

*EPIGENETIC RISKS
OF CLONING*

EPIGENETIC RISKS OF CLONING

EDITED BY

Akio Inui

Kagoshima University
Kagoshima, Japan



Taylor & Francis
Taylor & Francis Group

Boca Raton London New York Singapore

A CRC title, part of the Taylor & Francis imprint, a member of the
Taylor & Francis Group, the academic division of T&F Informa plc.

Published in 2006 by
CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

© 2006 by Taylor & Francis Group, LLC
CRC Press is an imprint of Taylor & Francis Group

No claim to original U.S. Government works
Printed in the United States of America on acid-free paper
10 9 8 7 6 5 4 3 2 1

International Standard Book Number-10: 0-8493-2527-7 (Hardcover)
International Standard Book Number-13: 978-0-8493-2527-4 (Hardcover)
Library of Congress Card Number 2005048532

This book contains information obtained from authentic and highly regarded sources. Reprinted material is quoted with permission, and sources are indicated. A wide variety of references are listed. Reasonable efforts have been made to publish reliable data and information, but the author and the publisher cannot assume responsibility for the validity of all materials or for the consequences of their use.

No part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, microfilming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, please access www.copyright.com (<http://www.copyright.com/>) or contact the Copyright Clearance Center, Inc. (CCC) 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. CCC is a not-for-profit organization that provides licenses and registration for a variety of users. For organizations that have been granted a photocopy license by the CCC, a separate system of payment has been arranged.

Trademark Notice: Product or corporate names may be trademarks or registered trademarks, and are used only for identification and explanation without intent to infringe.

Library of Congress Cataloging-in-Publication Data

Epigenetic risks of cloning / edited by Akio Inui
p. cm.
Includes bibliographical references and index.
ISBN 0-8493-2527-7 (alk. Paper)
1. Cloning. 2. Epigenesis. I. Inui, Akio, 1950-

QH442.2.E65 2005
660.6'5—dc22

2005048532

T&F informa

Taylor & Francis Group
is the Academic Division of T&F Informa plc.

Visit the Taylor & Francis Web site at
<http://www.taylorandfrancis.com>

and the CRC Press Web site at
<http://www.crcpress.com>

Preface

Cloning technology has the potential to be a valuable tool not only in basic research, but also in agriculture and clinical medicine. The agricultural and clinical applications that are being explored include reproductive cloning of farm animals and therapeutic cloning for human cell, tissue, and organ replacement [1,2]. Embryos produced by nuclear transfer from a patient's somatic cell offer one potential source of embryonic stem (ES) cells [3,4] that would be histocompatible with the patient's cells and in principle be a source of any other cell type. Studies in animal models show that transplantation of ES-derived cells can successfully treat a variety of chronic diseases, including cardiovascular diseases, diabetes, and traumatic spinal cord injury, that underlie the promising role of human ES cells in tissue regeneration and modern medicine [5].

Several laboratories have used a variety of somatic cell types to create cloned animals, including sheep, cattle, mice, pigs, and goats; the list is ever expanding. The present procedures have proved to be repeatable, but are very inefficient when only between 1 and 4% of reconstructed embryos typically develop to adulthood [1,2]. The low overall success rate is the cumulative result of inefficiencies at all stages of development, although species and donor cell types may differ in the precise pattern of loss. In addition to embryonic loss, somatic cell nuclear transfer is also associated with very high rates of fetal, perinatal, and neonatal loss, and production of abnormal offspring [1,2,6]. Common abnormalities include respiratory distress, increased birth weight, and major cardiovascular abnormalities. Other abnormalities that may develop later include failure of the immune system; structural abnormalities of the brain and other viscera; accelerated aging; and obesity, which may be influenced by species, genetic background, or donor cell type.

Increasing evidence from a range of mammals shows a propensity for epigenetic errors with embryo technologies; if paralleled in human embryos, the effect on tumorigenic and differentiation properties of ES cells needs to be established [7]. Epigenetic risks are also related to assisted reproductive technologies in humans as known for imprinting disorders such as Beck–Wiedemann and Angelman syndromes. Therefore, it is important to evaluate the consequences of cloning in resulting embryo and offspring before widespread use of the technology.

We hope that this book helps the reader understand embryonal, fetal, perinatal, neonatal, and postnatal development of clones of various species for further technological advances.

REFERENCES

1. Wilmut, I., and Paterson, L. Somatic cell nuclear transfer, *Oncol. Res.* 13, 303, 2003.
2. Wilmut, I. et al. Somatic cell nuclear transfer, *Nature* 419, 583, 2002.
3. Cowan, C.A. et al. Derivation of embryonic stem-cell lines from human blastocysts, *N. Engl. J. Med.* 350, 1353, 2004.
4. Hwang, W.S. et al. Evidence of a pluripotent human embryonic stem cell line derived from a cloned blastocyst, *Science* 303, 1669, 2004.
5. Stojkovic, M. et al. Derivation, growth and applications of human embryonic stem cells, *Reproduction* 128, 259, 2004.
6. Tamashiro, K.L. et al. Phenotype of cloned mice: development, behavior, and physiology, *Exp. Biol. Med. (Maywood)* 228, 1193, 2003.
7. Allegrucci, C. et al. Stem-cell consequences of embryo epigenetic defects, *Lancet* 364, 206, 2004.

Editor

Akio Inui completed his M.D. and Ph.D. degrees at Kobe University. In 1984, he was appointed assistant professor at the same university and became associate professor in 1998. Between 1985 and 1989, he also served as chief physician of the Medical Ward at Kobe University Hospital. Since 2001, Dr. Inui has been engaged as associate professor in the Division of Diabetes, Digestive and Kidney Diseases in the Department of Clinical Molecular Medicine at Kobe University Graduate School of Medicine. He is recognized for his studies in elucidating the role of gut–brain peptides in the regulation of gastrointestinal motility, feeding, and body weight, and the identification of the ghrelin–neuropeptide Y pathway from stomach to brain in the pathogenesis of obesity and cachexia. He has an interest in the role of gut–brain peptides in the development of behavior in animal models, including clones.

Dr. Inui received the Janssen Award of the American Gastrointestinal Association in 2004. He is editor of *Peptides*, *Nutrition*, and the *International Journal of Oncology*. Between 2000 and 2002, he also edited the *International Journal of Molecular Medicine*. His efforts are now focused on translational research on peptides that bridges the gap between basic and clinical disciplines for better understanding and management of human behavioral disorders, including obesity, cancer cachexia, and eating disorders.

Contributors

Pierre G. Adenot

INRA
Unite de Biologie du Developpement et
Reproduction
Jouy-en-Josas, France

Laurent Boulanger

INRA
Unite de Biologie du Developpement et
Reproduction
Jouy-en-Josas, France

Thomas D. Bunch

Animal Dairy and Veterinary Sciences
Department, Center for Integrated
Biosystems
Utah State University
Logan, Utah

Mireille Challah–Jacques

VIVALIS
Site Bio Quest
Saint-Herblain, France

Aimee S. Chang

Department of Obstetrics and
Gynecology
Washington University School of
Medicine
St. Louis, Missouri

Patrick Chesné

INRA
Unite de Biologie du Developpement et
Reproduction
Jouy-en-Josas, France

Peter Chrenek

RIAP
Nitra, Slovak Republic

Nathalie Daniel

BioProtein Technologies
Paris, France

Michael R. DeBaun

Department of Pediatrics, Division of
Genetics
Washington University School of
Medicine
St. Louis, Missouri

Robert Feil

Institute of Molecular Genetics, CNRS
Montpellier, France

Martha C. Gómez

Audubon Center for Research of
Endangered Species and Department
of Animal Sciences
Louisiana State University
New Orleans, Louisiana

J.B. Gurdon

Wellcome Trust/Cancer Research
U.K. Gurdon Institute and Department
of Zoology
Cambridge, United Kingdom

M. Hirabayashi

National Institute for Physiological
Sciences
Okazaki, Aichi, Japan

S. Hochi

Faculty of Textile Science and
Technology
Shinshu University
Ueda Nagano, Japan

Yoko Kato

Laboratory of Animal Reproduction,
College of Agriculture
Kinki University
Nakamachi, Nara, Japan

Guanpeng Li

Animal Dairy and Veterinary Sciences
Department, Center for Integrated
Biosystems
Utah State University
Logan, Utah

Pasqualino Loi

Department of Comparative Clinical
Services
University of Teramo
Teramo, Italy

Kelle H. Moley

Department of Obstetrics and
Gynecology
Washington University School of
Medicine
St. Louis, Missouri

Akira Onishi

Embryonic Technology Laboratory,
Developmental Biology Department
Institute of Insect and Animal Sciences,
National Institute of Agrobiological
Sciences
Tsukuba, Ibaraki, Japan

C. Earle Pope

Audubon Center for Research of
Endangered Species
Louisiana State University
New Orleans, Louisiana

Jean-Paul Renard

INRA
Unite de Biologie du Developpement et
Reproduction
Jouy-en-Josas, France

Randall R. Sakai

Department of Psychiatry
University of Cincinnati College of
Medicine
Cincinnati, Ohio

Kellie L.K. Tamashiro

Neuroscience Program and Department
of Psychiatry
University of Cincinnati College of
Medicine
Cincinnati, Ohio

Yukio Tsunoda

Laboratory of Animal Reproduction,
College of Agriculture
Kinki University
Nakamachi, Nara, Japan

Dirk K. Vanderwall

Northwest Equine Reproduction
Laboratory, Department of Animal
and Veterinary Science
University of Idaho
Moscow, Idaho

Xavier Vignon

INRA
Unite de Biologie du Developpement et
Reproduction
Jouy-en-Josas, France

Teruhiko Wakayama

Institute for Biogenesis Research
University of Hawaii School of
Medicine
Honolulu, Hawaii
Laboratory for Genomic
Reprogramming, Center for
Developmental Biology
Kobe, Japan

Michael Wangler

Department of Pediatrics, Division of
Genetics
Washington University School of
Medicine
St. Louis, Missouri

Kenneth L. White

Animal Dairy and Veterinary Sciences
Department, Center for Integrated
Biosystems
Utah State University
Logan, Utah

Gordon L. Woods

Northwest Equine Reproduction
Laboratory, Department of Animal
and Veterinary Science
University of Idaho
Moscow, Idaho

Yukiko Yamazaki

Institute for Biogenesis Research
University of Hawaii School of
Medicine
Honolulu, Hawaii

Ryuzo Yanagimachi

Institute for Biogenesis Research
University of Hawaii School of
Medicine
Honolulu, Hawaii

Table of Contents

Chapter 1

Health Consequences of Cloning Mice..... 1

*Kellie L.K. Tamashiro, Randall R. Sakai, Yukiko Yamazaki,
Ryuzo Yanagimachi, and Teruhiko Wakayama*

Chapter 2

Cloning Pigs from Somatic Cells and its Applications 17

Akira Onishi

Chapter 3

Amphibian Nuclear Transfer and Future Directions of Research..... 29

J.B. Gurdon

Chapter 4

Cloning in Cattle 33

Yukio Tsunoda and Yoko Kato

Chapter 5

Cloning the Equine..... 59

*Kenneth L. White, Gordon L. Woods, Dirk K. Vanderwall,
Guanpeng Li, and Thomas D. Bunch*

Chapter 6

Cloning in the Rabbit: Present Situation and Prospects..... 71

*Patrick Chesné, Peter Chrenek, Mireille Challah-Jacques,
Nathalie Daniel, Laurent Boulanger, Xavier Vignon,
Pierre G. Adenot, and Jean-Paul Renard*

Chapter 7

Evidence for and Against Associations between ART and
Congenital Malformation Syndromes 97

*Michael R. DeBaun, Aimee S. Chang, Michael Wangler, and
Kelle H. Moley*

Chapter 8

Current Concepts in Cat Cloning..... 111

Martha C. Gómez and C. Earle Pope

Chapter 9

Ovine Somatic Cell Nuclear Transfer: Retrospective Overview and
Analysis of Epigenetic and Phenotypic Effects of Cloning Procedures 153
Robert Feil and Pasqualino Loi

Chapter 10

Cloning in the Rat 165
M. Hirabayashi and S. Hochi