Current Clinical Oncology
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Marcella Macaluso *Editors*

Gynecological Cancers

Genetic and Epigenetic Targets and Drug Development

Springer

Current Clinical Oncology

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Editors

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Current Clinical Oncology
ISBN 978-3-319-32905-5 ISBN 978-3-319-32907-9 (eBook)
DOI 10.1007/978-3-319-32907-9

Library of Congress Control Number: 2016943122

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG Switzerland

The Editors, on behalf of all the contributors to this book, dedicate this work to all the women who are fighting with gynecologic cancers and to those involved in the research, prevention, treatment, and care of these diseases.

Preface

Over the years, the prevention and treatment of gynecologic cancers has improved as the result of strong multidisciplinary efforts, which allows for early detection of the disease and improved intervention strategies. In this book we have gathered all the molecular and cellular aspects of gynecological cancers together within one volume and provided a comprehensive resource of information on drug discovery and drug development for the treatment of these diseases.

The reader will find an overview of the genetic and epigenetic mechanisms underlying the formation and progression of gynecological cancers as well as detailed, up-to-date information on the etiology, diagnosis, and treatment of these diseases, which include ovarian cancer, uterine cancer, cervical cancer, vaginal cancer, and vulvar cancer. Fertility preservation and available options were also included in the book. In addition, emphasis was placed in providing the public with information on the racial/ethnic disparities in the treatment of gynecological cancers.

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Part I

Epigenetic Mechanisms in Gynecological Cancers

Epigenetic Mechanisms in Gynecological Cancer

1

Gavino Faa, Daniela Fanni, Giuseppina Pichiri, and Clara Gerosa

Abstract

The disruption of epigenetic regulatory mechanisms has been demonstrated to represent the prevalent carcinogenetic actor in cancer, aberrant epigenetic silencing of tumor suppressor genes, mainly due to DNA methylation, representing a relevant mechanism able of modifying the expression of key genes during carcinogenesis. In addition, epigenetic regulation has included microRNAs that regulate gene expression leading to inhibition and/or degradation of RNA target. In recent years, epigenetic silencing has been indicated as one of the major causes of gynecological cancer, being able to inactivate multiple pathways including cell cycle control, DNA repair, and apoptosis. In this chapter, the most important environmental factors interfering with the DNA methylation status in mammalian cells, leading to the insurgence of gynecological tumors will be discussed, including the dietary habits that have been indicated as main actors of DNA methylation. The role of epigenetics in the insurgence of ovarian cancer, endometrial cancer, cervical cancer, and endocervical cancer will be discussed. Finally, the role of microbioma in gynecological cancer insurgence and progression will be discussed. Here, a modern view of the relationship between genetics and epigenetics in gynecological cancer is presented. According to this view, genetics might be seen as a piano, a long one with a keyboard of 25,000 keys each one representing one human gene, whereas epigenetics could be represented by the piano tuner and by the pianist. The epigenetic approach is based on changing the pianist, i.e. the hyper- or hypomethylation status of target genes appears much more promising for the therapy of gynecological cancer than the previous ones based on modifying the piano, i.e. the genetic changes accumulating in tumor cells.

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A. Giordano, M. Macaluso (eds.), *Gynecological Cancers*, Current Clinical Oncology,
DOI 10.1007/978-3-319-32907-9_1