# Advances in Experimental Medicine and Biology

## Volume 1245

#### **Series Editors**

Wim E. Crusio, Institut de Neurosciences Cognitives et Intégratives d'Aquitaine, CNRS and University of Bordeaux UMR 5287, Pessac Cedex, France John D. Lambris, University of Pennsylvania, Philadelphia, PA, USA Heinfried H. Radeke, Institute of Pharmacology & Toxicology, Clinic of the Goethe University Frankfurt Main, Frankfurt am Main, Germany Nima Rezaei, Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran Advances in Experimental Medicine and Biology provides a platform for scientific contributions in the main disciplines of the biomedicine and the life sciences. This series publishes thematic volumes on contemporary research in the areas of microbiology, immunology, neurosciences, biochemistry, biomedical engineering, genetics, physiology, and cancer research. Covering emerging topics and techniques in basic and clinical science, it brings together clinicians and researchers from various fields.

Advances in Experimental Medicine and Biology has been publishing exceptional works in the field for over 40 years, and is indexed in SCOPUS, Medline (PubMed), Journal Citation Reports/Science Edition, Science Citation Index Expanded (SciSearch, Web of Science), EMBASE, BIOSIS, Reaxys, EMBiology, the Chemical Abstracts Service (CAS), and Pathway Studio.

2018 Impact Factor: 2.126.

More information about this series at http://www.springer.com/series/5584

Alexander Birbrair Editor

# Tumor Microenvironment

Extracellular Matrix Components – Part A



*Editor* Alexander Birbrair Department of Radiology Columbia University Medical Center New York, NY, USA

Department of Pathology Federal University of Minas Gerais Belo Horizonte, MG, Brazil

 ISSN 0065-2598
 ISSN 2214-8019
 (electronic)

 Advances in Experimental Medicine and Biology
 ISBN 978-3-030-40145-0
 ISBN 978-3-030-40146-7
 (eBook)

 https://doi.org/10.1007/978-3-030-40146-7
 ISBN 978-3-030-40146-7
 (eBook)

#### © Springer Nature Switzerland AG 2020

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, expressed 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 Switzerland AG The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

## Preface

This book's initial title was "Tumor Microenvironment." However, due to the current great interest in this topic, we were able to assemble more chapters than would fit in one book, covering tumor microenvironment biology from different perspectives. Therefore, the book was subdivided into several volumes.

This book Tumor Microenvironment: Extracellular Matrix Components -Part A presents contributions by expert researchers and clinicians in the multidisciplinary areas of medical and biological research. The chapters provide timely detailed overviews of recent advances in the field. This book describes major contributions of different extracellular matrix components in the tumor microenvironment during cancer development. Further insights into these mechanisms will have important implications for our understanding of cancer initiation, development, and progression. The authors focus on the modern methodologies and the leading-edge concepts in the field of cancer biology. In recent years, remarkable progress has been made in the identification and characterization of different components of tumor microenvironment in several tissues using state-of-the-art techniques. These advantages facilitated identification of key targets and definition of the molecular basis of cancer progression within different organs. Thus, the present book is an attempt to describe the most recent developments in the area of tumor biology which is one of the emergent hot topics in the field of molecular and cellular biology today. Here, we present a selected collection of detailed chapters on what we know so far about the extracellular matrix components in the tumor microenvironment in various tissues. Eight chapters written by experts in the field summarize the present knowledge about distinct extracellular matrix constituents during tumor development.

Maria Angelica Miglino and colleagues from the University of Sao Paulo wrote an introductory chapter on the role of different extracellular matrix components in the tumor microenvironment. Anthony J. Hayes and James Melrose from The University of Sydney discuss the role of keratan sulfate within the tumor. Laura Alaniz and colleagues from the Universidad Nacional del Noroeste de Buenos Aires compile our understanding of hyaluronan in the tumor microenvironment. Peter Qiao and Zheng-Rong Lu from Case Western Reserve University update us with what we know about fibronectin in the tumor microenvironment. Georgina Gonzalez-Avila and colleagues from Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas" summarize current knowledge on matrix metalloproteinases role in tumor microenvironment. Mary C. Farach-Carson and colleagues from The University of Texas Health Science Center at Houston describe the influence of perlecan and its modifiers in the tumor microenvironment. Evgenia Karousou and colleagues from the University of Insubria address the importance of heparan sulfate in the tumor microenvironment. Finally, Brad Walsh and colleagues from Glytherix Ltd. give an overview of the role of glypican-1 in the tumor microenvironment.

It is hoped that the articles published in this book will become a source of reference and inspiration for future research ideas. I would like to express my deep gratitude to my wife, Veranika Ushakova, and Mr. Murugesan Tamilsevan from Springer, who helped at every step of the execution of this project.

New York, NY, USA Belo Horizonte, MG, Brazil Alexander Birbrair

# Contents

1	The Tumor Microenvironment: Focus on Extracellular	
	Matrix. Nathia Nathaly Rigoglio, Ana Carolina Silveira Rabelo, Jessica Borghesi, Gustavo de Sá Schiavo Matias, Paula Fratini, Pedro Henrique Dias Moura Prazeres, Concepta Margaret Mc Manus Pimentel, Alexander Birbrair, and Maria Angelica Miglino	1
2	Keratan Sulphate in the Tumour Environment Anthony J. Hayes and James Melrose	39
3	<b>Hyaluronan in the Tumor Microenvironment</b> Fiorella Mercedes Spinelli, Daiana Lujan Vitale, Ina Sevic, and Laura Alaniz	67
4	Fibronectin in the Tumor Microenvironment Peter Qiao and Zheng-Rong Lu	85
5	Matrix Metalloproteinases' Role in Tumor Microenvironment. Georgina Gonzalez-Avila, Bettina Sommer, A. Armando García-Hernández, and Carlos Ramos	97
6	Flipping the Molecular Switch: Influence of Perlecan and Its Modifiers in the Tumor Microenvironment Lissette A. Cruz, Tristen V. Tellman, and Mary C. Farach-Carson	133
7	<b>Heparan Sulfate in the Tumor Microenvironment</b> Barbara Bartolini, Elena Caravà, Ilaria Caon, Arianna Parnigoni, Paola Moretto, Alberto Passi, Davide Vigetti, Manuela Viola, and Evgenia Karousou	147
8	<b>The Role of Glypican-1 in the Tumour Microenvironment</b> Maria E. Lund, Douglas H. Campbell, and Bradley J. Walsh	163
In	Index	

## Contributors

Laura Alaniz Laboratorio de Microambiente Tumoral, Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional de la Pcia. de Bs. As. Centro de Investigaciones y Transferencia del Noroeste de la Pcia. de Bs. As. (CIT NOBA, UNNOBA-CONICET), Junín, Buenos Aires, Argentina

**Barbara Bartolini** Department of Medicine and Surgery, University of Insubria, Varese, Italy

Alexander Birbrair Department of Radiology, Columbia University Medical Center, New York, NY, USA

Department of Pathology, Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

Jessica Borghesi Department of Surgery, School of Veterinary Medicine and Animal Science, University of Sao Paulo, Sao Paulo, Brazil

Douglas H. Campbell GlyTherix Ltd, Sydney, NSW, Australia

Ilaria Caon Department of Medicine and Surgery, University of Insubria, Varese, Italy

**Elena Caravà** Department of Medicine and Surgery, University of Insubria, Varese, Italy

**Lissette A. Cruz** Department of Diagnostic and Biomedical Sciences, School of Dentistry, The University of Texas Health Science Center at Houston, Houston, TX, USA

**Gustavo de Sá Schiavo Matias** Department of Surgery, School of Veterinary Medicine and Animal Science, University of Sao Paulo, Sao Paulo, Brazil

**Mary C. Farach-Carson** Department of Diagnostic and Biomedical Sciences, School of Dentistry, The University of Texas Health Science Center at Houston, Houston, TX, USA

**Paula Fratini** Department of Surgery, School of Veterinary Medicine and Animal Science, University of Sao Paulo, Sao Paulo, Brazil

**A. Armando García-Hernández** Laboratorio de Oncología Biomédica, Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Mexico City, Mexico **Georgina Gonzalez-Avila** Laboratorio de Oncología Biomédica, Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Mexico City, Mexico

Anthony J. Hayes Bioimaging Research Hub, Cardiff School of Biosciences, Cardiff University, Cardiff, Wales, UK

**Evgenia Karousou** Department of Medicine and Surgery, University of Insubria, Varese, Italy

Maria E. Lund GlyTherix Ltd, Sydney, NSW, Australia

**Zheng-Rong Lu** Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH, USA

**James Melrose** Graduate School of Biomedical Engineering, University of New South Wales, Sydney, NSW, Australia

Raymond Purves Laboratory, Institute of Bone and Joint Research, Kolling Institute, Northern Sydney Local Health District, Royal North Shore Hospital, St. Leonards, NSW, Australia

Sydney Medical School, Northern, The University of Sydney, Faculty of Medicine and Health at Royal North Shore Hospital, St. Leonards, NSW, Australia

**Maria Angelica Miglino** Department of Surgery, School of Veterinary Medicine and Animal Science, University of Sao Paulo, Sao Paulo, Brazil

**Paola Moretto** Department of Medicine and Surgery, University of Insubria, Varese, Italy

Arianna Parnigoni Department of Medicine and Surgery, University of Insubria, Varese, Italy

Alberto Passi Department of Medicine and Surgery, University of Insubria, Varese, Italy

**Concepta Margaret Mc Manus Pimentel** Department of Physiological Science, Institute of Biological Science, University of Brasilia, Brasilia, Brazil

**Pedro Henrique Dias Moura Prazeres** Department of Pathology, Institute of Biological Sciences, Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

**Peter Qiao** Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH, USA

Ana Carolina Silveira Rabelo Department of Surgery, School of Veterinary Medicine and Animal Science, University of Sao Paulo, Sao Paulo, Brazil

**Carlos Ramos** Laboratorio de Biología Celular, Departamento de Fibrosis Pulmonar, Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Mexico City, Mexico **Nathia Nathaly Rigoglio** Department of Surgery, School of Veterinary Medicine and Animal Science, University of Sao Paulo, Sao Paulo, Brazil

**Ina Sevic** Laboratorio de Microambiente Tumoral, Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional de la Pcia. de Bs. As. Centro de Investigaciones y Transferencia del Noroeste de la Pcia. de Bs. As. (CIT NOBA, UNNOBA-CONICET), Junín, Buenos Aires, Argentina

**Bettina Sommer** Departamento de Investigación en Hiperreactividad Bronquial, Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Mexico City, Mexico

**Fiorella Mercedes Spinelli** Laboratorio de Microambiente Tumoral, Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional de la Pcia. de Bs. As. Centro de Investigaciones y Transferencia del Noroeste de la Pcia. de Bs. As. (CIT NOBA, UNNOBA-CONICET), Junín, Buenos Aires, Argentina

**Tristen V. Tellman** Department of Diagnostic and Biomedical Sciences, School of Dentistry, The University of Texas Health Science Center at Houston, Houston, TX, USA

**Davide Vigetti** Department of Medicine and Surgery, University of Insubria, Varese, Italy

Manuela Viola Department of Medicine and Surgery, University of Insubria, Varese, Italy

**Daiana Lujan Vitale** Laboratorio de Microambiente Tumoral, Centro de Investigaciones Básicas y Aplicadas (CIBA), Universidad Nacional de la Pcia. de Bs. As. Centro de Investigaciones y Transferencia del Noroeste de la Pcia. de Bs. As. (CIT NOBA, UNNOBA-CONICET), Junín, Buenos Aires, Argentina

Bradley J. Walsh GlyTherix Ltd, Sydney, NSW, Australia