国外优秀科技著作出版专项基金资助

组织工程原理

Principles of Tissue Engineering

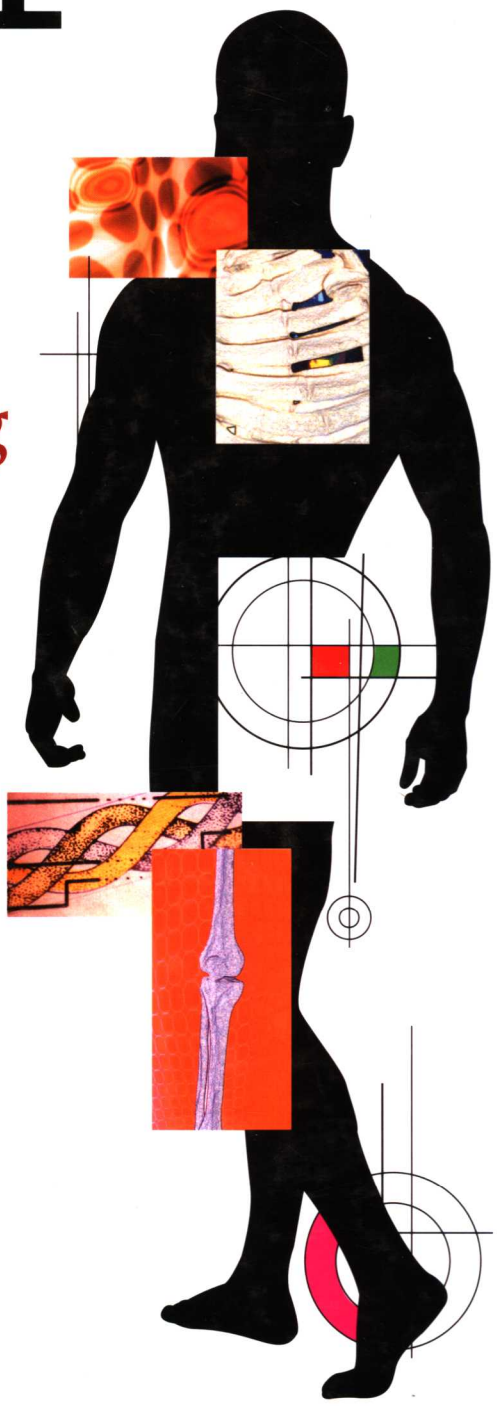
（原著第二版）
SECOND EDITION

[美] R. P. 兰扎
Robert P. Lanza

[美] R. 兰格　　主编
Robert Langer

[美] J. 瓦康提
Joseph Vacanti

杨志明　等译



化学工业出版社
现代生物技术与医药科技出版中心

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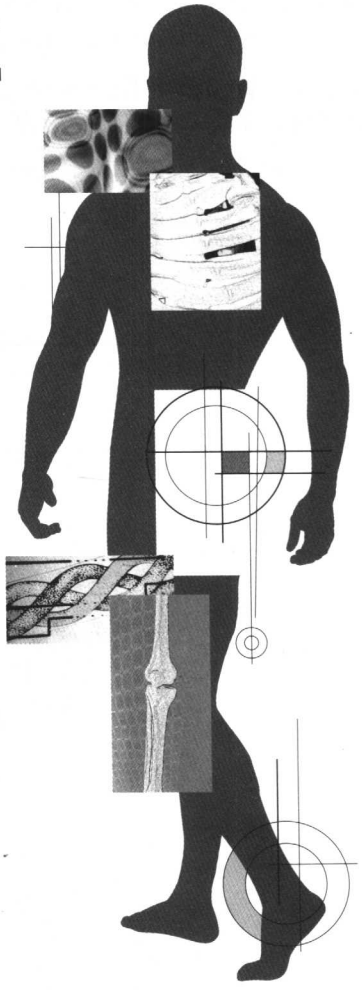

化学工业出版社
现代生物技术与医药科技出版中心

·北京·

图书在版编目（CIP）数据

组织工程原理：第2版/[美] 兰扎（Lanza，R.P.），兰格（Langer，R.），瓦康提（Vacanti，J.）主编；杨志明等译. —北京：化学工业出版社，2005.8
书名原文：Principles of Tissue Engineering
ISBN 7-5025-7604-5

Ⅰ. 组… Ⅱ. ①兰…②兰…③瓦…④杨… Ⅲ. 人体组织学 Ⅳ. R329

中国版本图书馆CIP数据核字（2005）第101844号

ISBN 0-12-436630-9

北京市版权局著作权合同登记号：01-2003-8467

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（原著第二版）
[美] R. P. 兰扎 R. 兰格 J. 瓦康提 主编
杨志明 等译
责任编辑：杨燕玲
责任校对：李 林
封面设计：关 飞
*
化 学 工 业 出 版 社
现代生物技术与医药科技出版中心 出版发行
（北京市朝阳区惠新里3号 邮政编码100029）
购书咨询：(010)64982530
(010)64918013
购书传真：(010)64982630
http://www.cip.com.cn
*
新华书店北京发行所经销
北京永鑫印刷有限责任公司印刷
三河市东柳装订厂装订
开本 787mm×1092mm 1/16 印张 57¾ 彩插 1 字数 1424千字
2006年1月第1版 2006年1月北京第1次印刷
ISBN 7-5025-7604-5
定 价：165.00元

国外优秀科技著作出版专项基金

FUND FOR FOREIGN BOOKS OF
EXCELLENCE ON SCIENCE AND TECHNOLOGY
(FFBEST)

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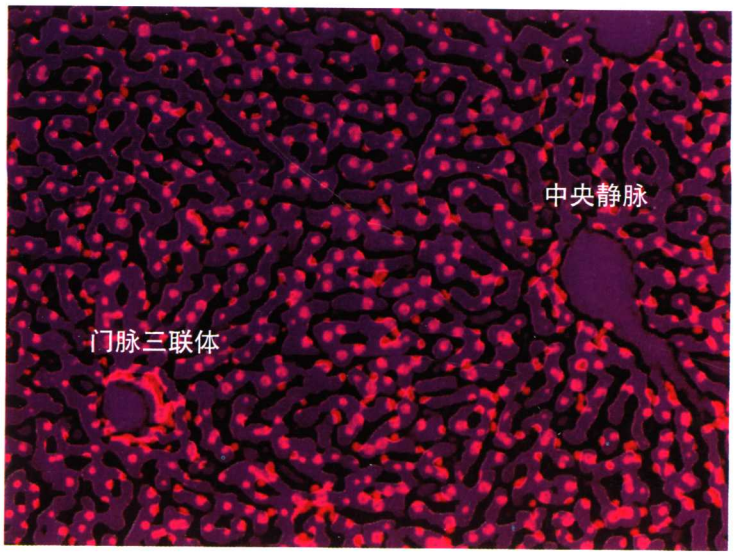

图 41-1　鼠肝切片显示门脉三联体、中央静脉和它们之间的肝细胞索

DNA染色，细胞核呈明亮的橙色。Huifei Liu 供图

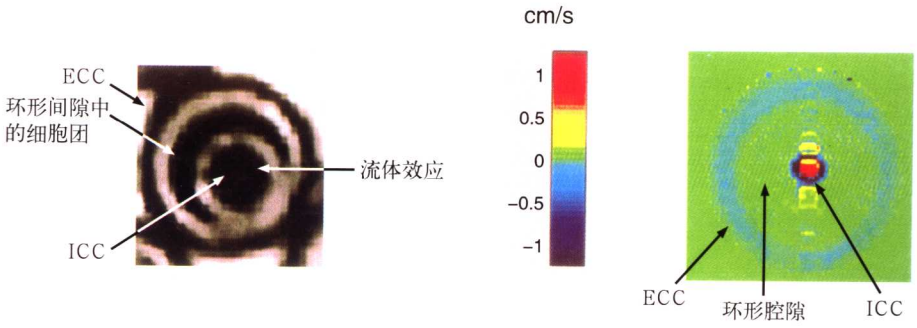

图 4l-8　T_2加权（a）和速度编码（b）共轴生物反应器图像

（a）与ECC中低速流水相比，ICC中的流体效应呈现低强度，含有肝细胞的环形间隙呈现为低强度。ECC和ICC中轴流的生理指标（b）可用实验性输入流体力学模型在T_2加权图像（a）得以分离，细胞分布可在扩散加权图像中获得。Macdonald等对T_2加权MRI（A）进行了修正（Macdonald等，NMR Spectros-copy and MRI investigation of a Potential Bioarticial Liver. NMR Biomed，11，55-66;©1998，经John Wiley & Sons，Inc. 许可）。

原著第一版序

尽管在组织工程各方面的单独的文献报道非常之多，但以前的工作还没有将这些新的边缘学科领域令人满意地结合起来。《组织工程原理》在一卷书里以对组织生长发育的总体理解为先决条件，将设计组织工程组织和器官的技术和理论知识，组织工程的应用与影响特定的器官系统的相关介绍都结合在了这部书里。我们努力写出一本全面的著作，一方面，打破与组织工程相关的学科（如生物学、化学、材料科学、工程学、免疫学和移植学等其他科学）多样性的平衡，另一方面，还要着重于那些对未来的医学最具价值的研究领域。

组织工程为医学发展提供的广度和深度是非凡的。据估计，仅在美国每年就有接近5000亿美元用于治疗因丧失组织或终末期器官衰竭而遭受病痛的患者；有超过400万烧伤、褥疮和皮肤溃疡的病人，超过1200万的糖尿病病人，还有200多万病人的病痛来自支持结构组织，如长骨、软骨、结缔组织和椎间盘等的缺损或缺失。组织工程其他潜在的应用方面还包括替代磨损的和功能极差的组织，例如衰老的肌肉或角膜；替代小管径的动脉、静脉、冠状动脉和外周支架；替代膀胱、输尿管和输卵管；修复细胞以产生必需的酶、激素和其他生物活性分泌产物去恢复组织的功能。

《组织工程原理》力图做到不仅是一本为生物医学工程学、细胞生物学和生物技术的高年级学生和研究生的医学课程准备的教科书，而且还是一本为研究和临床实验室准备的参考工具书。创作这本书对专业知识的要求远远超出了主编的能力，它是80多位学者和临床医生的智慧的集合，这些学者和医师们的前沿工作为展示这一极具吸引力的重要领域有很大帮助。我们深信，他们的知识和经验为本书中所提到的材料内容增加了必不可少的深度和权威性，并且在介绍的内容里，他们成功地勾画出和记录下了当这一新的领域——组织工程出现后，随之而来的兴奋、理解和期待。

Robert Lanza
Robert Langer
William Chick

（杨志明　张姝江　译）

原著第二版序

1997 年本书第一版问世，随后很快便成为组织工程领域一本全面的教科书。这一版本可当作为对组织工程感兴趣者、研究生、科研工作者、医师们准备的一本全面的教材，也可作为其他学科研究者们的参考书。本书力图涵盖组织工程的历史和基础原理以及近年来组织工程发展的概念和现在的技术工艺情况。

尽管已经有许多关于这方面的综述和教材出版，但还没有哪一本书像本书第一版那样对科学原理、涉及的相关学科、应用前景、对未来产业化和医学的潜在影响以及对所属领域的确定，做过如此深刻的阐述。

当人们知道某一图书最近有了新的版本出版，一定会猜想该学科的知识基础是否已经足以需要修订这本书。对于组织工程而言，自第一版出版以后，该领域发生了尤为显著的巨大发展。即使是该领域的专家也无法预言那些和这个学科发展相关的知识信息的爆炸。如今应用于制造工程化组织的各种新型多聚物和其他材料以指数级大量增长，这有相关的特殊应用的数据为证，人们在基础方面对细胞/生物材料相互作用的了解越来越多。自上一版出版以来，近年来的工作展示了在组织工程中使用干细胞的巨大潜力。有的研究小组致力于胚胎干细胞，而其他的则相信每一种特定的组织都含有祖细胞或干细胞，它们已经或多或少地发育成为完全分化的组织的不同特定细胞。

与这些进展相并行的是，并不仅仅是私人企业关注并大量“接纳”组织工程概念相关信息，还有许多学科的从业医师也是如此。这种不断增长的兴趣导致了组织工程的范围扩展，远远超过了 5 年前所能预见的范围，并且有助于组织工程的特殊应用发展到人体试验的阶段。

在本书中的各章节展示了国际上数百个科学研究者在同等的研究成就方面的结果。某种程度上本书的发展与整个领域的发展相平行，并真实反映了该领域所涉及的科学合作。

Robert P. Lanza
Robert Langer
Joseph Vacanti
（杨志明　张姝江　译）

前　言

当我们进入新千年的时候，回顾过去的成果和认清我们所处的位置是十分重要的。只有这样，我们才能现实地展望未来，去想像可能实现的目标。

组织工程最终给人类带来的深刻影响远远超出我们现在的想像力。它不仅将改变医学实践，帮助人们弄清发育生物学的机制，而且它影响生物技术产业经济发展的潜力远胜于过去几十年科学或医学的任何单项进步的影响力。

尽管我们能指出在历史上的各种各样里程碑式的成就，如组织工程所取得的成果，但是在重建丧失的组织功能方面的尝试，却只是在细胞生物学及材料科学领域有了相关进展后才成为可能的。直到细胞生物学的发展使得商业性可获得的酶和营养素能够大规模生产，从而能分离大量细胞并在孵箱中培养它们，这才使现代组织工程成为可能，或者说成为切实可行。现在可以清楚地看到，使用活细胞产生的组织功能水平比化学制剂、生长因子或激素刺激发育生长所得到的更高。实际上，从不同特定组织分离细胞的能力仅仅出现了几十年而已。即使在今天，特定细胞类型的增殖培养所取得的成功仍然有限。

早期将细胞再导入受者的方法非常简单，并且通常不能成功。最初细胞是被作为悬液注射进入体内的，主要是希望它们能随机移植。

对于大规模发展和应用组织工程还有一项更大的挑战就是免疫屏障。免疫学方面的进步以及使宿主认为异体细胞是“自己人”的技巧，最终可以让同种异体移植物，甚至异种移植物细胞产生功能组织。不幸的是，在当前这一历史时刻，可以用于构建能满足任何受者需要的商业性可获得细胞/多聚物结构支架的通用供体细胞类型的开发还仍然是一个梦想。

为了从活细胞中产生出新的功能组织，在努力尝试了几乎 20 年之后，我们已经了解了一些基本的概念。最重要的是，“违背大自然是不明智的”。考虑到这一点，当模拟自然状态时，许多尝试取得了最高程度的成功。我们所知道的只是所有活体各系统的组成、发育以及功能相关的进展里很小的一部分。尽管人们提出、探索了大量的理论，并且用更现代的假说替代它们，但是绝大多数的生物过程仍然是一个“黑箱”。

有时，作为一种自然科学和一种医学学科，组织工程被称为“非自然”。当人们切实考虑到医师们几个世纪以来所做的事情，这的确是事实真相。卫生保健的根本前提就是机体的自我愈合，医师们只能通过优化导向愈合的环境来支持病人的重要生命功能，主要是在中和有害因子的同时，试图加强机体自身愈合所需要的氧气和营养物质的供应。外科手术的基本原则就是：清除失活组织——这些组织是不良化学因子的来源；采用相似组织以保护组织不受有害环境的侵害；以及改善损伤部位的血液供应。在组织工程领域，我们也在努力达到同样的目标。坏死组织和瘢痕组织首先要被切除。损伤区域的活体细胞能阻止有害因素的扩散，就像支架一样提供结构线索来维持需要组织的结构和功能，而不是用残余的组织去消灭死腔。科学家们则用与医师们完全相同的方式制造出一个环境，即优化局部供氧和清除代谢的废物。在理想条件下，这将促进机体的自我愈合。组织工程的成就主要集中在相较于传统卫生保健中制造出的宏观环境而言的微环境。

最新组织工程的关键因素到现在才得到了更充分的探索，它就是使用的细胞来源。有数

个研究提示不成熟的细胞比特定组织充分分化的细胞在体外大量增殖的能力更强。与充分分化的细胞在体外的增殖相比，这些幼稚细胞或祖细胞能在体外被诱导分化，并在数代后产生功能。它们还似乎具有分化成许多在特定组织内发现的特定细胞的能力，这和它们所处的环境功能有关。

最后，我相信了解组织工程领域目前的局限和以之为基础的组织工程相关领域的发展是非常重要的。当该领域出现时，我们的期望必须和我们的能力相一致。在这一可接受的范围内，组织工程首次在人类的应用也许实际上是反映了组织工程作为治疗的一部分，替代特定器官所丧失的功能，而不是替代整个器官这一原理的运用。在肝脏和胰腺工程化的例子中，患者也许仅仅只是某种特殊的酶缺陷，或也许是产生某种重要的激素或生长因子能力的丧失，可能只需要一小团关键的功能组织，而不是整个器官。以此形式，人类应用的进步才能够与该领域科学的进步并驾齐驱，而不是产生不现实的幻想。

尽管人们相信这个领域的发展终将引起许多疾病治疗过程的巨大进步，但组织工程作为探索与发育生物学相关变化的研究模式，可以发挥和它在人类卫生保健事业方面的应用的同等能力。

总之，经过深思熟虑和有机发展的这门科学学科与组织工程领域的应用，能为人类在新千年带来诸多益处。

Charles A. Vacanti

（杨志明　张姝江　译）

原著编写人员名单

Patrick Aebischer
Division of Surgical Research and Gene Therapy Center
Centre Hospitalier Universitaire Vaudois (CHUV)
Lausanne CH-1011, Switzerland
Chapter 56

Richard A. Altschuler
Auditory Anatomy Laboratory
University of Michigan Medical School
Kresge Hearing Research Institute
Ann Arbor, Michigan 48109
Chapter 53

Pascal Ambrosini
Laboratoire d'Immunologie
Faculté de Médecine de Nancy
Vandoeuvre-les-Nancy 54500, France
Chapter 59

David J. Anderson
Departments of Electrical Engineering and Otolaryngology
University of Michigan
Ann Arbor, Michigan 48109
Chapter 53

Anthony Atala
Laboratory for Tissue Engineering
Children's Hospital
Boston, Massachusetts 02115
Chapter 46

François A. Auger
Department of Surgery
Laval University; and
Laboratoire d'Organogénèse Expérimentale/LOEX
Québec, Canada G1S 4L8
Chapter 50

Efstathios S. Avgoustiniatos
Department of Chemical Engineering
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Chapter 27

David W. Barnes
American Type Culture Collection
Manassas, Virginia 20110
Chapter 10

Eugene Bell
Department of Biology
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139; and
Tissue Engineering Inc.
Boston, Massachusetts 02210
Chapter 16

Marie C. Béné
Laboratoire d'Immunologie
Faculté de Médecine de Nancy
Vandoeuvre-les-Nancy 54500, France
Chapter 59

John G. Bishop
Center for Biologics Evaluation and Research (CBER)
U. S. Food and Drug Administration (FDA)
Rockville, Maryland 20852
Chapter 65

T. Bohrer
Department of Surgery
Philipps-University of Marburg
Marburg 35033, Germany
Chapter 37

Lawrence J. Bonassar
Department of Anesthesiology
Laboratory for Tissue Engineering
University of Massachusetts Memorial Health Care
Worcester, Massachusetts 01655
Chapter 47

Amy D. Bradshaw
Department of Vascular Biology
Hope Heart Institute
Seattle, Washington 98104
Chapter 11

Kelvin G. M. Brockbank
KGB Associates, Inc.
Charleston, South Carolina 29401
Chapter 33

Leon W. Browder
Department of Biochemistry and Molecular Biology
University of Calgary
Calgary, Alberta, Canada T2N 4N1
Chapter 8

Scott P. Bruder
Orthobiologics
DePuy Orthopaedics
Raynham, Massachusetts 02767
Chapter 48

Mary Bartlett Bunge
The Miami Project to Cure Paralysis
University of Miami School of Medicine
Miami, Florida 33136
Chapter 57

Arnold I. Caplan
Department of Biology
Skeletal Research Center
Case Western Reserve University
Cleveland, Ohio 44106
Chapter 48

Thomas Ming Swi Chang
Artificial Cells and Organs Research Center
Departments of Physiology, Medicine, and
Biomedical Engineering
McGill University
Montreal, Quebec, Canada H3G 1Y6
Chapter 42

Robert G. Chapman
Department of Chemistry
Harvard University
Cambridge, Massachusetts 02138
Chapter 18

Una Chen
Stem Cell Therapy Program
Biochemistry Institute
University of Giessen
Giessen D-35392, Germany
Chapter 43

Richard A. F. Clark
Department of Dermatology
State University of New York
Stony Brook, New York 11794
Chapter 61

Réjean Cloutier
Department of Physical Therapy
Laval University;
Hôpital du Saint-Sacrement; and
Laboratoire d'Organogénèse Expérimentale/LOEX
Québec, Canada G1S 4L8
Chapter 50

Clark K. Colton
Department of Chemical Engineering
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Chapter 27

Joanne C. Cousins
MRC Clinical Sciences Centre
Imperial College School of Medicine
Hammersmith Hospital
London W12 0NN, England
Chapter 52

Stephen C. Cowin
The Center for Biomedical Engineering
Department of Mechanical Engineering
The School of Engineering of The City College and
The Graduate School of The City University of New York
New York, New York 10031
Chapter 51

Gislin Dagnelie
Lions Vision Research & Rehabilitation Center
Johns Hopkins University School of Medicine
Baltimore, Maryland 21205
Chapter 54

Thomas F. Deuel
Division of Growth Regulation
Department of Medicine
Beth Israel Deaconess Medical Center and
Harvard Medical School
Boston, Massachusetts 02215
Chapter 12

Charles N. Durfor
Center for Devices and Radiological Health (CDRH)
U. S. Food and Drug Administration (FDA)
Rockville, Maryland 20852
Chapter 65

Brian E. Edwards
Department of Gynecology and Obstetrics
Division of Developmental Genetics
Johns Hopkins University School of Medicine
Baltimore, Maryland 21287
Chapter 29

Carol A. Erickson
Section of Molecular & Cellular Biology
University of California, Davis
Davis, California 95616
Chapter 3

Gilbert C. Faure
Laboratoire d'Immunologie
Faculté de Médecine de Nancy
Vandoeuvre-les-Nancy 54500, France
Chapter 59

Denise Faustman
Immunobiology Laboratories
Harvard Medical School
Massachusetts General Hospital
Charlestown, Massachusetts 02129
Chapter 25

Dario O. Fauza
Department of Surgery
Children's Hospital
Brookline, Massachusetts 02446; and
Harvard Medical School
Boston, Massachusetts 02115
Chapter 28

Eric G. Fine
Division of Surgical Research and Gene Therapy Center
Centre Hospitalier Universitaire Vaudois (CHUV)
Lausanne CH-1011, Switzerland
Chapter 56

Lee G. Fradkin
Valentis, Inc.
Burlingame, California 94010
Chapter 30

Lisa E. Freed
Division of Health Sciences & Technology
Harvard-Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Chapter 13

Claudia Gaffey
Center for Devices and Radiological Health (CDRH)
U. S. Food and Drug Administration (FDA)
Rockville, Maryland 20852
Chapter 65

John D. Gearhart
Department of Gynecology and Obstetrics
Division of Developmental Genetics
Johns Hopkins University School of Medicine
Baltimore, Maryland 21287
Chapter 29

Lucie Germain
Department of Surgery
Laval University; and
Laboratoire d'Organogénèse Expérimentale/LOEX
Québec, Canada G1S 4L8
Chapter 50

Francine Goulet
Department of Physical Therapy
Laval University; and
Laboratoire d'Organogénèse Expérimentale/LOEX
Québec, Canada G1S 4L8
Chapter 50

Howard P. Greisler
Department of Surgery
Loyola University Medical Center
Maywood, Ilinois 60153
Chapter 32

Alan J. Grodzinsky
Department of Electrical Engineering & Computer Science
Division of Bioengineering & Environmental Health
Center for Biomedical Engineering
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Chapter 17

Craig R. Halberstadt
Department of General Surgery Research
Carolinas Medical Center
Charlotte, North Carolina 28232
Chapter 31

Janet Hardin-Young
Organogenesis, Inc.
Canton, Massachusetts 02021
Chapters 23, 62

C. Hasse
Department of Surgery
Philipps-University of Marburg
Marburg 35033, Germany
Chapter 37

Matthias Hebrok[●]
Department of Molecular and Cellular Biology and
Howard Hughes Medical Institute
Harvard University
Cambridge, Massachusetts 02138
Chapter 6

Kiki B. Hellman
Center for Devices and Radiological Health (CDRH)
U. S. Food and Drug Administration (FDA)
Rockville, Maryland 20852
Chapter 65

Walter D. Holder
Department of General Surgery Research
Carolinas Medical Center
Charlotte, North Carolina 28232
Chapter 31

Edward Hsu
Department of Biomedical Engineering
Duke University Medical Center
Durham, North Carolina 27710
Chapter 41

Jeffrey A. Hubbell
Institute for Biomedical Engineering
ETH and University of Zürich
Zürich 8044, Switzerland
Chapter 20

Mark S. Humayun
Lions Vision Research & Rehabilitation Center
Johns Hopkins University School of Medicine
Baltimore, Maryland 21205
Chapter 54

H. David Humes
Department of Internal Medicine
University of Michigan Medical School
Ann Arbor, Michigan 48109
Chapter 45

Donald E. Ingber
Department of Pathology
Children's Hospital
Harvard Medical School
Boston, Massachusetts 02115
Chapter 9

Hugo O. Jauregui
Department of Pathology
Division of Pathology Research
Rhode Island Hospital
Providence, Rhode Island 02903
Chapter 39

● 现在地址：Diabetes Research Center，Department of Medicine，University of California San Francisco，California 94143.

Roger D. Kamm
Department of Mechanical Engineering
Division of Bioengineering & Environmental Health
Center for Biomedical Engineering
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Chapter 17

Ravi S. Kane
Department of Chemistry
Harvard University
Cambridge, Massachusetts 02138
Chapter 18

Jens O. M. Karlsson
Department of Surgery & Bioengineering
Shriner's Research Center
Cambridge, Massachusetts 02139
Chapter 24

Anne Kessinger
University of Nebraska Medical Center
Omaha, Nebraska 68198
Chapter 44

Byung-Soo Kim
Laboratory for Tissue Engineering
Children's Hospital and Harvard Medical School
Boston, Massachusetts 02115
Chapter 46

Naomi Kleitman
The Miami Project to Cure Paralysis
University of Miami School of Medicine
Miami, Florida 33136
Chapter 57

Joachim Kohn
Department of Chemistry
Rutgers University
Piscataway, New Jersey 08855
Chapter 22

Hiroshi Kubota
Departments of Cell & Molecular Physiology and Medicine
University of North Carolina
Chapel Hill, North Carolina 27514
Chapter 41

Robert P. Lanza
Tissue Engineering & Transplant Medicine
Advanced Cell Technology
Worcester, Massachusetts 01605
Chapter 36

Douglas A. Lauffenburger
Department of Chemical Engineering
Division of Bioengineering & Environmental Health
Center for Biomedical Engineering
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Chapter 17

Kuen Yong Lee
Department of Chemical Engineering, Biomedical Engineering, and Biologic & Materials Sciences
University of Michigan
Ann Arbor, Michigan 48109
Chapter 31

Peter I. Lelkes
Department of Medicine
University of Wisconsin Medical School
Milwaukee, Wisconsin 53201
Chapter 14

Robert E. London
Departments of Cell & Molecular Physiology and Medicine
University of North Carolina
Chapel Hill, North Carolina 27514
Chapter 41

Jack W. Love
CardioMend, LLC
Santa Barbara, California 93110
Chapter 34

Thomas L. Luntz
Departments of Cell & Molecular Physiology and Medicine
University of North Carolina
Chapel Hill, North Carolina 27514
Chapter 41

Michael J. Lysaght
Departments of Molecular Pharmacology, Physiology & Biotechnology
Division of Biology and Medicine
Brown University
Providence, Rhode Island 02912
Chapter 26

Jeffrey M. Macdonald
Departments of Cell & Molecular Physiology and Medicine
University of North Carolina
Chapel Hill, North Carolina 27514
Chapter 41

Manuela Martins-Green
Department of Cell Biology and Neurosciences
University of California, Riverside
Riverside, California 92521
Chapter 4

Robert W. Massof
Lions Vision Research & Rehabilitation Center
Johns Hopkins University School of Medicine
Baltimore, Maryland 21205
Chapter 54

John M. McPherson
Department of Cell and Protein Therapeutics
Genzyme Corporation
Framingham, Massachusetts 01701
Chapter 49

Douglas A. Melton
Department of Molecular and Cellular Biology and
Howard Hughes Medical Institute
Harvard University
Cambridge, Massachusetts 02138
Chapter 6

Antonios G. Mikos
Department of Chemical Engineering
Rice University
Houston, Texas 77005
Chapter 21

Josef M. Miller
Kresge Hearing Institute
Department of Otolaryngology and Biochemistry
University of Michigan
Ann Arbor, Michigan 48109
Chapter 53

Neal A. Miller
Laboratoire d'Immunologie
Faculté de Médecine de Nancy
Vandoeuvre-les-Nancy 54500, France
Chapter 59

David J. Mooney
Department of Chemical Engineering, Biomedical Engineering
and Biologic & Materials Sciences
University of Michigan
Ann Arbor, Michigan 48109
Chapters 31, 46

Jennifer E. Morgan
MRC Clinical Sciences Centre
Imperial College School of Medicine
Hammersmith Hospital
London W12 0NN, England
Chapter 52

Melvin L. Moss
Department of Anatomy and Cell Biology
College of Physicians and Surgeons and
School of Dental and Oral Surgery
Columbia University
New York, New York 10032
Chapter 51

Claudy Mullon
Research & Development
Circe Biomedical, Inc.
Lexington, Massachusetts 02421
Chapter 40

Christopher S. Muratore
Department of Surgery
Children's Hospital
Boston, Massachusetts 02115
Chapter 64

Gail K. Naughton
Advanced Tissue Sciences
La Jolla, California 92037
Chapter 63

Robert M. Nerem
Department of Bioengineering & Biosciences
Parker H. Petit Institute
Georgia Institute of Technology
Atlanta, Georgia 30332
Chapter 2

Björn Reino Olsen
Department of Cell Biology
Harvard Medical School; and
Harvard–Forsyth Department of Oral Biology
Harvard School of Dental Medicine
Boston, Massachusetts 02115
Chapter 5

Gregory M. Organ
Department of Surgery
Kaiser Permanente Medical Center
University of California, Davis
Oakland, California 94611
Chapter 38

James M. Pachence
Veritas Medical Technologies, Inc.
Princeton, New Jersey 08540
Chapter 22

Nancy L. Parenteau
Organogenesis, Inc.
Canton, Massachusetts 02021
Chapters 23, 62

Terence A. Partridge
MRC Clinical Sciences Centre
Imperial College School of Medicine
Hammersmith Hospital
London W12 0NN, England
Chapter 52

Jacques Penaud
Laboratoire d'Immunologie
Faculté de Médecine de Nancy
Vandoeuvre-les-Nancy 54500, France
Chapter 59

A. Robin Poole
Joint Diseases Laboratory
Shiners Hospital for Crippled Children;
McGill University
Montréal, Canada; and Laboratoire d'Organogénèse
Expérimentale/LOEX
Québec, Canada G1S 4L8
Chapter 50

Denis Rancourt
Department of Mechanical Engineering
Laval University and
Laboratoire d'Organogénèse Expérimentale/LOEX
Québec, Canada G1S 4L8
Chapter 50

Yehoash Raphael
Kresge Hearing Institute
Department of Otolaryngology and Biochemistry
University of Michigan
Ann Arbor, Michigan 48109
Chapter 53

A. H. Reddi
Centre for Tissue Regeneration and Repair
Department of Orthopaedic Surgery
University of California, Davis
Sacramento, California 95817
Chapter 7

Lola M. Reid
Departments of Cell & Molecular Physiology and Medicine
University of North Carolina
Chapel Hill, North Carolina 27514
Chapter 41

J. Dezz Ropp
Valentis, Inc.
Burlingame, California 94010
Chapter 30

Robert N. Ross
Medical/Science Analytics
Brookline, Massachusetts 02445
Chapters 23, 62

M. Rothmund
Department of General Surgery
Philipps-University of Marburg
Marburg 35033, Germany
Chapter 37

R. Bruce Rutherford
School of Dentistry
University of Michigan
Ann Arbor, Michigan 48109
Chapter 60

E. Helene Sage
Department of Vascular Biology
Hope Heart Institute
Seattle, Washington 98104
Chapter 11

Jacqueline Sagen
The Miami Project to Cure Paralysis
University of Miami School of Medicine
Miami, Florida 33136
Chapter 57

W. Mark Saltzman
Department of Chemical Engineering
Cornell University
Ithaca, New York 14853
Chapter 19

Gordon H. Sato
Department of Navy
Asmara, Eritrea
Africa
Chapter 10

Jochen Schacht
Kresge Hearing Institute
Department of Otolaryngology and Biochemistry
University of Michigan
Ann Arbor, Michigan 48109
Chapter 53

Michael J. Shamblott
Department of Gynecology and Obstetrics
Division of Developmental Genetics
Johns Hopkins University School of Medicine
Baltimore, Maryland 21287
Chapter 29

Graham Sharp
Department of Internal Medicine
Section of Oncology & Hematology
Omaha, Nebraska 68198
Chapter 44

Albert K. Shung
Department of Chemical Engineering
Rice University
Houston, Texas 77005
Chapter 21

Adam J. Singer
Department of Dermatology
State University of New York
Stony Brook, New York 11794
Chapter 61

Barry A. Solomon
Circe Biomedical, Inc.
Lexington, Massachusetts 02421
Chapter 40

Ruth R. Solomon
Center for Biologics Evaluation and Research (CBER)
U. S. Food and Drug Administration (FDA)
Rockville, Maryland 20852
Chapter 65

Susan J. Sullivan
Organogenesis, Inc.
Canton, Massachusetts 02021
Chapter 33

Shuichi Takayama
Department of Chemistry
Harvard University
Cambridge, Massachusetts 02138
Chapter 18

Jeffrey Teumer
Organogenesis, Inc.
Canton, Massachusetts 02021
Chapter 23

Robert C. Thomson
Medical Products Division
W. L. Gore and Associates
Flagstaff, Arizona 86002
Chapter 21

Mehmet Toner
Department of Surgery & Bioengineering
Shriners Research Center
Cambridge, Massachusetts 02139
Chapter 24

Vickery Trinkaus-Randall
Boston University School of Medicine
Boston, Massachusetts 02118
Chapter 35

Ross Tubo
Department of Cell and Protein Therapeutics
Genzyme Corporation
Framingham, Massachusetts 01701
Chapter 49

Brian R. Unsworth
Department of Biology
Marquette University
Milwaukee, Wisconsin 53233
Chapter 14

Charles A. Vacanti
Department of Anesthesiology
Laboratory for Tissue Engineering
University of Massachusetts Memorial Health Care
Worcester, Massachusetts 01655
Chapters 1, 47

Joseph P. Vacanti
Department of Surgery
Harvard Medical School and
Massachusetts General Hospital
Boston, Massachusetts 02114
Chapters 1, 38, 47, Epilogue

Martin P. Vacanti
Department of Anesthesiology
University of Massachusetts Medical School
Worcester, Massachusetts 01655
Chapter 58

Robert F. Valentini
Division of Surgical Research and Gene Therapy Center
Centre Hospitalier Universitaire Vaudois (CHUV)
Lausanne CH-1011, Switzerland
Chapter 56

Gordana Vunjak-Novakovic
Division of Health Sciences & Technology
Harvard-Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Chapter 13

Lars U. Wahlberg
NeuroSearch A/S
Glostrup DK-2600, Denmark
Chapter 55

Taylor G. Wang
Center for Microgravity Research and Applications
School of Engineering
Vanderbilt University
Nashville, Tennessee 37232
Chapter 36

John F. Warner
Gene-Based Therapeutics
Valentis, Inc.
Burlingame, California 94010
Chapter 30

George M. Whitesides
Department of Chemistry
Harvard University
Cambridge, Massachusetts 02138
Chapter 18

Jay M. Wilson
Department of Surgery
Children's Hospital
Boston, Massachusetts 02115
Chapter 64

Haiyun Wu
Department of Chemical Engineering
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Chapter 27

Arron S. L. Xu
Departments of Cell & Molecular Physiology and Medicine
University of North Carolina
Chapel Hilll, North Carolina 27514
Chapter 41

Lian Xue
Department of Surgery
Loyola University Medical Center
Maywood, Ilinois 60153
Chapter 32

Ioannis V. Yannas
Department of Mechanical Engineering
Fibers and Polymers Laboratory
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Chapter 15

Michael J. Yaszemski
Departments of Orthopedic Surgery and Bioengineering
Mayo Clinic
Rochester, Minnesota 55901
Chapter 21

Nan Zhang
Division of Growth Regulation
Department of Medicine
Beth Israel Deaconess Medical Center and
Harvard Medical School
Boston, Massachusetts 02215
Chapter 12