

Current Human Cell Research and Applications

Series Editors:

Nariyoshi Shinomiya

Department Integrative Physiology and Bio-Nano Medicine

National Defense Medical College

Tokorozawa, Saitama, Japan

Hiroaki Kataoka

Department of Pathology

University of Miyazaki

Miyazaki, Japan

Yutaka Shimada

Department of Nanobio Drug Discovery

Kyoto University

Sakyo-ku, Kyoto, Japan

This series covers basic and clinical research on human cells, including molecular diagnostics/targeted therapy, cell therapy, cancer stem cells, regenerative medicine, etc., and provides an up-to-date review of human-cell research. All volumes are contributed by leading experts in the field, and offer valuable resources for both cell biologists and clinical researchers in the areas of oncology, stem cell biology, regenerative medicine, and clinical medicine including gynecology, gastroenterology, etc.

Current Human Cell Research and Applications will be published in partnership with the Japan Human Cell Society

More information about this series at <http://www.springer.com/series/15107>

Haruhisa Inoue • Yukio Nakamura
Editors

Medical Applications of iPS Cells

Innovation in Medical Sciences

 Springer

Editors

Haruhisa Inoue
CiRA, Kyoto University
Kyoto
Japan

iPSC-based Drug Discovery
and Development Team
RIKEN BioResource Research Center
Kyoto
Japan

Medical-risk Avoidance based
on iPS Cells Team
RIKEN Center for Advanced
Intelligence Project
Kyoto
Japan

Yukio Nakamura
Cell Engineering Division
RIKEN BioResource Research Center
Tsukuba-shi
Ibaraki
Japan

ISSN 2522-073X ISSN 2522-0748 (electronic)
Current Human Cell Research and Applications
ISBN 978-981-13-3671-3 ISBN 978-981-13-3672-0 (eBook)
<https://doi.org/10.1007/978-981-13-3672-0>

Library of Congress Control Number: 2019930482

© Springer Nature Singapore Pte Ltd. 2019

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors, and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Singapore Pte Ltd. The registered company address is: 152 Beach Road, #21-01/04 Gateway East, Singapore 189721, Singapore

Preface

The creation of chimeric animals and the discovery of embryonic stem cells have had a profound effect on the study and treatment of diseases. The resulting animal models have enabled extraordinary insights on the very beginnings of a disease that can only be identified in its late stages in human patients. Of course, these models have limitations, mostly being that animals and humans, while sharing a great deal of similarities, differ in significant ways that are best summarized by Judah Folkman's remark, "if you have cancer and you are mouse, we can take good care of you."

The discovery of induced pluripotent stem (iPS) cells, specifically human iPS cells, began a new generation of modeling that invited the opportunity to watch a patient's cells develop the disease phenotype in real time. Understanding how to control the pluripotency network of a somatic cell has enabled scientists to reprogram easily accessible cells into those afflicted by the pathology and observing how development differs in healthy and diseases groups and even within diseased subgroups. That these experiments can be done using human cells invites comparisons with animal models and explanation as to why patients diagnosed with the same disease respond differently to an experimental medicine.

Thus, the very first report of human iPS cells was followed by a surge not only in research that explored the reprogramming mechanism but also in research that sought to exploit the power of reprogramming technology for new medical applications. These applications include the study of the pathogenesis of diseases along with new drug discoveries and cell therapies. In more recent years, the development of complementary technologies, such as gene editing and organoids, has only added to the expectation that iPS cells will provide solutions to what are currently intractable diseases.

Accordingly, we have invited authors who view iPS cells as a tool that advances medical treatments and use them to study disease development and generate cells for transplantation or to find candidate compounds. We have also invited authors

who use iPS cells to test their new technologies in gene editing, nanomachines, and organoids. Overall, the intention of this book is to provide readers with an impression of the reach iPS cells have in medicine and how their own research can benefit by incorporating iPS cell technology.

Kyoto, Japan
Tsukuba-shi, Ibaraki, Japan

Haruhisa Inoue
Yukio Nakamura

Acknowledgments

We want to thank Peter Karagiannis (Center for iPS Cell Research and Application) for his assistance with the editing and writing of this book.

Contents

Part I Introduction

- 1 Clinical Potential of Induced Pluripotent Stem Cells** 3
Peter Karagiannis

Part II Disease Modelling

- 2 Disease Modeling of Hematological and Immunological Disorders Using Induced Pluripotent Stem Cells** 15
Megumu K. Saito
- 3 iPSC Cell Technology for Dissecting Cancer Epigenetics** 29
Hirofumi Shibata and Yasuhiro Yamada
- 4 Recapitulating Hematopoietic Development in a Dish** 45
Kim Vanuytsel, Martin H. Steinberg, and George J. Murphy
- 5 Modeling Cardiomyopathies with iPSCs** 73
Jean-Sébastien Hulot

Part III Molecular Technologies

- 6 Endogenous Signal-Responsive Transgene Switch Systems for Visualization and Purification of Specific Cells** 99
Hideyuki Nakanishi and Hirohide Saito
- 7 Precision Genome Editing in Human-Induced Pluripotent Stem Cells** 113
Knut Woltjen

Part IV iPS Applications

- 8 Induced Pluripotent Stem Cell-Based Cell Therapy of the Retina . . . 133**
Seiji Takagi, Michiko Mandai, Yasuhiko Hiramami, Yasuo Kurimoto,
and Masayo Takahashi
- 9 Organoid Models of Development and Disease Towards Therapy . . . 149**
Yasunori Nio and Takanori Takebe
- 10 In Vivo Cell Conversion as a New Cell Therapy 169**
Hedong Li, Lei Zhang, Yuchen Chen, Zheng Wu,
Zhuofan Lei, and Gong Chen