institute of Biosciences and Bioengineering,  
Rice University,  
6100 S. Main,  
Houston, Texas 77005-1892, USA*

*and*

**LARRY V. MCINTIRE**

*Institute of Biosciences and Bioengineering,  
Rice University,  
6100 S. Main,  
Houston, Texas 77005-1892, USA*

### **1 Tissue engineering defined**

Tissue engineering is a relatively new and emerging interdisciplinary field that applies the knowledge of bioengineering, the life sciences, and the clinical sciences towards solving the critical medical problems of tissue loss and organ failure. It involves applying engineering principles of transport and reaction phenomena as well as methods of analysis towards understanding the complex biological processes that occur in tissue development and repair. Frequently, knowledge of molecular phenomena and cellular interactions with surface, biochemical, and mechanical environments are employed. Tissue engineering has been formally defined as 'the application of the principles and methods of engineering and the life sciences toward the fundamental understanding of structure-function relationships in normal and pathological mammalian tissues and the development of biological substitutes that restore, maintain, or improve tissue function' [1]. Implied in the above is the essence of tissue engineering: the use of living cells,