

Contents

<i>Contributors</i>	<i>ix</i>
1. STAT signaling in the intestine	1
Yael R. Nobel, Kenneth Stier, and Suneeta Krishnareddy	
1. Introduction	1
2. Mechanisms of JAK-STAT signaling in inflammatory bowel diseases (IBD)	4
3. JAK-STAT inhibition in the treatment of IBD	7
4. STAT signaling in other diseases of the gut	11
5. Infection	12
6. Cancer	13
7. Conclusion	14
References	15
2. The RAL signaling network: Cancer and beyond	21
Lisa H. Apken and Andrea Oeckinghaus	
1. The RAS family of small GTPases	22
2. RAL GTPases: An introduction	25
3. Regulation of RAL activity and function	27
4. The RAL signaling network: Effector proteins and regulated processes	46
5. RAL signaling in cancer	61
6. RALopathies	77
7. Inhibition of RAL activity	78
8. Conclusion	82
Acknowledgments	83
References	83
3. Implications of microgravity-induced cell signaling alterations upon cancer cell growth, invasiveness, metastatic potential, and control by host immunity	107
Randal K. Gregg	
1. Introduction	108
2. Models of microgravity	109
3. Microgravity-mediated mechanical to biochemical changes	112
4. Changes in cytoskeleton signaling associated with cell viability	125
5. Microgravity-mediated changes in signaling pathways of cancer cells	131

6. Microgravity-mediated changes in signaling pathways of primary anti-cancer effector cells	138
7. Conclusion	153
References	157
 4. Tyro3, Axl, Merck receptor-mediated efferocytosis and immune regulation in the tumor environment	 165
Liwen Zhou and Glenn K. Matsushima	
1. Introduction	166
2. Structure of TAM receptors	167
3. Ligand recognition of apoptotic cells	169
4. Virus molecular apoptotic mimicry	172
5. TAM receptor efferocytosis	174
6. TAM receptors in cancer	184
References	196
 5. Charting protein dephosphorylation triggered by Toll-like receptor (TLR) signaling in macrophages and its role in health and disease	 211
Aristóbol M. Silva and Thomas S. Postler	
1. Introduction	212
2. Protein phosphorylation and TLR signaling	214
3. Phosphorylation sites downregulated in TLR-stimulated macrophages	215
4. Using mass spectrometry to identify downregulated phosphorylation sites	228
5. Considerations and open questions	231
6. Concluding remarks	233
References	233
 6. The many-sided contributions of NF-κB to T-cell biology in health and disease	 245
Allison Voisin and Yenkel Grinberg-Bleyer	
1. The NF- κ B signaling pathway(s) in T cells	246
2. A short overview of T-cell flavors and functions in health and disease	248
3. NF- κ B in T-cell homeostasis: Proliferation, survival, cytokine expression	249
4. NF- κ B in CD4 ⁺ T cells	251
5. NF- κ B in CD8 ⁺ T cells	265
6. NF- κ B in other T-cell subsets	270
7. NF- κ B in pathological conditions: Toward NF- κ B-targeted therapies?	272

8. Concluding remarks	282
Acknowledgments	284
References	284
 7. A most versatile kinase: The catalytic subunit of PKA in T-cell biology	 301
Thomas S. Postler	
1. A brief introduction to PKA biology	302
2. PKA as a regulator of NF- κ B activity	304
3. The role of cAMP and PKA in T cells	305
4. The translational relevance of PKA	309
References	310