



Immunology An Introductory Textbook

edited by

Anil K. Sharma



Published by

Pan Stanford Publishing Pte. Ltd. Penthouse Level, Suntec Tower 3 8 Temasek Boulevard Singapore 038988

Email: editorial@panstanford.com Web: www.panstanford.com

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library.

Immunology: An Introductory Textbook

Copyright © 2019 by Pan Stanford Publishing Pte. Ltd.

All rights reserved. This book, or parts thereof, may not be reproduced in any form or by any means, electronic or mechanical, including photocopying, recording or any information storage and retrieval system now known or to be invented, without written permission from the publisher.

For photocopying of material in this volume, please pay a copying fee through the Copyright Clearance Center, Inc., 222 Rosewood Drive, Danvers, MA 01923, USA. In this case permission to photocopy is not required from the publisher.

ISBN 978-981-4774-51-2 (Hardcover) ISBN 978-1-315-15063-5 (eBook)

Contents

Prefe	асе		xiii					
1.	Introduction to Immunology							
	Priya Katyal Batra, Anil K. Sharma,							
	and Robinka Khajuria							
	1.1 Historical Attributes							
	1.2	Immunological Responses and Effectors	11					
		1.2.1 Innate and Adaptive Immunity	11					
		1.2.1.1 Innate immunity	12					
		1.2.1.2 Adaptive immunity	12					
	1.3	Summary	15					
2.	lmm	nunity	19					
	Sneha Choubey, Vikas Beniwal, and Anil K. Sharma							
	2.1	Basic Concept of Immunity	19					
	2.2	Historical Background of Immune Responses	20					
	2.3 Cell-Mediated Immune Responses							
	2.4 Processing of Endogenous Antigens: Cytosolic							
	Pathway							
	2.5							
		Pathway	26					
	2.6		27					
	2.7		29					
	2.8	1 1 5	29					
	2.9	Humoral Response to T-Independent Antigens	30					
3.	Prot	eins of the Immune System	33					
	Anil	Kumar Bhankhar and Vikas Beniwal						
	3.1	Antimicrobial Peptide	34					
	3.2	Pattern Recognition Receptor	35					
	3.3	Toll-Like Receptors	36					
		NOD Protein	39					
		Acute Phase Proteins	40					
		Interferon	42					
	3.7	Complement System	42					

		3.7.1 Function of Complement System	44
		3.7.2 Complement Nomenclature	44
	3.8	Activation of Complement Pathways	45
	3.9	Classical Pathway of the Complement System	46
	3.10	Lectin Pathway	49
	3.11	Alternative Pathway	51
	3.12	Small Fragments of the Complement Protein	
		Initiates Local Inflammatory Response	54
	3.13	Membrane Attack Complex (MAC) or Lytic	
		Pathway	55
	3.14	Regulation of Complement Protein	57
	3.15	Summary	58
1	Maio	r Histocompatibility Complex (MHC): Recent	
4.	_	ds and Relevance from Immunological Perspective	67
			07
	-	Bose, Navnit Kumar Mishra, and Anil K. Sharma	
	4.1	Introduction	67
	4.2	Nomenclature of HLA Antigens	69
	4.3	Frequency of Different HLA Alleles Molecular and Genetics Basis of MHC	70
	4.4	Polymorphisms	70
		4.4.1 Inheritance	70
		4.4.2 Expression	72
	4.5	MHC Molecules: Structure and Genetics	73
	т.5	4.5.1 MHC Class I vs. MHC Class II	74
		4.5.1.1 MHC Class I	74
		4.5.1.2 MHC Class II	78
	4.6	Role of MHC in Immune Response	81
		4.6.1 The Mixed Lymphocyte Reaction	81
		4.6.2 Antigen Processing and Presentation	81
		4.6.3 Some Points about MHC Class I and	
		Class II/TCR	83
	4.7	Antigen Processing and Presentation	84
	4.8	Langerhans Cells as APC	85
	4.9	Antigen Processing and Presentation by Class II	
		(Exogenous/Endocytic) Pathway	86
	4.10	Antigen Processing and Presentation by Class I	
		(Endogenous/Cytosolic) Pathway	87
		Significance of MHC-Peptide Presentation	89
	4 12	Clonal Selection of T-cells	90

					Contents	vii
	4 13	Generat	ion of Cytor	toxic T-Cells	92	
			Response		93	
			ment Factor		93	
		_		unctions of MHC Genes	94	
	4.17	Disease	and the Ma	jor Histocompatibility		
		Complex	K		94	
5.	Imm	une Syste	m of the Br	ain	99	
				seel, Suresh Pallikkuth, Sharma, and		
		nn vanaa hese K. Ge		Snarma, ana		
	_		•		100	
		Introduo Microgli			100 101	
	5.3				101	
	5.4	-	e Receptors		104	
	5.5		ammatory (106	
	5.6	Summai	-	by tokines	106	
6.	An O	verview o	of Immunod	leficiency Disorders	113	
	Varg	hese K. Ge	eorge, Sures	h Pallikkuth,		
	Anil	K. Sharmo	a, Ranjini Va	aliathan, and		
	Sudh	eesh Pila	kka Kanthik	reel		
	6.1	Introdu	ction		114	
	6.2	Primary	Immunode	eficiency Diseases	115	
	6.3	Classific	ation of Pr	imary Immunodeficiency	115	
		6.3.1	Severe Co	mbined Immunodeficiency	115	
			6.3.1.1	X-linked recessive		
				severe combined		
				immunodeficiency	116	
			6.3.1.2	Adenosine deaminase		
				deficiency	117	
		6.3.2		ned Syndromes with	445	
				eficiency	117	
			6.3.2.1	Wiskott-Aldrich		
				syndrome protein- interacting protein		
				deficiency	117	
			6.3.2.2	DiGeorge syndrome	117	
			6.3.2.3	Phospholipase Cg2	110	
			0.01210	gain-of-function mutations	118	

		6.3.3	Predomin	antly Antibody Defects	119
			6.3.3.1	Forms of	
				agammaglobulinemia	119
			6.3.3.2	Common variable	
				immunodeficiency	119
			6.3.3.3	Selective IgA deficiency	120
			6.3.3.4	CD21 deficiency	120
		6.3.4	Defects of	Immune Dysregulation	121
			6.3.4.1	Pallidin deficiency	121
			6.3.4.2	CD27 deficiency	121
		6.3.5	Defects in	Innate Immunity	121
			6.3.5.1	Differentiation of	
				neutrophils	121
			6.3.5.2	Anhidrotic ectodermal	
				dysplasia with	
				immunodeficiency (EDA-ID)	121
			6.3.5.3	Cytokine signaling and	
				immunodeficiencies	122
			6.3.5.4	NK cells	122
		6.3.6	Therapeu	tic Options for Primary	
			Immunod	eficiency	122
	6.4	Seconda	ry (Acquire	ed) Immunodeficiencies	123
		6.4.1	Acquired	Immunodeficiency Syndrome	123
		6.4.2	Immunop	athogenesis	124
		6.4.3	Non-Infec	tious Causes of Secondary	
			Immunod	eficiencies	125
			6.4.3.1	Malnutrition	125
			6.4.3.2	Diabetes mellitus and	
				uremia	125
			6.4.3.3	Immunodeficiencies	
				associated with aging	125
			6.4.3.4	Immunodeficiencies	
				associated with	
				malignancies and other	
				diseases	125
	6.5	Conclus	ions		126
7.	Tum	or Immun	ology		133
	Тара	ın K. Muki	herjee		
	7.1		gin of Cance	er Cells	133

7.2	Tumor (Cell and Car		134
7.3			latural Question: How	
			em Perceive Tumor and	100
	Cancer (CT 1.C	136
	7.3.1	_	on of Tumors and Cancers	406
	700	by Immune System		136
	7.3.2	Tumor Antigens and Their Role in		405
			nmunology	137
		7.3.2.1	O	
			generation of tumor	400
		= 0 0 0	antigens	138
		7.3.2.2	The tumor-specific	
			antigens and tumor-	4.40
		m) .	associated antigens	140
	7.3.3		unosurveillance of Tumor	141
		7.3.3.1	Evidence in favor of	
			immunosurveillance	
			hypothesis	142
		7.3.3.2	The process of	
			immunological reactions	
			against tumor and cancer	
			cells	142
7.4	_		n of Immune Responses	
	_		Cancer Cells	144
	7.4.1		k of CD8 ⁺ T Cells with CD4 ⁺	
		T Cells		145
	7.4.2		al Relevant T Cell	
			ations and Their Role in	
			ımunosurveillance	146
	7.4.3	_	om the Immunosurveillance	147
		7.4.3.1	Role of T regulatory cells in	
			tumor immunosuppression	148
		7.4.3.2	Role of tumor-associated	
			macrophages in tumor	
			immunosuppression	149
		7.4.3.3	Role of myeloid-derived	
			suppressor cells in escape	
			from immunosurveillance	150
	7.4.4		herapies against Tumor and	
		Cancer Ce	ells	151

	7.5	Types of	f Immunoth	nerapy	152
		7.5.1	Adoptive	Immunotherapy	152
			7.5.1.1	Adoptive immunotherapy	
				with tumor-reactive T cells	153
			7.5.1.2	Adoptive immunotherapy	
				with engineered dendritic	
				cells	154
			7.5.1.3	Adoptive immunotherapy	
				with monoclonal antibodies	154
			7.5.1.4	Adoptive immunotherapy	
				with cytokines	155
		7.5.2	Active-Sp	ecific Immunotherapy	156
			7.5.2.1	Feline leukemia virus	156
			7.5.2.2	Hepatitis B virus	156
		7.5.3	Regulator	y T Cells as a Target for	
			Tumor/Ca	ancer Cells Immunotherapy	156
		7.5.4	Tumor-As	ssociated Macrophages as a	
			Target for	Tumor/Cancer Cells	
			Immunotl	herapy	157
	7.6	Summai	ry		157
8.	Prev	iew of An	tibody Engi	neering and Diversity:	
٠.	Trends, Scope, and Relevance				169
				Aishra, and Anil K. Sharma	
	8.1	Introdu		,	169
	8.2		Structure o	of Antibody	170
	8.3			nunoglobulins	172
	8.4		-	asses and Their Biological	1,2
	0.1	Propert	_	asses and Then Bronegieur	173
	8.5	•	cation of An	tibodies	174
		8.5.1		l Antibodies	176
		8.5.2		al Antibodies	176
	8.6	Hvbrido		logy and Antibody	
		Enginee		- 8,	177
	8.7	_	_	noclonal Antibodies	178
	-	8.7.1		of Antibody Library	180
	8.8	-	_	s of Therapeutic Antibodies	180
	8.9			ibody Fragments	182
		8.9.1	_	ng Multivalency	183

		8.9.2	Engineering of Bispecific and	
			Multi-Specific Antibodies	183
		8.9.3	Fusion with Other Molecules	185
		8.9.4	Intrabodies	186
		8.9.5	Glycoengineered Antibodies	187
		8.9.6	Engineered Fcs	187
		8.9.7	Protein Engineering	188
	8.10		ment of Antigen-Binding Affinity and	
		Effector	Function	189
			Antigen-Binding Affinity Improvement	189
			Improvement of Effector Functions	190
	8.11	_	Pharmacokinetics	190
			Increased FcRn Binding	190
			PEGylation	191
		-	Produced by Transgenic Technology	191
	8.13	• •	ions and Future Perspectives	192
		8.13.1	General Application of Antibody	400
		0.400	Engineering	192
		8.13.2	Application of Antibody Engineering	400
	014	C 1 '	in Veterinary Medicine	193
	8.14	Conclusi	on	194
9.	Princ	iples of In	nmunodetection and Immunotechniques:	
	A Pre	view and	Emerging Applications	201
	Shelz	a Thakur,	Navnit Kumar Mishra,	
	Hard	eep Singh	Tuli, and Anil K. Sharma	
	9.1	Western		202
	9.2	ELISA	2.00	203
		9.2.1	Indirect ELISA	204
		9.2.2	Sandwich ELISA	204
		9.2.3	Competitive ELISA	206
	9.3	Flow Cyt	ometry	206
	9.4		munoassay	208
10.	Vacci	nes		213
	Rajas	sri Bhatta	charyya and Dibyajyoti Banerjee	
	-	Introduc		213
			al Background	214
		Definition	_	215
		Classifica		215

xii | Contents

	10.5 Immunization	21	3				
	10.6 Mechanism of Action	21	9				
	10.7 Immunization Schedule						
	10.8 Success Story of Vaccination	on 22	22				
	10.9 Emerging Vaccines and Re	cent Trends 22	23				
11.	Immunoinformatics: A Modern Immunotherapeutic						
	22	25					
	Navnit Kumar Mishra and Anil K. Sharma						
	11.1 Immunology	22	27				
	11.2 Immunological Databases	22	27				
	11.3 Conclusion	23	33				
Index	X	23	37				

Preface

Immunology has been consistently fascinating the scientific community to find out ways to counter many pathogens and other antigenic challenges we face time to time. It acts as a sort of bridge between sciences such as biochemistry, cell biology, structural biology, microbiology, biotechnology, genetics, and medicine. This subject has been referred to as a broad branch of biomedical science covering the study of all aspects of the immune system dealing with its physiological functioning in health and disease. This textbook presents a broader overview of the immune system in a logical and easy-to-understand manner and is a useful resource for undergraduate and postgraduate students of biotechnology. immunology, biosciences, and microbiology. The whole text has been divided into 11 chapters. It begins with an introduction to the immune system, organs, and cells of the immune system and further advances to proteins, immunogens, antibodies, and antibody diversity. Topics such as major histocompatibility complex, immune system of the brain, and immunological disorders have been elegantly covered in the book, increasing its broader perspective. Moreover, tumor immunology, immunoinformatics, vaccines, and principals of immunodetection are some other highlights of this book that will attract the broader attention of students and the research fraternity. The book also presents the latest trends and the scope of immunocomplex and immunodetection approaches for the appropriate diagnosis of diseases. It provides comprehensive, accessible, up-to-date information about immunological perspectives and an instant access to a wealth of data for biotechnologists, biomedical scientists, biochemists, molecular biologists, and students from diverse streams of biotechnology, microbiology, structural biology, and genetics.

I thank all the contributors of this book for their valuable scientific contributions and the reviewers for their precious comments and suggestions for improving the quality and scientific perspectives of the chapters. Finally, I would like to dedicate this book to my mother, who has been consistently fighting with

pituitary macroadenoma, which severely deteriorated her vision, making me go through various immunological aspects associated with the disease and further prompting me to come up with this book for the benefit of students and, above all, for mankind.

Anil K. Sharma