

.....

Parasites and Allergy

.....

Chemical Immunology and Allergy

Vol. 90

Series Editors

Johannes Ring Munich

Luciano Adorini Milan

Claudia Berek Berlin

Kurt Blaser Davos

Monique Capron Lille

Judah A. Denburg Hamilton

Stephen T. Holgate Southampton

Gianni Marone Napoli

Hirohisa Saito Tokyo

KARGER

.....

Parasites and Allergy

Volume Editors

Monique Capron Lille
François Trottein Lille

27 figures, 1 in color, and 2 tables, 2006

KARGER

Basel · Freiburg · Paris · London · New York ·
Bangalore · Bangkok · Singapore · Tokyo · Sydney

.....

Chemical Immunology and Allergy

Formerly published as 'Progress in Allergy' (Founded 1939),
continued 1990–2002 as 'Chemical Immunology'

Edited by Paul Kallos 1939–1988, Byron H. Waksman 1962–2002

.....

Monique Capron

Centre d'Immunologie et Biologie Parasitaire, Inserm U547
'Schistosomiase, Paludisme et Inflammation'

Université de Lille 2

Institut Pasteur de Lille, Lille, France

François Trottein

Centre d'Immunologie et Biologie Parasitaire, Inserm U547
'Schistosomiase, Paludisme et Inflammation'

Université de Lille 2

Institut Pasteur de Lille, Lille, France

Bibliographic Indices. This publication is listed in bibliographic services.

Disclaimer. The statements, options and data contained in this publication are solely those of the individual authors and contributors and not of the publisher and the editor(s). The appearance of advertisements in the book is not a warranty, endorsement, or approval of the products or services advertised or of their effectiveness, quality or safety. The publisher and the editor(s) disclaim responsibility for any injury to persons or property resulting from any ideas, methods, instructions or products referred to in the content or advertisements.

Drug Dosage. The authors and the publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

All rights reserved. No part of this publication may be translated into other languages, reproduced or utilized in any form or by any means electronic or mechanical, including photocopying, recording, microcopying, or by any information storage and retrieval system, without permission in writing from the publisher.

© Copyright 2006 by S. Karger AG, P.O. Box, CH–4009 Basel (Switzerland)

www.karger.com

Printed in Switzerland on acid-free paper by Reinhardt Druck, Basel

ISSN 1660–2242

ISBN 3–8055–7974–8

.....

Contents

XI Foreword

1 Helminth-Induced Immunoregulation of an Allergic Response to Food

C. Nagler-Anderson, Charlestown, Mass.

- 1 Abstract
- 1 Microbes and Allergy
- 3 Enteric Helminth Infection Acts as a Th2-Polarizing Mucosal Adjuvant
- 5 Enteric Helminth Infection Induces Th2 Responses without Atopy
- 8 How Does Helminth Infection Protect against Allergy: Immunoregulatory T or B Cells
- 11 Conclusions
- 11 References

14 The Mutual Influence of Nematode Infection and Allergy

D. Negrão-Corrêa, M.M. Teixeira, Belo Horizonte

- 14 Abstract
- 14 The Worldwide Relevance of Nematode Infections
- 15 Nematode Infections and the Hygiene Hypothesis
- 17 The Model of *S. venezuelensis* Infection in Rodents
- 18 *S. venezuelensis* Infection Induces Eosinophilic Airway Inflammation and Airway Hyperreactivity
- 20 Airway Hyperreactivity Is Shut Off by *S. venezuelensis* Infection but Prevents Parasite Infection
- 22 Role of a Th2 Immune Response for *S. venezuelensis* Elimination from the Intestine
- 25 Concluding Remarks

- 26 Acknowledgements
- 27 References

29 Human Schistosomiasis Decreases Immune Responses to Allergens and Clinical Manifestations of Asthma

M.I. Araujo, E.M. de Carvalho, Salvador

- 29 Abstract
- 29 Immunological Response and Clinical Forms of Schistosomiasis
- 31 Down-Modulation of Type 1 Immune Response in *S. mansoni* Infection
- 35 Immune Response in Atopy
- 36 Influence of Parasite Infection on the Development of Atopy and Asthma
- 42 References

45 Proteases in Helminth- and Allergen-Induced Inflammatory Responses

S. Donnelly, J.P. Dalton, Sydney; A. Loukas, Brisbane

- 45 Abstract
- 48 Proteases Are Major Allergens Derived from Various Organisms
- 49 How Do Proteases Act as Allergens?
 - 49 Disruption of the Epithelial Barrier
 - 50 Modulation of Dendritic Cell (DC) Function
 - 50 Modulation of B and T Cell Function
 - 50 Activation of Mast Cells Via Protease Activated Receptors
 - 51 Alteration of the Protease/Anti-Protease Balance
- 52 Proteases Provoke Allergenic Responses to Non-Peptidolytic Molecules
- 53 Do Parasites Exacerbate or Protect against Allergy?
- 54 Helminth Parasites Secrete Proteases
- 54 Can Parasite Proteases Sensitise Individuals to Environmental Proteases *Via* Cross-Reactive IgE?
- 57 Parasite Peptidolytic Activity May Sensitise Individuals to Allergens
 - 57 Degranulation of Mast Cells and Basophils
 - 57 Modulation of T Cell Responses
 - 58 Recruitment and Activation of Alternatively Activated Macrophages
- 58 Are Helminth Proteases Allergens?
- 61 Conclusion
- 62 Acknowledgements
- 62 References

65 Mechanisms Underlying Helminth-Induced Th2 Polarization: Default, Negative or Positive Pathways?

D. Jankovic, S. Steinfeldler, M.C. Kullberg, A. Sher, Bethesda, Md.

- 65 Abstract
- 66 The Immune Response during Infection with *Schistosoma mansoni*
- 67 Role of IL-4 in *S. mansoni*-Induced Th2 Polarization
- 69 *S. mansoni*-Induced Th2 Polarization Requires DC: Evidence against a Default Pathway
- 71 *S. mansoni* Th2 Polarization As A Negative Pathway: Down-Regulation of DC Functions

- 73 *S. mansoni* Th2 Polarization As A Positive Pathway: Selective Activation of DC
- 74 How Do SEA-Conditioned DC Promote IL-4 Secretion in CD4+ Cells?
- 77 Conclusions
- 77 Acknowledgements
- 78 References

82 Regulation of Dendritic Cell Function by Pathogen-Derived Molecules Plays a Key Role in Dictating the Outcome of the Adaptive Immune Response

E.J. Pearce, C.M. Kane, J. Sun, Philadelphia, Pa.

- 82 Abstract
- 83 Dendritic Cells and Their Role in Th Cell Activation
- 84 Th Response Polarization
- 85 The Interaction of SEA with DCs
- 86 Eggs and SEA Induce Different Responses – An Unexpected Finding
- 87 SEA Inhibits TLR-Initiated DC Maturation
- 88 TLR-Ligand-Activated DCs Provide Negative Instruction for Th2 Response Polarization
- 89 Acknowledgements
- 89 References

91 Glycans Modulate Immune Responses in Helminth Infections and Allergy

I. van Die, Amsterdam; R.D. Cummings, Oklahoma City, Okla.

- 91 Abstract
- 93 Glycan Ags in Schistosomes
- 95 Schistosome Glycan Ags Generate High Levels of Anti-Glycan Abs in Infection
- 97 Helminth- and Allergen-Derived Glycan Ags Induce Th2 Responses
- 98 Immunogenic Glycan Ags Shared between Helminths and Allergens Are IgE Epitopes
- 100 Glycan Ags Regulate Immune Responses via Interaction with Host Lectins
- 101 C-Type Lectins on Antigen-Presenting Cells Recognize Glycan Ags
- 102 Recognition of Schistosome- or Allergen-Derived Glycan Ags by Antigen-Presenting Cells
- 102 Schistosome Egg Glycan Ags Interact with DC-SIGN
- 103 L-SIGN Binds Schistosome Egg Glycan Ags
- 103 Interaction of Schistosome Glycan Ags with hMGL
- 104 The Mannose Receptor Recognizes Ags from Schistosome Eggs and House Dust Mite Der p 1
- 104 Host Protection Mechanisms May Include the Binding of Glycosylated Ags by Soluble Lectins in Schistosomiasis and Allergy
- 105 Interaction of Helminth Glycan Ags and Allergens with Collectins
- 105 Galectin-3 Recognizes LDN Glycan Ags within Schistosome SEA
- 106 Does IL-10 Production Induced by Parasite Glycans Contribute to Protection Against Allergy?
- 108 Concluding Remarks
- 109 Acknowledgements
- 109 References

113 Role of the Natural Killer T Lymphocytes in Th2 Responses during Allergic Asthma and Helminth Parasitic Diseases

F. Trottein, T. Mallevaey, C. Faveeuw, M. Capron, Lille; M. Leite-de-Moraes, Paris

- 113 Abstract
- 114 Classification and General Features of NK T Cells
- 115 NK T Cells in Autoimmune, Neoplastic and Infectious Diseases
- 117 NK T Cells in Th2 Inflammatory Response during Allergic Asthma
- 118 Mechanisms of NK T Cell Activation and Mode of NK T Cell Actions during Allergic Asthma
- 119 NK T Cells during Helminth Infection
- 122 Mechanisms by which NK T Cells Become Activated during Infection
- 122 NK T Cells in Regulatory Mechanisms during Th2-Related Inflammation
- 124 Conclusions
- 124 Acknowledgements
- 125 References

128 The Mast Cell and Gut Nematodes: Damage and Defence

J.L. Pennock, R.K. Grencis, Manchester

- 128 Abstract
- 129 Regulation of Mucosal Mast Cells
- 131 Adhesion and Homing of Mast Cells to the Gut
- 132 Effector Mechanisms
- 136 Current Ideas
- 137 Acknowledgements
- 138 References

141 Basophils, Basophilia and Helminth Infections

E. Mitre, T.B. Nutman, Bethesda, Md.

- 141 Abstract
- 142 Basophil Biology
 - 142 Lineage
 - 142 Growth and Development
 - 143 Trafficking
- 144 Basophil Function
 - 144 Basophil Activation
 - 144 IgE-Mediated Activation
 - 145 Non-IgE Activation
 - 146 Degranulation
 - 146 Activation Markers
 - 146 Effector Molecules
 - 147 Histamine
 - 147 Other Effector Molecules
 - 148 Immunomodulatory Capabilities
 - 148 Cytokine Release
 - 148 Immunomodulatory Properties of Histamine
- 149 Basophils and the Immune Response to Helminth Infections

- 150 Basophilia
- 151 Basophil Activation in Helminth Infections
- 151 Helminth Antigens as ‘Super Allergens’
- 152 Potential Roles of Basophils in Helminth Infections
- 154 References

157 Innate, Adaptive and Regulatory Responses in Schistosomiasis: Relationship to Allergy

*F.C. Hartgers, H.H. Smits, Leiden; D. van der Kleij, Rijswijk;
M. Yazdanbakhsh, Leiden*

- 157 Abstract
- 158 Innate Immune Responses in Schistosomiasis
- 160 Adaptive Immune Responses in Schistosomiasis
- 162 Downregulation of the Immune Response during Chronic Schistosome Infection
- 162 Modulation of Innate Responses
- 165 Modulation of Adaptive Responses
- 165 Modulation via Regulatory T Cells
- 167 Relationship between Schistosomiasis and Allergy
- 167 Prevention of Atopy
- 168 Role of Regulatory T Cells
- 169 IgG4 Antibodies and IL-13 Decoy Receptor
- 171 The Window of Immune Suppression
- 172 Concluding Remarks
- 172 Acknowledgements
- 172 References

176 Regulatory T Cells Induced by Parasites and the Modulation of Allergic Responses

M.S. Wilson, R.M. Maizels, Edinburgh

- 176 Abstract
- 177 The Cellular Basis of Allergic Diseases
- 179 Regulatory T Cell (Treg) Biology
- 181 Regulatory T Cells in Allergic Diseases
- 183 Helminth-Mediated Immune Regulation and Treg Cells
- 184 Helminth Infection and Allergic Disease
- 186 Model Systems for Infection and Allergy
- 189 Alternative Models
- 190 Molecular Mechanisms at the Parasite-Allergy Interface
- 191 Infectious Tolerance and the Specificity of Treg Cells
- 192 Conclusions
- 193 References

196 Author Index

197 Subject Index

.....

Foreword

One of the key words of immunology at the beginning of the 21st century is 'regulation'. Twenty-five years later the Th1/Th2 paradigm, the concept of regulatory cell populations, is now in the heart of our understanding of immune response.

Helminths and allergic conditions are recognized as the main Th2 cell inducers. The negative association of allergic manifestations and helminth infections has been debated for over 30 years. It is, however, only in the recent past, that modulation of allergy by helminth infections has been clearly substantiated and shown to be consistent with the activity of regulatory cell populations, which control effector mechanisms of both Th1 and Th2 types.

Although remarkable progress has been made in identifying the molecular events required for Th2 differentiation, a number of questions which are addressed in this volume point to essential challenges.

Several contributions illustrate the critical importance of characterization of helminth molecules with Th2 or regulatory inducing activities and their modes of action in dendritic cells.

The large emphasis given to glycan epitopes highlights the profound immunomodulatory properties of glycan antigens and their role in inducing two key regulatory cytokines IL-10 and TGF- β . It is striking that the specificity of helminth infection does not influence the profile of the regulatory response: Schistosomes, *Onchocerca*, *Wuchereria* or gut nematodes for instance, induce similar patterns of cytokine production, the regulation appearing more related to the chronicity of infections than to the pathogen itself.

Although the identification of regulatory cell populations has progressed, we are left with a global notion of heterogeneity and a rather unclear respective role of the various incriminated populations: regulatory T and B cells, natural killer T cells, mast cells and basophils, etc. The concept that primary and secondary regulatory populations may account for their heterogeneity is very stimulating, and the role of Fox p 3 as a master control gene is very attractive.

Whereas most of the contributions discuss the down-modulation of allergy by helminths, there is also some evidence that allergy or predisposition to atopic diseases may protect against helminth infections. It is, on the other hand, of particular interest that removal or inhibition of regulatory T cells leads to the effective clearance of infection and restoration of antigen specific activity.

In practical terms, one may expect that allergen-specific immunotherapy, which generates populations of allergen-specific regulatory T cells, producing IL-10 and TGF- β , can significantly reduce allergic manifestations. Conversely, successful immunization against helminth infections and the development of efficient vaccines will certainly rely on a subtle balance between the induction of appropriate effector mechanisms and the expression of regulatory responses.

In this context, the various contributions to this volume dedicated to Parasites and Allergy reveal a new dimension of host-parasite interactions and of the importance of anti-inflammatory responses in chronic helminthiasis. They also provide a novel insight on the possible modes of down-modulation of unwarranted immune responses. They finally pave the way to new directions of research for the successful immunization against helminths and the prevention of inflammatory responses in allergic and autoimmune diseases.

André and Monique Capron, Lille