

Contents

1 Evolution of Resistance Genes in Plants	1
Shunyuan Xiao, Wenming Wang, and Xiaohua Yang	
1 Evolution of the Plant <i>R</i> Gene System	2
2 Conservation and Diversity of Plant <i>R</i> Genes	3
3 NBS, LRR and TIR – Domains of Defense	6
4 Proliferation and Diversification of <i>NBS-LRR</i> Genes in Plants	9
5 Mechanisms of R-Avr Recognition	10
5.1 Direct R-Avr Interaction – the “Gene-For-Gene” Hypothesis .	10
5.2 Indirect R-Avr Interaction – the “Guard” Hypothesis	11
6 Patterns of <i>R</i> -Avr Coevolution	13
6.1 Diversifying Selection Results from Direct R-Avr Recognition? .	14
6.2 Balancing Selection Results from Indirect Recognition?	15
6.3 A General Model for Evolution of the Plant <i>R</i> Gene System	17
7 New Perspectives	19
References	20
2 The Path Less Explored: Innate Immune Reactions in Cnidarians	27
Thomas C.G. Bosch	
1 Cnidaria Are Among the Earliest Multicellular Animals	
in the Tree of Life	28
2 Immune Reactions in Invertebrates	30
3 Immune Reactions in Cnidaria	30
3.1 How to Fight for a Space to Live? Intraspecies	
Competition in Sea Anemones	31
3.2 How to Detect Approaching Allogeneic Cells	
as Foreign and to Eliminate Them? Allore cognition	
and Cell Lineage Competition in Colonial <i>Hydractinia</i>	32
3.3 How to Detect and Disarm Microbial Attackers?	
Antimicrobial Defense Reactions in the Freshwater	
Polyp <i>Hydra</i> and the Jellyfish <i>Aurelia</i>	34

3.4	How to Distinguish Between Friends and Foes: Symbiotic Relationships in Corals and <i>Hydra</i>	36
4	How to Explore the Path They Went? Why Cnidarians Matter	38
	References	39
3	Bug Versus Bug: Humoral Immune Responses in <i>Drosophila melanogaster</i>	43
	Deniz Ertürk-Hasdemir, Nicholas Paquette, Kamna Aggarwal, and Neal Silverman	
1	Introduction	44
1.1	A Brief History	44
1.2	Overview of the <i>Drosophila</i> Immune Response	45
2	Microbial Recognition – the Peptidoglycan Recognition Proteins	45
2.1	Peptidoglycan	47
2.2	NF-κB Proteins	48
3	The Toll Pathway	49
4	The IMD Pathway	55
5	Down-Regulation of the IMD Pathway by PGRP Amidases	60
6	JAK/STAT Pathway	61
7	Concluding Remarks	62
	References	63
4	Cellular Immune Responses in <i>Drosophila melanogaster</i>	73
	Adrienne Ivory, Katherine Randle, and Louisa Wu	
1	Introduction	74
2	Encapsulation	75
2.1	Recognition Centers on Membrane Differences	76
2.2	Lamellocyte Proliferation: Necessary for Successful Encapsulation Response	78
2.3	Adhesion Requires Integrins, Rac, and Rho	78
2.4	Encapsulation Terminates with the Formation of Basement Membrane	82
3	Phagocytosis	83
3.1	Proteins Opsonize Invading Bacteria and Fungi to Promote Phagocytosis	84
3.2	Transmembrane and Circulating Peptidoglycan Recognition Proteins are Involved in the Recognition of Bacteria	85
3.3	Receptors with Scavenger-Like Activity Recognize a Variety of Microbes	86
3.4	Phagocytosis Requires Reorganization of the Actin Cytoskeleton	88
3.5	Engulfed Pathogens are Degraded in Phagolysosomes	89
3.6	Interactions Between Cellular and Humoral Immune Responses	90
	References	91

5 Immune Reactions in the Vertebrates' Closest Relatives, the Urochordates	99
Konstantin Khalturin, Ulrich Kürn, and Thomas C.G. Bosch	
1 Introduction	100
2 Urochordates are at the Root of Vertebrate Evolution	100
3 Natural History and Ecology of Urochordates	101
4 Immunity in Urochordates	102
4.1 Antimicrobial Peptides from Urochordates	103
4.2 Allore cognition in Urochordates	104
4.3 Complement in Urochordates	106
4.4 Despite the Absence of MHC, Urochordate Blood Contains NK-Like Cells	107
5 Conclusion	108
References	108
6 Innate Immune System of the Zebrafish, <i>Danio rerio</i>	113
Con Sullivan and Carol H. Kim	
1 Overview	114
2 Components of Innate Immunity	115
2.1 General Description	115
2.2 <i>Drosophila</i> Toll: Identification and Recognition of a Dually Functioning Pathway	116
2.3 TLRs and TIR-Bearing Adaptor Proteins	117
3 Zebrafish as a Model for Infectious Disease and Innate Immune Responses	118
3.1 Overview	118
3.2 Forward and Reverse Genetics	119
3.3 An Infectious Disease and Innate Immunity Model	120
4 NK-Like Cells	122
5 Additional Innate Immunity Receptors in Zebrafish	124
6 Zebrafish Phagocytes	126
7 Conclusion	126
References	127
7 Toll-Like Receptors in the Mammalian Innate Immune System	135
Andrei E. Medvedev and Stefanie N. Vogel	
1 Introduction	136
2 TLRs as Primary Sensors of Pathogenic PAMPs and Endogenous "Danger" Molecules	137
3 TLR Signaling Pathways	141
3.1 Interaction of TLRs with PAMPs and Co-Receptors Initiates Signaling	141
3.2 Role of TIR-Containing Adapter Molecules in TLR Signaling	142

3.3	TLR Specificity for PAMPs in the Ectodomain and Adapters in the TIR Domain Underlie a Dual Recognition/Response System	146
3.4	The IRAK Family: Key Regulators of TLR Signaling	147
4	Mutations in TLRs and IRAK-4: Implications for Disease	149
5	Conclusions	155
	References	156
8	NLRs: a Cytosolic Armory of Microbial Sensors Linked to Human Diseases	169
	Mathias Chamaillard	
1	Introduction	170
2	NLRs, a Conserved Cytosolic Arm of the Innate Immune System	171
3	Physiological Role of NLRs in Innate and Adaptive Immunity: NLRs Join TLRs	174
3.1	Host Sensing of Non-TLR PAMPs: Lessons from NOD1 and NOD2 Studies	174
3.2	NLRs Promote Maturation of TLR-Induced IL-1 β and IL-18 Release	176
4	What Can we Learn from NLRs Linked to Human Diseases?	177
4.1	NOD1 and NOD2 Mutations Linked to Chronic Inflammatory Diseases	178
4.2	Auto-Inflammatory Diseases	179
4.3	Reproduction Diseases	179
5	Concluding Remarks: Towards the Development of “Magic” Bullets	179
	References	180
9	Antimicrobial Peptides as First-Line Effector Molecules of the Human Innate Immune System	187
	Regine Gläser, Jürgen Harder, and Jens-Michael Schröder	
1	Introduction	188
2	Epithelial Antimicrobial Peptides and Proteins	189
2.1	Lysozyme	189
2.2	Human Beta Defensins	189
2.3	Human Alpha Defensins	194
2.4	RNases	195
2.5	S100 Proteins: S100 A7 (Psoriasin)	196
2.6	Others	198
3	Phagocyte Antimicrobial Peptides	200
3.1	Human Alpha Defensins	200
3.2	Cathelicidins	200
3.3	S100 Proteins: S100 A8/9 (Calprotectin) and S100A12 (Calgranulin C)	201
3.4	Others	202

Contents

4	Putative Action of Antimicrobial Peptides in the Healthy Human	202
5	Antimicrobial Peptides and Diseases	205
5.1	Skin Diseases	205
5.2	Wound Healing	206
5.3	Diseases of the Airway Epithelia: Cystic Fibrosis	207
5.4	Gastrointestinal Diseases: Inflammatory Bowel Diseases	208
5.5	Diseases Associated with Phagocyte Dysfunction	209
6	General Conclusion and Future Aspects	210
	References	210
10	The Complement System in Innate Immunity	219
	K.R. Mayilyan, Y.H. Kang, A.W. Dodds, and R.B. Sim	
1	The Complement System in Mammals	220
1.1	Classical Pathway	221
1.2	The Lectin Pathway	223
1.3	Alternative Pathway	225
1.4	Regulation of the Complement System	228
1.5	Complement Receptors	229
2	The Structure of Complement Proteins	230
3	Complement Across Species	232
	References	233
Index		237