

Contents

1	Introduction on Cancer Immunology and Immunotherapy	1
	Nima Rezaei, Seyed Hossein Aalaei-Andabili, and Howard L. Kaufman	
1.1	Introduction	1
1.2	Cancer Immunity	2
1.3	Cancer and Immune System Impairment	3
1.4	Immune System Reaction to Cancer	3
1.5	Genetic and Environmental Carcinogenesis	4
1.5.1	Cancer Cells Escape from Host Immunosurveillance	4
1.5.2	Cancer Immunodiagnosis	4
1.6	Cancer Treatment	5
1.6.1	Cancer Immunotherapy	5
1.6.2	Cancer Cell “Switch”	6
1.7	Concluding Remarks	6
	References	7
2	Inflammatory and Innate Immune Cells in Cancer Microenvironment and Progression	9
	Patrick Brennecke, Paola Allavena, Ilaria Laface, Alberto Mantovani, and Barbara Bottazzi	
2.1	Introduction	9
2.2	Heterogeneity of Myeloid Cells in the Tumor Microenvironment	10
2.2.1	Myeloid Subsets in the Tumor Microenvironment	10
2.2.2	Recruitment of Myeloid Cells in Tumors	12
2.2.3	Tumor-Derived Factors Affecting Myeloid Differentiation and Polarized Functions	13
2.3	Pro-tumoral Functions of Tumor-Associated Myeloid Cells	13
2.3.1	Tumor Proliferation and Survival	14
2.3.2	Angiogenesis	15

2.3.3	Cancer Cell Dissemination	16
2.3.4	Suppression of Adaptive Immunity	18
2.4	Selected Aspects of Therapeutic Targeting of TAMC	19
2.5	Concluding Remarks	20
	References	21
3	Role of Innate Immunity in Cancers and Antitumor Response	29
	Masahisa Jinushi and Muhammad Baghdadi	
3.1	Introduction	29
3.2	Role of Innate Immune Cells in Cancer and Antitumor Immunity	30
3.2.1	Natural Killer (NK) Cells	30
3.2.2	Natural Killer T (NKT) Cells	31
3.2.3	$\gamma\delta$ -T Cells	31
3.2.4	Macrophages	31
3.2.5	Dendritic Cells	32
3.2.6	Granulocytes	32
3.3	The Role of Innate Immune Receptors on Innate Immune Cells in Cancer and Antitumor Immunity	32
3.3.1	Toll-Like Receptors (TLRs)	32
3.3.2	RIG-I-Like Helicases (RLHs)	33
3.3.3	NOD-Like Receptors (NLRs)	33
3.3.4	Phagocytosis Receptors	33
3.3.5	C-Type Lectin-Like Receptors (CLRs)	34
3.3.6	NK Cell Receptors	34
3.3.7	B7 Family	37
3.4	The Role of Effectors Produced from Innate Immune Cells in Cancer and Antitumor Immunity	37
3.4.1	Interferons (IFNs)	37
3.4.2	Other Cytokines	38
3.4.3	Chemokines	39
3.5	Concluding Remarks	40
	References	40
4	B Cells in Cancer Immunology: For or Against Cancer Growth?	47
	Qiao Li, Qin Pan, Huimin Tao, Xiao-Lian Zhang, Shiang Huang, and Alfred E. Chang	
4.1	Introduction	48
4.2	CD40-Activated B (CD40-B) Cells	48
4.3	Tumor Killer B Cells	50
4.4	Tumor-Infiltrating B Cells (TIL-Bs) in Cancer	52
4.5	Resting B Cells and Regulatory B Cells in Cancer	53
4.6	Concluding Remarks	55
	References	57

5 The Role of Exhaustion in Tumor-Induced T Cell Dysfunction in Cancer	61
Heriberto Prado-Garcia, Susana Romero-Garcia, and Jose Sullivan Lopez-Gonzalez	
5.1 Introduction	61
5.2 T Cell Activation	62
5.3 T Cell Anergy	63
5.3.1 T Cell Anergy in Cancer	64
5.4 T Cell Exhaustion	65
5.4.1 Mechanisms for Inducing T Cell Exhaustion	65
5.4.2 Identification of Exhausted T Cells	66
5.5 T Cell Exhaustion in Cancer	67
5.5.1 A Particular Case: T Cell Exhaustion in Lung Cancer Patients	69
5.6 Concluding Remarks	72
References	72
6 Regulatory T Cells and Th17 Cells in Cancer	
Microenvironment	77
Chang H. Kim	
6.1 Introduction	77
6.2 Diversity of Tumor Microenvironments and Tumor Tissue Factors	79
6.3 Generation of Tregs and Th17 Cells	80
6.4 Impact of Tumor-Derived Factors on Regulation of T-Cell Differentiation	81
6.5 Migration of Tregs and Th17 Cells into Tumors	82
6.6 Impact of Tregs and Th17 Cells on Antitumor Immune Responses	84
6.7 Concluding Remarks	85
References	86
7 Role of Cytokines in Tumor Immunity and Immune Tolerance to Cancer	93
Murugaiyan Gopal	
7.1 Introduction	93
7.2 Cytokine Regulation of the Antitumor Immune Response	94
7.2.1 IL-12	95
7.2.2 IL-27	100
7.3 Cytokines in Immune Tolerance to Cancer	101
7.3.1 TGF- β	101
7.3.2 IL-17	105
7.3.3 IL-23	108
7.3.4 IL-35	108
7.3.5 IL-10	109
7.4 Concluding Remarks	111
References	111

8 Role of Chemokines and Chemokine Receptors in Cancer	121
Mathieu Paul Rodero, Christophe Combadière, and Alexandre Boissonnas	
8.1 Introduction	121
8.2 Chemokines and Chemokine Receptors	123
8.3 Control of Tumor Cell Behavior	125
8.3.1 Chemokines and Chemokine Receptor Alterations During Neoplastic Transformation	125
8.3.2 Metastasis/Homing	126
8.3.3 Senescence, Proliferation, and Survival	127
8.4 Control of Immune Cell Behaviors	128
8.4.1 Chemokines Involved in T-Cell Antitumor Immune Response	128
8.4.2 Chemokines in Innate Immune Components	130
8.4.3 Chemokine and Tumor-Induced Tolerance	131
8.5 Alternative Tumor-Associated Physiological Functions of Chemokines	132
8.5.1 Angiogenesis	132
8.5.2 Fibrosis and Extracellular Matrix Remodeling	132
8.6 Clinical Aspect	133
8.6.1 Prognosis	133
8.6.2 CC Chemokines/Chemokine Receptors	133
8.6.3 CXC Chemokines	135
8.6.4 CX3C Chemokine Receptors	135
8.6.5 Chemokine Circulating Expression	135
8.6.6 Therapeutic Strategies	136
8.7 Concluding Remarks	137
References	138
 9 The CD95/CD95L Signaling Pathway: A Role in Carcinogenesis	143
Amélie Fouqué and Patrick Legembre	
9.1 Introduction	143
9.2 TNF Receptor Family	144
9.2.1 TNFR1 Signaling Pathways	144
9.2.2 TNF/TNFR: A Gold Mine for Therapeutic Tools	145
9.3 CD95: A Death Receptor?	146
9.3.1 Structure/Function	146
9.3.2 Type I/II Signaling Pathways	148
9.3.3 What Can We Learn from CD95 Mutations?	148
9.3.4 Regulation of the Initial Steps of CD95-Mediated Signaling	150
9.3.5 Programmed Necrosis Also Known as Necroptosis	152
9.3.6 CD95L, an Inflammatory/Oncogenic Cytokine?	152
9.4 Concluding Remarks	155
References	156

10 MHC Class I Molecules and Cancer Progression:	
Lessons Learned from Preclinical Mouse Models	161
Irene Romero, Ignacio Algarra, and Angel M. Garcia-Lora	
10.1 Introduction	161
10.2 MHC-I Cell Surface Expression on Tumor Cells and Primary Tumor Growth	162
10.2.1 Studies in GR9 Tumor Model: H-2 Antigen Surface Expression and Tumorigenic Capacity	164
10.3 MHC-I Expression and Metastatic Progression	166
10.3.1 MHC Class I Expression on Primary Tumor Cells May Determine Spontaneous Metastatic Capacity	166
10.3.2 Different MHC-I Surface Expression on GR9 Tumor Clones Determines Their Spontaneous Metastatic Capacity	167
10.4 Immunotherapy as a Treatment Against Cancers Expressing Different MHC-I Surface Expression	169
10.4.1 Immunotherapy as a Treatment Against Primary Tumors with Different Levels of MHC-I Expression	169
10.4.2 Immunotherapy as a Treatment Against Metastatic Progression Derived from Primary Tumors with Different MHC-I Expression	170
10.5 Concluding Remarks	170
References	171
11 Role of Plasmacytoid Dendritic Cells in Cancer	177
Michela Terlizzi, Aldo Pinto, and Rosalinda Sorrentino	
11.1 Introduction	177
11.2 Localization and Trafficking Patterns of Plasmacytoid Dendritic Cells (pDCs)	178
11.3 Plasmacytoid Dendritic Cells (pDCs) Phenotype	179
11.4 Activation of pDCs	180
11.5 pDCs: Bridging the Gap Between Innate and Adaptive Immunity	183
11.6 pDCs and Human Diseases	184
11.6.1 Role of pDCs in Human Infections	184
11.6.2 Role of pDCs in Autoimmune Diseases	185
11.6.3 Role of pDCs in Cancer	186
11.7 Potential Therapies: Clinical Significance	189
11.8 Concluding Remarks	189
References	190

12 Cancer Immunoediting: Immunosurveillance, Immune Equilibrium, and Immune Escape	195
Alka Bhatia and Yashwant Kumar	
12.1 Introduction	195
12.2 Cancer Immunoediting with Its Three Es: Reflection of the Dual Role of Immunity in Cancer	196
12.2.1 Immune Elimination: Evidences For and Against	197
12.2.2 The Equilibrium Phase: The Most Controversial and the Least Understood Phase	200
12.2.3 Immune Escape: The Best Studied Phase	201
12.3 Tumor Antigens and Cancer Immunoediting	203
12.4 The Tumor Microenvironment During Cancer Immunoediting	204
12.5 Clinical Relevance of the Immunoediting Process in Cancer	205
12.6 Concluding Remarks	206
References	206
13 Apoptosis and Cancer	209
Mei Lan Tan, Heng Kean Tan, and Tengku Sifzizul Tengku Muhammad	
13.1 Introduction	209
13.2 Mechanisms of Apoptosis	211
13.2.1 Extrinsic Apoptosis Pathway	212
13.2.2 Intrinsic Apoptosis Pathway	213
13.3 Apoptosis and Cancer	217
13.4 Apoptosis Signaling Pathways and Therapeutic Targets in Cancer	220
13.4.1 TRAIL (TRAIL Ligands, Monoclonal Antibodies Against TRAIL-R1 and TRAIL-R2)	220
13.4.2 Bcl-2 Family Proteins (BH3 Mimetics and Bcl-2 Antisense)	225
13.4.3 Proteasome Inhibitors	227
13.4.4 Inhibitor of Apoptosis Protein (IAP) Antagonists	229
13.5 Concluding Remarks	230
References	231
14 Autophagy and Necroptosis in Cancer	243
Mei Lan Tan, Heng Kean Tan, Ahmed Ismail Hassan Moad, and Tengku Sifzizul Tengku Muhammad	
14.1 Introduction	243
14.2 Autophagy and Cancer	247
14.3 Autophagy Signaling Pathways and Therapeutic Strategies in Cancer	249
14.3.1 mTOR Signaling Pathway Inhibitors	249
14.3.2 Pro-autophagics	250
14.3.3 Autophagy Inhibitors	251
14.4 Mechanisms of Necroptosis	252

14.5	Necroptosis and Possible Therapeutic Targets in Cancer	260
14.6	Crosstalk in Apoptosis, Autophagy, and Necroptosis	261
14.7	Future Directions	263
14.8	Concluding Remarks	263
	References	264
15	Prognostic Value of Innate and Adaptive Immunity in Cancers	275
	Fabio Grizzi, Giuseppe Di Caro, Federica Marchesi, and Luigi Laghi	
15.1	Introduction	275
15.2	Immune Infiltration as a Major Player of the Tumor Microenvironment	276
15.3	Cellular Players of the Innate Immunity in Cancer	277
15.3.1	Tumor-Associated Macrophages (TAM)	277
15.3.2	Tumor-Associated Neutrophils (TAN)	278
15.4	Cellular Players of the Adaptive Immunity in Cancer	278
15.5	Prognostic Value of Innate and Adaptive Cells of the Immune System in Cancer	279
15.6	Concluding Remarks	281
	References	281
16	Epigenetics and microRNAs in Cancer	285
	Petra M. Wise, Kishore B. Challagundla, and Muller Fabbri	
16.1	Introduction	285
16.2	MiRNAs Regulate Effectors of the Epigenetic Machinery	286
16.3	MiRNAs Are Epigenetically Regulated in Several Types of Human Cancers	289
16.4	Concluding Remarks	291
	References	292
17	Immunogenetics of Cancer	295
	Armin Hirbod-Mobarakeh, Ali Akbar Amirzargar, Behrouz Nikbin, Mohammad Hossein Nicknam, Anton Kutikhin, and Nima Rezaei	
17.1	Introduction	295
17.2	Cancers: Why Are There Different Faces?	296
17.3	Immune Polymorphism	296
17.4	Immunogenetics	298
17.4.1	Background	298
17.4.2	Immunogenetic Tools	298
17.5	Immunogenetics: A Champion in Fighting the Losing Battle Against Cancer	303
17.6	Human Leukocyte Antigen	304
17.6.1	Background	304
17.6.2	Genes Behind HLA	304
17.6.3	From Polymorphisms to Clinic	306

17.6.4 HLA Typing and HLA Association Studies:	
Lessons from the Past	308
17.6.5 Typing Methods.	311
17.6.6 Environmental Factors	311
17.6.7 Linkage Disequilibrium	311
17.7 The Cytokine Network	312
17.7.1 Background.....	312
17.7.2 Interleukin-1 Superfamily.....	313
17.7.3 Interleukin-4	316
17.7.4 Interleukin-6 (IL-6).....	317
17.7.5 Interleukin-8	318
17.7.6 Interleukin-10	319
17.7.7 Interleukin-12	323
17.7.8 Tumor Necrosis Factor- α and Lymphotoxin- α	324
17.7.9 Interferon Gamma (IFN- γ)	330
17.7.10 Transforming Growth Factor- β (TGF- β).....	330
17.8 Concluding Remarks.....	333
References	333
18 Primary Immunodeficiencies and Cancers	343
Mona Hedayat, Waleed Al-Herz, Asghar Aghamohammadi, Kim E. Nichols, and Nima Rezaei	
18.1 Introduction.....	344
18.2 Primary Antibody Deficiencies	344
18.2.1 Common Variable Immunodeficiency.....	344
18.2.2 X-Linked Agammaglobulinemia.....	345
18.2.3 Selective IgA Deficiency.....	346
18.3 Combined Immunodeficiencies.....	346
18.3.1 IL-2-Inducible T-Cell Kinase Deficiency	346
18.3.2 Purine Nucleoside Phosphorylase Deficiency.....	347
18.3.3 Dediator of Cytokinesis 8 Deficiency	348
18.3.4 RHOH Deficiency	349
18.3.5 MAGT1 Deficiency.....	350
18.4 Phagocyte Defects.....	351
18.4.1 Severe Congenital Neutropenia (Kostmann Syndrome)	351
18.4.2 Shwachman–Diamond Syndrome.....	352
18.4.3 GATA2 Deficiency	352
18.5 Defects in Innate Immunity.....	353
18.5.1 Epidermodysplasia Verruciformis	353
18.5.2 Warts, Hypogammaglobulinemia, Infections, and Myelokathexis Syndrome	354
18.6 Diseases of Immune Dysregulation	354
18.6.1 X-Linked Lymphoproliferative Disease	354
18.7 Syndromes with Autoimmunity	355
18.7.1 Autoimmune Lymphoproliferative Syndrome	355
18.7.2 Autoimmune Polyendocrinopathy with Candidiasis and Ectodermal Dystrophy	356

18.8 Other Well-Defined Immunodeficiencies	356
18.8.1 DNA Repair Defects	356
18.8.2 Signal Transducer and Activator of Transcription 3 Deficiency	357
18.8.3 Wiskott–Aldrich Syndrome	360
18.8.4 Chromosome 22q11.2 Deletion Syndrome	361
18.9 Concluding Remarks	361
References	361
19 Immunosenescence, Oxidative Stress, and Cancers	377
Tamas Fulop, Graham Pawelec, Gilles Dupuis, Rami Kotb, Bertrand Friguet, and Anis Larbi	
19.1 Introduction	377
19.2 Immune System and Cancer	378
19.2.1 Immunosenescence or Immune Aging	378
19.2.2 Innate Immune System	379
19.2.3 Adaptive Immune System	383
19.2.4 Interaction Between Innate and Adaptive Immune Responses: Effect of Aging	384
19.3 Inflammation Aging and Oxidative Stress	385
19.4 Immunosenescence and Cancer	387
19.5 Modulation	388
19.6 Concluding Remarks	388
References	389
20 Nutrition, Immunity, and Cancers	395
Hassan Abolhassani, Niyaz Mohammadzadeh Honarvar, Terezie T. Mosby, and Maryam Mahmoudi	
20.1 Introduction	395
20.2 Role of Nutrition in Predisposition of Cancer from an Immunologic View	396
20.2.1 Protein-Calorie Balance	396
20.2.2 Essential Fatty Acids	397
20.2.3 Antioxidants (Selenium, Vitamin E, and Vitamin C)	397
20.2.4 Vitamin D	397
20.2.5 Vitamin B6	397
20.2.6 Folate	397
20.2.7 Calcium	397
20.3 Aging as a Confounder of the Triangle of Nutrition, Immunity, and Cancer	398
20.4 Role of Cancer in Predisposition to Malnutrition from an Immunologic View	398
20.5 Role of Nutritional Support in Immune Restoration of Cancer Patients	399
20.5.1 Arginine	400
20.5.2 Glutamine	400
20.5.3 Branched Chain Amino Acids	400

20.5.4 Nucleotides, Long-Chain Omega-3 Polyunsaturated Fatty Acids, and Eicosapentaenoic Acid	400
20.5.5 Fructooligosaccharides	400
20.5.6 Bioactive Compounds	400
20.5.7 Vitamins C and E	400
20.5.8 Vitamin A	401
20.6 Concluding Remarks	401
References	401
21 Allergies and Cancers	407
<i>Delia Rittmeyer and Axel Lorentz</i>	
21.1 Introduction	407
21.2 Molecular Mechanisms of Allergy	408
21.3 Types of Allergic Diseases	409
21.4 Molecular Basics of Carcinogenesis	409
21.5 Types of Cancers	410
21.6 Antitumor Immunity	410
21.7 Relationship Between Allergies and Cancers in General	411
21.7.1 Cancers Positively Correlated with Allergies	411
21.7.2 Tumor-Promoting Effects of Allergies	412
21.7.3 Cancers Negatively Correlated with Allergies	413
21.8 Tumor-Protecting Effects of Allergies	414
21.9 Concluding Remarks	415
References	416
22 Cancer Immunology of Transmissible Cancers	419
<i>Katrina Marie Morris and Katherine Belov</i>	
22.1 Introduction	419
22.2 Canine Transmissible Venereal Tumor	420
22.2.1 Prevalence and Transmission	420
22.2.2 Histology and Clonality	420
22.2.3 Disease Progression	421
22.2.4 Immunology	421
22.3 Devil Facial Tumor Disease	422
22.3.1 Prevalence and Appearance	422
22.3.2 Transmission	422
22.3.3 Immunology	422
22.3.4 Do Devils Have an Impaired Immune System?	423
22.3.5 Devils Have Low MHC Diversity	423
22.3.6 Expression of Immunosuppressive Cytokines	423
22.3.7 Regulation of Cell Surface MHC	423
22.4 Comparison of DFTD and CTVT	424
22.5 Evolution of Transmissible Cancers	424
22.6 Transmissible Tumors as a Cancer Model	425
22.7 Concluding Remarks	426
References	426

23	Envisioning the Application of Systems Biology in Cancer Immunology	429
	Julio Vera, Shailendra K. Gupta, Olaf Wolkenhauer, and Gerold Schuler	
23.1	Introduction	429
23.1.1	The “Omics” Paradigm and the Use of Statistical Models	430
23.1.2	Mathematical Modeling and Systems Theory: Dissecting the Complexity Emerging Out of the Structure of Biochemical Networks	431
23.1.3	Bridging Biological Scales Through the Integration of Biological Data in Multi-scale Models	431
23.2	One Step Further: Integrating the Different Perspectives of Systems Biology into a Unified Framework	431
23.3	Does Cancer Immunology Need a Systems Biology Approach?	434
23.4	A Quick View on Current Results	434
23.4.1	Computational Biology, Bioinformatics, and High-Throughput Data Analysis Used in the Design of Immune Therapies for Cancer	434
23.4.2	Mathematical Models Used in Basic Oncology Research	440
23.5	Concluding Remarks	446
	References	447
24	Principles of Immunological Diagnostic Tests for Cancers	451
	Amber C. Donahue and Yen-lin Peng	
24.1	Introduction	451
24.2	Overview of Antibodies	452
24.2.1	Monoclonal vs. Polyclonal Antibodies	452
24.2.2	Antibody Fragments	453
24.2.3	Reporter Labeling	454
24.2.4	Primary and Secondary Antibodies	454
24.3	Immunoprecipitation	454
24.4	Immunoblotting	455
24.5	Radioimmunoassays	457
24.6	Enzymatic Immunoassays	457
24.7	Immunocytochemical and Immunohistochemical Assays	460
24.8	Flow Cytometry	461
24.9	Bead-Based Assays	464
24.10	Antibody Arrays	465
24.11	Concluding Remarks	468
	References	468

25 Flow Cytometry in Cancer Immunotherapy:	
Applications, Quality Assurance, and Future	471
Cécile Gouttefangeas, Steffen Walter, Marij J.P. Welters, Christian Ottensmeier, Sjoerd H. van der Burg, Cedrik M. Britten, and Cliburn Chan	
25.1 Introduction	471
25.2 Main Flow Cytometry Assays in Cancer Immunotherapy	472
25.3 Panel Development and Quality Assurance	474
25.4 Proficiency Programs Addressing Flow Cytometry Assays	477
25.5 Structured Reporting of Immune Assay Experiments	478
25.6 Organization of Immune Monitoring in Multicenter Trials	479
25.7 Towards Automated Analysis	480
25.8 New Methods and Technologies	482
25.9 Concluding Remarks	485
References	486
26 Immunohistochemistry of Cancers	491
Alireza Ghanadan, Issa Jahanzad, and Ata Abbasi	
26.1 Introduction	492
26.2 Immunohistochemistry of Skin Tumors	492
26.2.1 Markers of Normal Skin	492
26.2.2 Epithelial Tumors	494
26.2.3 Sweat Gland Tumors	495
26.2.4 Trichogenic Tumors	495
26.2.5 Sebaceous Tumors	496
26.2.6 Melanocytic Tumors	496
26.2.7 Prognostic Markers of Melanoma	497
26.2.8 Specific Mesenchymal Tumors of the Skin	497
26.3 Immunohistochemistry of Head and Neck Tumors	499
26.3.1 Tumors of the Nasal Cavity and Paranasal Sinuses	499
26.3.2 Tumors of the Larynx, Nasopharynx, and Oropharynx	500
26.3.3 Tumors of the Salivary Glands	501
26.3.4 Immunohistochemistry of Salivary Gland Tumors	502
26.3.5 Tumors of Thyroid and Parathyroid Glands	505
26.4 Immunohistochemistry of Lung Tumors	505
26.4.1 Adenocarcinoma	505
26.4.2 Mesothelioma	506
26.5 Immunohistochemistry of Gastrointestinal Tumors	507
26.5.1 Liver	508
26.5.2 Esophagus	509
26.5.3 Stomach	509

26.5.4	Small Intestine.....	511
26.5.5	Colon.....	511
26.5.6	Anal.....	511
26.5.7	Appendix.....	511
26.5.8	Pancreas.....	511
26.5.9	Gastrointestinal Stromal Tumor	513
26.5.10	Neuroendocrine Carcinomas.....	513
26.6	Immunohistochemistry of the Urinary Tract.....	513
26.6.1	Kidney	513
26.6.2	Bladder	514
26.7	Immunohistochemistry of Female and Male Genital Tumors	516
26.7.1	Uterine Cervix.....	516
26.7.2	Vulva and Vagina.....	516
26.7.3	Uterine Corpus	516
26.7.4	Ovary.....	517
26.7.5	Breast	517
26.7.6	Prostate	520
26.7.7	Testis	521
26.8	Immunohistochemistry of Lymphoma	521
26.9	Immunohistochemistry of Soft Tissue and Bone Tumors	522
26.9.1	Epithelial Markers.....	523
26.9.2	Myogenic Markers	526
26.9.3	Nerve and Schwann Cell Markers.....	530
26.9.4	Endothelial Markers	530
26.9.5	Fibrohistiocytic Markers.....	531
26.9.6	Lipocytic Markers.....	533
26.9.7	Chondrocyte Markers	533
26.9.8	Osteogenic Markers	533
26.9.9	Unknown-Origin Soft Tissue Tumors	534
26.10	Immunohistochemistry of the Nervous System	534
26.10.1	Neuroepithelial Tumors.....	535
26.10.2	Non-neuroepithelial Tumors.....	536
26.10.3	Undifferentiated Tumors.....	538
26.10.4	Proliferative Markers.....	538
26.11	Immunohistochemistry of Pediatric Tumors.....	538
26.12	Immunosurveillance, Immune Editing, Immune Constant of Rejection, Immune Contexture, and Immune Scoring of Cancers.....	541
26.13	Concluding Remarks.....	545
	References	545
	Index	561