

CONTENTS

Contributors

ix

1. New Insights into Adaptive Immunity in Chronic Neuroinflammation

1

Volker Siffrin, Alexander U. Brandt, Josephine Herz, and Frauke Zipp

1. Introduction: Multiple Sclerosis Is a Heterogeneous Inflammatory Disease of the Nervous System 2
2. Experimental Autoimmune Encephalomyelitis as a Model for MS 3
3. Current Knowledge About Induction and Perseveration of Chronic Neuroinflammation 5
4. Therapeutic Approaches to Chronic Neuroinflammation 20
- Acknowledgments 29
- References 29

2. Regulation of Interferon- γ During Innate and Adaptive Immune Responses

41

Jamie R. Schoenborn and Christopher B. Wilson

1. Introduction 43
2. IFN- γ -Producing Cells 45
3. Signaling Pathways Controlling IFN- γ Production by NK Cells 48
4. Control of IFN- γ Production by NKT Cells 52
5. Signaling Pathways in the Differentiation of CD4 and CD8 T Cells 53
6. Transcription Factors Downstream of the TCR, Activating NK Receptors, and Cytokine Receptors 60
7. Epigenetic Processes Govern Plasticity of Cell Fate Choices and Help to Identify Distal Regulatory Elements 72
8. Transcriptional Regulatory Elements Within the *Ifng* Gene 74
9. Functional Analysis of Candidate Distal Regulatory Elements in the *Ifng* Locus 82
10. Conclusions and Future Directions 84
- Acknowledgments 85
- References 85

3. The Expansion and Maintenance of Antigen-Selected CD8⁺ T Cell Clones	103
Douglas T. Fearon	
1. Background	105
2. The Behavior of the CD8 ⁺ T Cell in Persistent Viral Infections	111
3. Clarifying the Role of IL-2 in the Clonal Expansion and Effector Differentiation of the CD8 ⁺ T Cell	115
4. Coreceptors Mediating IL-2-Independent CD8 ⁺ T Cell Clonal Expansion	118
5. Modifying the Antiproliferative Effects of Types I and II IFN	120
6. Transcriptional Control of Replicative Senescence: Bmi-1, Blimp-1, and BCL6/BCL6b	123
7. A Refined Model for CD8 ⁺ T Cell Clonal Expansion: Sequential Phases of CD27-Dependent Self-Renewal and IL-2-Dependent Differentiation	126
8. Clinical Extensions of the TCR/CD27 Pathway: Adoptive CD8 ⁺ T Cell Therapy	127
Acknowledgments	129
References	129
 4. Inherited Complement Regulatory Protein Deficiency Predisposes to Human Disease in Acute Injury and Chronic Inflammatory States	 141
Anna Richards, David Kavanagh, and John P. Atkinson	
1. Altered Self Triggers Innate Immunity	143
2. Regulation of the Alternative Complement Pathway	145
3. Lessons from Homozygous Complement Regulatory Protein Deficiencies	153
4. Complement and Atypical Hemolytic Uremic Syndrome	154
5. Complement and Age-Related Macular Degeneration	160
6. Immunopathogenesis of aHUS and AMD	163
7. Treatment of aHUS and AMD	167
8. Conclusions: Lessons and Implications	168
References	169
 5. Fc-Receptors as Regulators of Immunity	 179
Falk Nimmerjahn and Jeffrey V. Ravetch	
1. Introduction	180
2. The Family of Activating and Inhibitory FcRs	181
3. Activating and Inhibitory FcR Signaling Pathways	183
4. The Role of Activating and Inhibitory FcRs on Innate Immune Effector Cells	185

5. Modulation of Antibody Activity	188
6. Activating and Inhibitory FcR Expression on DCs	190
7. FcγRIIB as a Master Regulator of Humoral Tolerance and Plasma Cell Survival	192
8. Summary and Outlook	195
Acknowledgments	196
References	196
<i>Index</i>	205
<i>Content of Recent Volumes</i>	211
<i>See Color Plate Section in the back of this book</i>	