



VOLUME ONE HUNDRED AND SIXTEEN

ADVANCES IN  
**PROTEIN CHEMISTRY AND  
STRUCTURAL BIOLOGY**

Intracellular Signalling Proteins

Edited by

**ROSSEN DONEV**

*MicroPharm Ltd,  
United Kingdom*



**ACADEMIC PRESS**

An imprint of Elsevier

# Contents

*Contributors*

*xi*

<b>1. Voices from the dead: The complex vocabulary and intricate grammar of dead cells</b>	<b>1</b>
Jerrold S. Levine and David S. Ucker	
1. Introduction	2
2. The language of cell death	4
3. An expanded view of the role of cell death in homeostasis	6
4. A universally heard language	14
5. Paradigm	18
6. A complex language	21
7. Inbuilt mechanisms that improve the signal-to-noise ratio	66
8. An intricate grammar	67
9. Conclusions	69
References	69
<b>2. Nucleobindins and encoded peptides: From cell signaling to physiology</b>	<b>91</b>
Adelaine Kwun-Wai Leung, Naresh Ramesh, Christine Vogel, and Suraj Unniappan	
1. Introduction	92
2. Structural characteristics of the NUCB protein family	93
3. Biochemical and structural properties of NUCB	98
4. Structure of the EF-hand pair in NUCB1	99
5. Calcium induces conformational changes in NUCB1	101
6. DNA binding property of NUCB1	102
7. Post-translational modification	102
8. Subcellular distribution	104
9. NUCB protein-protein interactions that mediate different physiological functions	104
10. NUCB encoded peptides	109
11. Perspectives and considerations for future research	126
Acknowledgments	127
References	127

<b>3. Estrogen receptor signaling mechanisms</b>	<b>135</b>
Nathalie Fuentes and Patricia Silveyra	
1. Estrogens: Definition and history	136
2. Estrogen biosynthesis	137
3. Estrogen metabolism	141
4. Physiological functions of estrogens	142
5. The estrogen receptors: History and discovery	142
6. Structural properties of estrogen receptors	143
7. Mechanims of estrogen receptor signaling	146
8. Nuclear estrogen receptors: Direct genomic signaling	147
9. Nuclear estrogen receptors: Indirect genomic signaling	148
10. Membrane receptor: Indirect non-genomic signaling	150
11. Genomic and non-genomic signaling crosstalk	151
12. Estrogen receptor ligand independent signaling	152
13. Estrogen receptor coregulators and transcriptional control	153
14. Endogenous and exogenous estrogen receptors ligands	154
15. Discussion	157
Acknowledgments	158
References	158
<b>4. Intracellular signaling of the AMP-activated protein kinase</b>	<b>171</b>
Miribane Dërmaku-Sopjani and Mentor Sopjani	
1. The protein enzyme AMPK	172
2. AMPK-mediated downstream targets	176
3. Conclusions and perspectives	196
References	197
<b>5. Relationship between mitofusin 2 and cancer</b>	<b>209</b>
Alessandro Allegra, Vanessa Innao, Andrea Gaetano Allegra, and Caterina Musolino	
1. Mitochondria as signaling organelles	209
2. Mitochondrial fission and fusion	212
3. Mitofusin 1 and mitofusin 2	214
4. Mitofusin 2 and cancer	217
5. MFN 2 in solid tumors	220
6. Future perspective	226
References	228
Further reading	236

<b>6. Molecular signaling in bone cells: Regulation of cell differentiation and survival</b>	<b>237</b>
Lilian I. Plotkin and Angela Bruzzaniti	
1. Introduction	238
2. Osteoblasts and osteocytes	239
3. Osteoclast signaling mechanisms	250
4. Regulation of bone cell differentiation and function through cell-to-cell contact	261
5. Concluding remarks	267
Acknowledgments	268
References	268
<b>7. Activating mutations of the gp130/JAK/STAT pathway in human diseases</b>	<b>283</b>
Juliane Lokau and Christoph Garbers	
1. Introduction: The IL-6 family of cytokines	284
2. Intracellular signaling cascades activated by IL-6-type cytokines	286
3. Mutations in IL-6 family cytokines	289
4. Mutations in the $\alpha$ -receptors IL-6R, IL-11R, and CNTFR	290
5. Mutations in gp130 and related receptors	292
6. Mutations in Janus kinases	293
7. Mutations in STAT transcription factors	297
8. Concluding remarks	299
References	300
<b>8. Aquaporin water channels: New perspectives on the potential role in inflammation</b>	<b>311</b>
Margherita Sisto, Domenico Ribatti, and Sabrina Lisi	
1. Introduction	312
2. AQPs structure, function and regulation	313
3. Physiological role of mammalian AQPs	316
4. AQPs in inflammation	326
5. Potential role of AQPs in different models of inflammation	326
6. Conclusions	334
Acknowledgment	335
References	335

<b>9. Intracellular protein complexes involved in synapse assembly in presynaptic neurons</b>	<b>347</b>
Kyung Ah Han, Ji Won Um, and Jaewon Ko	
1. Introduction	348
2. Intracellular synaptic signaling by presynaptic neuroligins	349
3. Intracellular synaptic signaling by presynaptic LAR-RPTPs	356
4. Other presynaptic membrane proteins	361
5. Conclusions and future directions	363
Acknowledgments	364
References	364
<b>10. Dopamine signaling in the striatum</b>	<b>375</b>
Emmanuel Valjent, Anne Biever, Giuseppe Gangarossa, and Emma Puighermanal	
1. Introduction	376
2. Distribution of DA receptors and intracellular signaling in the striatum	376
3. Modulation of histone H3 phosphorylation by dopamine	378
4. Regulation of the ribosomal protein S6 by dopamine	386
5. Future directions	389
Acknowledgments	390
References	390
<b>11. Recent advances in computational studies of GPCR-G protein interactions</b>	<b>397</b>
Jinan Wang and Yinglong Miao	
1. Introduction	397
2. Bioinformatics of GPCR-G protein interactions	401
3. Protein-protein docking on GPCR-G protein interactions	402
4. Molecular dynamics simulations of GPCR-G protein interactions	403
5. Discussions and outlook	411
Acknowledgments	413
References	413
<b>12. From traveler to homebody: Which signaling mechanisms sponge larvae use to become adult sponges?</b>	<b>421</b>
Ilya Borisenko, Olga I. Podgornaya, and Alexander V. Ereskovsky	
1. Introduction	422
2. Embryonic development	423

---

3. Morphology of the metamorphosis	426
4. The fate of ciliated cells during metamorphosis of <i>H. dujardini</i>	428
5. A journey from the outside inward: How ciliated cells become detached	432
6. Signaling pathways in sponges	433
7. Conclusions and perspective	442
Acknowledgments	443
References	443
Further reading	449