

CONTENTS

<i>Contributors</i>	<i>xiii</i>
<i>Preface</i>	<i>xvii</i>
1. Estrogen-Mediated Mechanisms to Control the Growth and Apoptosis of Breast Cancer Cells: A Translational Research Success Story	1
Russell E. McDaniel, Philipp Y. Maximov, and V. Craig Jordan	
1. Introduction	2
2. Clinical Presentation of Breast Cancer	3
3. Targeted Therapy	6
4. Transition to Tamoxifen	15
5. Selective Estrogen Receptor Modulation	20
6. Acquired Drug Resistance and the Surprise of SERMs	22
7. Estrogen-Induced Apoptosis: Back to the Beginning	24
8. The Legacy of Tamoxifen	29
Acknowledgments	35
References	35
2. The Epidemiology and Molecular Mechanisms Linking Obesity, Diabetes, and Cancer	51
Rosalyn D. Ferguson, Emily J. Gallagher, Eyal J. Scheinman, Rawan Damouni, and Derek LeRoith	
1. Introduction	52
2. Type 2 Diabetes and Breast Cancer	52
3. The Role of Cholesterol in Cancer Growth	64
4. Obesity, Estrogen, and Breast Cancer	70
5. Current Medications for Type 2 Diabetes: Relationship to Breast Cancer	77
6. Conclusions and Future Directions	82
References	82
3. Sex Hormone Receptors in Breast Cancer	99
Nina D'Abreo and Alexander A. Hindenburg	
1. Introduction	100
2. Historical Perspective	101
3. Receptor Structure and Function	105

4. ER Agonists and Antagonists	111
5. Molecular Mechanisms of Estrogen Signaling	112
6. Implications in Breast Cancer	116
7. Future Directions	120
References	123
4. Modulation of Estrogen Receptor Alpha Activity and Expression During Breast Cancer Progression	135
Gwennege Kerdivel, Gilles Flourirot, and Farzad Pakdel	
1. Introduction	136
2. DNA Methylation	140
3. ER α Transcriptional Regulation by <i>cis</i> - and <i>trans</i> -Acting Elements	142
4. ER α Gene Mutations and Splice Variants	143
5. MicroRNA Deregulation	144
6. Cross Talk with Growth Factor Receptor Signaling	145
7. ER Posttranslational Modifications	146
8. Hypoxia	148
9. ER Coregulators	149
10. Breast Cancer Stem-Like Cells	150
11. Pioneer Factors and Endocrine-Resistant Specific Cistromes	150
12. Conclusions and Future Directions	151
Acknowledgments	152
References	152
5. Targeting Progesterone Receptors in Breast Cancer	161
Sebastián Giulianelli, Alfredo Molinolo, and Claudia Lanari	
1. Introduction	162
2. Progestins and Breast Cancer Risk	162
3. Progestins Stimulating Breast Cancer Growth in Animal Models	162
4. <i>In Vitro</i> Studies	165
5. Progestins Inhibiting Breast Cancer Growth	168
6. The Systemic Effect of Progestins	169
7. PRs and Gene Expression	170
8. Regulation of PR Activity	174
9. PRs as Therapeutic Targets for Breast Cancer Treatment	174
Acknowledgments	175
References	175

6. The Hyperplastic Phenotype in PR-A and PR-B Transgenic Mice: Lessons on the Role of Estrogen and Progesterone Receptors in the Mouse Mammary Gland and Breast Cancer	185
Rocio Sampayo, Sol Recouvreur, and Marina Simian	
1. Introduction	186
2. Developmental Stages in the Mouse Mammary Gland	187
3. Spatiotemporal Expression of Estrogen and Progesterone Receptors in the Mouse Mammary Gland	188
4. The Generation of PR-A and PR-B Transgenic Mice	190
5. Breast Cancer and PRs	195
6. PRs and Mammary Stem Cells	197
7. Conclusion and Future Directions	198
Acknowledgments	198
References	198
7. FOXP1 and Estrogen Signaling in Breast Cancer	203
Nobuhiro Ijichi, Kazuhiro Ikeda, Kuniko Horie-Inoue, and Satoshi Inoue	
1. Introduction	204
2. FOXP1 and FOXA1 in ER α -Positive Breast Cancer Cells	204
3. Clinicopathological Significances of FOXP1 and FOXA1 in ER-Positive Breast Cancer	207
4. Conclusions and Future Directions	209
Acknowledgments	209
References	210
8. Role of KLF5 in Hormonal Signaling and Breast Cancer Development	213
Rong Liu, Jin-Tang Dong, and Ceshi Chen	
1. Introduction	213
2. Progesterone—PR Signaling, KLF5, and Breast Cancer	215
3. Estrogen—ER Signaling and KLF5 in Breast Cancer	217
4. Androgen/AR Signaling, KLF5, and Breast Cancer	219
5. Summary and Perspectives	220
Acknowledgments	221
References	221

9. Dynamic Regulation of Steroid Hormone Receptor Transcriptional Activity by Reversible SUMOylation	227
Todd P. Knutson and Carol A. Lange	
1. Introduction	228
2. Mechanisms of Protein SUMOylation	230
3. SR SUMOylation/deSUMOylation	233
4. SR SUMOylation Modulates Transcriptional Action and Promoter Selectivity	242
5. Conclusions	253
References	255
 10. Beta-Endorphin Neuron Regulates Stress Response and Innate Immunity to Prevent Breast Cancer Growth and Progression	 263
Dipak K. Sarkar and Changqing Zhang	
1. Introduction	264
2. Neuroendocrine Response to Stress	264
3. Chronic Stress and Its Effect on Immune Functions	265
4. Neuroendocrine-Immune Pathway of Cancer	266
5. Beta-Endorphin Neurotransmission Reduces the Body's Stress Response	268
6. Beta-Endorphin Neurotransmission Enhances Innate Immunity	268
7. Beta-Endorphin Cell Transplantation Effects on the Neuroendocrine-Immune Pathway of Cancer	269
8. Conclusions	273
Acknowledgment	274
References	274
 11. The Functional Role of Notch Signaling in Triple-Negative Breast Cancer	 277
Jodi J. Speiser, Çağatay Erşahin, and Clodia Osipo	
1. Background—Triple-Negative Breast Cancer and Notch	278
2. Notch—Breast Oncogenes	280
3. Notch in TNBC	281
4. Notch in Luminal Versus Basal-Like Breast Cancer	283
5. ER and Notch	285
6. PR and Notch	288
7. HER-2 and Notch	289
8. Prognostic Makers for Survival Associated with Notch in TNBC	290
9. Therapeutic Strategies in TNBC	292
References	297

12. ADAM22 as a Prognostic and Therapeutic Drug Target in the Treatment of Endocrine-Resistant Breast Cancer	307
Jarlath C. Bolger and Leonie S. Young	
1. Introduction	308
2. ADAM Proteins in Breast Cancer	309
3. ADAM22 and Breast Cancer	310
4. A Functional Role for ADAM22	316
5. ADAMs as Therapeutic Targets	317
6. Conclusions	318
References	319
13. Alpha-Actinin 4 and Tumorigenesis of Breast Cancer	323
Kuo-Sheng Hsu and Hung-Ying Kao	
1. Introduction	324
2. Overview of ACTNs	325
3. The Function of ACTN4 in Breast Cancer	331
4. ACTN4 and Other Cancers	339
5. Conclusion and Future Direction	344
Acknowledgments	345
References	345
14. Adherence Rates and Correlates in Long-term Hormonal Therapy	353
Julia Dunn and Carolyn Gotay	
1. Introduction	353
2. Nonadherence in Clinical Practice	356
3. Patient-Reported Barriers to Adherence to Adjuvant Hormonal Therapies	367
4. Interventions to Increase Adherence	368
5. Discussion	370
6. Conclusion	371
References	372
Index	377