

TABLE OF CONTENTS

TABLES	VIII
FIGURES (PLATES)	IX
KEY WORDS	X
PREFACE & INTRODUCTION	XI
FOREWORD (KATALIN PALOCZI)	XIII
PREFACE (H. DAVID KAY)	XV
A PREFACE FROM A CLOSE COLLABORATOR AND FRIEND (JOSEPH C. HORVATH)	XXII
1. THE INNATE IMMUNE SYSTEM	1
1.1. The Universal Ancestor(s)	1
1.2. Chemokines and Toll-like Receptors Make Their Appearance	7
1.3. Nod	12
1.4. Viral Evolution	13
1.5. Interferons and Small Interfering RNAs	17
1.6. The Ascidian Haemocyte and Its Followers	24
1.7. Programmed Cell Death	25
1.8. Bactericidal Substances	39
1.9. Some Simple Interactions	39
1.10. Oncogenic Mutations	40
2. THE ADAPTIVE IMMUNE SYSTEM	43
2.1. Primordial Adaptive Elements	43
2.2. Retrotransposons	44
2.3. Host and Viral Genetic Refinements	45
2.4. The Placenta	63
2.5. The Thymus, Bursa of Fabricius and MALT	67
2.6. The Host Confronts Mutagenes and Pathogenes Attacking Lymphoid Tissues	69
2.7. DC, NK, T, B, T_{REG} Cells	73
2.8. Humoral and Cell-Mediated Immunity	75

3. TUMOR IMMUNOLOGY AND IMMUNOTHERAPY	89
3.1. Cancer Vaccines	89
3.2. Natural and Artificial Hybridoma Formations by Cell Fusions	92
3.3. Lymphocytes Cytotoxic to Human Tumor Cells	115
3.4. Adoptive Immune Lymphocyte Therapy	128
4. AUTOIMMUNITY AND LYMPHOMAGENESIS	137
4.1. Hashimoto Thyroiditis	137
4.2. Systemic Lupus Erythematosus	140
4.3. Malignant Thymoma and Autoimmunity	144
5. CYTOTOXIC LYMPHOCYTES AGAINST CELLULAR AND VIRAL INFECTIOUS AGENTS	149
5.1. Complex Eukaryotic Pathogens	149
5.1.1. Worms	149
5.1.2. Unicellular Parasites	151
5.1.3. Fungal Pathogens	156
5.2. Septic Shock	157
5.3. Interaction with Intracellular Bacteria and Mycobacteria	159
5.3.1. Bacteria	159
5.3.2. Mycobacteria	163
5.4. Anti-Oncoviral Immunity	170
5.4.1. Retroviruses	170
5.4.2. DNA Viruses	187
6. A CONCISE SYNOPSIS (2007-8)	215
6.1. From RNA Concentrates to Synthrophus and Upward	215
6.1.1. Another Ancient Microorganism	215
6.1.2. The RNA Prevails	216
6.1.3. Avian Retroviruses and Herpesviruses Compete for the Malignant Transformation of Their Host Cells	218
6.1.4. Unicellular Eukaryotes Emerge and Evolve	219
6.1.5. Transposable Elements Sustain the Plasticity of the Genomes	221
6.1.6. The Pluripotent Stem Cell	224
6.2. Innate Immune Faculties Regulate the Lymphocytes	225
6.2.1. Land Plants Derive from Green Algae and Develop Defensive Reactions	225
6.2.2. Circulating Cells Arise in the Service of Multicellular Hosts	226
6.2.3. Molecular Defensins Predating Antibodies	227
6.2.4. Subverted Cytokines of the Host Serve the Tumor	230
6.2.5. The Most Advanced Hosts Still Mobilize Innate Defenses	231

6.3.	Innate and Adaptive Interactions in Infections and in Malignancies	233
6.3.1.	<i>CpG Islands</i>	233
6.3.2.	<i>The Pathogens Strike Back. Treacherous Cytokines</i>	234
6.3.3.	<i>The Immunosuppression of Pregnancy</i>	236
6.3.4.	<i>Co-evolving Viruses Establish a "Criminal Collusion"</i>	241
6.3.5.	<i>The Immuno-evasive Skills of the Viral Genome is Matched by Protozoa</i>	256
6.4.	Latest Events in Human Cancer Immunology and Immunotherapy	257
6.4.1.	<i>Epigenetics</i>	257
6.4.2.	<i>Ancient TLRs Knew How to Induce Apoptosis</i>	258
6.4.3.	<i>Obstacles to Antitumor Immune Reactions of the Host</i>	259
6.4.4.	<i>Cancer Vaccines Induce Antitumor Immune Reactions but the Tumor Survives</i>	261
6.4.5.	<i>Adoptive Immune Lymphocyte Therapy</i>	262
SUMMARY		269
APPENDIX I.		281
APPENDIX II. (ADDED AT PROOF-READING)		285
AUTHOR'S POSTSCRIPT		293
REFERENCES		295
ACKNOWLEDGEMENTS		377
ABOUT THE AUTHOR		381
SUBJECT INDEX		383