

新生物学丛书

HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE

人类基因组编辑

科学·伦理·管理 (中英对照)

“人类基因编辑：科学、医学和伦理决策”委员会
美国科学院研究理事会

裴端卿 等 译



科学出版社

本书由广州再生医学与健康广东省实验室资助

HUMAN GENOME EDITING

Science, Ethics, and Governance

人类基因组编辑

科学 · 伦理 · 管理

(中英对照)

“人类基因编辑：科学、医学和伦理决策”委员会
美国科学院研究理事会

编

裴端卿 等 译

科学出版社

北京

图字：01-2019-2325 号

内 容 简 介

基因组编辑是一个强有力的新工具，可以精确地改变生物体的遗传物质。最近的科学进展使基因组编辑比以往任何时候都更有效率、更精确和更灵活。这些进展促使全球范围内人们对通过基因组编辑改善人类健康的方式产生了兴趣。这些技术的发展和运用引起许多决策者和利益相关方的关切，如是否有适当的制度来管理这些技术，以及公众如何、何时参与这些决策。本书从人类基因组编辑和管理的总体原则、基因编辑技术的基础研究应用、体细胞基因组编辑、可遗传性基因组编辑、基因强化、公众参与等方面进行了阐述。

本书可供从事基因组编辑相关研究的科研人员及企业人员参考使用。

This is a translation of *Human Genome Editing: Science, Ethics, and Governance*, National Academy of Sciences; National Academy of Medicine; National Academies of Sciences, Engineering, and Medicine; Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations ©2017 National Academy of Sciences. First Published in English by National Academies Press. All rights reserved.

图书在版编目 (CIP) 数据

人类基因组编辑：科学·伦理·管理；汉英对照 / 美国“人类基因编辑：科学、医学和伦理决策”委员会，美国科学院研究理事会编；裴端卿等译. —北京：科学出版社，2019.6

书名原文：Human Genome Editing: Science, Ethics, and Governance

ISBN 978-7-03-061360-8

I. ①人… II. ①美… ②美… ③裴… III. ①人类基因—基因组—研究—汉、英 IV. ①Q987

中国版本图书馆CIP数据核字 (2019) 第103655号

责任编辑：王 静 罗 静 刘 晶 / 责任校对：郑金红

责任印制：张 伟 / 封面设计：刘新新

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>

北京虎彩文化传播有限公司印刷

科学出版社发行 各地新华书店经销

*

2019年6月第 一 版 开本：889×1194 1/16

2019年6月第一次印刷 印张：19 1/4

字数：560 000

定价：180.00元

(如有印装质量问题，我社负责调换)

译校者名单

List of Translators

(按姓氏笔画排序)

王 飞	王 波	王付卉	王学聪	石 曦	匡俊企	邢 琦
朱洁滢	朱艳玲	朱菲艳	刘 鹤	孙 昊	孙 薇	苏整会
李 婷	李长朋	李宇航	李林鹏	杨 肖	吴 芳	吴琳琳
岑晓彤	何江平	何松蔚	余致君	张 田	张一心	张炳文
张祖明	张梦丹	张燕琪	陈金龙	陈聪玲	林立龙	周纯华
郑 辉	单永礼	赵 圆	钟肖芬	侯红明	姚 姣	徐慧娟
高铭蔚	郭 婧	郭 琳	郭宜平	黄 可	曹 凡	龚举成
商必志	梁丽宁	梁泽川	梁锦川	喻 佩	裴端卿	樊琛语

美国国家科学院、工程院和医学院

美国国家科学院是在 1863 年根据时任美国总统林肯签署的一项国会法案成立的，这是一个私营的非政府机构，旨在就科学和技术问题向美国政府提供建议。成员由对研究做出突出贡献的同行选出，由 Marcia K. McNutt 博士担任院长。

美国国家工程院是在 1964 年根据美国国家科学院的章程成立的，旨在将工程实践引入国家建设。成员由对工程做出特别贡献的同行选举产生，由 C. D. Mote Jr. 博士担任院长。

美国国家医学院（原医学研究院）是在 1970 年根据美国国家科学院的章程成立的，旨在就医疗和健康问题为美国政府提供建议。成员由为医学和健康做出杰出贡献的同行选举产生，由 Victor J. Dzau 博士担任院长。

这三个研究院合称为美国国家科学院、工程院和医学院，为美国政府提供独立、客观的分析和建议，并开展其他活动来解决复杂的问题，为公共政策决策提供信息。美国国家科学院还鼓励教育和研究，确认对知识的杰出贡献，并增进公众对科学、工程和医学的了解。

有关美国国家科学院、工程院和医学院的更多信息，请访问 www.national-academies.org。

The National Academies of **SCIENCES • ENGINEERING • MEDICINE**

The **National Academy of Sciences** was established in 1863 by an Act of Congress, signed by President Lincoln, as a private, nongovernmental institution to advise the nation on issues related to science and technology. Members are elected by their peers for outstanding contributions to research. Dr. Marcia K. McNutt is president.

The **National Academy of Engineering** was established in 1964 under the charter of the National Academy of Sciences to bring the practices of engineering to advising the nation. Members are elected by their peers for extraordinary contributions to engineering. Dr. C. D. Mote, Jr., is president.

The **National Academy of Medicine** (formerly the Institute of Medicine) was established in 1970 under the charter of the National Academy of Sciences to advise the nation on medical and health issues. Members are elected by their peers for distinguished contributions to medicine and health. Dr. Victor J. Dzau is president.

The three Academies work together as the **National Academies of Sciences, Engineering, and Medicine** to provide independent, objective analysis and advice to the nation and conduct other activities to solve complex problems and inform public policy decisions. The National Academies also encourage education and research, recognize outstanding contributions to knowledge, and increase public understanding in matters of science, engineering, and medicine.

Learn more about the National Academies of Sciences, Engineering, and Medicine at www.national-academies.org.

美国国家科学院、工程院和医学院

本报告记录了专家创作委员会基于证据的共识，包括根据委员会和委员会审议收集的信息得出的发现、结论和建议。报告由同行评审，并由美国国家科学院、工程院和医学院批准。

会议记录了在研讨会、专题讨论会或其他会议上的陈述和讨论。会议记录中的陈述和意见是与会者的陈述和意见，没有得到其他与会者、计划委员会，或者国家科学院、工程院和医学院的认可。

有关美国国家科学院其他产品和活动的信息，请访问 nationalacademies.org/whatwedo。

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Reports document the evidence-based consensus of an authoring committee of experts. Reports typically include findings, conclusions, and recommendations based on information gathered by the committee and committee deliberations. Reports are peer reviewed and are approved by the National Academies of Sciences, Engineering, and Medicine.

Proceedings chronicle the presentations and discussions at a workshop, symposium, or other convening event. The statements and opinions contained in proceedings are those of the participants and have not been endorsed by other participants, the planning committee, or the National Academies of Sciences, Engineering, and Medicine.

For information about other products and activities of the National Academies, please visit nationalacademies.org/whatwedo.

“人类基因编辑：科学、医学和伦理决策”委员会
COMMITTEE ON HUMAN GENE EDITING:
SCIENTIFIC, MEDICAL, AND ETHICAL CONSIDERATIONS

R. ALTA CHARO (*Co-Chair*), Sheldon B. Lubar Distinguished Chair and Warren P. Knowles Professor of Law & Bioethics, University of Wisconsin–Madison

RICHARD O. HYNES (*Co-Chair*), Investigator, Howard Hughes Medical Institute, Daniel K. Ludwig Professor for Cancer Research, Massachusetts Institute of Technology

DAVID W. BEIER, Managing Director, Bay City Capital

ELLEN WRIGHT CLAYTON, Craig Weaver Professor of Pediatrics, Professor of Law, Vanderbilt University

BARRY S. COLLER, David Rockefeller Professor of Medicine, Physician in Chief, and Head, Allen and Frances Adler Laboratory of Blood and Vascular Biology, Rockefeller University

JOHN H. EVANS, Professor, University of California, San Diego

JUAN CARLOS IZPISUA BELMONTE, Professor, Gene Expression Laboratory, Salk Institute for Biological Studies

RUDOLF JAENISCH, Professor of Biology, Massachusetts Institute of Technology

JEFFREY KAHN, Andreas C. Dracopoulos Director, Johns Hopkins Berman Institute of Bioethics, Johns Hopkins University

EPHRAT LEVY-LAHAD, Director, Fuld Family Department of Medical Genetics, Shaare Zedek Medical Center; Faculty of Medicine, Hebrew University of Jerusalem

ROBIN LOVELL-BADGE, Senior Group Leader, Laboratory of Stem Cell Biology and Developmental Genetics, The Francis Crick Institute

GARY MARCHANT, Regents' Professor of Law, Arizona State University **JENNIFER MERCHANT**, University Professor, Université de Paris II (Panthéon-Assas)

LUIGI NALDINI, Professor of Cell and Tissue Biology and of Gene and Cell Therapy, San Raffaele University, and Director of the San Raffaele Telethon Institute for Gene Therapy

DUANQING PEI, Professor and Director General of Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences

MATTHEW PORTEUS, Associate Professor of Pediatrics, Stanford School of Medicine **JANET ROSSANT**, Senior Scientist and Chief of Research Emeritus, Hospital for Sick Children, University of Toronto

DIETRAM A. SCHEUFELE, John E. Ross Professor in Science Communication and Vilas Distinguished Achievement Professor, University of Wisconsin–Madison

ISMAIL SERAGELDIN, Founding Director, Bibliotheca Alexandrina **SHARON TERRY**, President & CEO, Genetic Alliance

JONATHAN WEISSMAN, Professor, Department of Cellular and Molecular Pharmacology, University of California, San Francisco

KEITH R. YAMAMOTO, Vice Chancellor for Science Policy and Strategy, University of California, San Francisco

研究人员(*Study Staff*)

KATHERINE W. BOWMAN, Study Director

MONICA L. GONZALEZ, Associate Program Officer

JOANNA R. ROBERTS, Senior Program Assistant

ANDREW M. POPE, Director, Board on Health Sciences Policy

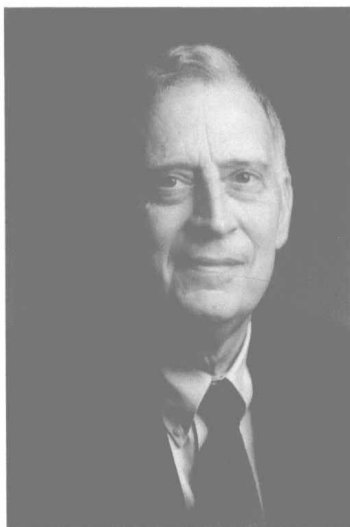
FRANCES E. SHARPLES, Director, Board on Life Sciences

顾问(*Consultants*)

RONA BRIERE, Editor

HELAINÉ RESNICK, Editor

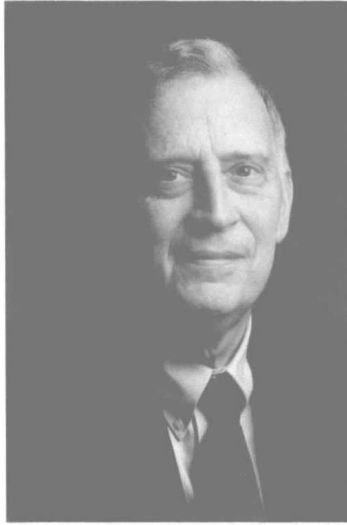
题 词



Ralph Cicerone 博士 (1943—2016) 于 2015 年担任美国国家科学院院长，当时他与美国国家医学院院长合作宣布了一项关于人类基因组编辑的倡议，该倡议包括科学、伦理和管理。他指出，美国国家科学院、工程院和医学院将努力引导，为许多新兴和有争议的遗传学和细胞生物学领域制定负责任的综合政策，如人类胚胎干细胞研究、人类克隆和“功能获得”研究。最值得注意的是它包含了 1975 年阿西洛马尔会议之前的关键事件。但 Cicerone 博士在接受《自然》杂志采访时说，阿西洛马尔时代和今天有着重要的区别，因为 1975 年很少有研究人员从事重组 DNA 的研究，而现代的基因组编辑技术更易于使用，并且能被广泛使用，这使他得出结论，这种情况需要一种“比阿西洛马尔更国际化的方案”。

Cicerone 博士言行一致。他与来自中国和英国的科学院和医学院合作，发起了一项与国际首脑会议有关的倡议。由此，承诺今后将举行首脑会议，并成立一个研究委员会，成员来自加拿大、中国、埃及、法国、德国、以色列、意大利、西班牙、英国和美国，或在这些国家工作。本报告是该委员会工作的成就，也是对这位伟大的美国国家科学院院长的致敬。

Dedication



Dr. Ralph Cicerone (1943-2016) was President of the National Academy of Sciences in 2015 when, in partnership with the President of the National Academy of Medicine, he announced a human genome-editing initiative that would encompass science, ethics, and regulation. He noted that the National Academies of Sciences, Engineering, and Medicine have led the effort to develop responsible, comprehensive policies for many emerging and controversial areas of genetics and cell biology, such as human embryonic stem cell research, human cloning, and “gain-of-function” research. Most notable was its involvement in key events leading up to the 1975 Asilomar conference. But there are important differences between the Asilomar era and today, Dr. Cicerone said in an interview with *Nature*, because few researchers were pursuing recombinant DNA research in 1975. Modern genome-editing techniques are easy to use and widely accessible, leading him to conclude that the situation requires an approach that is “really more international than Asilomar ever had to be.”

Dr. Cicerone was as good as his word. In collaboration with science and medicine academies from China and the United Kingdom, an initiative was launched with an international summit. From this came a commitment to future summits, and the formation of a study committee, with members hailing from or working in Canada, China, Egypt, France, Germany, Israel, Italy, Spain, the United Kingdom, and the United States. This report is the culmination of the work by that committee and is dedicated to this great leader of the National Academy of Sciences.

致 谢

本报告由选取具有不同观点和技术专长的个人对草稿进行审查。本次独立审查的目的是提供坦诚和批评性的评论，以帮助本机构尽可能完善已公布的报告，并确保报告符合机构标准和对研究费用的相关制度标准。为保护审议程序的完整性，审查意见和稿件草稿保密。我们要感谢以下各人对本报告的审核：

Eli Adashi, 布朗大学

George Annas, 波士顿大学

Dana Carroll, 犹他大学

Michael Dahlstrom, 爱荷华州立大学

Hank Greely, 斯坦福大学

J. Benjamin Hurlbut, 亚利桑那州立大学

Maria Jasin, 纪念斯隆 - 凯特林癌症中心

James Lawford-Davies, 亨普森律师事务所, 英国

Andrew Maynard, 亚利桑那州立大学

Krishanu Saha, 威斯康星大学

Fyodor Urnov, 阿尔蒂乌斯研究所

Keith Wailoo, 普林斯顿大学

尽管上述审查人员提供了许多建设性意见和建议，但并不要求他们认可这些结论或建议，他们也没有看到报告发布前的最终版本。该报告的审查由 Harvey Fineberg (穆尔基金会) 和 Jonathan Moreno (宾夕法尼亚大学) 负责。他们负责确保按照机构程序对本报告进行独立审查，并仔细考虑所有审查意见。本报告的最终内容完全由编写委员会和机构负责。

Reviewers

This report was reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

Eli Adashi, Brown University

George Annas, Boston University

Dana Carroll, University of Utah

Michael Dahlstrom, Iowa State University

Hank Greely, Stanford University

J. Benjamin Hurlbut, Arizona State University

Maria Jasin, Memorial Sloan Kettering Cancer Center

James Lawford-Davies, Hempsons Law Firm, United Kingdom

Andrew Maynard, Arizona State University

Krishanu Saha, University of Wisconsin-Madison

Fyodor Urnov, Altius Insitute

Keith Wailoo, Princeton University

Although the reviewers listed above provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by **Harvey Fineberg** (Moore Foundation) and **Jonathan Moreno** (University of Pennsylvania). They were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

序 言

基因组编辑是一套比以往更准确、更灵活地改变 DNA 的方法，曾被《自然 - 方法》杂志誉为 2011 年年度方法，CRISPR/CAS9 基因组编辑系统被《科学》杂志评为 2015 年年度突破。由于它可以用于洞察基本的生物过程，以及为人类健康可能带来的进步，这项技术在全球范围内引起了人们的兴趣。但是随着研究的进步，出现了许多问题，包括在避免不必要的影响的同时达到预期效果的技术方面，以及一系列的用途，这些用途不仅可以治愈病人，而且还可以预防我们自己和后代的疾病，甚至改变与健康需求无关的特征。现在是时候考虑这些问题了。使用编辑过的人体细胞进行的临床试验已经在进行中，并且已经有了更多的预期。为了有助于应用基因组编辑以广泛促进人类福祉，有必要审查其提出的科学、伦理和社会问题，并评估管理系统确保其负责任的发展和使用的。这样做还需要阐明一些更崇高的原则，这些原则应该是这些系统的基础。

这些并非易事，但我们非常感谢加入我们的委员会成员。他们愿意并且深思熟虑地将他们不同的观点带到我们的讨论中，我们感谢他们对这项研究的承诺，以及他们在过去一年中投入了如此多的时间和精力。和他们一起工作是一种乐趣和荣幸。本报告还得到了与会发言者的许多介绍和讨论，这些发言者的贡献提供了丰富的信息和见解。我们感谢他们与我们分享他们的研究和观点。最后，我们代表委员会感谢美国国家科学院、工程院和医学院的工作人员，他们在整个研究过程中与我们一起工作，他们的想法和支持对于项目的成功至关重要；同时感谢该研究的发起人，他们对该研究的潜力有着广阔视野。

R. Alta Charo 和 Richard O. Hynes

“人类基因编辑：科学、医学和伦理决策”委员会的共同主持人

Preface

Genome editing—a suite of methods for creating changes in DNA more accurately and flexibly than previous approaches—was hailed as the 2011 Method of the Year by *Nature Methods*, and the CRISPR/Cas9 system of genome editing was named the 2015 Breakthrough of the Year by *Science*. The technology has excited interest across the globe because of the insights it may offer into fundamental biological processes and the advances it may bring to human health. But with these advances come many questions, about the technical aspects of achieving desired results while avoiding unwanted effects, and about a range of uses that may include not only healing the sick, but also preventing disease in this and future generations, or even altering traits unrelated to health needs. Now is the time to consider these questions. Clinical trials using edited human somatic cells are already underway, and more are anticipated. To help direct the use of genome editing toward broadly promoting human well being, it is important to examine the scientific, ethical, and social issues it raises, and assess the capacity of governance systems to ensure the technologies' responsible development and use. Doing so also entails articulating the larger principles that should underlie such systems.

These were not easy tasks, but we are profoundly grateful to the committee members who joined us in tackling our charge. They willingly and thoughtfully brought their diverse perspectives to bear on our discussions, and we thank them for their commitment to this study and for devoting so much of their time and energy over the past year. It has been a pleasure and a privilege to work with them. The report was also informed by many presentations and discussions with speakers whose contributions provided a wealth of information and insight. We thank them for sharing their research and viewpoints with us. Finally, on behalf of the committee, we would like to thank the staff of the National Academies of Sciences, Engineering, and Medicine for working alongside us throughout the study—their ideas and support were crucial to bringing the project to fruition—and thank the sponsors of the study, who had an expansive vision for its potential.

R. Alta Charo and Richard O. Hynes, *Co-Chairs*

Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations

目 录

总论	1
基因组编辑应用和政策问题概述	2
人类基因组编辑的应用	4
监管人类基因组编辑的原则	10
建议	12
1 概述	14
研究现况	16
研究背景	19
研究方法	25
报告概要	25
2 人类基因组编辑监管的总体原则	27
人类基因组编辑的监管原则	27
美国基因治疗技术的监管	32
其他国家的监管细节	53
总结和建议	53
3 基因组编辑技术的基础研究应用	57
基因组编辑基本方法	57
基因组编辑技术的飞速发展	63
人类细胞和组织基础实验研究进展	65
哺乳动物繁殖与发育基础实验研究进展	66
基础研究中的伦理和监管问题	75
总结和建议	76
4 体细胞基因组编辑	78
研究背景	79
基因编辑较传统基因治疗和早期方案的优势	81
基于核酸酶的同源与非同源重组编辑修复技术	85
人类体细胞基因编辑技术的潜在应用	86
基因编辑的设计和应用涉及的科技考量	88
体细胞基因编辑产生的伦理和监管问题	97
总结和建议	103