

# Trends in Stem Cell Proliferation and Cancer Research

Rodrigo R. Resende · Henning Ulrich  
Editor

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 Springer

*Editors*

Rodrigo R. Resende  
Instituto de Ciências Biológicas  
Universidade Federal de Minas Gerais  
Belo Horizonte  
São Paulo  
Brazil

Henning Ulrich  
Depto. Bioquímica  
Inst. Química  
Universidade de São Paulo  
São Paulo  
Brazil

ISBN 978-94-007-6210-7                      ISBN 978-94-007-6211-4 (eBook)

DOI 10.1007/978-94-007-6211-4  
Springer Dordrecht Heidelberg New York London

Library of Congress Control Number: 2013933025

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Printed on acid-free paper

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# Invited Preface

## **Convergent and Divergent Signaling Pathways in Stem Cells and Cancer**

The rapid progress in research in areas of stem cells and cancer calls for frequent comprehensive and critical overviews of these fields. This book, presenting a compilation of the most recent reviews from these areas, is an excellent example of such needed overviews. The Editors were able to engage a large number of expert authors who present 23 chapters devoted to critical appraisal of the important topics at the forefront of the research in these fields. The collection of reviews on both the subjects, the stem cells and cancer, in a single volume, offers the reader an opportunity and convenience to learn and compare on similarities and disparities in the signaling pathways and regulatory machineries in these respective states of cell growth versus malignancy.

Of particular interest, widely covered in several chapters, is the role of stem cells in cancer genesis, development, progression, and as a potential target for cancer therapy. There is still a lot of uncertainty in identification of cancer stem cells, particularly in solid tumors, problems with their isolation, growth, and characterization of their drug sensitivity. Effectiveness of anticancer drugs on cancer stem cells cannot be properly recognized because it is still based on assessment of a decrease in tumor mass (“cancer response”) where the cancer stem cells are in a minor proportion. Therefore their sensitivity may be unrelated to tumor mass shrinkage. The knowledge on identification and properties of cancer stem cells, presented in these chapters, provides the necessary background needed for further advances towards development of more effective anticancer strategies.

Among many attention-grabbing chapters the article describing embryonic rest hypothesis of cancer development is especially exciting. Based on evidence of the presence of very small embryonic/epiblast-like stem cells (VSELs) in different tissues the authors of this chapter resurrect the 150-year-old hypothesis of Rudolf Virchow and Julius Cohnheim who proposed that cancer may develop from embryonic cell remnants that remain in the developing organs following embryogenesis (“embryonic rest hypothesis of cancer development”). Their contention that the primitive epiblast-germline-derived VSELs represent the Virchow’s

hypothetical embryonic cells from which cancer develops is exciting, calls for further experiments testing, and if confirmed, opens new avenues for cancer prevention and possibly the treatment.

Several chapters are devoted to anticancer strategies aimed toward selective killing cancer—while sparing normal—cells. Some strategies are focused on modulation of the mechanism of cell death by the mode of apoptosis, autophagy, and other means of cell demise. Among these chapters very exhaustive and stimulating is the review describing the role of BH3-only proteins, a class of small molecules of the Bcl-2 family, in regulation of cell propensity to undergo apoptosis. In this chapter the authors present attractive ideas of how to exploit mechanisms involving BH3-only proteins for selective elimination of cancer cell, offering one more cancer treatment strategy.

Cancer can be considered as primarily a disease of the cell cycle. While normal cells enter into—and progress through—the cell cycle only when triggered by the respective growth factors or mitogens, cancer cells are constitutively recruited to the cycle by the persistent stimulation of many signaling pathways mobilized by the defective oncogenes and/or tumor suppressor genes. A number of chapters address these differences and discuss the cell cycle-oriented anticancer strategies. The last chapter (23) of this volume specifically addresses targeting the cell cycle for anticancer treatment. It offers a very comprehensive review of the cell cycle regulatory machinery, describes the cancer-related changes in this machinery, and lists pharmaceutical agents targeting individual constituents of the machinery and the associated signaling pathways.

All in all, this book is a valuable compendium covering the most important topics related to cancer and stem cells and presenting comprehensive and state-of-the-art reviews. It can be of assistance to researchers who are already deeply engaged in the respective fields in cancer and stem cell biology. It can be of even greater assistance to newcomers to these fields giving them a possibility to see the diversity of the subjects and also, through the depth of the field covered in individual reviews, the outlook of entirety of the up-to-date research progress along these subjects. Because several chapters contain novel ideas on anticancer strategies as well as on a potential role of stem cells in regenerative medicine, the book will intellectually stimulate readers in these directions.

Dr. Zbigniew Darzynkiewicz  
Director of the Brander Cancer Research Institute  
New York Medical College  
Valhalla, NY, USA

# Editor Preface

More and more scientists and physicians are being confronted with the advancement in stem and cancer cell research and mechanisms of proliferation and cell survival. Throughout life, complex genetic systems regulate the balance between cell birth and death in response to growth and death signals. In this dynamic process, stem cells are essential for development, tissue repair, as well as aging and cancer. Major importance is given to mechanisms resulting from genetic and epigenetic alterations that result in changes of pathways mediating normal cellular activities.

This book provides comprehensive coverage of the current state-of-science of molecular stem and cancer research with discussion of controversial issues, directed to a wide range of audience including scientists working in the field, physicians, and all others who need to understand the molecular mechanisms that govern the functioning of stem cells in normal physiology and malfunctioning of tumor cells.

Experts in the field contributed 23 chapters, grouped into four parts. The first part “*Molecular Bases of Stem and Cancer Cell Proliferation*” focuses on mechanisms of proliferation control, initiated by an introductory chapter and followed by a chapter on the participation of extracellular matrix in the establishment of stem and cancer cells and the embryonic hypothesis of cancer development, suggesting that tumor genesis occurs from remaining stem cells as a development-related process. Furthermore, maintenance of pluripotency and proliferation processes are strictly regulated by intracellular pathways events. Induction of intracellular calcium transients as well as sphingolipid formation and lipid droplet biogenesis acting as inducible organelles play an important roles in cell signaling.

The part “*Signaling Pathways Underlying Tumor Genesis, Proliferation and Cell Death*” aims to highlight signaling processes and pro-and anti-apoptic mechanisms which decide over proliferation or cell death. A chapter discusses the breakthrough immunomodulatory mechanisms of CL-B and its importance in anti-tumor responses. The importance of BH3-only proteins in regulation apoptosis is described in addition to the participation of  $\beta$ -catenin/JNK and NF-KB signaling in carcinogenesis and cell death.

The third part focuses on “*Functions and Dysfunctions of Physiological Processes Involved in Tumor Genesis and Malignancy*” including the role of

chemokines, autophagy, epigenetic features, and immune response mechanisms exerted by tumor-associated neutrophils with implications in tumor development and malignancy. Mesenchymal stem–cancer stem interactions as well as regulatory functions exerted by microRNAs provide further mechanisms and possible targets for combating tumor cells. The final part “*Strategies for Cancer Treatment*” includes a contribution on cancer stem cell markers for characterization of the tumor and prognosis of patient treatment and survival. Furthermore, cancer cell dormancy and cell cycle regulation provide molecular targets for anticancer therapy.

In summary, together with aspects of stem cell biology, this book puts together knowledge on various molecular aspects of cancer, the disease with the highest predicted mortality in the twenty-first century, and encourages physicians and researchers from various disciplines to join their experience and efforts in combating this disease.

Belo Horizonte, November 2012  
São Paulo

Rodrigo R. Resende  
Henning Ulrich

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# Contributors

**Maria Jimena Amaya** Section of Digestive Diseases, Department of Internal Medicine, Yale University School of Medicine, New Haven, CT 06520-8019, USA

**Roya Babaei-Jadidi** Division of Pre-Clinical Oncology, Nottingham Digestive Diseases Centre Biomedical Research Unit, Cancer Genetics and Stem Cell Group, School of Clinical Sciences, University of Nottingham, Nottingham NG7 2UH, UK

**Jason Bennett** Department of Medicine, Centre for Cell Signalling and Inflammation, Imperial College London, Hammersmith Hospital Campus, Du Cane Road, London W12 0NN, UK

**Gabriel Bidaux** INSERM U1003, LabEx ICST, Université Lille 1, Villeneuve d'Ascq 59655, France

**Sarah A. Bliss** UMDNJ-New Jersey Medical School, Newark, NJ, USA

**Sylwia Borkowska** James Graham Brown Cancer Center, Stem Cell Institute, University of Louisville, Louisville, KY 40202, USA; Department of Physiology, Pomeranian Medical University, Szczecin, Poland

**Anne-Sophie Borowiec** INSERM U1003, LabEx ICST, Université Lille 1, Villeneuve d'Ascq 59655, France

**Patricia T. Bozza** Laboratory of Immunopharmacology, Oswaldo Cruz Institute, FIOCRUZ, Rio de Janeiro, Brazil

**Dora Brites** Faculdade de Farmácia, Research Institute for Medicines and Pharmaceutical Sciences, Universidade de Lisboa, Lisbon, Portugal

**Silvia Bruno** Department of Experimental Medicine, Human Anatomy Section, University of Genoa, 16132 Genoa, Italy

**Thierry Capiod** INSERM U807, Faculté de Médecine, 156 rue de Vaugirard, Paris 75730, France; Université Paris Descartes, 156 rue de Vaugirard, Paris Cedex 15 75730, France; IFR 94-Institut Fédératif de Recherche Necker-Enfants Malades, Tour Lavoisier 7, 149 rue de Sèvres, Paris 75015, France; Hôpital Necker-Enfants Malades, 149 rue de Sèvres, Paris Cedex 15 75743, France

**Shuang Chen** Department of Medicine, Massey Cancer Center and Virginia Commonwealth University, Richmond, VA 23298, USA

**Patrice Codogno** INSERM U984, University Paris-Sud 11, Châtenay-Malabry 92296, France

**André L. S. Cruz** Division of Cellular Biology, National Cancer Institute (INCA), Rio de Janeiro, Brazil

**Yun Dai** Department of Medicine, Massey Cancer Center and Virginia Commonwealth University, Richmond, VA 23298, USA

**Franco Fais** Department of Experimental Medicine, Human Anatomy Section, University of Genoa, 16132 Genoa, Italy

**Guido Franzoso** Department of Medicine, Centre for Cell Signalling and Inflammation, Imperial College London, Hammersmith Hospital Campus, Du Cane Road, London W12 0NN, UK

**Fabio Ghiotto** Department of Experimental Medicine, Human Anatomy Section, University of Genoa, 16132 Genoa, Italy

**Olivier Gires** Department of Otorhinolaryngology, Head and Neck Surgery, Grosshadern Medical Center, Ludwig-Maximilians-University of Munich, Marchioninstr. 15, Munich 81377, Germany

**Talita Glaser** Departamento de Bioquímica, Instituto de Química, Universidade de São Paulo, São Paulo, Brazil

**Kátia N. Gomes** Cell Signaling and Nanobiotechnology Laboratory, Department of Biochemistry and Immunology, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil; Universidade José do Rosário Vellano, Campus Divinópolis, MG, Brazil

**Vânia A. M. Goulart** Cell Signaling and Nanobiotechnology Laboratory, Department of Biochemistry and Immunology, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil

**Rodrigo Guabiraba** Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, UK; Laboratório de Imunofarmacologia, Departamento de Bioquímica e Imunologia, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

**Silvia Guatimosim** Cardiomyocyte Intracellular Signaling Laboratory, Department of Physiology and Biophysics, Institute of Biological Sciences, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil

**Ahmed Hamaï** INSERM U984, University Paris-Sud 11, Châtenay-Malabry 92296, France

**Kirsten Hattermann** Department of Anatomy, University of Kiel, 24098 Kiel, Germany

**Janka Held-Feindt** Department of Neurosurgery, University Medical Center Schleswig-Holstein UKSH, Campus Kiel, 24105 Kiel, Germany

**Ronald A. Hill** Department of Basic Pharmaceutical Sciences, University of Louisiana, Monroe, LA, USA

**Salman B. Hosain** Department of Basic Pharmaceutical Sciences, University of Louisiana, Monroe, LA, USA

**Lina Hu** Laboratory of Obstetrics and Gynecology, The Second Affiliated Hospital, Chongqing Medical University, Chongqing 400010, China; Key Laboratory of Obstetrics and Gynecology, Chongqing Bureau of Health, Chongqing 400010, China

**Ping Huang** Department of General Surgery, The First Affiliated Hospital, Chongqing Medical University, Chongqing 400016, China

**Suzana A. Kahn** Institute of Biomedical Sciences, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

**Eliana Kalakouti** Cancer Genetics and Stem Cell Group, Division of Pre-Clinical Oncology, Nottingham Digestive Diseases Centre Biomedical Research Unit, School of Clinical Sciences, University of Nottingham, Nottingham NG7 2UH, UK

**Reena V. Kartha** Department of Experimental and Clinical Pharmacology, Center for Orphan Drug Research, University of Minnesota, Minneapolis, MN, USA

**Alexandre H. Kihara** Núcleo de Cognição e Sistemas Complexos, Centro de Matemática, Computação e Cognição, Universidade Federal do ABC, Santo André, SP, Brazil

**Mark A. LaBarge** Life Science Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA

**Luiz O. Ladeira** Nanomaterials Laboratory, Department of Physics, Federal University of Minas Gerais, Belo Horizonte, Brazil

**Nataša Levičar** Department of Systems Biology and Biotechnology, National Institute of Biology, Večna pot 111, 1000 Ljubljana, Slovenia

**Yong-Yu Liu** Department of Basic Pharmaceutical Sciences, University of Louisiana, Monroe, LA, USA

**James B. Lorens** Department of Biomedicine, University of Bergen, Bergen 5009, Norway

**Maryam Mehrpour** INSERM U984, University Paris-Sud 11, Châtenay-Malabry 92296, France

**Gustavo Batista Menezes** Laboratório de Imunobiofotônica, Departamento de Morfologia, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil; Laboratório de Imunofarmacologia, Departamento de Bioquímica e Imunologia, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

**Rolf Mentlein** Department of Anatomy, University of Kiel, Kiel 24098, Germany

**Lorena E. Mora-Blanco** Life Science Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA

**Marta Moretti** Department of Medicine, Centre for Cell Signalling and Inflammation, Imperial College London, Hammersmith Hospital Campus, Du Cane Road, London W12 0NN, UK

**Helena Motaln** Department of Genetic Toxicology and Cancer Biology, National Institute of Biology, Ljubljana, Slovenia

**Vivaldo Moura Neto** Institute of Biomedical Sciences, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

**Jessian L. Munoz** UMDNJ-New Jersey Medical School, Newark, NJ, USA

**Abdolrahman S. Nateri** Cancer Genetics and Stem Cell Group, Division of Pre-Clinical Oncology, Nottingham Digestive Diseases Centre Biomedical Research Unit, School of Clinical Sciences, University of Nottingham, Nottingham NG7 2UH, UK

**Garth L. Nicolson** Department of Molecular Pathology, The Institute for Molecular Medicine, Huntington Beach, CA 92647, USA

**André Gustavo Oliveira** Laboratório de Imunobiofotônica, Departamento de Morfologia, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

**Jacqueline M. Park** UMDNJ-New Jersey Medical School, Newark, NJ, USA

**Micheli Mainardi Pillat** Departamento de Bioquímica, Instituto de Química, Universidade de São Paulo, São Paulo, Brazil

**Pranela Rameshwar** UMDNJ-New Jersey Medical School, Newark, NJ, USA

**Mariusz Z. Ratajczak** James Graham Brown Cancer Center, Stem Cell Institute, University of Louisville, Louisville, KY 40202, USA; Department of Physiology, Pomeranian Medical University, Szczecin, Poland

**Rodrigo R. Resende** Cell Signaling and Nanobiotechnology Laboratory, Department of Biochemistry and Immunology, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil

**Ana Rotter** Department of Surgery and Cancer, Imperial College London, Hammersmith Hospital, Du Cane Road, London W12 0NN, UK

**Anderson K. Santos** Cell Signaling and Nanobiotechnology Laboratory, Department of Biochemistry and Immunology, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil

**Telma Tiemi Schwindt** Departamento de Biologia Celular e do Desenvolvimento, Instituto de Ciências Biomédicas, Universidade de São Paulo, São Paulo, Brazil

**Karol Serwin** James Graham Brown Cancer Center, Stem Cell Institute, University of Louisville, Louisville, KY 40202, USA; Department of Physiology, Pomeranian Medical University, Szczecin, Poland

**Daniel A. F. Silva** Cell Signaling and Nanobiotechnology Laboratory, Department of Biochemistry and Immunology, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil

**Subbaya Subramanian** Department of Surgery, University of Minnesota, Minneapolis, MN 55455, USA

**Urška Tajnšek** Department of Genetic Toxicology and Cancer Biology, National Institute of Biology, Ljubljana, Slovenia

**Maciej Tarnowski** James Graham Brown Cancer Center, Stem Cell Institute, University of Louisville, Louisville, KY 40202, USA; Department of Physiology, Pomeranian Medical University, Szczecin, Poland

**Mauro Martins Teixeira** Laboratório de Imunofarmacologia, Departamento de Bioquímica e Imunologia, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

**Claudia Tenca** Department of Experimental Medicine, Human Anatomy Section, University of Genoa, 16132 Genoa, Italy

**Anil K. Thotakura** Department of Medicine, Centre for Cell Signalling and Inflammation, Imperial College London, Hammersmith Hospital Campus, Du Cane Road, London W12 0NN, UK

**Yasushi Toh** Department of Gastroenterological Surgery, National Kyushu Cancer Center, 3-1-1 Notame, Minami-ku, Fukuoka 811-1395, Japan

**Fernanda M. P. Tonelli** Cell Signaling and Nanobiotechnology Laboratory, Department of Biochemistry and Immunology, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil

**Laura Tornatore** Department of Medicine, Centre for Cell Signalling and Inflammation, Imperial College London, Hammersmith Hospital Campus, Du Cane Road, London W12 0NN, UK

**Emilia Torrado** Faculdade de Farmácia, Research Institute for Medicines and Pharmaceutical Sciences, Universidade de Lisboa, Lisbon, Portugal; Institute of Biomedical Sciences, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil;

**Henning Ulrich** Departamento de Bioquímica, Instituto de Química, Universidade de São Paulo, São Paulo, Brazil

**K. Venuprasad** Departments of Oncology, Immunology, and Microbiology, Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI 48201, USA

**João P. B. Viola** Division of Cellular Biology, National Cancer Institute (INCA), Rio de Janeiro, Brazil

**Miriam B. F. Werneck** Laboratory of Immunopharmacology, Oswaldo Cruz Institute, FIOCRUZ, Rio de Janeiro, Brazil; Division of Cellular Biology, National Cancer Institute (INCA), Rio de Janeiro, Brazil

**Minghe Wu** Physical Electronics School, University of Electronic Science and Technology of China, Chengdu 610054, China

**Minhui Xu** Department of Neurosurgery, Daping Hospital, Institute of Field Surgery, Third Military Medical University, Chongqing 400042, China

**Liang Yi** Department of Neurosurgery, Daping Hospital, Institute of Field Surgery, Third Military Medical University, Chongqing 400042, China

**Tinghe Yu** Laboratory of Obstetrics and Gynecology, The Second Affiliated Hospital, Chongqing Medical University, Chongqing 400010, China; Key Laboratory of Obstetrics and Gynecology, Chongqing Bureau of Health, Chongqing 400010, China