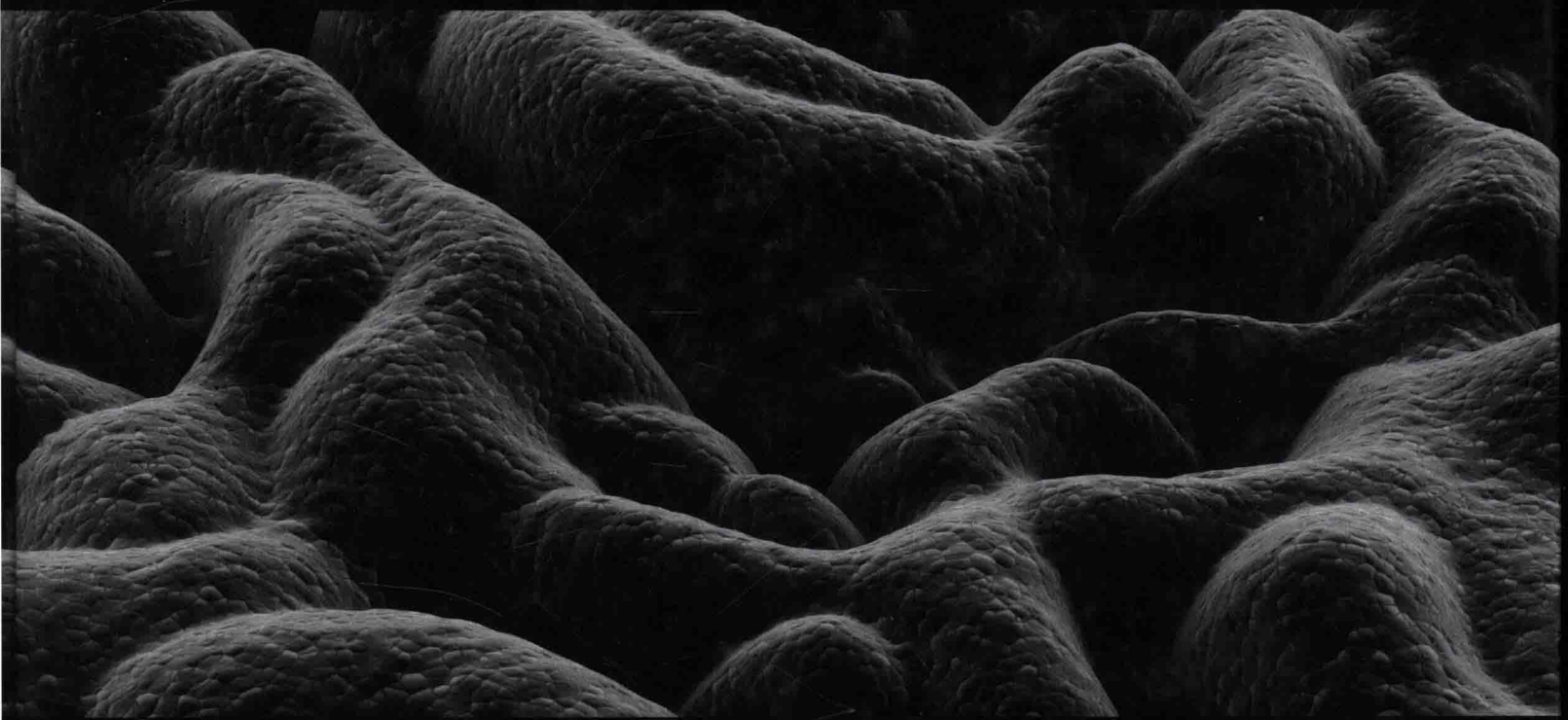
Fourth Edition

Mucosal Immunology

Volume 2



EDITED BY
Jiri Mestecky, Warren Strober,
Michael W. Russell, Brian L. Kelsall,
Hilde Cheroutre, Bart N. Lambrecht

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Edited by

Jiri Mestecky
Departments of Microbiology and Medicine, University of Alabama, Birmingham, AL, USA;
Institute of Microbiology, Czech Academy of Sciences and Department of Immunology and Microbiology,
School of Medicine, Charles University, Prague, Czech Republic

Warren Strober
Chief, Mucosal Immunity Section, Laboratory of Host Defenses, National Institute of Allergy and
Infectious Diseases, National Institutes of Health, Bethesda, MD, USA

Michael W. Russell
Departments of Microbiology/Immunology and Oral Biology, University at Buffalo, Buffalo, NY, USA

Brian L. Kelsall
Mucosal Immunobiology Section, Laboratory of Molecular Immunology, National Institute of Allergy
and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA

Hilde Cheroutre
Division of Developmental Immunology, La Jolla Institute for Allergy and Immunology, La Jolla, CA, USA

Bart N. Lambrecht
VIB Inflammation Research Center, Ghent University, and Department of Respiratory Medicine,
University Hospital Ghent, Ghent, Belgium

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Mucosal Immunology

In Memoriam

Malcolm Artenstein
Thomas Brown
John Cebra
Merrill W. Chase
Arlette Darfeuille-Michaud
Anne Ferguson
Robert Good
Joseph Heremans
Graham Jackson
Martin Kagnoff
Otakar Koldovsky
Hilary Koprowski
Frederick Kraus
Henry Kunkel
Leo LeFrançois
Lloyd Mayer
Goro Mogi
Eva Orlans
Richard Rothberg
Roberta Shahin
Jaroslav Sterzl
Masaharu Tsuchiya
Robert Waldman
Martin Zeitz

For their lasting contributions
to the field of Mucosal Immunology

Arlette Darfeuille-Michaud, who completed Chapter 48 for this edition before her passing, discovered the adherent-invasive biotype of *Escherichia coli* and its role in inflammatory bowel disease. Leo LeFrançois, who co-authored Chapter 35, was a leader in the field of mucosal T cells including intestinal intraepithelial γδ- and αβ- T cells and he was one of the first to introduce the concept of tissue-resident memory T cells. Lloyd Mayer, an editor of the third edition, was a noted clinical immunologist who first demonstrated that intestinal epithelial cells had a critical role in gut immune responses and could present antigen to T cells. Hilary Koprowski pioneered the first oral vaccine against polio and later became director of the Wistar Institute where he contributed to an improved rabies vaccine. John Cebra's seminal finding that intestinal IgA antibody-secreting cells had their origins in Peyer's patches was instrumental in developing the concept of the common mucosal immune system. Jaroslav Sterzl more than 50 years ago initiated studies on the fundamental role of intestinal microbiota in the development and function of the immune system in gnotobiotic animals. Thomas Brown contributed importantly to studies on IgA function and the induction of IgA subclass antibody responses. Martin Zeitz's major contribution was to define the gastrointestinal abnormalities caused by HIV infection; he was the first to show that HIV infection caused an enteropathy resulting in malabsorption and entry of bacterial products into the internal milieu. He contributed Chapter 77 to this edition before his passing.

Contributors

Valérie Abadie (Ch 80) Sainte-Justine Hospital Research Centre, University of Montreal, Montreal, QC, Canada

Clara Abraham (Ch 30) Yale University, CT, USA

David H. Adams (Ch 90) University of Turku, Turku, Finland; NIHR Biomedical Research Unit in Liver Disease, Centre for Liver Research, University of Birmingham, Edgbaston, Birmingham, UK

William W. Agace (Ch 40) Lund University, Lund, Sweden; Danish Technical University, Copenhagen, Denmark

Jennifer Alexander-Brett (Ch 53) Washington University School of Medicine, Saint Louis, MO, USA

Omar Alkhairy (Ch 73) Karolinska University Hospital, Huddinge, Stockholm, Sweden; King Abdulaziz Medical City, Riyadh, Saudi Arabia

Ines Ambite (Ch 106) Institute of Laboratory Medicine, Lund University, Lund, Scania, Sweden

Deborah J. Anderson (Ch 109) Boston University School of Medicine, Boston, MA, USA

David Artis (Ch 54) Institute for Immunology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

Robert L. Atmar (Ch 57) Baylor College of Medicine, Houston, TX, USA

Laetitia Aymeric (Ch 50) Unité de Pathogénie Microbienne Moléculaire, Institut Pasteur, Paris, France; Collège de France, Paris, France

Claus Bachert (Ch 100) Upper Airways Research Laboratory, University Hospital Ghent, De Pintelaan, Ghent, Belgium

Jantine E. Bakema (Ch 20) VU University Medical Center, Amsterdam, The Netherlands

Kristi Baker (Ch 19) Harvard Medical School, Brigham and Women's Hospital, Boston, MA, USA

Kenneth W. Beagley (Ch 107) Queensland University of Technology, Kelvin Grove, QLD, Australia

A.D. Befus (Ch 43) University of Alberta, Edmonton, AB, Canada

Mats Bemark (Ch 33) Mucosal Immunobiology and Vaccine Center, Institute of Biomedicine, University of Gothenburg, Gothenburg, Sweden; Sahlgrenska University Hospital, Gothenburg, Sweden

M. Cecilia Berin (Ch 84) Department of Pediatrics, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Margot Berings (Ch 100) Upper Airways Research Laboratory, University Hospital Ghent, De Pintelaan, Ghent, Belgium

Jay A. Berzofsky (Ch 75) National Institutes of Health, Bethesda, MD, USA

Martin Bilej (Ch 9) Institute of Microbiology of the Academy of Sciences of the Czech Republic, v.v.i., Prague, Czech Republic

Nabanita Biswas (Chs 108, 110) Geisel School of Medicine at Dartmouth, Lebanon, NH, USA

Richard S. Blumberg (Chs 19, 27) Division of Gastroenterology, Hepatology and Endoscopy, Harvard Medical School, Brigham and Women's Hospital, Boston, MA, USA

John Bienenstock (Introduction) McMaster University, Hamilton, ON, Canada

Dimitrios Bogdanos (Ch 87) Institute of Liver Studies, Transplantation Immunology and Mucosal Biology, King's College London School of Medicine, King's College Hospital, London, UK

Monica Boirivant (Ch 79) Immune-mediated Diseases Section, Parasitic and Immune-mediated Diseases, Istituto Superiore di Sanità, Roma, Italy

Kobporn Boonnak (Ch 59) National Institute of Allergy and Infectious Diseases (NIAID), NIH, Bethesda, MD, USA

Ken R. Bracke (Ch 97) Laboratory for Translational Research in Obstructive Pulmonary Diseases, Department of Respiratory Medicine, Ghent University Hospital, Ghent, Belgium

Per Brandtzaeg (Chs 31, 103) Laboratory for Immunohistochemistry and Immunopathology (LIIPAT), Center for Immune Regulation (CIR), University of Oslo, and Department of Pathology, Oslo University Hospital, Rikshospitalet, Oslo, Norway

Jonathan Braun (Ch 5) Department of Pathology and Laboratory Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Marie-Agnès Bringer (Ch 48) UMR1071 Inserm/ Université d'Auvergne, INRA, France

Andrew J. Broadbent (Ch 59) National Institute of Allergy and Infectious Diseases (NIAID), NIH, Bethesda, MD, USA

Richard Bronson (Ch 111) Stony Brook University School of Medicine, Stony Brook, NY, USA

Guy G. Brusselle (Ch 97) Laboratory for Translational Research in Obstructive Pulmonary Diseases, Department of Respiratory Medicine, Ghent University Hospital, Ghent, Belgium

Judith N. Bulmer (Ch 114) Newcastle University, Newcastle upon Tyne, UK

J.E. Butler (Ch 116) Carver College of Medicine, The University of Iowa, Iowa City, IA, USA

Paul A. Cardenas (Ch 6) National Heart and Lung Institute, Imperial College London, London, UK; Universidad de las Americas, Center for Translational Research, Quito, Ecuador

John J. Cebra (Introduction) University of Pennsylvania, Philadelphia, PA, USA

Marina Cella (Ch 52) Washington University School of Medicine, St Louis, MO, USA

Andrea Cerutti (Ch 32) Icahn School of Medicine at Mount Sinai, New York, NY, USA

Stephen J. Challacombe (Ch 102) Department of Oral Medicine, King's College London and Guys & St Thomas Hospitals, London, UK, and University of Sheffield, Sheffield, UK

Kuldeep Chattha (Ch 68) Canadian Food Inspection Agency, Lethbridge, AB, Canada

Hilde Cheroutre (Chs 1, 35, 72) Head, Division of Developmental Immunology, La Jolla Institute for Allergy and Immunology, La Jolla, CA, USA

Tsutomu Chiba (Ch 88) Department of Gastroenterology and Hepatology, Kyoto University Graduate School of Medicine, Kyoto, Japan

Alejo Chorny (Ch 32) Icahn School of Medicine at Mount Sinai, New York, NY, USA

John D. Clements (Ch 61) Tulane University, School of Medicine, New Orleans, LA, USA

Marco Colonna (Ch 52) Washington University School of Medicine, St Louis, MO, USA

William O.C. Cookson (Ch 6) National Heart and Lung Institute, Imperial College London, London, UK

Lynette B. Corbeil (Ch 68) UCSD Medical Center, University of California – San Diego, San Diego, CA, USA

Blaise Corthésy (Ch 21) R&D Laboratory, Division of Immunology and Allergy, University State Hospital (CHUV), Lausanne, Switzerland

Allan W. Cripps (Chs 11, 101) Griffith University, Gold Coast, QLD, Australia

Koen van Crombruggen (Ch 100) Upper Airways Research Laboratory, University Hospital Ghent, De Pintelaan, Ghent, Belgium

Andre Pires da Cunha (Ch 41) Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Susanna Cunningham-Rundles (Ch 74) Weill Cornell Medical College, New York, NY, USA

Roy Curtiss, 3rd (Ch 64) Arizona State University, Tempe, AZ, USA

Arlette Darfeuille-Michaud (Ch 48) UMR1071 Inserm/ Université d'Auvergne, INRA, France

Wouter J. de Jonge (Ch 46) Tytgat Institute for Gastrointestinal and Liver Research, Academic Medical Centre, Meibergdreef, Amsterdam, The Netherlands

Livija Deban (Ch 37) Cancer Research UK, London, UK; King's College London, London, UK

Timothy L. Denning (Ch 26) Georgia State University, Atlanta, GA, USA

James P. Di Santo (Ch 39) Innate Immunity Unit, Inserm U668, Institut Pasteur, Paris, France

Andreas Diefenbach (Ch 3) University of Mainz Medical Centre, Mainz, Germany

Victor J. DiRita (Ch 49) University of Michigan Medical School, Ann Arbor, MI, USA

Jordan Downey (Ch 93) Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

Ming-Qing Du (Ch 89) University of Cambridge, Cambridge, UK

Karen L. Edelblum (Ch 12) The University of Chicago, Chicago, IL, USA

Marjolein van Egmond (Ch 20) VU University Medical Center, Amsterdam, The Netherlands

H.-J. Epple (Ch 77) Charité – Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin, Germany

Sidonia Fagarasan (Ch 23) Research Center for Integrative Medical Sciences, Riken Yokohama, Yokohama, Japan

John V. Fahey (Chs 108, 110) Geisel School of Medicine at Dartmouth, Lebanon, NH, USA

Michael J. Ferris (Ch 7) Louisiana State University Health Sciences Center, New Orleans, LA, USA

Stefan Fichtner-Feigl (Ch 91) University Medical Center Regensburg, Regensburg, Germany

Paul L. Fidel Jr. (Ch 112) Louisiana State University Health Science Center, New Orleans, LA, USA

Melanie Flach (Ch 3) University of Mainz Medical Centre, Mainz, Germany; Institute of Microbiology and Hygiene, University of Freiburg Medical Centre, Freiburg, Germany

Richard Flavell (Ch 38) School of Medicine, Yale University, New Haven, CT, USA; Howard Hughes Medical Institute, Chevy Chase, MD, USA

Howard B. Fleit (Ch 111) Stony Brook University School of Medicine, Stony Brook, NY, USA

Genoveffa Franchini (Ch 75) National Institutes of Health, Bethesda, MD, USA

Lucy C. Freytag (Ch 61) Tulane University, School of Medicine, New Orleans, LA, USA

Anja Fuchs (Ch 52) Washington University School of Medicine, St Louis, MO, USA

kohtaro Fujihashi (App2) University of Alabama at Birmingham, Birmingham, AL, USA

Ivan J. Fuss (Chs 81, 86) Mucosal Immunity Section, Laboratory of Host Defenses, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA

Nicola Gagliani (Ch 38) School of Medicine, Yale University, New Haven, CT, USA

Marta Rodriguez Garcia (Chs 108, 110) Geisel School of Medicine at Dartmouth, Lebanon, NH, USA

Wendy S. Garrett (Ch 42) Harvard School of Public Health, Boston, MA, USA; Harvard Medical School, Boston, MA, USA; Dana-Farber Cancer Institute, Boston, MA, USA; Broad Institute of Harvard and MIT, Cambridge, MA, USA

M. Eric Gershwin (Ch 87) University of California, Davis School of Medicine, Davis, CA, USA

Philippe Gevaert (Ch 100) Upper Airways Research Laboratory, University Hospital Ghent, De Pintelaan, Ghent, Belgium

Maree Gleeson (Ch 11) University of Newcastle, NSW, Australia

Gabriela Godaly (Ch 106) Institute of Laboratory Medicine, Lund University, Lund, Scania, Sweden

Randall M. Goldblum (Ch 115) Pediatric Child Health Research Center, University of Texas Medical Branch, Galveston, TX, USA

Naina Gour (Ch 93) Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Mayda Gursel (Ch 62) Middle East Technical University, Department of Biological Sciences, Ankara, Turkey

George Hajishengallis (Ch 15) University of Pennsylvania School of Dental Medicine, Philadelphia, PA, USA

Hamida Hammad (Ch 29) Ghent University, Ghent, Belgium; VIB, Ghent, Belgium

Lennart Hammarström (Chs 71, 73) Department of Laboratory Medicine, Division of Clinical Immunology and Transfusion Medicine, Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm, Sweden

Arno Hänninen (Ch 90) University of Turku, Turku, Finland; NIHR Biomedical Research Unit in Liver Disease, Centre for Liver Research, University of Birmingham, Edgbaston, Birmingham, UK

Lars Å. Hanson (Ch 117) Göteborg University, Göteborg, Sweden

Adrian Hayday (Ch 37) Cancer Research UK, London, UK; King's College London, London, UK

Ronit Herzog (Ch 74) Weill Cornell Medical College, New York, NY, USA

Douglas C. Hodgins (Ch 68) Ontario Veterinary College, University of Guelph, Guelph, ON, Canada

Stephen T. Holgate (Ch 96) School of Medicine, Southampton General Hospital, Southampton, UK

Jan Holmgren (Chs 51, 56) Department of Microbiology and Immunology, Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden

Michael J. Holtzman (Ch 53) Washington University School of Medicine, Saint Louis, MO, USA

Edward W. Hook III (Ch 112) University of Alabama at Birmingham, Birmingham, AL, USA

Samuel Huber (Ch 38) University Hospital Hamburg-Eppendorf, Hamburg, Germany

Julia L. Hurwitz (Ch 49) St Jude Children's Research Hospital, Memphis, TN, USA

Juraj Ivanyi (Ch 95) Guy's Campus of Kings College London, London, UK

Akiko Iwasaki (Ch 25) Howard Hughes Medical Institute, Yale University, New Haven, CT, USA

Bana Jabri (Ch 80) University of Chicago, Chicago, IL, USA

Susan Jackson (App1) University of Alabama at Birmingham, Birmingham, AL, USA

Jonathan Jacobs (Ch 5) Division of Digestive Diseases, Department of Medicine, Los Angeles, CA, USA

Sirpa Jalkanen (Ch 90) University of Turku, Turku, Finland; NIHR Biomedical Research Unit in Liver Disease, Centre for Liver Research, University of Birmingham, Edgbaston, Birmingham, UK

Edward N. Janoff (Ch 58) Mucosal and Vaccine Research Program Colorado (MAVRC); University of Colorado Denver, Aurora, CO, USA; Veterans Affairs Medical Center, Denver, CO, USA

Ann E. Jerse (Ch 107) Uniformed Services University of the Health Sciences, Bethesda, MD, USA

Mangalakumari Jeyanathan (Ch 66) McMaster University, Hamilton, ON, Canada

Bruce A. Julian (Ch 105) School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA

Imre Kacskovics (Ch 116) Eötvös Loránd University, Budapest, Hungary

Charlotte S. Kaetzel (Chs 18, 19) Department of Microbiology, Immunology and Molecular Genetics, University of Kentucky College of Medicine, Lexington, KY, USA

Charu Kaushic (Ch 107) McMaster University, Hamilton, ON, Canada

Brian L. Kelsall (Chs 1, 24, 25, 78) Mucosal Immunobiology Section, Laboratory of Molecular Immunology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA

Sarah Kessans (Ch 65) Arizona State University, Tempe, AZ, USA

Rebecca Kesselring (Ch 91) University Medical Center Regensburg, Regensburg, Germany

Mogens Kilian (Chs 21, 22) Department of Biomedicine (Medical Microbiology and Immunology), Aarhus University, Aarhus, Denmark

Hiroshi Kiyono (Ch 65) University of Tokyo, Minato-ku, Tokyo, Japan

Dennis M. Klinman (Ch 62) Cancer and Infammation Program, National Cancer Institute, Frederick, MD, USA

Marina Korotkova (Ch 117) Göteborg University, Göteborg, Sweden

Mitchell Kronenberg (Ch 36) Division of Developmental Immunology, La Jolla Institute for Allergy and Immunology, La Jolla, CA, USA

Olga Krysko (Ch 100) Upper Airways Research Laboratory, University Hospital Ghent, De Pintelaan, Ghent, Belgium

Yuichi Kurono (Ch 101) Kagoshima University, Kagoshima, Japan

Miloslav Kverka (Ch 8) Laboratory of Cellular and Molecular Immunology, Institute of Microbiology, Academy of Sciences of the Czech Republic, Prague, Czech Republic

Bart N. Lambrecht (Chs 1, 25, 92, 94, 98) VIB Inflammation Research Center, Ghent University, and Department of Respiratory Medicine, University Hospital Ghent, Ghent, Belgium

Michael E. Lamm (Introduction) Case Western Reserve University, Cleveland, OH, USA

Olivier Lantz (Ch 36) Institut Curie, Paris, France

Gendie E. Lash (Ch 114) Newcastle University, Newcastle upon Tyne, UK

E.C. Lavelle (Ch 63) School of Biochemistry and Immunology, Trinity Biomedical Sciences Institute, Trinity College Dublin, Ireland

Leo Lefrancois (Ch 35) Division of Immunology, University of Connecticut Health Center, Farmington, CT, USA

Patrick S.C. Leung (Ch 87) University of California, Davis School of Medicine, Davis, CA, USA

Myron M. Levine (Ch 56) University of Maryland School of Medicine, Baltimore, MD, USA

David J. Lim (Ch 101) University of California, Los Angeles, CA, USA

John Lippolis (Ch 116) Ruminant Disease of Cattle Research Unit, Ames, IA, USA

Nancy A. Louis (Ch 45) Emory University School of Medicine, Atlanta, GA, USA

Andrew D. Luster (Ch 40) Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Nataliya Lutay (Ch 106) Institute of Laboratory Medicine, Lund University, Lund, Scania, Sweden

Nils Lycke (Ch 33) Mucosal Immunobiology and Vaccine Center, Institute of Biomedicine, University of Gothenburg, Gothenburg, Sweden

Andrew J. Macpherson (Ch 23) University Hospital of Bern, Bern, Switzerland

Nicholas J. Mantis (Ch 21) Division of Infectious Disease, Wadsworth Center, New York State Department of Health, Albany, NY, USA

Harold Marcotte (Ch 71) Department of Laboratory Medicine, Division of Clinical Immunology and Transfusion Medicine, Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm, Sweden

David H. Martin (Ch 7) Louisiana State University Health Sciences Center, New Orleans, LA, USA

Hugh S. Mason (Ch 65) Arizona State University Tempe, AZ, USA

Helen M. Massa (Ch 101) Griffith University, Gold Coast, QLD, Australia

Nobuyuki Matoba (Ch 65) University of Louisville School of Medicine, Louisville, KY, USA

Lloyd Mayer (Ch 27) Immunology Center, Mount Sinai Medical Center, New York, NY, USA

Craig L. Maynard (Ch 34) University of Alabama at Birmingham, Birmingham, AL, USA

M. Juliana McElrath (Ch 60) Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA

C. McEntee (Ch 63) School of Biochemistry and Immunology, Trinity Biomedical Sciences Institute, Trinity College Dublin, Ireland

Jerry R. McGhee (Introduction) University of Alabama at Birmingham, Birmingham, AL, USA

Michael A. McGuckin (Ch 14) Mater Research Institute–The University of Queensland, Translational Research Institute, Woolloongabba, QLD, Australia

Jiri Mestecky (Chs 1, 17, 55, 104, 105, 108, 112) Departments of Microbiology and Medicine, University of Alabama, Birmingham, AL, USA; Institute of Microbiology, Czech Academy of Sciences and Department of Immunology and Microbiology, School of Medicine, Charles University, Prague, Czech Republic

Zamaneh Mikhak (Ch 40) Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Robert D. Miller (Ch 10) University of New Mexico, Albuquerque, NM, USA

Zina Moldoveanu (App1, App2) University of Alabama at Birmingham, Birmingham, AL, USA

Paul C. Montgomery (Ch 99) Department of Immunology and Microbiology, Wayne State University School of Medicine, Detroit, MI, USA

Tsafrir Mor (Ch 65) Arizona State University Tempe, AZ, USA

Markus F. Neurath (Chs 82, 91) University of Erlangen-Nuremberg, Erlangen, Germany

Katrijn Neyt (Ch 94) VIB Inflammation Research Center, Ghent, Belgium

Lindsay K. Nicholson (Ch 58) Mucosal and Vaccine Research Program Colorado (MAVRC); University of Colorado Denver, Aurora, CO, USA; Veterans Affairs Medical Center, Denver, CO, USA

Jan Novak (Ch 105) School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA

Stella Nowicki (Ch 115) Department of Microbiology and Immunology, Meharry Medical College, Nashville, TN, USA

D.T. O'Hagan (Ch 63) Novartis Vaccines and Diagnostics, Cambridge, MA, USA

Nancy L. O'Sullivan (Ch 99) Department of Immunology and Microbiology, Wayne State University School of Medicine, Detroit, MI, USA

Pearay Ogra (Ch 117) University of Buffalo School of Medicine, Buffalo, NY, USA

Carlos Orihuela (Ch 49) University of Texas Health Science Center San Antonio, San Antonio, TX, USA

André J. Ouellette (Ch 16) Department of Pathology & Laboratory Medicine, Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA

Robert L. Owen (Ch 13) University of California San Francisco, San Francisco, CA, USA; Veterans Affairs Medical Center, San Francisco, CA, USA

Oliver Pabst (Ch 41) Institute of Immunology, Hannover Medical School, Hannover, Germany

Charles A. Parkos (Ch 45) Emory University School of Medicine, Atlanta, GA, USA

Viviana Parreño (Ch 68) Instituto de Virología, Centro de Investigación en Ciencias Veterinarias y Agronómicas, Instituto Nacional de Tecnología Agropecuaria, Castelar, Buenos Aires, Argentina

Mickey V. Patel (Chs 108, 110) Geisel School of Medicine at Dartmouth, Lebanon, NH, USA

Claudina Perez-Novo (Ch 100) Upper Airways Research Laboratory, University Hospital Ghent, De Pintelaan, Ghent, Belgium

Darren J. Perkins (Ch 30) University of Maryland, Baltimore (UMB), MD, USA

Calman Prussin (Ch 83) Laboratory of Allergic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA

Jeffrey Pudney (Ch 109) Boston University School of Medicine, Boston, MA, USA

Sukanya Raghavan (Ch 51) Department of Microbiology and Immunology, Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden

Pascal Rainard (Ch 116) INRA Centre Val de Loire et Universite' Francois Rabelais de Tours, UMR, Nouzilly, France

Sasirekha Ramani (Ch 57) Baylor College of Medicine, Houston, TX, USA

Troy D. Randall (Ch 4) University of Alabama at Birmingham, Birmingham, AL, USA

Milan Raska (Chs 67, 105) School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA; Palacky University Olomouc, Olomouc, Czech Republic

Gourapura J. Renukaradhya (Ch 68) Food Animal Health Research Program, Ohio Agricultural Research and Development Center, Department Veterinary Preventive Medicine, The Ohio State University, Wooster, OH, USA

Maria Rescigno (Ch 28) European Institute of Oncology, Milano, Italy

Kenneth L. Rosenthal (Ch 66) McMaster University, Hamilton, ON, Canada

Marc E. Rothenberg (Ch 44) Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

Frank M. Ruemmele (Ch 85) Université Sorbonne Paris Cité, Université Paris Descartes, Hôpital Necker Enfants Malades, Service de Gastroentérologie Pédiatrique, Paris, France

Michael W. Russell (Chs 1, 15, 18, 21, 22, 55, 98, 104, 112) Departments of Microbiology/Immunology and Oral Biology, University at Buffalo, Buffalo, NY, USA

Linda J. Saif (Ch 68) Food Animal Health Research Program, Ohio Agricultural Research and Development Center, Department Veterinary Preventive Medicine, The Ohio State University, Wooster, OH, USA

Irene Salinas (Ch 10) University of New Mexico, Albuquerque, NM, USA

Marko Salmi (Ch 90) University of Turku, Turku, Finland; NIHR Biomedical Research Unit in Liver Disease, Centre for Liver Research, University of Birmingham, Edgbaston, Birmingham, UK

Henri Salmon (Ch 116) INRA Centre Val de Loire et Universite' Francois Rabelais de Tours, UMR, Nouzilly, France

Hugh A. Sampson (Ch 84) Department of Pediatrics, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Philippe Sansonetti (Ch 50) Unité de Pathogénie Microbienne Moléculaire, Institut Pasteur, Paris, France; Collège de France, Paris, France

T. Schneider (Ch 77) Charité – Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin, Germany

Nicolas Serafini (Ch 39) Innate Immunity Unit, Inserm U668, Institut Pasteur, Paris, France

Dolly Sharma (Ch 117) University of Buffalo School of Medicine, Buffalo, NY, USA

Zheng Shen (Ch 108) Geisel School of Medicine at Dartmouth, Lebanon, NH, USA

Hai Ning Shi (Ch 2) Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

Penelope J. Shirlaw (Ch 102) Department of Oral Medicine, King's College London and Guys & St Thomas Hospitals, London, UK, and University of Sheffield, Sheffield, UK

Sourima B. Shivhare (Ch 114) Newcastle University, Newcastle upon Tyne, UK

Phillip D. Smith (Ch 26) University of Alabama at Birmingham, Birmingham, AL, USA; VA Medical Center, Birmingham, AL, USA

Patrick M. Smith (Ch 42) Harvard School of Public Health, Boston, MA, USA

Daniel J. Smith (Ch 69) The Forsyth Institute, Cambridge, MA, USA; Harvard School of Dental Medicine, Boston, MA, USA

Lesley E. Smythies (Ch 26) University of Alabama at Birmingham, Birmingham, AL, USA

Jo Spencer (Chs 33, 89) King's College London School of Medicine, Guy's King's College, Thomas Hospitals, London, UK

Warren Strober (Chs 1, 24, 47, 70, 72, 78, 81, 86, 88) Chief, Mucosal Immunity Section, Laboratory of Host Defenses, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA

Kanta Subbarao (Ch 59) National Institute of Allergy and Infectious Diseases (NIAID), NIH, Bethesda, MD, USA

Catharina Svanborg (Ch 106) Institute of Laboratory Medicine, Lund University, Lund, Scania, Sweden

Ann-Mari Svennerholm (Ch 51) Department of Microbiology and Immunology, Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden

Martin A. Taubman (Ch 69) The Forsyth Institute, Cambridge, MA, USA; Harvard School of Dental Medicine, Boston, MA, USA

Esbjörn Telemo (Ch 117) Göteborg University, Göteborg, Sweden

Martin H. Thornhill (Ch 102) Department of Oral Medicine, King's College London and Guys & St Thomas Hospitals, London, UK, and University of Sheffield, Sheffield, UK

David J. Thornton (Ch 14) Wellcome Trust Centre for Cell-Matrix Research, University of Manchester, Manchester, UK

Eva Thuenemann (Ch 65) Institute of Food Research, Norwich Research Park, Norwich, UK

Helena Tlaskalova-Hogenova (Ch 8) Laboratory of Cellular and Molecular Immunology, Institute of Microbiology, Academy of Sciences of the Czech Republic, Prague, Czech Republic

Debra Tristram (Ch 113) Department of Pediatrics, Albany Medical Center, Albany, NY, USA

Palak Trivedi (Ch 90) University of Turku, Turku, Finland; NIHR Biomedical Research Unit in Liver Disease, Centre for Liver Research, University of Birmingham, Edgbaston, Birmingham, UK

Elaine Tuomanen (Ch 49) St Jude Children's Research Hospital, Memphis, TN, USA

Jaroslav Turanek (Ch 67) Veterinary Research Institute, Brno, Czech Republic

Jerrold R. Turner (Ch 12) The University of Chicago, Chicago, IL, USA

Brian J. Underdown (Ch 70) McMaster University, Hamilton, ON, Canada

Mary J. van Helden (Ch 94) VIB Inflammation Research Center, Ghent, Belgium

Ronald S. Veazey (Ch 76) Tulane National Primate Research Center, Tulane University School of Medicine, Covington, LA, USA

Elena F. Verdu (Ch 8) Farncombe Family Digestive Health Research Institute, McMaster University, Hamilton, ON, Canada

Anastasia Vlasova (Ch 68) Food Animal Health Research Program, Ohio Agricultural Research and Development Center, Department Veterinary Preventive Medicine, The Ohio State University, Wooster, OH, USA

Harissios Vliagoftis (Ch 43) University of Alberta, Edmonton, AB, Canada

Stefanie N. Vogel (Ch 30) University of Maryland, Baltimore (UMB), MD, USA

W. Allan Walker (Ch 2) Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

Xiaolei Wang (Ch 76) Tulane National Primate Research Center, Tulane University School of Medicine, Covington, LA, USA

Tomohiro Watanabe (Ch 88) Department of Gastroenterology and Hepatology, Center for Innovation in Immunoregulative Technology and Therapeutics, Kyoto University Graduate School of Medicine, Kyoto, Japan; National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA

Casey T. Weaver (Ch 34) University of Alabama at Birmingham, Birmingham, AL, USA

Howard L. Weiner (Ch 41) Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Jerry M. Wells (Ch 8) Host-Microbe Interactomics Group, Department of Animal Sciences, Wageningen University, Wageningen, The Netherlands

Ting Wen (Ch 44) Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

Judith Whittum-Hudson (Ch 112) Wayne State University, Detroit, MI, USA

Jeffrey A. Whitsett (Ch 14) Perinatal Institute, Cincinnati Children's Hospital, OH, USA; University of Cincinnati, OH, USA

Ifor R. Williams (Ch 13) Emory University School of Medicine, Atlanta, GA, USA

Marsha Wills-Karp (Ch 93) Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Charles R. Wira (Chs 108, 110) Geisel School of Medicine at Dartmouth, Lebanon, NH, USA

Jenny M. Woof (Chs 17, 20) Division of Cancer Research, University of Dundee Medical School, Dundee, UK

Andrew C. Wotherspoon (Ch 89) The Royal Marsden NHS Trust, London, UK

Zhou Xing (Ch 66) McMaster University, Hamilton, ON, Canada

Huanbin Xu (Ch 76) Tulane National Primate Research Center, Tulane University School of Medicine, Covington, LA, USA

Colby Zaph (Ch 54) University of British Columbia, Vancouver, BC, Canada

Sebastian Zeissig (Ch 27) Department of Internal Medicine I, Kiel University, Kiel, Germany

M. Zeitz (Ch 77) University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Preface to the First Edition

Only 25 years ago, a multidisciplinary group of some three dozen individuals met for the first time in Vero Beach, Florida, under the auspices of the National Institute of Child Health and Human Development (NICHHD) to discuss a recently identified immunoglobulin, secretory IgA. Since that historic workshop, seven international congresses have been held to discuss secretory immunoglobulins and mucosal immunology, and there have been a number of scientific meetings on immunological mechanisms in such mucosal sites as respiratory tract, gut, genital tract, mammary glands, and periodontal tissues. The last International Congress of Mucosal Immunology, held in 1992 in Prague, Czechoslovakia, was attended by nearly 1000 participants.

The recognition that defenses are mediated via mucosal barriers dates back several 1000 years. Ingestion of Rhus leaves to modify the severity of reactions to poison ivy is a centuries old practice among native North Americans. The modern concepts of local immunity, however, were developed by Besredka in the early 1900s, followed by the discovery of IgA in 1953 and its isolation and characterization in 1959. Studies in the early 1960s demonstrated the presence of IgA in a unique form in milk and, shortly thereafter, in other external secretions. These studies were followed by the discovery of the secretory component and the identification of the J chain. These remarkable observations were soon complemented by the characterization of the bronchus-associated lymphoid tissue (BALT) and the gut-associated lymphoid tissue (GALT), the observation of circulation of antigen-sensitized or reactive IgA B cells from BALT and GALT to other mucosal surfaces such as the genital tract and the mammary glands, and the definition of mucosal T cells. Since 2004, our concept of the mucosal immune system has been expanded to include M cells and mechanisms of mucosal antigen processing, regulatory T lymphocytes and other effector cell mechanisms, neuropeptides, and the network of interleukins and other cytokines. Finally, the biological significance of the mucosal immune system increasingly is being realized in the context of human infections acquired via mucosal portals of entry, including conventional infections as well as new syndromes such as acquired immune deficiency associated with infection by HIV.

Despite the tremendous progress made in the acquisition of new knowledge concerning the common mucosal immune system, mucosal infections, and oral immunization, no single text covering the entire spectrum of mucosal immunity was available. Therefore, this handbook was organized to develop a perspective of the basic biology of the components that constitute the framework of the common mucosal immune system, as well as of the infectious and immunologically mediated disease processes of the mucosae. Virtually all chapters have been authored by original investigators responsible for key observations on which current concepts are based.

Part I, Cellular Basis of Mucosal Immunity, provides an introductory overview and a historical perspective of the mucosal immune system (Chapter 1), followed by 10 comprehensive chapters (Section A) on development and physiology of mucosal defense (Chapters 2–11). These chapters address structure and function of mucosal epithelium, cellular basis of antigen transport, mucosal barrier, innate humoral factors, bacterial adherence, development and function of mucosal immunoglobulin, and epithelial and hepatobiliary transport. Section B (Chapters 12–19) focuses on cells, regulation, and specificity in inductive and effector sites. The inductive site chapters discuss characteristics of mucosa-associated lymphoid tissue (MALT), Peyer's patches, regulation of IgA B cell development, diversity and function of mucosal antigen-presenting cells, oral tolerance, peptidergic circuits, role of B-1 cells, and lymphocyte homing. The chapters on effector sites (Section C) present information about cytokines, mucosal Ig-producing cells, regulatory T cells, intraepithelial cells, mucosal IgE, inflammation and mast cells, cytokines in liver, cytotoxic T cells in mucosal effector sites, and immunity to viruses (Chapters 20–29). Section D addresses mucosal immunization and the concepts of mucosal vaccines. These chapters discuss passive immunization, vaccine development for mucosal surfaces, antigen delivery systems, mucosal adjuvants, and approaches for generating specific secretory IgA antibodies (Chapters 30–34).

Part II, Mucosal Diseases, addresses the secretory immune system with special reference to mucosal diseases. Section E consists of chapters on the stomach, intestine, and liver, and includes diseases of GALT and intestinal tract, a chain and related lymphoproliferative disorders, gastritis and peptic ulcer, malabsorption syndrome, food allergy, intestinal infections, and diseases of the liver and biliary

tract (Chapters 35–42). Section F covers selected areas of lung and lower airway and includes chapters on BALT and pulmonary diseases, mucosal immunity in asthma, respiratory infections, and inhalant allergy (Chapters 43–46). Section G presents information on the oral cavity, upper airway, and mucosal regions in the head and neck (Chapters 47–50), as well as ocular immunity, tonsils and adenoids, and middle ear. Sections H and I are devoted to mammary glands and genitourinary tract, respectively. These sections consist of chapters on milk, immunological effects of breast feeding (Chapters 51 and 52), IgA nephropathy, immunology of female and male reproductive tracts, endocrine regulation of genital immunity, mucosal immunopathophysiology of HIV infection, and genital infections relative to maternal and infant disease (Chapters 53–58).

The information reviewed in the different chapters in this handbook will be of considerable interest to diverse groups of clinicians, basic and clinical immunologists, biologists, veterinarians, and public health workers interested in understanding the application of basic biology to virtually all immunological or infection-mediated disease processes of external mucosal surfaces. This handbook will be of particular importance to students of medicine and pediatrics, including individuals studying gastroenterology and pulmonology, ophthalmology, gynecology, infectious disease, otolaryngology, periodontal disease, sexually transmitted disease, and especially mucosal immunology.

Pearay L. Ogra
Jiri Mestecky
Michael E. Lamm
Warren Strober
Jerry R. McGhee
John Bienenstock