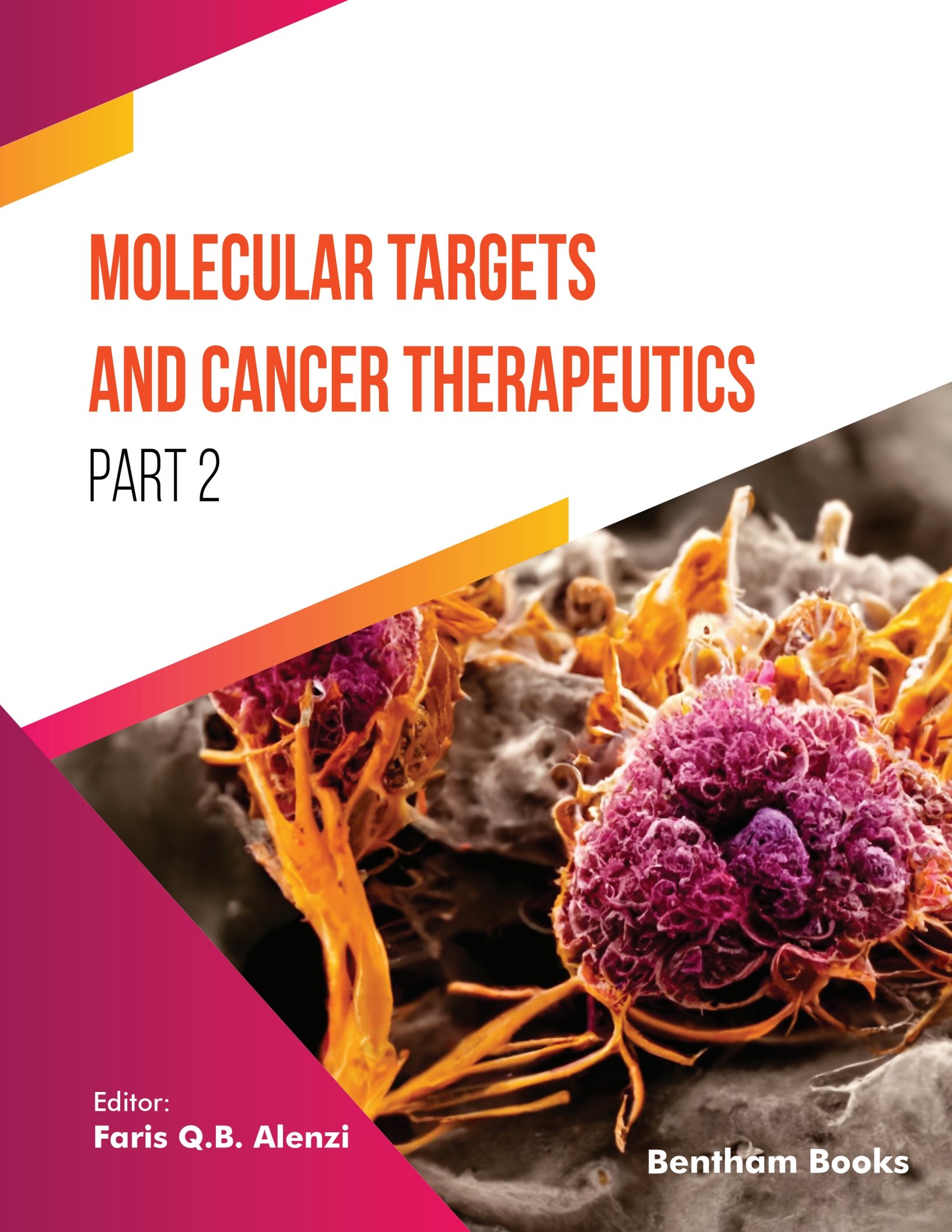


MOLECULAR TARGETS AND CANCER THERAPEUTICS

PART 2

Editor:
Faris Q.B. Alenzi

Bentham Books



Molecular Targets and Cancer Therapeutics (Part 2)

Edited by

Faris Q.B. Alenzi

Professor of Immunology

College of Applied Medical Sciences

Prince Sattam Bin Abdulaziz University

Saudi Arabia

Molecular Targets and Cancer Therapeutics (Part 2)

Editor: Faris Q.B. Alenzi

ISBN (Online): 978-981-5124-60-6

ISBN (Print): 978-981-5124-61-3

ISBN (Paperback): 978-981-5124-62-0

© 2023, Bentham Books imprint.

Published by Bentham Science Publishers Pte. Ltd. Singapore. All Rights Reserved.

First published in 2023.

BENTHAM SCIENCE PUBLISHERS LTD.

End User License Agreement (for non-institutional, personal use)

This is an agreement between you and Bentham Science Publishers Ltd. Please read this License Agreement carefully before using the book/echapter/ejournal (“**Work**”). Your use of the Work constitutes your agreement to the terms and conditions set forth in this License Agreement. If you do not agree to these terms and conditions then you should not use the Work.

Bentham Science Publishers agrees to grant you a non-exclusive, non-transferable limited license to use the Work subject to and in accordance with the following terms and conditions. This License Agreement is for non-library, personal use only. For a library / institutional / multi user license in respect of the Work, please contact: permission@benthamscience.net.

Usage Rules:

1. All rights reserved: The Work is the subject of copyright and Bentham Science Publishers either owns the Work (and the copyright in it) or is licensed to distribute the Work. You shall not copy, reproduce, modify, remove, delete, augment, add to, publish, transmit, sell, resell, create derivative works from, or in any way exploit the Work or make the Work available for others to do any of the same, in any form or by any means, in whole or in part, in each case without the prior written permission of Bentham Science Publishers, unless stated otherwise in this License Agreement.
2. You may download a copy of the Work on one occasion to one personal computer (including tablet, laptop, desktop, or other such devices). You may make one back-up copy of the Work to avoid losing it.
3. The unauthorised use or distribution of copyrighted or other proprietary content is illegal and could subject you to liability for substantial money damages. You will be liable for any damage resulting from your misuse of the Work or any violation of this License Agreement, including any infringement by you of copyrights or proprietary rights.

Disclaimer:

Bentham Science Publishers does not guarantee that the information in the Work is error-free, or warrant that it will meet your requirements or that access to the Work will be uninterrupted or error-free. The Work is provided "as is" without warranty of any kind, either express or implied or statutory, including, without limitation, implied warranties of merchantability and fitness for a particular purpose. The entire risk as to the results and performance of the Work is assumed by you. No responsibility is assumed by Bentham Science Publishers, its staff, editors and/or authors for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products instruction, advertisements or ideas contained in the Work.

Limitation of Liability:

In no event will Bentham Science Publishers, its staff, editors and/or authors, be liable for any damages, including, without limitation, special, incidental and/or consequential damages and/or damages for lost data and/or profits arising out of (whether directly or indirectly) the use or inability to use the Work. The entire liability of Bentham Science Publishers shall be limited to the amount actually paid by you for the Work.

General:

1. Any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims) will be governed by and construed in accordance with the laws of Singapore. Each party agrees that the courts of the state of Singapore shall have exclusive jurisdiction to settle any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims).
2. Your rights under this License Agreement will automatically terminate without notice and without the

need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.

3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

Bentham Science Publishers Pte. Ltd.

80 Robinson Road #02-00

Singapore 068898

Singapore

Email: subscriptions@benthamscience.net



CONTENTS

PREFACE	i
DEDICATION	ii
LIST OF CONTRIBUTORS	iii
CHAPTER 1 CANCER TYPES	1
<i>Amal F. Alshammary, Mashael Al-Toub, Maha F. Almutairi, Mohammed Bakar, Haifa F. Alshammary, Arwa F.Q.B. Alanazi, Amani F.Q.B. Alanazi, Norah A. Alturki, Haifa Alhawas and Asma Alanazi</i>	
INTRODUCTION	2
Definition	2
Nomenclature	3
CHARACTERISTICS OF BENIGN AND MALIGNANT TUMOURS	4
CLASSIFICATION	6
Carcinoma	6
<i>Lung Cancer</i>	7
<i>Breast Cancer</i>	16
<i>Pancreatic Cancer</i>	19
<i>Prostate Cancer</i>	23
Types of Prostate Cancer	25
<i>Acinar Adenocarcinoma</i>	25
<i>Prostatic Ductal Adenocarcinoma</i>	25
<i>Transitional Cell or Urethral Cancer</i>	25
<i>Squamous Cell Cancer</i>	25
<i>Small Cell Prostate Cancer</i>	25
<i>Neuroendocrine Tumors</i>	26
<i>Sarcoma</i>	26
Pathophysiology	26
Approach to Diagnosis and Further Assessment	26
Colorectal Cancer	28
<i>Epidemiology and Risk Factors</i>	28
<i>Symptoms</i>	29
<i>Screening</i>	29
Cervical Cancer	31
<i>Epidemiology</i>	31
<i>Pathophysiology</i>	31
Sarcoma	33
<i>Bone Tumor</i>	33
<i>Cartilage Tumor</i>	35
<i>Liposarcoma</i>	37
<i>Brain Tumor</i>	40
Mixed-Origin Carcinoma-Sarcoma Tumors	41
<i>Gastrointestinal Cancer</i>	41
Melanoma	43
<i>Skin Cancer</i>	43
Hematological Malignancies	46
<i>Leukemia</i>	46
<i>Lymphoid Malignancy</i>	60
Germ Cell Tumors	71
<i>Testicular Germ Cell Tumors</i>	71

<i>Ovarian Germ Cell Tumors</i>	72
Blastoma	76
<i>Neuroblastoma</i>	76
CONCLUSION	77
CONSENT FOR PUBLICATION	77
CONFLICT OF INTEREST	78
ACKNOWLEDGEMENTS	78
REFERENCES	78
CHAPTER 2 DIAGNOSIS OF CANCER	96
<i>Fayez Alelyani, Anas Abdulhamid Sedayo, Mashaal Al-Toub and Adnan Alwatban</i>	
INTRODUCTION	96
BIOPSY	97
ENDOSCOPY	99
DIAGNOSTIC IMAGING	101
The Use of Imaging Diagnoses	102
Imaging Tests are Used for Cancer in Many Ways	104
Perfections of Imaging Diagnosis	104
Imaging Scan Types	105
BLOOD TESTS (TUMOR MARKERS)	105
Tumor Markers (Cancer Biomarkers)	106
Circulating Tumor Markers	107
<i>CTCs</i>	112
<i>CEA</i>	112
<i>PSA</i>	113
CONCLUSION	114
CONSENT FOR PUBLICATION	115
CONFLICT OF INTEREST	115
ACKNOWLEDGEMENT	115
REFERENCES	115
CHAPTER 3 TREATMENT OF CANCER	122
<i>Naif AlEnazi, Ayisha Q. Alanazi, Mohammed W. Al-Rabia and Fahad Albisi</i>	
INTRODUCTION	122
Types of Cancer Surgery	123
DIAGNOSTIC SURGERY	123
Open Biopsy	124
Advantages of Open Biopsy	124
Disadvantages of Open Biopsy	124
<i>Incisional Biopsy</i>	125
<i>Punch Biopsy</i>	126
<i>Excisional Biopsy</i>	126
Needle Biopsy	127
<i>Fine-Needle Aspiration</i>	128
<i>Core Needle Biopsy</i>	128
ENDOSCOPY	130
Laparoscopy	131
Laparotomy	131
Analysis of the Biopsy Results	132
STAGING SURGERY	133
Clinical Staging and Pathological Staging	133
Sentinel Lymph Node Mapping and Biopsy	134

CURATIVE SURGERY	135
Types of Curative Surgery	136
<i>Excisional Surgery</i>	136
<i>Laser Surgery</i>	136
<i>Cryosurgery</i>	137
<i>Electrosurgery</i>	138
<i>Mohs Micrographic Surgery</i>	139
Preoperative or Post-Operative Chemotherapy and Radiation	140
Preoperative Chemotherapy and Radiation	140
Post-Operative Chemotherapy and Radiation	140
Preoperative Chemotherapy with Post-Operative Radiation Therapy	141
DEBULKING	141
Patient Suitability for Debulking	141
Debulking for Ovarian Cancer	142
Complications of Debulking	142
PALLIATIVE SURGERY	143
Bowel Surgery	143
Palliative Mastectomy	144
Suture Ligation	144
Insertion of a Feeding Tube	144
Prevent Broken Bones	144
PREVENTATIVE SURGERY	144
Mastectomy	145
Oophorectomy	146
Colectomy	146
Thyroidectomy	146
Removal of Precancerous Polyps	146
RECONSTRUCTIVE SURGERY	146
Breast Reconstructive Surgery	147
Head and Neck Restorative Surgery	147
ACCESS SURGERY	148
PRACTICALITIES OF SURGERY	148
Before Surgery	148
Prepping for Surgery	149
After Surgery	149
Palliative Treatment	150
Soft Tissue Cancer of the Head and Neck (Except Salivary Glands and Thyroid Gland)	150
Skin	151
Malignant Melanoma (Including Skin, Ocular, or Mucosal Melanomas), as Described in Either A, B, or C	151
Soft Tissue Sarcoma	152
Lymphoma (Including Mycosis Fungoides but Excluding T-Cell Lymphoblastic Lymphoma)	152
Leukemia	152
Multiple Myeloma (Confirmed by Appropriate Serum or Urine Protein Electrophoresis and Bone Marrow Findings)	153
Salivary Glands: Carcinoma or Sarcoma with Metastases Beyond the Regional Lymph Nodes	153
<i>Thyroid Gland</i>	153
<i>Breast (Except Sarcoma)</i>	154
<i>Skeletal System (Sarcoma)</i>	154

<i>Maxilla, Orbit, or Temporal Fossa</i>	155
<i>Nervous System</i>	155
<i>Lungs</i>	156
<i>Pleura or Mediastinum</i>	156
<i>Esophagus or Stomach</i>	156
Small Intestine: Carcinoma, Sarcoma, or Carcinoid	157
Large Intestine: (from Ileocecal Valve to and Including Anal Canal)	157
Liver or Gallbladder: Cancer of the Liver, Gallbladder, or Bile Ducts Pancreas	157
Kidneys, Adrenal Glands, or Ureters Carcinoma	158
Urinary Bladder Carcinoma	158
Cancers of the Female Genital Tract-Carcinoma or Sarcoma (Including Primary Peritoneal Carcinoma)	158
Prostate Gland: Carcinoma	159
CONCLUSION	160
CONSENT FOR PUBLICATION	160
CONFLICT OF INTEREST	161
ACKNOWLEDGEMENT	161
REFERENCES	161
CHAPTER 4 IMMUNOTHERAPY AND CANCER STEM CELLS	165
<i>Ravi Teja Chitturi Suryapakash, Mohammad Ayman Abdulkarim Safi, Noufa Alonazi, Ahdab A. Alsaieedi cpf Omar Kujan</i>	
INTRODUCTION	166
MONOCLONAL ANTIBODIES (MABS)	166
Classification of Chemotherapeutic Monoclonal (CmMab) Antibodies	167
Mechanism of Action of Monoclonal Antibodies for the Treatment of Cancer	168
<i>Constraint and Cost</i>	170
TARGETED THERAPY USING SMALL MOLECULES	171
Small Molecules Blocking PD1 and PD-L1	171
<i>Small Molecules Blocking IDO1</i>	172
Small Molecules Targeting Tregs	173
Small Molecules Activating Toll-Like Receptors (TLRs)	173
Small Molecules Activating cGAS/STING Pathway	174
Small Molecules Targeting Chemokine Receptors	175
<i>Other Small Molecule Inhibitors</i>	175
LIGAND TARGETED THERAPY	176
Transforming Growth Factor β (TGF- β)	176
<i>NKG2D Signalling Pathway</i>	177
<i>B7 Family of Immune-Regulatory Ligands</i>	177
Targeting CSC by CAR T-Cells	178
Targeting CSC by Dendritic Cell-Based Vaccines	179
CANCER STEM CELL-TARGETED IMMUNOTHERAPY	179
Targeting CSC by Oncolytic Viruses	180
Cancer Immunotherapy	181
NON-SPECIFIC TUMOR IMMUNOTHERAPY	181
Targeting Pattern Recognition Receptors (PRRs)	181
Cytokine Based Therapy	184
Immune Checkpoint Blockage	185
SPECIFIC IMMUNOTHERAPY	187
Adoptive T Cell Transfer	187
Tumor-Infiltrating Lymphocytes (TILs) Therapy	188

TCR Gene Therapy	189
CAR T-Cell Therapy	191
Vaccination	193
Coley's Vaccine (Toxin)	194
Fusion (Loading) of Human Dendritic Cell	195
<i>General Information About Dendritic Cell</i>	195
<i>Method of Preparation</i>	197
Gen Vaccines (DNA and RNA Vaccines)	198
<i>Vaccines using Viral Vectors</i>	199
Tumor-Associated Antigens <i>Versus</i> Tumor Neoantigens Vaccines	201
CONCLUSION	202
CONSENT FOR PUBLICATION	202
CONFLICT OF INTEREST	202
ACKNOWLEDGEMENTS	202
REFERENCES	202
CHAPTER 5 NANOTECHNOLOGY AND PRECISION MEDICINE	236
<i>Noufa Alonazi, Talat Abdullah Albukhari cpf Naif M. Alruwaili</i>	
INTRODUCTION	237
Unique Roles of Nanotechnology in Cancer	237
The Role of Nanotechnology in Cancer	238
Nanotechnology and Cancer	238
Passive Tumor Accumulation	239
Active Tumor Targeting	240
Transport Across Tissue Barriers	241
DELIVERING NANOMEDICINE TO SOLID TUMORS	242
INTRODUCTION	242
BARRIERS TO NANOMEDICINE DELIVERY	243
POOR BLOOD PERFUSION	244
ELEVATED IFP	244
ECM DENSE	245
HIGH TUMOR STROMAL CELLS (TSC)	245
MODULATION OF THE TUMOR MICROENVIRONMENT	246
Tumor Perfusion Enhancement	246
ENHANCEMENT OF NANOMEDICINE EXTRAVASATION	248
ENHANCEMENT OF INTERSTITIAL TRANSPORT OF NANOMEDICINES	251
ELECTROCHEMOTHERAPY	255
INTRODUCTION	255
PRINCIPLE OF ECT	256
APPLICATION OF ECT IN MEDICINE	257
ADVANTAGES AND DISADVANTAGES OF ECT	259
Advantages	259
Disadvantages	259
POTENTIAL AND CHALLENGES	260
CONCLUSION	260
CONSENT FOR PUBLICATION	261
CONFLICT OF INTEREST	261
ACKNOWLEDGEMENTS	261
REFERENCES	261
CHAPTER 6 CANCER SURVEILLANCE	271

Amal F. Alshammary, Mashael Al-Toub, Talat Abdullah Albukhari cpf Waheed A. Filimban

INTRODUCTION TO CANCER SURVEILLANCE	272
NON-IMMUNE SURVEILLANCE	273
Genetic Surveillance	273
Epigenetic Surveillance	274
Intracellular Surveillance	275
Intercellular Surveillance	277
IMMUNE SURVEILLANCE	278
OVERVIEW OF IMMUNE SURVEILLANCE	279
Historical Perspective	279
Evidence for and Against Immune Surveillance	280
Tumor Antigens	281
<i>Definition</i>	282
<i>Classification</i>	282
A New Approach to Immunosurveillance	284
MECHANISMS OF TUMOR IMMUNOEDITING	284
Elimination	285
Equilibrium	286
Escape	287
Role of Innate and Adaptive Immunity During the Elimination	288
<i>T Cells</i>	288
<i>Effect of Tregs on NKT Cells</i>	289
<i>Effect of $\gamma\delta$ T Cells and NKT Cells</i>	290
How Immunosurveillance Recognises Cancer	290
EVIDENCE OF IMMUNOEDITING IN ANIMAL MODELS	292
Overview of Mice Models	293
<i>Spontaneous Tumor Development in Immunodeficient Mice</i>	295
<i>Carcinogen-Induced Tumors in Immunodeficient Mice</i>	297
Components Implicated in Animal Immunoeediting	299
EVIDENCE FOR CANCER IMMUNOEDITING IN HUMANS	300
Immunosuppressed Patients	300
Microsatellite Instability in Human Tumors	302
Human Tumor-Infiltrating Lymphocytes	303
Paraneoplastic Autoimmune Syndromes	305
WHY DOES IMMUNE SURVEILLANCE FAIL?	306
HLA Class I Defects	307
T Cell Immune Dysfunction	309
Dendritic Cell System Malfunction	314
CANCER PREVENTION AND SCREENING	315
Cancer Prevention	316
<i>Policy and Action for Cancer Prevention</i>	317
<i>Diet and Cancer Prevention</i>	318
Cancer Screening	320
<i>Balancing the Benefits and Screening Risks</i>	321
<i>Optimizing Screening Participation</i>	322
<i>Discrete Factors of Cancer Screening Involvement</i>	322
CONCLUSION	324
CONSENT FOR PUBLICATIONS	326
CONFLICT OF INTEREST	327
ACKNOWLEDGEMENTS	327
REFERENCES	327
SUBJECT INDEX	564

PREFACE

Cancer is a complex disease that affects all anatomical sites in the human body, causing a significant global health burden since it is considered the second leading cause of death worldwide. Recent advances in science and technology have improved the understanding of cancer evolution to discover new effective therapies. This book provides a state-of-art review of advances in cancer, including a broad overview of cancer classifications, surveillance, diagnosis and cancer treatment with a focus on innovative therapeutic approaches, such as immunotherapy, vaccines, nanomedicine, and precision medicine, in addition to cancer's surveillance.

Faris Q.B. Alenzi

Professor of Immunology
College of Applied Medical Sciences
Prince Sattam Bin Abdulaziz University
Saudi Arabia

DEDICATION

I dedicate this book to those who lost their lives because of this disease. May Allah bless them all!

To,

Fatema S. Albady Alanazi

Talal H. Almosaieed Alanazi

Saeed A. Baqader

Abdulla S. Alsiary

Moqaeem A. Alanazi

Nadda F. Alhassainan

Shaikha A. Alhabrdi

Hawazn W. Alnaam

Halah F. Alnaam

Hanan G. Alanazi

Eida S. Alhussani

Fryah A.M. Alshammari

Abdulrahman Zekri

Ghaytha Alshammari

List of Contributors

Adnan Alwatban	Radiology Department, KFMC, Riyadh, Saudi Arabia
Ahdab A. Alsaieedi	Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences, King Abdulaziz University, Riyadh, Kingdom of Saudi Arabia
Amal F. Alshammary	Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia
Amani F.Q.B. Alanazi	Department of RT, Al-Marafah University, Riyadh, Saudi Arabia
Anas Abdulhamid Sedayo	Radiology Department, Maternity and Children Hospital, Ministry of Health, Makkah, Saudi Arabia
Arwa F.Q.B. Alanazi	Department of Dentistry, Riyadh Elm University, Riyadh, Saudi Arabia
Asma Alanazia	College of Medicine, King Saud bin Abdulaziz University for Health Sciences (KSAU-HS), Riyadh, Saudi Arabia
Ayisha Q. Alanazi	Department of Pharmacy, KAMC, Riyadh, Saudi Arabia
Fahad Albisi	Department of Surgery, Military Hospital, Riyadh, Saudi Arabia
Fayez Alelyani	Department of Neurological Surgery, King Khalid University, Medical City Abha, Saudi Arabia
Haifa Alhawas	College of Medicine, King Saud Bin Abdulaziz for Health Sciences, Riyadh, Saudi Arabia
Haifa F. Alshammary	College of Applied Medical Sciences, Riyadh Elm University, Riyadh, Saudi Arabia
Maha F. Almutairi	College of Medicine, Dar Al Uloom University, Riyadh, Saudi Arabia
Mashaël Al-Toub	Department of Clinical Laboratory Sciences, College of Applied Medical Sciences King Saud University, Riyadh, Saudi Arabia
Mohammad Ayman Abdulkarim Safi	Department of Medical Microbiology and Parasitology, Faculty of Medicine, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia
Mohammed Bakar	Department of Medicine, Prince Mohamed bin Nasser Hospital, Jazan, Saudi Arabia
Mohammed W. Al-Rabia	Department of Clinical Microbiology and Immunology, King Abdulaziz University, KAU Hospital, Jeddah, Saudi Arabia
Naif M. Alruwaili	Department of RT, Prince Mohamed Hospital, Riyadh, Saudi Arabia
Naif AlEnazi	Department of Surgery, Al-Diriyah Hospital, Riyadh, Saudi Arabia
Norah A. Alturki	Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia
Noufa Alonazi	Department of Paediatrics, Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia
Omar Kujan	UWA Dental School, The University of Western Australia, Nedlands, 6009 WA, Australia

iv

Ravi Teja Chitturi	UWA Dental School, The University of Western Australia, Nedlands,
Suryaprakash	6009 WA, Australia
Talat Abdullah Albukhari	Um Al Qura University, Makkah, Saudi Arabia
Waheed A. Filimban	Pathology Department, Faculty of Medicine, Um Al Qura University, Makkah, Saudi Arabia

CHAPTER 1**Cancer Types**

Amal F. Alshammary^{1,*,#}, Mashaal Al-Toub^{1,*,#}, Maha F. Almutairi², Mohammed Bakar³, Haifa F. Alshammary⁴, Arwa F.Q.B. Alanazi⁵, Amani F.Q.B. Alanazi⁶, Norah A. Alturki¹, Haifa Alhawas⁷ and Asma Alanazi^{7,8}

¹ Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia

² College of Medicine, Dar Al Uloom University, Riyadh, Saudi Arabia

³ Department of Medicine, Prince Mohamed bin Nasser Hospital, Jazan, Saudi Arabia

⁴ College of Applied Medical Sciences, Riyadh Elm University, Riyadh, Saudi Arabia

⁵ Department of Dentistry, Riyadh Elm University, Riyadh, Saudi Arabia

⁶ Department of RT, Al-Marafah University, Riyadh, Saudi Arabia

⁷ College of Medicine, King Saud Bin Abdulaziz University for Health Sciences (KSAU-HS), Riyadh, Saudi Arabia

⁸ King Abdullah International Medical Research Center, Riyadh, Saudi Arabia

Abstract: Normally, to replace damaged cells or for the purpose of growth, healthy cells can divide according to the proliferation potency, in a systematic and controlled manner. When this mechanism is interfered with in such a way that the cell multiplies beyond the control system, a neoplasm may originate. The name (neoplasm) comes from the ancient Greek words *neo*, which means “new,” and *plasma*, which means “creation, formation.” Even after the underlying trigger is removed, a neoplasm's growth is disorganized with that of the healthy surrounding tissue, and it continues to grow abnormally. When this abnormal neoplastic growth creates a mass, it is referred to as a “tumor”. There are four primary types of neoplasms (tumor): benign (non-cancerous), *in situ*, malignant (cancerous), and neoplasms of unclear or unidentified behaviour, which follow the pattern of cell development. Oncology is concerned with malignant neoplasms, which are commonly known as malignancies or cancers. In Oncology, many cancer classifications emerged, however, the most notable of which is based on the nomenclature by the type of tissue from which it arises, or by the primary site in the body where it originally appeared. Herein, this chapter will go over the definition of cancer, classifications as well as the key differences between the types of cancers. This chapter will also cover the pathophysiology and epidemiology of the many types of cancers.

Keywords: Cancer, Carcinoma, Neoplasm, Pathophysiology, Sarcoma, Tumors.

* Corresponding authors Amal F. Alshammary & Mashaal Al-Toub: Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia;
E-mails: aalshammary@ksu.edu.sa, altoub@ksu.edu.sa

Contributed equally.

Faris Q.B. Alenzi (Ed.)

All rights reserved-© 2023 Bentham Science Publishers

INTRODUCTION

Cancer is a prominent cause of death across the globe, as each year has caused millions of deaths on a global scale. The threatening nature of the diseases has a significant impact across the social, health, and economic burdens, amongst all other diseases. While it is not the main cause of mortality in all countries, it exerts a significant burden to be among the top five leading causes of death. Globally, WHO (2021) reports that cancer killed at least ten million people in 2020 and was the leading cause of death. Cancer is of many types, and many of them are yet to have a significantly established cause and cure. This chapter will examine the understanding of cancer so far and explore established classifications based on their origin.

Definition

Cancer is a general term used to refer to hundreds of diseases that occur anywhere in the body as a result of abnormal cell growth [1]. The abnormalities result from numerous factors and arise from different body parts; leading to a classification system to allow ease of identification. Cancer cells are also known as malignant cells, depending on the course of their progression. Cancer development has numerous risk factors that could lead to the abnormal growth of cells. Many factors have been put forward, including environmental or personal factors. These include certain viruses such as the Human Papilloma Virus, radiation, certain chemical compounds, genetics, dietary problems, age, stress, hormones such as estrogen, and many others [2].

The onset of cancer is marked with signs and symptoms like any other disease, which are reliant on the type of cancer. The location, for example, can be a determining factor in what symptoms would be felt first. For example, cancer located in the brain regions could have major symptoms of seizures, while for breast cancer, lumps on the breast could be felt. However, in some forms of cancer, the symptoms often do not appear until it is too late [3]. However, some general signs and symptoms are recommended to follow up on in case they occur, including but not limited to loss of appetite and weight for no reason, persistence in nausea and fatigue, increasing pain in parts that were not so before, and recurrent infections without reason.

Cancer development is not straightforward, and the presence of a carcinogen does not always imply it will develop. A series of complex processes and procedures are always inhibited at every stage through the body's defence mechanisms. However, upon failure of these mechanisms, cancer will develop through a series of changes that allow the carcinogens of agents in the body to produce factors that

promote tumor growth. These carcinogens often target the cells at the DNA level to destroy or reduce the function of these cells to carry out their expected roles and thus, over time, render the cell a good site to start developing uncontrollable growth. Sometimes these cells escape and move from their initial site to neighbouring cells and cause further damage to these new cells, thus causing significant spread.

Nomenclature

Cancers are classified into numerous categories, as mentioned depending on the site or origin or the cause. The classification into the correct types through naming is known as nomenclature. According to Singer *et al.*, the process is critical for various reasons, including ensuring a correct diagnosis [4]. Discovering the right type of cancer means that the response would be highly specific since different types of cancers have their own responses and therapeutics that would be best for the patient at that given time. For example, breast cancer might be treated differently from brain cancer due to the location of the tumors. Since cancers are not fully understood, researchers are still building profiles and uncovering new information about the different types of cancers that occur in people. Therefore, having the right naming system can help researchers further understand what they are dealing with. It has also been shown that correct naming and identification of cancer allows oncologists to inform the patient more clearly on the progression of the disease, the aetiology, and expectations. Most importantly, the different types of cancers are now being studied using far more advanced methods, such as biomarker studies that have identified specific genes and molecules within the body that could be targeted far more precisely compared to if randomised studies were used. A good example is the identification of the HER2+ gene; a growth factor that impacts women to cause aggressive breast cancer and has a high fatality rate. By correctly identifying whether women with breast cancer are positive for the gene, they can be treated with advanced medication specifically made for the gene, and their progress tracked using biomarker studies, thus increasing the chances of quickly identifying what works and what works does not. This is because, as mentioned, there are hundreds of cancers and not all are well understood. Therefore, nomenclature becomes essential.

As cancer is a collection of diseases rather than a single disease, arising from different parts, the nomenclature is based on the origin of the cell as well as the possible cause. This is so because the biological properties in the cells provide a common origin or shared characteristics. As the cancer cells develop, they involve numerous tissues, carcinogens, and mechanisms, thus, tracking it based on where it affects has been seen as not ideal to some degree. One of the most common

Diagnosis of Cancer

Fayez Alelyani^{1,*}, Anas Abdulhamid Sedayo², Mashaal Al-Toub³ and Adnan Alwatban⁴

¹ Department of Neurological Surgery, King Khalid University, Medical City Abha, Saudi Arabia

² Radiology Department, Maternity and Children Hospital, Ministry of Health, Makkah, Saudi Arabia

³ Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia

⁴ Radiology Department, KFMC, Riyadh , Saudi Arabia

Abstract: Cancer has a higher chance of being cured when it is diagnosed, detected, and treated early. Diagnosis of cancer in its early stages also results in the highest chance of survival with the improvement of lifestyle of cancer patients. A comprehensive physical exam and a full family medical history are needed before a cancer diagnosis can be made. Self-examination or other screening procedures will normally detect visible forms of cancers, such as melanoma and breast cancer, before the condition progresses. However, several forms of other types of cancer are discovered and diagnosed after disease development and severe signs have already occurred. This chapter discusses the diagnostic approaches that are often utilized to aid in the diagnosis of cancer.

Keywords: Biopsy, Cancer, Diagnosis, Endoscopy, Imaging, Sample, Tumors Markers, Tumor.

INTRODUCTION

Cancer is suspected depending on a person's symptoms, physical examination results, and, in some cases, screening test results. Screening procedures are used to predict the presence of a disease before symptoms appear. Until performing screening tests, the physicians will evaluate whether the patient has any risk factors for cancer due to age, gender, family background, previous history, or lifestyle. Further examination confirms or disproves the results. When a physician suspects a patient has cancer, diagnostic tests are performed. As cancer is discove-

* Corresponding author Fayez Alelyani: Department of Neurological Surgery, King Khalid University, Medical City Abha, Saudi Arabia; E-mail: m.almakhfor@kku.edu.sa

red, staging testing can help assess how advanced the cancer is in terms of its spread. When cancer is diagnosed, staging tests help assess the extent of the disease in terms of its position, size, and metastasis to proximal or distal organ systems. Staging tests help physicians to assess the best course of treatment as well as the prognosis. The primary goal of this chapter is to improve our comprehension of widely used cancer diagnosis strategies: Biopsy, Endoscopy, Diagnostic Imaging and Blood tests.

BIOPSY

Tumor biopsy is the cornerstone of the diagnostic approaches for most of the tumors in the human body. It provides a significant amount of information for oncologists and radiotherapists regarding a histopathological diagnosis, staging of the disease and genetic profile for the tumors, to guide diagnostic and therapeutic approaches [1]. With the rapid growth of imaging and image guidance technologies, the utilization of the biopsies technique has advanced significantly. It is, usually, performed by either surgeons or/and interventional radiologists [2].

Nowadays, image-guided percutaneous biopsies are widely adopted as an abridgment of molecular and biomarker methodology. This approach has several benefits, including detecting prognosis, planning a therapeutic response, assessing treatment resistance, and detecting disease progression. Therefore, biopsies are essential in clinical trials where we aim to evaluate the effects of drugs, identify the most related biomarkers and detect genetic mutations of the tumors [3].

We can associate biopsies adoption expansion with the increased integration of biomarker studies into clinical trials [4 - 6]. In the past, obtaining samples from metastatic tumors is known to be challenging due to logistical reasons since most of those metastatic lesions are inoperable. Accordingly, the demand increased to create a new biospecimen methodology for an easier, safer, and more efficient method for metastatic lesion analysis.

Clinical biopsy-type specimens, such as liquid biopsies, are considered next-generation biospecimens. Usually, it is collected from tissues at predetermined time points according to a prespecified treatment plan. Thereafter, the collected samples are ready for further analysis using multidimensional high-throughput technologies. The aforementioned analysis can use either a targeted approach or a global (comprehensive) approach. The former is utilized to evaluate cases such as cancer-related alterations, while the latter is used for sequencing of whole genome and epigenetic profiling, for instance [7, 8]. In contrast to this approach, the conventional hospital-based biobanks generally consist of specimen sections collected from surgical resection, which are mostly the residue of primary tumors

used for diagnostic purposes [9 - 12]. Table 2.1 illustrates the differences between traditional tumor biobanks and next-generation biobanks.

Table 2.1. The table illustrates the differences in variables between the traditional tumor techniques vs. next-generation tumor sampling.

Variables	Traditional Tumor Biobank	Next-Generation Tumor Biobank
Sample collector	Pathologists and surgeons	Interventional radiologists, surgeons, pulmonologists, dermatologists, and other physicians
Biopsy location	Primary site (usually surgical excisions)	Either primary recurrence or mets to other organ systems
Quantity of the biopsy	Abundant	Minimal
Time of collection	Initial diagnosis	Various time points
Sample preservation method	FFPE or Flsh-frozen	FFPE, Flash-Frozen, collected in tissue preserver, or OCT-embedded
Sample sharing	Common	Uncommon
Clinical data	Limited	Detailed

Abbreviations: Mets, Metastasis; FFPE, formalin-fixed paraffin-embedded tissue; OCT, optimal cutting temperature compound.

Different types of cancers respond to the same targeted therapy, although they harbor the exact same mutations. Hence, conventional histopathology derives its BRAF V600E mutations are frequent in skin cancer and central nervous system astrocytoma patients with excellent response rates to BRAF inhibitors. Contrary to colorectal cancer cases with the same mutation, the latter demonstrates an inadequate response rate [13]. In the field of surgery, several studies have confirmed that micropapillary and solid histologic subtypes are predictors of inadequate prognosis and high local recurrence, even in entirely surgical excision early-stage lung adenocarcinomas. This demonstrates the significance of the histological classification of invasive lung adenocarcinoma tumors with respect to recurrence patterns and post-recurrence survival rate [14, 15]. The limited knowledge we possess regarding the molecular correlates of the aforementioned subtypes generates a poor understating of this issue, indicating the importance of histological classification and genetic profiles of each tumor.

Regardless of the significant progress in molecular tumor characterization, some issues have remained unresolved thus far. These issues jeopardize our ability to move forward in molecular medicine. For instance, a large phase II precision trial was discontinued due to a temporary analysis indicating that only 87% of submitted cases were good enough to be used for tumor testing [16]. In addition,

Treatment of Cancer

Naif AlEnazi^{1,*}, Ayisha Q. Alanazi², Mohammed W. Al-Rabia³ and Fahad Albisi⁴

¹ Department of Surgery, Al-Diriyah Hospital, Riyadh, Saudi Arabia

² Department of Pharmacy, KAMC, Riyadh, Saudi Arabia

³ Department of Clinical Microbiology and Immunology, King Abdulaziz University, KAU Hospital, Jeddah, Saudi Arabia

⁴ Department of Surgery, Military Hospital, Riyadh, Saudi Arabia

Abstract: Surgery, the oldest cancer treatment, is a mainstay in the cure and control of most cancers. Indeed, for many patients, surgery, usually in combination with chemotherapy, is the only hope for long-term survival or cure. But surgery can do more than treat cancer; it can also diagnose cancer (diagnostic surgery), investigate cancer further (staging surgery), debulk tumors (debulking surgery), relieve pain (palliative surgery), prevent cancer from occurring in the first place (preventative surgery), restore the appearance or function of the body after cancer surgery (reconstructive surgery) and help medical staff to administer chemotherapy (access surgery). This chapter looks at each of these purposes of cancer surgery in detail.

Keyword: Biopsy, Cancer, Endoscopy, Resection, Surgery.

INTRODUCTION

Cancer is one of the leading causes of death worldwide [1]. More than a quarter of people will be affected by cancer at some point in their lives [2]. There are many types of cancer treatments, of which surgery is the oldest. Surgery, where a surgeon cuts the tumor from the patient's body, is also one of the most common cancer treatments. Still to this day, surgery remains a mainstay in the cure and control of most cancers. This chapter will discuss cancer surgery in detail.

* Corresponding author Naif AlEnazi: Department of Surgery, Al-Diriyah Hospital, Riyadh, Saudi Arabia; Email: Dr.NaifAlEnazi@gmail.com

Types of Cancer Surgery

When people hear the term ‘cancer surgery’, they usually think of the removal of cancer from a patient’s body. However, it is important to understand that there are many other reasons why cancer patients have surgery. The most common reasons cancer patients have surgery are:

- **Diagnostic surgery** to determine whether a patient has cancer or not.
- **Staging surgery** to determine where the cancer is located, whether the cancer has spread and whether the cancer affects other organs in the body.
- **Curative surgery** to try to remove the cancer from the body and cure the patient.
- **Debulking surgery** to remove some, but not all, of a cancer tumor. This is not the ideal option, but it can be the only option in cases where removing an entire tumor (curative surgery) might damage an organ or the body.
- **Palliative surgery** to ease cancer symptoms in late-stage cancer patients.
- **Preventative surgery** to prevent cancer from occurring in the first place.
- **Reconstructive surgery** to restore function and normal appearance after curative surgery.
- **Access surgery** to make it easier for doctors and nurses to administer chemotherapy medications.

This chapter will now discuss each of these types of cancer surgery in turn.

DIAGNOSTIC SURGERY

Before cancer is treated, the medical team must get an accurate diagnosis. Sometimes cancer can be diagnosed based on the patient’s history, physical tests, lab tests, and imaging studies alone. However, these methods can be unreliable. To get the most accurate diagnosis, by far, the most reliable and common way is surgery.

When doctors perform surgery for diagnosis reasons, it is called ‘diagnostic surgery’ or a tissue diagnosis. This is where a surgeon makes an incision into the skin and removes some or all of the suspicious tissue. A pathologist then examines the tissue under a microscope and writes a report based on the finding.

Diagnostic cancer surgery comes with risks because cutting into any patient is invasive. Complications of surgery include hematoma, wound problems and can even spread the tumor. The goal of any biopsy is to obtain an adequate amount of tissue for a pathologist to make an accurate diagnosis, in the least invasive

manner, while avoiding risks and avoiding jeopardizing future surgical management.

Because every patient is different, many different techniques have evolved to diagnose cancer. These techniques vary depending on the type of cancer, its location, and the patient. The main techniques are open biopsy, needle biopsy, endoscopy and laparotomy, which will now be discussed in detail.

Open Biopsy

Open biopsy is known by several other names, including surgical biopsy, wide local excision, wide local surgical biopsy, incisional biopsy and lumpectomy. It is the gold standard for soft tissue mass diagnosis due to its high accuracy [3]. The procedure is very simple and involves making a one- to two-inch cut in the skin to remove all or part of the abnormal lump.

Open biopsy has several advantages and disadvantages compared to other cancer diagnostic methods.

Advantages of Open Biopsy

- Very high accuracy of 94% to 99% [4].
- More reliable at establishing the exact diagnosis than needle biopsy [3].
- The surgeon works with direct sight, thereby minimizing sampling error.

Disadvantages of Open Biopsy

- Expensive (between \$4321 and \$7234) [3].
- Invasive.
- Has a complication rate of up to 16%, including hematoma, tumor spread, and wound problems that may interfere with adjuvant treatments [4, 5].

As with all types of surgery, open biopsy carries risk of complications, although usually, these complications are not serious. Potential complications of open surgery include:

- Bleeding at the surgical site.
- Hematoma formation.
- Infection.
- Nerve damage.

The risk of bleeding and hematoma can be lowered by applying pressure dressings and ice to the site after the operation, while the risk of infection can be

CHAPTER 4**Immunotherapy and Cancer Stem Cells****Ravi Teja Chitturi Suryaprakash¹, Mohammad Ayman Abdulkarim Safi², Noufa Alonazi³, Ahdab A. Alsaieedi^{4,5} and Omar Kujan^{1,*}**¹ *UWA Dental School, The University of Western Australia, Nedlands, 6009 WA, Australia*² *Department of Medical Microbiology and Parasitology, Faculty of Medicine, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia*³ *Department of Paediatrics, Prince Sultan Military Medical City, Riyadh, Saudi Arabia*⁴ *Department of Medical Laboratory Sciences, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah, Saudi Arabia*⁵ *Vaccines and Immunotherapy Unit, King Fahd Medical Research Center, King Abdulaziz University, Jeddah 21589, Saudi Arabia*

Abstract: Immunotherapy is one of the important modalities in the treatment of cancer since it can directly target the tumor and its microenvironment with lesser side effects and cytotoxicity. The main goal of immunotherapy in the treatment of cancer is the reactivation of the immune system against cancer cells. In this way, the body fights against cancer using its immune system rather than relying on external agents which might be harmful to other healthy parts of the body. The development of monoclonal antibodies (Mabs) has delivered a significant therapeutic effect. Mab therapy is one of the most evolving techniques in cancer immunotherapy and has shown efficacy in controlling several types of malignancies. There are several other methods by which the activation of the immune system can be achieved, such as by using small molecules or by targeting ligands. Interestingly, studies have demonstrated that cancer stem cells have also been found as a target for effective immunotherapy. Additionally, the complete elimination of the cancer cells requires longer sustainability of tumor-specific T cells. Primitive results suggest that these T cells can be localized to tumor cells, mediating highly effective immunotherapy. However, despite these huge successes, several problems still persist and must be overcome. This chapter discusses the current and cutting-edge immunotherapeutic approaches to fight against cancer cells.

Keywords: Cancer, Immunotherapy, Monoclonal therapy, Stem cells, Tumour microenvironment, Vaccines.

* **Corresponding authors Omar Kujan:** UWA Dental School, The University of Western Australia, Nedlands, 6009 WA, Australia; Email: omar.kujan@uwa.edu.au

INTRODUCTION

The recent advances in understanding the molecular landscape and pathogenesis of cancer have led to the successful introduction of targeted therapies for several types of human malignancies that involve a wide range of direct and indirect approaches. Monoclonal antibodies (Mabs) target signalling molecules and small molecules that interfere with the target proteins are regarded as direct approaches. Tumor antigens that are expressed on the cell surface serve as target devices for ligands containing different kinds of effector molecules when targeted is termed to be an indirect approach. Thus, in these approaches, using tumor-specific Mabs or peptide ligands binding to receptors on tumor cells can be effectively used to target tumors. These types of cancer therapeutic approaches seem to be more effective than currently available treatments as they are less harmful to normal cells. Two types of monoclonal antibodies are utilized:

1- Naked monoclonal antibodies – These form most of the antibodies used currently. They are plain antibodies that are used without alteration.

2- Conjugated monoclonal antibodies – As the name indicates, these are joined to another element, which is either cytotoxic or radioactive. Chemotherapeutic drugs are routinely used toxic chemicals, but other toxic chemicals can also be employed. When used, the antibody binds to the specific antigens on the surface of tumor cells and regulates the drug or the amount of radiation delivered to the tumor. Once the antibodies are linked to these radioactive compounds, they are alluded to as radiolabelled. When these antibodies are coupled with chemotherapeutic drugs or toxins, they are reputed as chemolabelled or immunotoxins, respectively [1, 2].

MONOCLONAL ANTIBODIES (MABS)

Immunotherapy, in recent years, has evolved in the treatment of cancer, moving from non-specific treatment such as chemotherapy surgery and radiotherapy to specific treatment immunotherapy. Immunotherapy is one of the important modalities in the treatment of cancer since it can directly target the tumor and its microenvironment with lesser side effects and cytotoxicity [3, 4]. The main goal of immunotherapy in the treatment of cancer is the reactivation of the immune system against cancer cells. One of the main cancer immunotherapy methods is monoclonal antibodies. Antibodies are a very important component of the immune system. The multifunction of the antibodies includes facilitating cellular and humoral reactions to different antigen's self or non-self-substance.

Antibodies are either polyclonal molecules produced from a single B cell clone or produced by several B lymphocytes or monoclonal molecules, where they have a different specificity for the target antigen. Antibodies can recognize the epitope regions on the antigen. When an antibody is produced against a single epitope instead of an entire epitope, this antibody is called a monoclonal antibody (Mab) [5].

The hybridoma technology was discovered in 1975, and Mab was initially produced by this technology. The first Mabs developed as potential human therapeutic agents were mouse antibodies. Clinical trials showed that with repeatedly administering mouse Mab because of their short half-life, their immunogenicity in humans decreased with poor ability to induce human immune effector responses. This is caused by the high immunity of mouse antibodies in the human body and the development of a human anti-mouse antibody (HAMA) response [6 - 8].

Chimeric, humanized and fully human monoclonal antibodies have been developed to overcome these problems. Chimeric antibodies are encoded by genes from more than one species, with antigen-binding regions from mouse genes and constant regions from human genes. On the other hand, humanized antibodies are genetically engineered mouse antibodies in which the protein sequence has been modified to mimic that of human antibodies [9, 10].

Antibodies are sectioned into two antigen-binding fragments (Fab), as well as the crystallisable fragment (Fc) forming the Y shape. The Fab is composed of the variable region, which forms the antigen-binding site of the antibody and confers antigen specificity. The Fc can bind to immune effector cells and complement that can both mediate antibodies directed the immune killing. The revolution in anticancer therapy in the last century with using of monoclonal and then the development of chemotherapy monoclonal antibodies (CmMabs), which have become the standard therapeutic agent for many human malignancies [10].

Classification of Chemotherapeutic Monoclonal (CmMab) Antibodies

Advanced genetic engineering produces 4 types of CmAbs: murine, chimeric, humanized and human Cm-Mabs.

1. Murine source Mabs is a rodent Mabs with excellent affinities and specificity generated using conventional hybridoma technology. It's derived from mice. The patient treated with murine Mab developed a human anti-mouse antibody (HAMA) response. The disadvantages of this type are: rapid clearance of the Mab, poor tumor penetration and hypersensitivity reactions.

Nanotechnology and Precision Medicine

Noufa Alonazi^{1,*}, Talat Abdullah Albukhari² and Naif M. Alruwaili³

¹ Department of Paediatrics, Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia

² Umm AlQura University, Makkah, Saudi Arabia

³ Department of RT, Prince Mohamed Hospital, Riyadh, Saudi Arabia

Abstract: Nanoscience and Nanotechnology are now almost in every field of Science. The field has been growing since it was started in 1959 when the Nobel Prize American physicist, Richard Feynman introduced the concept of nanotechnology; since then, it has involved in almost every field of Science, including chemistry, biology, computer science, physics, and engineering. Nanoscience and nanotechnology are now at the frontline of modernistic research. The term 'nano' referred to a Greek prefix meaning "dwarf" with a scale of one thousand millionths of a meter (10^{-9} m). Nanoscience is the study of particles and structures on the scale of nanometers.

Early detection of cancer plays an important role in successful treatment. The detection of cancer in the early stage has been delayed by the limits of conventional cancer detection methods. Recently, the uprising in the use of Nanomedicine and nanotechnology in health care offers hope for the detection, prevention, and treatment of cancer. Nanomedicine drugs have been observed to be involved in the treatment of solid tumors. Also, it is based on enhanced Permeability and Retention (EPR). The main characteristics of EPR are related to tumor vessel permeability which allows enhanced permeability (EP) of large particles (macro molecules proteins, micelles & liposomes). Nanomedicine transport can be hindered from Tumor-associated microphage (TAM) by poor blood perfusion, high Extracellular Matrix (ECM) dense and high tumor stromal cells. Electrochemotherapy is commonly used in palliative settings for the treatment of patients with unresectable tumors to relieve pain and improve the quality of life. It is also frequently used in the treatment of neoplasia at a late stage and when comprehensive surgical treatment is not possible due to the size, location, and the number of the lesion. As the treatment does not involve tissue heating, so Electrochemotherapy is used for the treatment of tumors near or close to important structures like vessels and nerves. Electrochemotherapy has a favorable side effect in the form of local and transient, moderate local pain, edema, erythema, and muscle contractions during electroporation.

* Corresponding author **Noufa Alonazi:** Department of Paediatrics, Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia; E-mail: dralonazi@gmail.com

Keywords: Nanotechnology, Nanomedicine, Electrochemotherapy.

INTRODUCTION

Unique Roles of Nanotechnology in Cancer

Nanoscience and Nanotechnology are now almost in every field of Science. The field has been growing since it was started in 1959 when the Nobel Prize American physicist Richard Feynman introduced the concept of nanotechnology; since then, it has become involved in almost every field of Science, including chemistry, biology, computer science, physics, and engineering. Nanoscience and nanotechnology are now at the frontline of modernistic research. The term 'nano' referred to a Greek prefix meaning “dwarf” with a scale of one thousand millionths of a meter (10^{-9} m). Nanoscience means studying particles and structures on the nanoscale. Nanotechnology is the application of nanoscience in useful products [1].

In 2008, Nanomachines were successfully able to walk along DNA paths and manipulate structures. The application of nanotechnology in medicine is currently used to deliver drugs more efficiently, as in vaccines filled with nanoparticles of iron and gold to ensure sterility and help uptake into the human bloodstream. It is used to coat surgical equipment to keep them sterile. Nanotechnology also showed a promise in the treatment for different types of cancer.

In cancer therapy, the oncologist is looking for a tumor-specific anticancer agent to reduce the side effects and increase the efficacy of chemotherapeutic drugs in the patients. To overcome these barriers and increase the survival rate of patients with Cancer, Nanotechnology displays the unique and safe delivery of cancer therapy agents [2].

A lot of research was conducted to develop a novel therapeutic formulation to target cancer cells and avoid the cytotoxic effect on healthy cells [3].

A wide range of Nanostructures such as liposomes, Nano-diamonds, quantum dots, peptides, cyclodextrin, carbon nanotubes (CNTs), graphene, and metal-based nanoparticles, are used for diagnostic or therapeutic purposes [4].

The small size and large surface area of nanoparticles allow them to cross the cellular membranes and avoid detection by the reticular endothelial system, so they will not be debased, making them ideal for medical uses [5].

Nano drugs are unique and complex, so we must understand their structure, chemical, and physical characteristics. The targeting with nano drugs based on

delivery systems could be selectively targeted to the tumors *via* (selective targeting) using a peptide or an antibody that can specifically bind to a molecule that is selectively expressed on targeted cancer cells. Another mechanism is passive targeting where drugs should “passively target” cell-specific functions or local environments to facilitate the uptake and accumulation in tumor tissues and inflammatory sites with significant clinical success [6].

The Role of Nanotechnology in Cancer

Early detection of cancer plays an important role in successful treatment. The detection of cancer in the early stage has been delayed by the limits of conventional cancer detection methods. Recently the uprising in the use of Nanomedicine and nanotechnology in health care offers hope for the detection, prevention, and treatment of cancer. With the increase in the number of cancer cases which was estimated by GLOBOCAN 2018, 18.1 million with 9.6 million cancer-related death, with a prediction of 30 million death each year by 2030 [7, 8].

The present biomedical imaging, such as X-ray and computer-assisted diagnosis (CAD), and histopathology techniques are carried out to help clinicians in cancer diagnosis and treatment [9]. Nonetheless, most of these methods cannot effectively and independently be used to detect cancer at the early stage [10]. Therefore, the detection of cancer at an early stage before metastasis is a major challenge. To overcome the obstacles in the existing methodology and to improve outcomes, nanotechnology is used as a diagnostic method in the clinical setting, so the conjunction of nanotechnology with the current screening technologies will lead to an increase in the percentage of cancers that are diagnosed in the early stage and improved outcomes for cancer patients [10].

Nanoparticles (NPs) are used to capture cancer biomarkers, such as cancer-associated proteins, circulating tumor DNA, circulating tumor cells, and exosomes [11]. The main advantage of applying nanoparticles for cancer detection is based on their large surface area to volume ratio relative to bulk material [12]. So the nanoparticle surface can be covered with antibodies, peptides, and other moieties that can bind and identify specific cancer molecules [10].

Nanotechnology and Cancer

Nanoscale devices are one hundred to ten thousand times smaller than human cells. They are similar in size to biomolecules such as enzymes and receptors.

Cancer Surveillance

Amal F. Alshammary^{1,*,#}, Mashaal Al-Toub^{1,*,#}, Talat Abdullah Albukhari² and Waheed A. Filimban³

¹ Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia

² Um Al Qura University, Makkah, Saudi Arabia

³ Pathology Department, Faculty of Medicine, Um Al Qura University, Makkah, Saudi Arabia

Abstract: Surveillance against tumors is governed by both intrinsic (non-immune) and extrinsic (immune) surveillance. While research on non-immune surveillance started as early as the 1960s when it was demonstrated that cell environment within and around can induce tumor-suppressing mechanisms, a major part of the progress is missing compared to immune surveillance. Part of the reason could be due to the fact that immune surveillance is seen to have more potential in therapeutic application in curing cancerous tumors compared to non-immune surveillance mechanisms. Many of the non-immune mechanisms are still under investigation as theories, although a few studies have shown their possibility. Contrary to this, there is a plethora of studies on immune surveillance. The immune system has been proven to have a role in the surveillance against tumors, thus conferring a certain degree of protection. However, not all tumor cells are successfully detected by innate immunity, and many of them have developed strategic ways of escaping adaptive immunity. The immunosurveillance in both animal models and humans shows overwhelmingly that cells with immunodeficiencies are more susceptible to tumor development. However, it is confounding that even immune-competent individuals develop tumors, and thus a significant process is responsible. Thus, immunoediting was proposed as a theory to explain why tumors can escape immunosurveillance. This chapter provides detailed evidence from animal and human tumors and analyses the mechanisms, pathways, and components implicated in tumor immune surveillance. The findings suggest that while immune surveillance could be the key to promoting immune function against the development of tumors, there is more research and understanding needed in the various mechanisms and cells implicated. This is because most, if not all, of the therapeutic studies using immune effectors have proved to be poor in preventing, treating, or regulating the development of tumors.

* Corresponding authors Mashaal Al-Toub & Amal F. Alshammary: Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia; Emails: altoub@ksu.edu.sa, aalshammary@ksu.edu.sa

Contributed equally.

Faris Q.B. Alenzi (Ed.)

All rights reserved-© 2023 Bentham Science Publishers

Keywords: DC, Immunosurveillance, Prevention, Screening, Tregs.

INTRODUCTION TO CANCER SURVEILLANCE

In multicellular organisms, the protection from irregular and abnormal growth of cells is necessary and constant as much as the protection against external threats. The surveillance system is designed to keep checks on the cell processes and provide an appropriate trigger mechanism to initiate the right response. These surveillance mechanisms for the prevention of both benign and malignant cells, are divided into the most common and well-known forms, like immune surveillance. However, other mechanisms exist that do not utilize the immune surveillance direct response. The non-immune surveillance mechanisms are independent and rely on certain cellular structures. This section will introduce what some of them are. The non-immune surveillance system is known as intrinsic surveillance, while the immune surveillance is extrinsic. While most malignant cancers arise from virus-induced tumors, the surveillance system always works to suppress both viral and carcinogenic tumors. Those tumors that escape such surveillance, mutate, and adapt are those capable of causing further growth and eventual cancer to an individual. Both intrinsic and extrinsic immune surveillance mechanisms are always working together in a continuous manner rather than being independent.

Immune surveillance as the main type of protection against cancer was, at first, a theory that was proposed by Thomas and MacFarlane [1]. With time, the theory has been proven through experiments in a lab that have shown that immune surveillance is present and always works to keep tumors at bay. While it has been proposed to be successful in many instances, immune surveillance has also failed in many because cancer incidents are increasing. This has been attributed to certain mechanisms in the cancer cells to possess the ability to either evade surveillance or suppress and escape it altogether. Tumor genesis does not bode well for most of the immune surveillance because mechanisms are deployed that lead to loss of function. Besides immune surveillance, other types of protection are implemented and include genetic surveillance, which is mainly involved in the repair of DNA to allow proper functions within the cell. Intracellular activities form a type of surveillance that utilize apoptosis. Epigenetics and intercellular activities have also been implicated. The subsequent sections will discuss these in detail.

NON-IMMUNE SURVEILLANCE

Genetic Surveillance

Genetic surveillance is a defense mechanism that occurs within the DNA itself. When tumors start to develop, there are chances that mutations in the DNA have an effect. This means that by carefully ensuring control of the processes like mitosis, the tumors will be kept at bay. The genes initiate control at the chromosomal level to prevent aspects like loss of heterozygosity or microsatellite instability [2]. The most known mechanism of genetic surveillance is that of the p53 pathway that tends to be present to repair the damage done to the DNA. This protein often appears when there has been damage to the DNA, and increases in number significantly until complete healing occurs. The gene binds itself to DNA in order to stop any growth or mutation process from occurring. This protein thus initiates healing and repair within the DNA itself through growth arrest and self-repair. After the DNA has managed to repair itself, the p53 levels decrease within the cell, and the process of cell division, growth and other cell functions resume [3]. In cells that are unable to complete the healing and repair process, another mechanism known as apoptosis is initiated, as will be discussed later.

Based on studies done on the role of p53 in tumor cells, it has been found that cells with tumors have up to 50% mutations in the p53 gene. This is significant and shows that p53 does play a role not just through the focus on healing, but by the fact that cancer cells seek to alter or eliminate its functions [4]. The impairments mostly relate to the ability of the gene to bind itself to DNA and thus serve its ability to regulate the DNA repairs. These aberrant cells thus contain DNA mutated at the basic level, no control or healing mechanism, and mitotic capacity to continue dividing. Therefore, cells arising from this are mutated at a micro level and hence the possibility of malignant cancer.

The genes controlling the mutation process have significant roles to play in ensuring the efficiency of DNA chromosomal separation, DNA repair and proper replication procedures are followed. One of the earliest cases of failure of genetic surveillance is a skin cancer condition known as Xeroderma pigmentosa. As the name suggests, the skin condition is characterized by pigments of the dermis that are caused by an inability of the DNA to repair itself. The main pathway implicated in this failure is a recessive mutation in the nucleotide repair system. This system is responsible for protection against ultraviolet (UV) rays from the sun, and upon their mutation, they become useless. Therefore, any form of light affects the skin of these patients because of the inability of thymidine dimers to protect them. These patients have to remain away from any form of UV light at all times. However, it is never enough, as these patients develop several carcinomas

SUBJECT INDEX**A**

Acid 251, 254, 319
 folic 319
 hyaluronic 251, 254
 Activities 28, 33, 173, 179, 184, 195, 309
 immune 184
 immunosuppressive 173, 184
 immunotherapeutic 179
 lymphocyte 195
 metabolic 28
 telomerase 33
 tumor-suppressing 309
 Acute 47, 48, 50, 51, 56, 58, 59, 107, 108,
 109, 110, 170, 178
 myelogenous leukemia 107
 myeloid leukemia (AML) 47, 48, 50, 51,
 56, 58, 59, 108, 109, 170, 178
 promyelocytic leukemia (APL) 48, 110
 Adenocarcinomas 7, 12, 15, 21, 25, 29, 31, 32,
 42, 112, 157, 201, 296
 cervical 31, 32
 gastric 42
 mammary gland 296
 pancreatic 21
 Adenosquamous carcinoma 12, 13
 Adenoviruses 180, 199
 Adoptive cell therapy 188
 Aggressive systemic mastocytosis (ASM) 55
 Alzheimer's disease 112
 Anaplastic large cell lymphoma (ALCL) 67,
 68, 69, 70
 Anemia, iron deficiency 29
 Anesthesia 149, 258
 Angiogenic signalling pathways 247
 Angiography 100
 Anticancer therapy 154, 167
 Antigen(s) 108, 114, 190, 195, 198, 248, 280,
 283, 291, 292, 307
 carcinoembryonic 108, 114, 190, 283
 deficiencies 307
 melanoma-associated 190

-presenting cells (APCs) 195, 198, 248,
 291, 292
 Anti-tumor immunity 180, 278, 307
 Apoptosis 247, 255, 272, 273, 275, 276, 277,
 284, 285, 315, 324
 Astrocytomas 41, 155
 Autoimmune syndromes 306

B

Basal cell carcinoma (BCC) 45, 46, 136, 139,
 182
 Biopsies technique 97
 Bladder 107, 109, 169, 170, 169, 253
 cancer 107, 109, 169, 170
 carcinoma 253
 tumor antigen (BTA) 107
 Blastoid plasmacytoid dendritic cell neoplasm
 (BPDCN) 47, 48, 50, 51
 Blastomas 76, 77
 Bleomycin 73, 255, 258
 Blood carcinoembryonic antigen 112
 Body mass index (BMI) 24, 28, 42, 315, 316
 Bone 27, 111
 marrow toxicity 111
 metastasis 27
 Breast cancer 2, 3, 16, 17, 18, 19, 20, 108,
 109, 111, 112, 135, 145, 170, 201, 257,
 321
 cancer therapy 201
 carcinoma 18, 20, 201
 inflammatory 19
 Bronchoscopy 130
 Burkitt lymphoma 50, 65
 Burton's tyrosine kinase (BTK) 254

C

Cancer 6, 25, 41, 42, 43, 44, 45, 46, 110, 111,
 125, 126, 127, 134, 135, 138, 139, 146,
 147, 176, 180, 200, 257, 258, 272, 273,
 277, 281

Faris Q.B. Alenzi (Ed.)

All rights reserved-© 2023 Bentham Science Publishers

Subject Index

gastrointestinal 41, 42, 43, 258
hepatocellular 180
liver 110, 176
malignant 6, 46, 272, 273, 277
neck 147
neuroendocrine 25
oral 147
pancreas 257
renal 200
skin 43, 44, 45, 46, 125, 126, 127, 134, 135, 138, 139
surveillance of immunity 281
thyroid 111, 146
Carcinogenesis 22, 298, 303, 325, 326
pancreatic 22
Carcinogen-induced tumors 297, 299
Carcinomas 5, 6, 7, 20, 109, 151, 153, 154, 155, 156, 157, 158, 159, 160, 176, 252, 273, 276, 283, 325
hepatocellular 109, 176, 283
inflammatory 154
malignant 276
mammary 252
Cervical 31, 32, 105, 136, 187, 189, 194, 321
cancer 31, 32, 136, 187, 189, 194, 321
carcinogenesis 33
carcinomas 31, 194
pathogenesis 32
screening cytology 105
Chronic 10, 53, 54, 55, 56, 57, 61, 107, 109, 112, 153, 175
lymphocytic leukemia (CLL) 61, 107, 109, 153
myeloid leukemia (CML) 53, 54, 56, 57, 107, 175
neutrophilic leukemia (CNL) 53, 55
obstructive pulmonary disease (COPD) 10, 112
CNS malignancies 40
Colon cancer 28, 135, 146, 178, 200, 274, 304
Colonoscopy 28, 30, 100, 105, 130, 320, 321
Colorectal 28, 29, 100, 108, 109, 110, 111, 112, 169, 171, 190, 274, 283, 302, 303, 304

Molecular Targets and Cancer Therapeutics (Part 2) 343

adenocarcinoma 190
adenoma 274
cancer 28, 29, 108, 109, 110, 111, 112, 169, 171, 283, 302, 303, 304
neoplasia 100
Colposcopy 130, 322
Complement-mediated-cytotoxicity 168
Computed tomography (CT) 27, 43, 67, 101, 102, 105, 127, 190
Connective tissue growth factor 253
Cytokine(s) 54, 173, 174, 177, 180, 184, 185, 188, 192, 193, 195, 197, 285, 286, 287, 288, 290, 310
based therapy 184
homeostatic 188
immunomodulatory 180
immunosuppressive 287
production, inflammatory 54
release syndrome (CRS) 192, 193
Cytosolic DNA sensors (CDS) 182, 183
D
Dendritic cells (DCs) 173, 174, 178, 179, 181, 183, 194, 195, 196, 253, 285, 287, 291, 314, 315
Diffuse large B-cell lymphoma (DLBCL) 49, 50, 63, 64, 65, 152
Disease 2, 3, 4, 7, 10, 19, 20, 21, 22, 26, 27, 37, 54, 77, 97, 102, 112, 156, 160, 242, 289, 305, 321
autoimmune 289
brain 242
chronic obstructive pulmonary 10, 112
genetic 37
metastatic 7, 156, 160
neoplastic 305
neurological 242
Disorders 50, 60, 70, 185, 186, 278, 305
autoimmune 185, 186, 305
cytogenetic 50
immune 278
DNA 6, 32, 42, 44, 72, 106, 145, 195, 272, 273, 274, 277, 297

anti-double-stranded 297
genomic 72
Dysfunction 278, 309, 314
immune 278, 309
Dysgerminoma 73, 74, 75
Dysplasia 34, 55, 57, 58, 59
fibrous 34
granulocytic 55, 57
multilineage 58, 59

E

Egg phosphatidyl glycerol (EPG) 254
Electrochemotherapy 236, 237, 255, 257, 258,
259, 260, 261
Electrosurgery 138, 145
Embryonal carcinomas 72, 73, 75
Endochondral ossification 36
Endoscopy 28, 96, 97, 99, 100, 122, 124, 126,
130, 131
Enzymes 113, 287
glycoprotein serine protease 113
immunoregulatory 287
Ependymoblastoma 155
Epidermal growth factor receptor (EGFR) 16,
19, 22, 168, 246
inhibitor (EGFRI) 246
Epstein-Barr virus (EBV) 42, 50, 282
Erdheim-Chester disease 15, 108
Erythrocytosis 54
Erythromelalgia 54

F

Fibroblast 168, 246, 252
activation protein (FAP) 168, 252
growth factor 246
Fibrosarcoma 5, 297, 298, 299
Follicular lymphoma (FL) 49, 60, 61, 62

G

Gastric 42, 43, 108, 169
cancer 42, 43, 108, 169

lymphoepitheliomas 42
Gastritis 186
Gene 21, 58, 64
expression profiling (GEP) 64
hypermethylation 58
malformation 21
Genetic 21, 42
malformation 21
polymorphisms 42
Glioblastoma 169, 180
Global cancer deaths 19
Guillain-Barre syndrome 306

H

Hairy cell leukemia (HCL) 49, 61, 62, 108
Herpes simplex virus 200
Hippel-Lindau syndrome 22
Hodgkin lymphoma (HL) 50, 60, 64, 66, 67,
68, 69, 108, 110, 133, 152
Hydraulic conductivity 244
Hypophysectomy 136
Hypoxia-inducible factors (HIF) 247
Hysterectomy 31

I

Immune 284, 304, 306, 314
surveillance process 306, 314
surveillance reaction 304
tolerance 284
Immunity, antibody-mediated 192
Immunogenic tumor cell death (ITCD) 285
Immunosurveillance theory 278

J

Juvenile myelomonocytic leukemia (JMML)
57, 60

K

Kaposi sarcoma 184

Subject Index

Klinefelter syndrome 71

L

Lesions 62, 67, 97, 125, 126, 127, 236, 255,
258, 259, 261, 304

metastatic 97

osteolytic 67

Leukocytosis 53

Listeria monocytogenes 201

Liver cirrhosis 112

Lung fibrosis 112

Lymphadenopathy 26

Lymphoblastic leukemia 53

Lymphocytes 62, 67, 73, 175, 177, 178, 195,
196, 278, 280, 281, 285, 286, 288, 325

antitumor 178

inflammatory 73

Lymphocytic leukemia 169

Lymphoproliferative disorder 70

Lynch syndrome 303

M

Magnetic resonance imaging (MRI) 27, 39,
67, 101, 102, 105, 249

Major histocompatibility complex (MHC)
173, 189, 194, 253, 280, 282, 291, 308,
309

Malignancies, hematologic 105

Malnutrition 143

Mastocytosis 53, 55

Metastatic 46, 110, 304

melanoma 46, 304

prostate cancer 110

Monoclonal antibodies 165, 166, 167, 168,
169, 170, 240, 253, 280, 295, 297

chemotherapeutic 170

Monocytosis 57

Mononuclear phagocytic system (MPS) 239

Mucocutaneous ulcer 50

Mucoepidermoid carcinoma 14

Multiple 66, 107, 110, 153, 169, 190, 305

myeloma 66, 107, 110, 153, 169, 190

Molecular Targets and Cancer Therapeutics (Part 2) 345

sclerosis (MS) 305

Myeloid 48, 53, 55, 57, 59, 60, 188, 248, 287,
311

-derived suppressor cells (MDSCs) 188,
248, 287, 311

leukemia 48

neoplasms 53, 55, 57, 59, 60

Myeloproliferative neoplasms 53, 54, 55, 56

Myoepithelial tumors 15

Myoepithelioma 15

Myofibroblasts 252

N

Neoplasms 1, 46, 60, 293

lymphoid 60

malignant 1, 46, 293

Neuroendoscopy 130

Neurofibromatosis 60

Non-Hodgkin lymphoma (NHL) 60, 64, 66,
67, 68, 108, 152, 193

P

Paget's disease 19

Paraneoplastic neurological syndrome (PNSs)
305, 306

Pathways 172, 174, 241, 247, 249, 271, 273,
274, 275, 288, 295, 298, 310

metabolic 241

mitogen-activated protein kinase-dependent
249

Peripheral blood 178, 187, 189, 197, 301, 304

lymphocytes (PBL) 178, 189, 301, 304

mononuclear cells (PBMCs) 187, 197

Phagocytosis 246

Platelet-derived growth factor (PDGF) 245,
247, 251

POEMS syndrome 66

Polymerase chain reaction (PCR) 302

Positron emission tomography (PET) 101, 102

Prostate cancer 23, 24, 25, 26, 27, 110, 111,
112, 113, 137, 307, 309, 320, 321

Prostatitis 27

Proteins 32, 33, 106, 107, 171, 190, 191, 197, 198, 201, 273, 274, 275, 276, 282, 287, 319
anti-apoptotic 201
transmembrane 287
Pulmonary 14, 15, 259
fibrosis 259
hamartoma 14
myxoid sarcoma 15

R

Radiation therapy 35, 45, 46, 104, 140, 141, 202
Reactive oxygen species (ROS) 42, 44, 45, 247, 252, 254
Renal cell carcinoma (RCC) 169, 184, 185, 186, 187, 189, 310
RNA 107, 183, 198, 199, 255
ligands 183
messenger 198
polymerase 198
replicons 199
synthetic 198
vaccines 198

S

Sarcoma 1, 5, 26, 33, 48, 151, 153, 154, 155, 156, 157, 158, 160, 299, 325
immunogenic 299
myeloid 48
Sarcomatoid carcinoma 12
Single 72, 101
nucleotide polymorphisms (SNPs) 72
-photon emission computed tomography (SPECT) 101
Small 10, 60
B-cell lymphoid neoplasms 60
-cell lung carcinomas (SCLC) 10
Smoldering systemic mastocytosis (SSM) 55
Soft tissue 33, 37, 150, 151, 152, 257
cancers 33, 150, 151
sarcoma 33, 37, 152, 257

Solid tumors 110, 111, 133, 135, 172, 173, 174, 176, 182, 183, 184, 242, 243, 261
Systemic mastocytosis (SM) 55

T

Testicular germ cell tumors (TGCTs) 71, 72, 73
Thrombocytosis 53, 54, 56, 57
Thrombopoiesis 54
Thyroidectomy 146
Transplantation 160, 296, 301
allogeneic 160
Tumor 42, 181, 193, 195, 201, 248, 278, 293, 301
immunotherapy 181, 278, 293
necrosis factor (TNF) 42, 195, 301
vaccines 193, 201, 248
Tumor-associated 188, 190, 194, 199, 201, 242, 244, 246, 251, 252, 253, 282, 283, 293, 294, 307, 308, 326
antigens (TAAs) 188, 190, 194, 199, 201, 282, 283, 293, 294, 307, 308, 326
fibroblast (TAF) 242, 244, 246, 251, 252, 253

V

Vaccine-based immunotherapy regimen (VBIR) 200
Vascular endothelial growth factor (VEGF) 168, 169, 176, 244, 247, 248, 249, 287, 314
Viruses 10, 180
measles 180
oncogenic 10
oncolytic 180

W

Waldenström macroglobulinemia (WM) 49, 62, 110
Willebrand's disease 54

Y

Yolk sac tumors (YST) 71, 72, 74, 75



Faris Q.B. Alenzi

Prof. Faris Alenzi received his MSc and PhD from Imperial College London in 2003. Prof. Faris is a passionate educator and researcher in allergy, immunology and cancer. Prof. Faris's interests go further than teaching as he is keen on serving his community through his community work. He is the founder of multiple charities including: The Saudi Society for Allergy, Asthma and Immunology, Saudi Society for Cell Death, Moafa Health Charity, Roya Fekrya Charity. He is also an editor and publisher for five Arabic books. Prof. Faris is a recipient of the British Journal of Hematology Award & the Leukemia Research Fund Award, London, UK. He obtained many research grants in total ~2M USD. In March 2019, he was among the Professional Achievement Award Finalists. In October 2022, he was selected among The Stanford University top 2% researchers in the world.