
Contents

The Orphanin FQ/Nociceptin (OFQ/N) System

OLIVIER CIVELLI	1
1 Discovery of OFQ/N	1
2 Pharmacology and Cellular Responses Induced by OFQ/N	2
3 Synthesis and Inactivation of OFQ/N	3
4 The OFQ/N and Opioid Systems	4
5 Tissue Distribution of the OFQ/N System	6
6 The Functional Implications of the OFQ/N System	8
6.1 Locomotion	8
6.2 Pain	9
6.3 Drug Dependence	10
6.4 Anxiety and Stress	11
6.5 Learning and Memory	12
6.6 Depression	12
6.7 Seizures	13
6.8 Food Intake	13
6.9 Cardiovascular and Renal Systems	14
6.10 Cough and Bronchial Constriction	14
6.11 Immune System	15
7 Conclusions	15
References	17

Orexins and Orexin Receptors:

From Molecules to Integrative Physiology

TAIZO MATSUKI, TAKESHI SAKURAI	27
1 Introduction	27
2 Orexin and Orexin Receptors	28
2.1 Identification of Orexin (Hypocretin) by Deorphaning of Two GPCRs	28
2.2 Orexin Receptors	29
2.3 Distribution of Orexin Neurons	29
2.4 Distributions of Orexin Receptors	30
3 Neural Circuits of Orexin Neurons	30
3.1 Neuronal Afferents	30

3.2	Local Interneurons	32
3.3	Efferents of Orexin Neurons	32
4	Roles of Orexins in Regulation of Sleep/Wake States	32
4.1	Interaction with Sleep and Arousal Centers	32
4.2	Interaction with Waking Centers	35
5	Roles of Orexins in Feeding Behavior	37
5.1	Interaction with Hypothalamic Neurons	37
5.2	Regulation of Orexin Neurons by Humoral Factors	38
5.3	Mechanism of Orexin-mediated Feeding	38
5.4	Orexin as Effector of Food Entrainable Oscillator (FEO)	39
6	Roles of Orexins in Reward Systems	41
6.1	Input from Reward Systems	41
6.2	Output to Reward Systems	41
7	Orexins in Emotion, Stress Responses and Autonomic Nervous System	42
7.1	Input from Mesolimbic System	42
7.2	Stress Response	44
7.3	Orexin in Autonomic Nervous System	44
8	Clinical Implications	45
8.1	Orexin Deficiency and Narcolepsy-Cataplexy	45
8.2	Orexin Agonists	45
8.3	Orexin Antagonists	47
9	Conclusion	48
	References	48

Prolactin-Releasing Peptide

STEVEN H. LIN	57
1 Molecular Pharmacology	57
1.1 PrRP	57
1.2 PrRP Receptor	59
2 Anatomical Distribution	62
2.1 PrRP	62
2.2 PrRP Receptor	63
2.3 Comparison Between PrRP and PrRP Receptor Expression	65
3 Functional Implications	69
3.1 Prolactin Release	70
3.2 Stress and Anxiety Response	70
3.3 Food Intake and Energy Homeostasis	72
3.4 Pain Processing	73
3.5 Sexual and Reproductive Functions	74
3.6 Sleep and Arousal	75
3.7 Pressor Effects	76
3.8 Other Actions	77

4	Conclusion	78
	References	79

Structure and Function of Ghrelin

	MASAYASU KOJIMA, KENJI KANGAWA	89
1	Introduction	89
2	Discovery and Structure Determination of Ghrelin	90
3	Des-Acyl Ghrelin	91
4	Ghrelin Gene and the Structure of the Ghrelin Precursor	93
5	Enzyme for Acyl-Modification of Ghrelin	93
6	Ghrelin Receptor Family	94
7	Ghrelin and Motilin	95
8	Distribution of Ghrelin	96
8.1	Plasma Ghrelin	96
8.2	Gastric and Intestinal Ghrelin	96
8.3	Pancreatic Ghrelin	98
8.4	Pituitary Ghrelin	99
8.5	Ghrelin in the Brain	99
9	Physiological Functions of Ghrelin	99
9.1	Growth Hormone Releasing Activity of Ghrelin	100
9.2	Appetite Stimulating Activity of Ghrelin	101
9.3	Pathway of the Ghrelin Signal; from Peripheral Tissues to the Central Nervous System	103
9.4	Ghrelin and Eating Disorders	104
9.5	Cardiovascular Function of Ghrelin	105
9.6	Gastrointestinal Function of Ghrelin	105
9.7	Ghrelin and Pancreatic Function	106
9.8	Ghrelin and the Process of Learning and Memory	106
10	Obestatin, a Ghrelin Precursor-Derived Peptide?	107
11	Epilogue	108
	References	108

GPR54 and Kisspeptins

	W. H. COLLEDGE	117
1	Introduction	117
2	The GPR54 Receptor	119
3	Kiss1	119
4	Role in Metastasis	121
5	Role in Reproduction	122
5.1	GPR54 Mutations in Hypogonadotropic Hypogonadism	122
5.2	Hypothalamic Expression Pattern	124
5.3	Stimulation of Gonadotropin Secretion	126
5.4	Activation at Puberty	128
5.5	Kiss1 Regulation by Sex Steroids	129

5.6	Kiss1 Expression During the Estrus Cycle	131
5.7	Seasonal Breeding	132
5.8	Lactation	133
6	Kisspeptin Action at Non-Hypothalamic Sites	133
6.1	Pituitary	133
6.2	Metabolism	134
6.3	Ovary/Testes	136
6.4	Placenta	136
	References	137

Neuropeptide S:

Anatomy, Pharmacology, Genetics and Physiological Functions

RAINER K. REINSCHIED	145
1 Identification and Structure of NPS	145
2 Anatomy and Neurochemistry of the NPS System	147
3 Pharmacology and Genetics of NPSR	148
4 Modulation of Arousal and Wakefulness by NPS	150
5 Anxiolytic-Like Effects of NPS	151
6 Modulation of Feeding Behavior by NPS	152
7 The NPS System as Part of Neural Networks	153
8 Conclusions	154
References	155

The Melanin-Concentrating Hormone System and Its Physiological Functions

YUMIKO SAITO, HIROSHI NAGASAKI	159
1 Introduction: MCH from Fish Scales	159
2 MCH Gene and Its Primary Functions in Mammals	161
3 MCH Receptors and Receptor Signaling	164
3.1 Discovery of MCH Receptor Through Orphan Receptor Strategies	164
3.2 Characterization of the MCH1R-Signaling Pathway	167
4 Effects of MCH1R Antagonism on Physiological Responses	169
4.1 Efficacy of Feeding Behavior and Energy Balance	169
4.2 Efficacy in Anxiety, Depression, and Stress	170
5 Peripheral Roles of the MCH–MCH Receptor System	171
6 Conclusions	173
References	173

Biological Function of Prokineticins

Q.-Y. ZHOU, R. MEIDAN	181
1 Introduction	181
2 Distribution of Prokineticin Receptors	182
3 Regulatory Function of PK2 in Circadian Rhythms	182

4	Function of PK2 in Neurogenesis	186
5	Functions in Angiogenesis	188
6	Functions in the Reproductive System	189
7	Prokineticins as Regulators of Gastrointestinal Motility . . .	191
8	Prokineticins and Pain Perception	192
9	Role of Prokineticins in the Development and Function of Blood Cells	193
10	Summary and Perspectives	194
	References	194

Neuromedin S: Discovery and Functions

	KENJI MORI, MIKIYA MIYAZATO, KENJI KANGAWA	201
1	Discovery of Neuromedin S	201
2	Structure of Neuromedin S	203
3	Receptors for Neuromedin S	204
4	Distribution of Neuromedin S	204
5	Functions of Neuromedin S	205
5.1	Circadian Oscillator System	206
5.2	Feeding Regulation	207
5.3	Gonadotropic Axis	208
5.4	Antidiuretic Action	209
6	Summary	209
	References	210

Relaxin-3, INSL5, and Their Receptors

	CHANGLU LIU, TIMOTHY W. LOVENBERG	213
1	Insulin Peptide Superfamily	214
2	Is LGR7 the Physiological Receptor for R3?	216
3	GPCR135 is Likely the Physiological Receptor for R3	216
4	GPCR135 and R3 are Highly Conserved Across Species . . .	218
5	Is There an Additional Receptor for R3?	218
6	Does GPCR142 Play a Significant Role in Higher Species? . .	221
7	Is There an Additional Ligand for GPCR142?	221
8	INSL5 Is Likely the Endogenous Receptor for GPCR142 . . .	223
9	Insulin Family of Peptides Activate Three Different Classes of Receptors	223
10	Relaxin-3, the Ancestor Gene for the Relaxin Subfamily of Peptides	225
11	Creation of Selective Pharmacological Tools for GPCR135 In Vivo Studies	226
11.1	R3/I5 Chimeric Peptides as a Selective Agonist for GPCR135 and GPCR142 over LGR7	226

11.2	R3 Chimeric Peptide Studies Shed Light on the Mechanism of the Ligand/Receptor Interactions Between Relaxin-Related Peptides and Their Receptors . . .	228
11.3	[¹²⁵ I]R3/I5 Is a Valuable Tool for Mapping GPCR135 Binding Sites in the Brain	228
11.4	R3(BΔ23-27)R/I5 Is a Selective Antagonist for GPCR135 and GPCR142	231
12	GPCR135 Selective Agonist (R3/I5) Stimulates Feeding in Rats, an Effect Blocked by Co-Administration of a GPCR135 Selective Antagonist [R3(BΔ23-27)R/I5] . . .	232
13	Summary	233
	References	234

The NPB/NPW Neuropeptide System and Its Role in Regulating Energy Homeostasis, Pain, and Emotion

	MARI HONDO, MAKOTO ISHII, TAKESHI SAKURAI	239
1	Introduction	239
2	Identification of NPB and NPW	240
3	Structures of NPB and NPW	240
4	Structure-Activity Relationships of NPB and NPW	242
5	Structures and Functions of NPBWR1 and NPBWR2	243
6	Tissue Distributions of NPB/NPW and NPBWR1/NPBWR2	244
6.1	Neuropeptide B	244
6.2	Neuropeptide W	246
6.3	NPBWR1 (GPR7)	246
6.4	NPBWR2 (GPR8)	247
7	Pharmacological Activities of NPB as NPW	247
7.1	Feeding and Energy Homeostasis	247
7.2	Effect on Inflammatory Pain	248
7.3	Neuroendocrine Regulation	249
7.4	Autonomic Regulation	250
8	Emotion and Behavior	250
8.1	Effects on Circadian Rhythm	251
9	Peripheral Actions	251
10	Phenotypes of NPBWR1- and NPB-Deficient Mice	253
10.1	NPBWR1-Deficient Mice	253
10.2	NPB-Deficient Mice	253
11	Discussion	254
	References	255

Subject Index	257
--------------------------------	------------

Orphan G Protein-Coupled Receptors and Novel
Neuropeptides

Civelli, O.; Zhou, Q.-Y. (Eds.)

2008, XV, 259 p., Hardcover

ISBN: 978-3-540-78350-3