

HANDBOOK OF STEM CELLS

VOLUME 1

Embryonic

干细胞手册

第一卷：胚胎干细胞

EDITORS

Robert Lanza

John Gearhart Brigid Hogan

Douglas Melton Roger Pedersen

James Thomson Michael West



英文原版名作
中文导读系列



科学出版社

www.sciencep.com

Q2
421

Handbook of Stem Cells

Volume 1

Embryonic

干细胞手册

第一卷：胚胎干细胞

EDITORS

Robert Lanza

John Gearhart

Brigid Hogan

Douglas Melton

Roger Pedersen

James Thomson

Michael West

科学出版社

北京

图字:01-2006-0538 号

This is an annotated version of

Handbook of Stem Cells

Robert Lanza et al. eds.

Copyright © 2004 Elsevier Inc.

ISBN 0-12-436643-0

All rights reserved.

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, recording, or any information storage and retrieval system, without permission in writing from the publisher.

Published by arrangement with **Elsevier Pte Ltd.**

AUTHORIZED EDITION FOR SALE IN P. R. CHINA ONLY

本版本只限于在中华人民共和国境内销售

图书在版编目(CIP)数据

干细胞手册=Handbook of Stem Cells/(美)兰扎(Lanza,R.)等编.—北京:科学出版社,2006

(Elsevier 英文原版名作中文导读系列)

ISBN 7-03-016709-0

I. 干… II. 兰… III. 干细胞-手册-英文 IV. Q24-62

中国版本图书馆 CIP 数据核字(2005)第 155558 号

责任编辑:马学海 盖宇

责任印制:钱玉芬/封面设计:耕者设计工作室

科学出版社 出版

北京东黄城根北街16号

邮政编码:100717

<http://www.sciencep.com>

中国科学院印刷厂 印刷

科学出版社发行 各地新华书店经销

*

2006年1月第一版 开本:889×1194 1/16

2006年1月第一次印刷 印张:116 1/2 插页:4

印数:1—2 500 字数:2 749 000

定价:320.00元(全二卷)

(如有印装质量问题,我社负责调换〈科印〉)

目 录

Contents

参编人员

Contributors

序言

PREFACE

Robert Lanza

前言

FOREWORD

Bruce Alberts

胚胎干细胞的前景

Embryonic Stem Cells in Perspective

Mani Manolagkos

“干性”：定义，规范

“Stemness”: Definition, Standardization

Douglas A. Melton and Chuan Chen

胚胎干细胞简介

Introduction to embryonic stem cells

1. 胚胎干细胞研究历史

History of Embryo Stem Cells

Robert G. Edwards

2. 哺乳动物来源的全能干细胞：前景与挑战

第一部分

基础生物学/机制

PART ONE

Basic biology/mechanisms

3. 全能性的分子基础

Molecular Facets of Pluripotency

Fabrizio Cavallari and Hans Schöler

4. 干细胞自我更新的机制

Mechanisms of Stem Cell Self-Renewal

Hiroshi Niwa

ED I T O R B O A R D 导读编译者

裴雪涛 教授 (军事医学科学院)

(以下按汉语拼音排序)

管利东 刘大庆 刘庆斌 李艳华 王韞芳

刁佳飞 闫 舫 姚海雷 赵敬湘 张 鹏

Pluripotential Stem Cells from Vertebrate Embryos: Present Perspective and Future Challenges

Richard L. Gardner

Mechanisms of Stem Cell Self-Renewal

Hiroshi Niwa

5. 胚胎干细胞的细胞周期调控

图书: 03-2004-0534 号

This is an annotated version of
Handbook of Stem Cells
Robert Lanza et al. eds.
Copyright © 2004 Elsevier Inc.
ISBN 9-78-0-12-436643-0

All rights reserved.

No part of this publication may be reproduced or transmitted
in any form or by any means, electronic or mechanical, including
photocopying, recording, or any information storage and retrieval
system.

EDITORIAL BOARD

Published by arrangement with
(科学出版社) 人民卫生出版社
AUTHORIZED REPRINTING IN THE P. R. CHINA ONLY
本版本只限在中国大陆地区
科学出版社, 2004
(Elsevier 英文名称)
ISBN 7-03-016799-0
科学出版社发行
中国版本图书馆 CIP 数据

Peter Andrews
Jose Cibelli
Robert Edwards
Sir Martin Evans
Richard Gardner
Ronald Green
Joseph Itskovitz-Eldor
Rudolf Jaenisch
Dame Anne McLaren
Sir Martin Pera
Benjamin Reubinoff
Hans Schöler
Austin Smith
Davor Solter
Alan Trounson

责任编辑: 王学敏

责任印制: 魏本芬/陈海霞/曹会成/工作室

科学出版社出版

北京东黄城根北街16号

100717

<http://www.sciencep.com>

北京科信印刷厂印刷

科学出版社发行 各地新华书店经销

2004年1月第1版 开本: 889×1194 1/16

2004年1月第1次印刷 印张: 115 1/2 插页: 1

印数: 1-2500 定价: 320.00元

(含邮费)

(如有印装质量问题, 请负责调换(科印))

Contributors

Numbers in parentheses indicate the chapter to which the author contributed.

Russell C. Addis (43)

Johns Hopkins University School of Medicine, Institute for Cellular Engineering, Baltimore, MD

Bruce Alberts, PhD (Foreword)

President, National Academy of Sciences, Washington, DC

Michal Amit, PhD (40)

Bruce Rappaport Faculty of Medicine, Technion - Israel Institute of Technology, Haifa, Israel

Peter W. Andrews (9, 56)

Arthur Jackson Professor of Biomedical Science, Department of Biomedical Science, The University of Sheffield, Western Bank, United Kingdom

Hitomi Aoki (20)

Department of Tissue and Organ Development, Regeneration and Advanced Medical Science, Gifu University Graduate School of Medicine, Japan

Makoto Asashima, PhD (46)

Dean and Professor, Department of Life Sciences, University of Tokyo, Meguro-ku, Tokyo, Japan

Joyce Axelman (43)

Johns Hopkins University School of Medicine, Institute for Cellular Engineering, Baltimore, MD

Daniel Becker, MD (69)

Department of Neurology, Vanderbilt University Medical Center, Nashville, TN

Nissim Benvenisty, MD, PhD (53, 66)

Professor of Genetics, Department of Genetics, Institute of Life Sciences, The Hebrew University of Jerusalem, Jerusalem, Israel

Mickie Bhatia, PhD (38, 50)

Director and Scientist, Stem Cell Biology and Regenerative Medicine, Robarts Research Institute, The Krembil Centre for Stem Cell Biology, Associate Professor, Faculty of Medicine, University of Western Ontario, London, Ontario, Canada

C. Clare Blackburn, PhD (37)

Leukaemia Research Fund Senior Fellow, Institute for Stem Cell Research, University of Edinburgh, Edinburgh, United Kingdom

Michele Boiani, PhD (64)

Department of Animal Biology, University of Pennsylvania (New Bolton Center), Kennett Square, PA

Susan Bonner-Weir, PhD (71)

Associate Professor/Senior Investigator, Diabetes Center, Harvard University, Boston, MA

Contributors

Josephine Bowles, PhD (33)

Institute for Molecular Bioscience, The University of Queensland, Brisbane, Queensland, Australia

Richard L. Boyd, PhD (67)

Associate Professor, Department of Pathology and Immunology, Monash University, Melbourne, Victoria, Australia

Marianne Bronner-Fraser, PhD (19)

California Institute of Technology, Division of Biology, Beckman Institute, Pasadena, CA

Eric W. Brunskill, PhD (58)

Professor, Division of Cardiology, University of Cincinnati College of Medicine, Cincinnati, OH

Scott Bultman, PhD (6)

Department of Genetics, University of North Carolina, Chapel Hill, NC

Frederick Charles Campbell, MD (35)

Professor, Department of Surgery, Cancer Centre, Queen's University of Belfast, Belfast, Antrim, Northern Ireland

Anne Camus, PhD (11)

Department of Developmental Biology, Institut Jacques Monod, Paris, France

Melissa K. Carpenter, PhD (38, 52)

Stem Cell Biology and Regenerative Medicine, Robarts Research Institute, Associate Professor, Faculty of Medicine, University of Western Ontario, London, Ontario, Canada

Fatima Cavaleri (3)

Max Planck Institute for Molecular Biomedicine, Department of Cell and Developmental Biology, Münster, Germany

Constance Cepko, PhD (22)

Professor, Department of Genetics, Investigator, Howard Hughes Medical Institute, Harvard Medical School, Boston, MA

Yijing Chen, PhD (60)

Department of Genetics, University of North Carolina, Chapel Hill, NC

Susana M. Chuva de Sousa Lopes, PhD (12)

Professor, Hubrecht Laboratory, University of Utrecht, Utrecht, The Netherlands

Gregory O. Clark, MD (43)

Johns Hopkins University School of Medicine, Institute for Cellular Engineering, Baltimore, MD

Jérôme Collignon, PhD (11)

Department of Developmental Biology, Institut Jacques Monod, Paris, France

Paul Collodi, PhD (47)

Professor, Department of Animal Sciences, Purdue University, West Lafayette, IN

Chad Cowan, PhD (Foreword)

Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA

George Q. Daley, MD, PhD (25)

Division of Hematology/Oncology, Children's Hospital, Boston, MA

Christian Dani, PhD (31)

Director of Research INSERM, Centre de Biochimie CNRS UMR6543, Institute of Signaling, Developmental Biology and Cancer, University of Nice-Sophia Antipolis, Nice, France

Joshua D. Dowell, MD, PhD (70)

Department of Medicine, Indiana University School of Medicine, Indianapolis, IN

Jonathan S. Draper, PhD (56)

Department of Biomedical Science, University of Sheffield, Sheffield, United Kingdom

Gregory R. Dressler, PhD (32)

Associate Professor, Department of Pathology, University of Michigan, Ann Arbor, MI

Micha Drukker (66)

Department of Genetics, Silberman Institute of Life Sciences, The Hebrew University, Jerusalem, Israel

Gabriela Durcova-Hills, PhD (42)

Professor, The Wellcome Trust/Cancer Research UK Gurdon Institute, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom

Robert G. Edwards (1)

Chief Editor, Reproductive BioMedicine Online, Duck End Farm, Dry Drayton, Cambridge, United Kingdom

Rebecca S. Eisenberg, JD (79)

Robert and Barbara Luciano Professor of Law, University of Michigan Law School, Ann Arbor, MI

Ravindra Elluru (36)

Divisions of Neonatology and Pulmonary Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Contributors

Sir Martin Evans, PhD (39)

Director and Professor, Cardiff School of Biosciences,
Cardiff University, Wales, United Kingdom

Lianchun Fan, PhD (47)

Research Associate, Department of Animal Sciences, Purdue
University, West Lafayette, IN

Margaret A. Farley, PhD (76)

Gilbert Stark Professor of Christian Ethics, Divinity School
and Department of Religious Studies, Yale University,
New Haven, CT

Donna M. Fekete, PhD (22)

Department of Neurobiology, Harvard Medical School,
Boston, MA

Loren J. Field, PhD (70)

Professor of Medicine, Department of Medicine, Indiana
University School of Medicine, Indianapolis, IN

Donald W. Fink Jr., PhD (77)

Biologist, Division of Cell and Gene Therapy, Center for
Biologics Evaluation and Research/US Food and Drug
Administration, Rockville, MD

Lesley M. Forrester, PhD (34)

John Hughes Bennett Laboratories, Department of
Oncology, University of Edinburgh, Western General
Hospital, Edinburgh, United Kingdom

Margaret T. Fuller, PhD (14)

Professor, Departments of Developmental Biology and
Genetics, Stanford University School of Medicine,
Stanford, CA

Miho Furue, DDS, PhD (46)

Department of Biochemistry and Molecular Biology,
Kanagawa Dental College, Yokosuka, Kanagawa, Japan

David L. Garbers, PhD (15)

Director of The Cecil H. and Ida Green Center for
Reproductive Biology Sciences, Investigator, Howard
Hughes Medical Institute, Professor of Pharmacology, The
University of Texas Southwestern Medical Center at Dallas,
Dallas, TX

Richard L. Gardner (2)

E P Abraham Research Professor of the Royal Society in the
University of Oxford, Department of Zoology, University of
Oxford, Oxford, United Kingdom

John D. Gearhart, PhD (43)

Johns Hopkins University School of Medicine, Institute for
Cellular Engineering, Baltimore, MD

Sharon Gerech-Nir, PhD (30)

Bruce Rappaport Faculty of Medicine, Technion-Israel
Institute of Technology, Haifa, Israel

Jason W. Gill, PhD (67)

Department of Pathology and Immunology, Monash
University, Melbourne, Victoria, Australia

Rodolfo Gonzalez, MS (68)

Joint Program in Molecular Pathology, The Burnham
Institute and the University of California, San Diego, La
Jolla, CA

Daniel H.D. Gray, PhD (67)

Department of Pathology and Immunology, Monash
University, Melbourne, Victoria, Australia

Ronald M. Green, PhD (75)

Director, Ethics Institute, Eunice and Julian Cohen Professor
for the Study of Ethics and Human Values, Chair,
Department of Religion, Dartmouth College, Hanover, NH

Michal Gropp, PhD (55)

The Hadassah Embryonic Stem Cell Research Center, The
Goldyne Savad Institute of Gene Therapy, Hadassah
University Hospital, Jerusalem, Israel

Alexandra Haagenen (71)

Section on Islet Transplantation and Cell Biology, Joslin
Diabetes Center, Harvard Medical School, Boston, MA

F. Kent Hamra, PhD (15)

Department of Pharmacology and The Cecil H. and Ida
Green Center for Reproductive Biology Sciences, The
University of Texas Southwestern Medical Center at Dallas,
Dallas, TX

Richard P. Harvey, PhD (28)

Sir Peter Finley Professor of Cardiac Research, Head,
Developmental Biology Program, Victor Chang Cardiac
Research Institute, Darlinghurst, New South Wales, Australia

Susan M. Hawes, PhD (48)

Research Fellow, Institute for Reproduction and
Development, Monash University, Melbourne, Victoria,
Australia

Shin-Ichi Hayashi, MD, PhD (27)

Professor, Division of Immunology, Department of
Molecular and Cellular Biology, School of Life Science,
Faculty of Medicine, Tottori University, Tottori, Japan

Anne L. Hazlehurst (78)

Center for Biomedical Engineering, Brown University,
Providence, RI

Contributors

- Hiroaki Hemmi, PhD (27)**
Ralph Steinman Laboratory, Cellular Physiology and Immunology, Rockefeller University, New York, NY
- Hiroshi Hisatsune (29)**
Department of Molecular Genetics, Graduate School of Medicine, Kyoto University, Kyoto, Japan
- James Huettner, PhD (69)**
Center for the Study of Nervous System Injury and the Restorative Treatment and Research Program, Department of Cell Biology and Physiology, Washington University School of Medicine, St. Louis, MO
- Bradley Huntsman, BS (58)**
Division of Developmental Biology, Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH
- Catherine Iéhlé, PhD (31)**
Senior Scientist, Unité de Virologie, Institut Pasteur de Madagascar, Antananarivo, Madagascar
- Jamie Imitola, MD (68)**
Department of Neurology, Brigham and Women's Hospital, Boston, MA
- Joseph Itskovitz-Eldor, MD, DSc (30, 40)**
Professor and Director, Department of Obstetrics and Gynecology, Rambam Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel
- Rudolf Jaenisch, MD (10)**
Professor of Biology, Whitehead Institute for Biomedical Research, Department of Biology, Massachusetts Institute of Technology, Cambridge, MA
- Penny A. Johnson, PhD (9)**
Senior Research Scientist, Intercytex Ltd., Manchester, United Kingdom
- D. Leanne Jones, PhD (14)**
Department of Developmental Biology, Stanford University School of Medicine, Stanford, CA
- Elizabeth A. Jones, MA, MB, BChir, MRCP, PhD (34)**
Institute of Human Genetics, University of Newcastle upon Tyne, Newcastle upon Tyne, United Kingdom
- Gerard Karsenty, MD, PhD (26)**
Professor of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX
- Gil Katz, PhD (66)**
The Lautenberg Center for General and Tumor Immunology, Hadassah Medical School, The Hebrew University, Jerusalem, Israel
- Pritinder Kaur, PhD (72)**
Head, Epithelial Stem Cell Biology Laboratory, Stem Cell Program, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia
- Robert G. Kelly (28)**
Department of Genetics and Development, Columbia University, New York, NY
- Kathleen C. Kent (43)**
Johns Hopkins University School of Medicine, Institute for Cellular Engineering, Baltimore, MD
- Candace L. Kerr, PhD (43)**
Johns Hopkins University School of Medicine, Institute for Cellular Engineering, Baltimore, MD
- Ali Khademhosseini, MSc (73)**
Division of Biological Engineering, Massachusetts Institute of Technology, Cambridge, MA
- Hanita Khaner, PhD (49)**
Research Associate, The Hadassah Embryonic Stem Cell Research Center, Goldyne Savad Institute of Gene Therapy, Hadassah University Hospital, Jerusalem, Israel
- Chris Kintner, PhD (18)**
Professor, Molecular Neurobiology Laboratory, The Salk Institute for Biological Studies, La Jolla, CA
- Irina Klimanskaya, PhD (41)**
Senior Scientist, Advanced Cell Technology, Worcester, MA
- Nobuyuki Kondoh (29)**
Satomi Nishikawa, Riken Center for Developmental Biology, Kobe, Japan
- Peter Koopman, PhD (33)**
Professor of Developmental Biology, Institute for Molecular Bioscience, The University of Queensland, Brisbane, Queensland, Australia
- Naoko Koyano-Nakagawa, PhD (18)**
Assistant Professor, Department of Neuroscience, University of Minnesota, Minneapolis, MN
- Jennifer N. Kraszewski (43)**
Johns Hopkins University School of Medicine, Institute for Cellular Engineering, Baltimore, MD
- Robb Krumlauf, PhD (19)**
Scientific Director, Stowers Institute for Medical Research, Kansas City, MO
- Tilo Kunath, PhD (17, 45)**
Institute for Stem Cell Research, University of Edinburgh, Edinburgh, United Kingdom

Contributors

Takahiro Kunisada, PhD (20)

Professor, Department of Tissue and Organ Development, Regeneration and Advanced Medical Science, Gifu University Graduate School of Medicine, Gifu, Japan

Robert Langer, ScD (73)

Professor, Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, MA

Robert Lanza, MD (Preface)

Vice President, Medical and Scientific Development, Advanced Cell Technology, Adjunct Professor of Surgical Sciences, Institute of Regenerative Medicine, Wake Forest University School of Medicine, Winston-Salem, NC

Jean Pyo Lee, PhD (68)

Department of Neurology, Beth Israel Deaconess Medical Center, Boston, Massachusetts

Shulamit Levenberg, PhD (73)

Research Associate, Langer Laboratory, Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, MA

Haifan Lin, PhD (13)

Associate Professor, Department of Cell Biology, Duke University Medical School, Durham, NC

John W. Littlefield, MD (43)

Johns Hopkins University School of Medicine, Institute for Cellular Engineering, Baltimore, MD

Michael J. Lysaght, PhD (78)

Professor and Director, Center for Biomedical Engineering, Brown University, Providence, RI

Fiona A. Mack (7)

Cell Growth and Cancer Graduate Group, University of Pennsylvania, Philadelphia, PA

Terry Magnuson, PhD (6, 60)

Professor, Department of Genetics, University of North Carolina, Chapel Hill, NC

Anna Malashicheva, PhD (5)

Laboratory of Molecular Basis of Cell Differentiation, Institute of Cytology, St. Petersburg, Russia

Ofer Mandelboim (66)

The Lautenberg Center for General and Tumor Immunology, Hadassah Medical School, The Hebrew University, Jerusalem, Israel

Nancy R. Manley, PhD (37)

Associate Professor, Department of Genetics, University of Georgia, Athens, GA

Klaus I. Matthaei, PhD (59)

Senior Fellow and Head, Gene Targeting Laboratory, The John Curtin School of Medical Research, The Australian National University, Canberra, ACT, Australia

Yoav Mayshar, (53)

Department of Genetics, The Silberman Institute for Life Sciences, The Hebrew University, Jerusalem, Israel

John W. McDonald, MD, PhD (69)

Associate Professor of Neurology, Neurological Surgery and Anatomy and Neurobiology, Director of the Spinal Cord Injury Program, Restorative Treatment and Research Center, Washington University School of Medicine, St. Louis, MO

Dame Anne McLaren, PhD (16, 42)

Professor, The Wellcome Trust/Cancer Research UK Gurdon Institute, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom

Jill McMahon, MSc (41)

Molecular and Cellular Biology Department, Harvard University, Cambridge, MA

Alexander Meissner, Dipl Ing (10)

Whitehead Institute for Biomedical Research, Massachusetts Institute of Technology, Cambridge, MA

Harald von Melchner, MD, PhD (61)

Professor of Cell Biology and Molecular Genetics, Department of Molecular Hematology, University of Frankfurt Medical School, Frankfurt am Main, Germany

Douglas A. Melton, PhD (Foreword)

Thomas Dudley Cabot Professor in the Natural Sciences, Department of Molecular and Cellular Biology, Harvard University, Investigator, Howard Hughes Medical Institute, Cambridge, MA

Nathan Montgomery (6)

Department of Genetics, University of North Carolina, Chapel Hill, NC

Mary Tyler Moore (80)

International Chairman, Juvenile Diabetes Research Foundation, New York, NY

Tsutomu Motohashi, PhD (20)

Department of Tissue and Organ Development, Regeneration and Advanced Medical Science, Gifu University Graduate School of Medicine, Gifu, Japan

Franz-Josef Mueller, MD (68)

Program in Developmental and Regenerative Cell Biology, The Burnham Institute, La Jolla, CA

Christine Mummery, PhD (12)

Professor, Hubrecht Laboratory, University of Utrecht, Utrecht, The Netherlands

Contributors

Satomi Nishikawa (29)

Riken Center for Developmental Biology Kobe, Japan

Shin-Ichi Nishikawa, MD, PhD (29)

Group Director, Stem Cell Research Group, Riken Center for Developmental Biology, Kobe, Japan

Andras Nagy, PhD (57)

Senior Scientist, Mount Sinai Hospital, Samuel Lunenfeld Research Institute, Professor, Department of Medical Genetics and Microbiology, University of Toronto, Toronto, Ontario, Canada

Hitoshi Niwa, MD, PhD (4)

Laboratory for Pluripotent Cell Studies, Riken Center for Developmental Biology (CDB), Kobe, Hyogo, Japan

Hiromi Okuyama (21)

Center for Cells and Gene Therapy, Takara Bio Inc., Ostu, Shiga, Japan

Jitka Ourednik, PhD (68)

Associate Professor, Department of Biomedical Sciences, Iowa State University, Ames, IA

Vaclav Ourednik, PhD (68)

Associate Professor, Department of Biomedical Sciences, Iowa State University, Ames, IA

Masahito Oyamada, MD, PhD (8)

Associate Professor, Department of Pathology and Cell Regulation, Kyoto Prefectural University of Medicine, Kyoto, Japan

Yumiko Oyamada, MD, PhD (8)

Department of Pathology and Cell Regulation, Kyoto Prefectural University of Medicine, Kyoto, Japan

Virginia E. Papaioannou, PhD (24)

Professor of Genetics and Development, Department of Genetics and Development, College of Physicians and Surgeons of Columbia University, New York, NY

Kook I. Park, MD (68)

Professor, Department of Pediatrics and Pharmacology, Yonsei University College of Medicine, Seoul, Korea

Ethan S. Patterson (43)

Johns Hopkins University School of Medicine, Institute for Cellular Engineering, Baltimore, MD

Larry T. Patterson, MD (58)

Professor, Division of Nephrology and Hypertension, Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH

Alice Pébay, PhD (51)

Monash Institute of Reproduction and Development, Monash University, Clayton, Victoria, Australia

Martin F. Pera, BA, PhD (48, 51)

Associate Professor, Monash Institute of Reproduction and Development, Monash University, Clayton, Victoria, Australia

Aitana Perea-Gomez, PhD (11)

Department of Developmental Biology, Institut Jacques Monod, Paris, France

Anthony C.F. Perry, PhD (62)

Head of Laboratory, Laboratory of Mammalian Molecular Embryology, Riken Center for Developmental Biology, Kobe, Japan

James N. Petite, PhD (44)

Professor, Department of Poultry Science, College of Agriculture and Life Sciences, North Carolina State University, Raleigh, NC

Blaine W. Phillips, PhD (31)

Research Scientist, ES Cell International, Singapore

S. Steven Potter, PhD (58)

Professor, Division of Developmental Biology, Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH

Arti K. Rai (79)

Professor of Law, Duke Law School, Duke University, Durham, NC

Christopher Reeve (81)

Chairman, Christopher Reeve Paralysis Foundation, Springfield, NJ

Benjamin Reubinoff, MD, PhD (49, 55)

Associate Professor in Obstetrics and Gynecology, Director, The Hadassah Embryonic Stem Cell Research Center, The Goldyne Savad Institute of Gene Therapy, Department of Obstetrics and Gynecology, Hadassah University Hospital, Jerusalem, Israel

Janet Rossant, PhD (17, 45, Foreword)

Senior Investigator, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario, Canada

Michael Rubart, MD (70)

Department of Medicine, Indiana University School of Medicine, Indianapolis, IN

Pierre Savatier, PhD (5)

Director of Research, U371 "Cerveau et Vision", Institut National de la Santé et de la Recherche Médicale, Bron, France

Hans Schöler (3, 64)

Max Planck Institute for Molecular Biomedicine, Department of Cell and Developmental Biology, Münster, Germany

Contributors

Cordula Schulz, PhD (14)

Research Investigator, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY

Nikolaus Schultz, PhD (15)

The Cecil H. and Ida Green Center for Reproductive Biology Sciences, The University of Texas Southwestern Medical Center at Dallas, Dallas, TX, Freie Universität Berlin, Institut für Biochemie, Thielallee 63, Berlin, Germany

Michael J. Shamblott, PhD (43)

Johns Hopkins University School of Medicine, Institute for Cellular Engineering, Baltimore, MD

Richard L. Sidman, MD (68)

Bullard Professor of Neuropathology, Emeritus, Harvard Medical School, Boston, MA

M. Celeste Simon, PhD (7)

Associate Investigator, Howard Hughes Medical Institute, Associate Professor, Abramson Family Cancer Research Institute and Department of Cell and Developmental Biology, University of Pennsylvania School of Medicine, Philadelphia, PA

Evan Y. Snyder, MD, PhD (68)

Professor and Director, Program in Developmental and Regenerative Cell Biology, The Burnham Institute, La Jolla, CA

A. Francis Stewart, PhD (61)

Professor, Department of Genomics, BioInnovationZentrum, Dresden University of Technology, Dresden, Germany

Lorenz Studer, MD (21, 62)

Developmental Biology and Neurosurgery, Memorial Sloan Kettering Cancer Center, New York, NY

Azim Surani, PhD (65)

Wellcome Trust/Cancer Research UK Gurdon Institute, University of Cambridge, Cambridge, United Kingdom

Tetsuro Takamatsu, MD, PhD (8)

Professor, Department of Pathology and Cell Regulation, Kyoto Prefectural University of Medicine, Kyoto, Japan

Yang D. Teng, MD, PhD (68)

Assistant Professor, Department of Neurosurgery, Harvard Medical School/Children's Hospital, Boston/Brigham and Women's Hospital, Boston, and SCI Laboratory, VA Boston Healthcare System, Boston, MA

Irma Thesleff, DDS (23)

Professor, Research Director, Institute of Biotechnology, University of Helsinki, Helsinki, Finland

James A. Thomson, VMD, PhD, Dipl. ACVP (54)

John D. MacArthur Professor, Department of Anatomy, University of Wisconsin-Madison Medical School, The Wisconsin National Primate Research Center, Madison, WI

David Tosh, PhD (34)

Biology and Biochemistry, University of Bath, Bath, United Kingdom

Paul Trainor, PhD (19)

Stowers Institute for Medical Research, Kansas City, MO

Alan O. Trounson, PhD (67)

Professor of Stem Cell Sciences, Monash Immunology and Stem Cell Laboratories, Monash University, Clayton, Victoria, Australia

Motokazu Tsuneto (27)

Division of Immunology, Department of Molecular and Cellular Biology, School of Life Science, Tottori University, Tottori, Japan

Mark Tummers, MSc (23)

Developmental Biology Programme, Institute of Biotechnology, University of Helsinki, Finland

Edward Upjohn, MD (72)

Department of Dermatology, Royal Children's Hospital, Melbourne, Victoria, Australia

George Varigos, MB, BS, PhD, FACD (72)

Department of Dermatology, Royal Melbourne and Children's Hospitals, Parkville, Victoria, Australia

Cécile Vernochet, PhD (31)

Centre de Biochimie CNRS UMR6543, Institute of Signaling, Developmental Biology and Cancer, University of Nice-Sophia Antipolis, Nice, France

Jay L. Vivian, PhD (60)

Department of Genetics, University of North Carolina, Chapel Hill, NC

Zhongde Wang, PhD (10)

Whitehead Institute for Biomedical Research, Massachusetts Institute of Technology, Cambridge, MA

Gordon C. Weir, MD (71)

Professor of Medicine, Harvard Medical School, Head, Section on Islet Transplantation and Cell Biology, Diabetes Research and Wellness Foundation, Chair, Joslin Diabetes Center, Boston, MA

Susan E. Wert (36)

Divisions of Neonatology and Pulmonary Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Contributors

Jeffrey A. Whitsett, MD (36)
Professor of Pediatrics, Chief, Section of Neonatology,
Pulmonary, and Perinatal Biology, Cincinnati Children's
Hospital Medical Center, University of Cincinnati College of
Medicine, Cincinnati, OH

J. David Winger, PhD (63)
Wake Forest University Baptist Medical Center, Program for
Assisted Reproduction, Department of Obstetrics and
Gynecology, Winston-Salem, NC

Zhuoru Wu, PhD (15)
Department of Pharmacology, The University of Texas
Southwestern Medical Center at Dallas, Dallas, TX

Chunhui Xu, PhD (52)
Senior Scientist, Geron Corporation, Menlo Park, CA

Toshiyuki Yamane, PhD (20, 27)
Irving Weissman Laboratory, Department of Pathology,
Stanford University School of Medicine, Stanford, CA

Jun Yamashita (29)
Department of Molecular Genetics, Graduate School of
Medicine, Kyoto University, Kyoto, Japan

Yukiko M. Yamashita, PhD (14)
Department of Developmental Biology, Stanford University
School of Medicine, Stanford, CA

Hidetoshi Yamazaki, DDS, PhD (27)
Associate Professor, Division of Regenerative Medicine and
Therapeutics, Department of Genetic Medicine and
Regenerative Therapeutics, Institute of Regenerative
Medicine and Biofunction, Tottori University Graduate
School of Medical Science, Division of Immunology,
Department of Molecular and Cellular Biology, School of
Life Science, Faculty of Medicine, Tottori University,
Tottori, Japan

Laurie Zoloth, PhD (74)
Professor of Medical Humanities and of Religion, Medical
Humanities and Bioethics, Feinberg School of Medicine,
Northwestern University, Chicago, IL

Thomas P. Zwaka, MD (54)
The Wisconsin National Primate Research Center,
Madison, WI

Robert Zweigerdt, PhD (70)
Department of Medicine, Heinrich Heine University,
Duesseldorf, Germany

Preface

New discoveries in the field of stem cells increasingly dominate the news and scientific literature. Wave upon wave of papers has led to an avalanche of new knowledge and research tools that may soon lead to new therapies for cancer, heart disease, diabetes, and a wide variety of other diseases that afflict humanity. The *Handbook of Stem Cells* integrates this exciting area of biology, combining in two volumes the prerequisites for a general understanding of adult and embryonic stem cells; the tools, methods, and experimental protocols needed to study and characterize stem cells and progenitor populations; as well as a presentation by the world's experts of what is currently known about each specific organ system. No topic in the field of stem cells is left uncovered, including basic biology/mechanisms,

early development, ectoderm, mesoderm, endoderm, methods (such as detailed descriptions of how to derive and maintain animal and human embryonic stem cells), application of stem cells to specific human diseases, regulation and ethics, and patient perspectives from Mary Tyler Moore (diabetes) and Christopher Reeve (spinal cord injury). The result is a comprehensive two-volume reference that will be useful for students and experts alike. It represents the combined effort of 12 editors and more than 300 scholars and scientists whose pioneering work has defined our understanding of stem cells.

Robert Lanza, MD
Boston, Massachusetts

序 言

干细胞领域的新发现越来越影响着新闻和科学文献。大量文章的出现引发的新知识和研究手段的涌现，最终将产生针对肿瘤、心脏病、糖尿病，以及影响人类健康的许多其他疾病的新的治疗手段。《干细胞手册》这部书分为上下两册，整合了该领域有关成体干细胞和胚胎干细胞必备的生物学知识、手段、方法、研究和描述干/祖细胞的特征所用的实验方案，以及国际专家对于每一个特定的器官系统相关知识发展现状的介绍。干细胞领域的所有主题无一例外地收录其中，包括基础生物学/机制、早期发育、外胚层、中胚层、内胚层、方法（例如如

何分离和培养动物和人胚胎干细胞的具体描述）、针对特定人类疾病的干细胞的应用、法规与伦理，以及分别来自 Mary Tyler Moore（糖尿病患者）和 Christopher Reeve（脊髓损伤患者）的观点。这两册书将成为学生和科研人员必备的全面的参考书目，它们凝集了 12 位编辑和超过 300 位学者和科学家的共同努力，正是他们开拓性的工作使得我们对干细胞有了精确的理解。

Robert Lanza, MD
波士顿，马萨诸塞州

前 言

对于这样一部收集了国际专家的权威性文章、几乎涵盖干细胞领域所能想见的每个方面的著作而言，在前言中写些什么才是有用的呢？我将尝试从科学，尤其是现代细胞与发育生物学更广的层面来回答这个问题。

我对于这部书中科学问题的看法源于一些在大学中工作了30年，致力于探询细胞发育过程中分子细节的研究人员的观点。随着时间的流逝，越来越多的新发现令我们对于细胞的理解飞速提高。这种知识的提高是相辅相成、相互促进的：我们对细胞理解的不断深入致使新的研究手段不断产生，后者又直接加速了我们对细胞的认识，如此循环。例如，上册第58章和下册第3章描述的DNA芯片技术使得研究人员同时研究成千上万个基因的表达成为可能。从1961年令人震惊的DNA杂交技术的诞生发展到这项新技术经历了无数小的进步，而它对未来的影响是难以估量的。

这与科学自身的发展规律是一样的，就像国家科学院在“超越发现”的系列小文章中反复强调的。为了向普通公众普及科学知识，每个8页纸的小册子都讲述了一个有关人类重大突破的由来——例如，全球定位系统（GPS）的产生和小儿白血病的治疗等。每一个故事中，最终的发现都有赖于大量科学家、工程师数十年来的不懈努力和知识积累。每一个独立看来无什么用处的知识，一经与其他知识意外地结合就会产生几近神奇的结果。

每一个伟大的科学发现，几乎都源于人类对于这个世界的好奇心迸发的火花——例如，人们为了解释在夜空中行星的运动而进行的科学活动，最终改变了我们的世界。而且，由于新的知识总是建筑于旧知识的基础之上，随着旧知识的积累，新知识的更新速度不断加快。因此，我们有理由相信本世纪有助于人类发展

的发明创造将比上世纪更加引人注目。当然，任何对未来将会发展成什么样子的预言也必将是徒劳的。

这些又与干细胞有什么关系呢？从我个人的体会讲，每当我听到有人要求讲出这项研究对人类的确切的利益，尤其还要加上一个期限时，我就特别不舒服，尽管科学发展的历史已经证明关于干细胞的研究最终将为人类健康带来无限的益处，甚至有些尚无法估量。最终，我们将利用我们渊博的生物学知识构建出新的、可供安全移植到病人体内的器官，而且干细胞的工作无疑会为这项突破作出巨大贡献。这部著作中所勾勒的研究进展也足以为肿瘤或其他众多的不知名的，甚至起源神秘的严重危害人类健康的疾病的治疗带来希望。

国家科学院委员会主席 Bert Vogelstein 在题为“干细胞与再生医学的未来”的报告讲到：“干细胞的争论引发了科学家、非科研人员等等对于我们是谁，我们之所以为人的原因等一系列主题的有意义的思索。”而且这样的争论使我们清楚，现代社会的成功将依赖于更加重视基于对科学本质理念传播的教育系统的建立。

要实现这个目标需要新的认识，这源于科学家不仅在大学层面的教育，还需要对5~18岁的学生群体以咨询教育为基础的有别于其他但十分必要的知识普及。在我国，即便在最优越的教育环境下，这种以科学为本的教育体系的传播也需要十年的时间，这是我们必需面对的现实。最后，科学家的生命终将改变——对于作为一名科学家意味着什么的更为深刻的见地，以及多数人安排时间的方式的改变。因此，在某种意义上讲，我们科学家应把对于干细胞研究的争论视为一种健康的警示和召唤，召唤我们在因我们令人震惊的发现而越发影响着新闻的新世纪行动起来。

Bruce Alberts, PhD

Foreword

What can usefully be said about stem cells in a foreword to a collection of definitive articles by the world's experts, inasmuch as this volume already covers every conceivable aspect of the subject? In response to this question, I shall attempt to place the work described here in the broader context of science—and of modern cell and developmental biology specifically.

My view of the science in this book comes from the perspective of someone who spent 30 years in universities probing the molecular details of basic cell processes. Over this time, our understanding of cells increased at a rate that startled even those most closely involved in the wave upon wave of new discoveries. This increase in knowledge was catalytic: As our understanding of cells advanced, it allowed new research tools to be developed that directly sped further advances in understanding, which in turn led to new tools, and so on. Consider, for example, the DNA chip technology described in Chapter 58 of Volume one and Chapter three of Volume two, which allows an investigator to examine the expression of tens of thousands of genes simultaneously. Because hundreds of small steps were needed to move from the striking initial discovery of DNA hybridization in 1961¹ to this new technology, its development was unpredictable in advance.

It is the same for the advance of science itself, as emphasized repeatedly in the "Beyond Discovery" series of brief articles from the National Academy of Sciences.² Designed to explain science to the general public, each of these eight-page documents traces the path leading to a breakthrough of great human benefit—such as the global positioning system (GPS) or the cure for childhood leukemia. In every case, the final discovery depended on knowledge developed over decades

through the efforts of a large number of independent scientists and engineers. Each piece of knowledge, often seemingly useless on its own, was combined in unexpected ways with other knowledge to produce a final result whose power seems almost magical.

The great enterprise of science, sparked simply by human curiosity about how the world works—for example, an attempt to account for the motions of the planets in the night sky—has transformed our world. And because new knowledge builds on old knowledge, the pace continually accelerates as the amount of old knowledge increases. Thus, we should expect the inventions that benefit humans in this new century to be even more dramatic than those of the last century. But we can be equally sure of the futility of attempting to predict what they will be in advance.

What does all this have to do with stem cells? Personally, I become uncomfortable whenever I hear claims that describe the precise benefits to be derived from this research—especially when they are associated with a timeline. Nevertheless, the history of science makes it certain that the knowledge derived from research on stem cells will eventually lead to enormous benefits for human health, even if they are unpredictable. Eventually, we will be able to use our profound understanding of biology to grow new organs that can be safely transplanted into human patients, and the work with stem cells will no doubt make important contributions to this breakthrough. But the research outlined in this volume is equally certain to contribute to cures for cancer and for a large number of other less famous diseases—many of mysterious origin—that are terrible afflictions for humanity.

Bert Vogelstein, the chairman of the National Academies committee that produced the report "Stem Cells and the Future of Regenerative Medicine" reminds us that "The stem cell debate has led scientists and nonscientists alike to contemplate profound issues, such as who we are and what makes us human."³ The debate has also made it clear that the success of modern societies will depend on education systems that place a much higher value on conveying an understanding of the nature of science to everyone.

Accomplishing such a goal will require new recognition by scientists of their teaching responsibilities at the college level as well as of their different but critical roles in the support of inquiry-based science education for students from 5 to 18 years old.⁴ We must all face the realization that, even under the best of circumstances, the transitions to the science-centered education systems that our nations need will require decades. In the end, the life of a scientist must change—incorporating a much broader view of what it means to be a scientist and changing the way that most of us apportion our time. In a sense, therefore, we scientists should view

the controversy over stem cell research as a healthy wake-up call—a call to action in a new century in which our startling discoveries will increasingly dominate the news.

Bruce Alberts, PhD

REFERENCES

1. Marmur, J., and Doty, P. (1961). Thermal renaturation of DNA. *J. Mol. Biol.* 3, 585–594.
2. National Academy of Sciences. "Beyond Discovery" series. Available at: <http://www.BeyondDiscovery.org>.
3. National Research Council. (2002). "Stem Cells and the Future of Regenerative Medicine." National Academies Press, Washington, DC. Available for purchase at: <http://www.nap.edu/catalog/10195.html>.
4. National Research Council. (1996). "National Science Education Standards." National Academies Press, Washington, DC. Available for purchase or download at: <http://www.nap.edu/catalog/4962.html>.