Handbook on Immunosenescence

Handbook on Immunosenescence

Basic Understanding and Clinical Applications

1

Editors

Tamas Fulop
University of Sherbrooke, Quebec, Canada

Claudio Franceschi
University of Bologna, Bologna, Italy

Katsuiku Hirokawa
Institute for Health and Life Sciences, Tokyo, Japan

Graham Pawelec
University of Tübingen, Tübingen, Germany

Springer

Editors
Tamas Fulop
Research Center on Aging
Division of Geriatrics
Dept. of Medicine, Faculty of Medicine
1036 Rue Belvedere
Sherbrooke J1H 4C4
Canada
tamas.fulop@usherbrooke.ca

Claudio Franceschi
CIG Interdepartmental Center
"L. Galvani"
University of Bologna
Department of Experimental Pathalogy
Via San Giacomo 12
40126 Bologna
Italy
claudio.franceschi@unibo.it

Katsuiku Hirokawa
Institute for Health and Life Sciences
4-6-22 Kohinato
Tokyo
Bunkyo-ku
112-0006 Japan

Graham Pawelec
University of Tübingen
ZMF - Zentrum Med. Forschung
Abt. Transplant./ Immunologie
Waldhörnlestr. 22
72072 Tübingen
Germany
graham.pavelec@uni-tuebingen.de

ISBN: 978-1-4020-9062-2 e-ISBN: 978-1-4020-9063-9

Library of Congress Control Number: 2008944075

Printed on acid-free paper

9 8 7 6 5 4 3 2 1

springer.com

Preface

What is Immunosenescence?

The number of elderly people is steadily increasing in most countries. Concomitantly, the number of age-related diseases is unfortunately also increasing. One of the leading causes of death in the very elderly is infection, with cardio-vascular diseases and cancer less prevalent than in younger elderly. All three major pathologies are to some extent related to the immune system due to its well-known but still imperfectly investigated deregulation during aging.

Thus, the large amount of data accumulated during the last decade or more has allowed a better but still incomplete understanding of all the complex alterations affecting the immune system with aging. Although we do not know everything, we feel that it is important for the scientific community to become more acquainted with the corpus of knowledge recently generated in this domain, presented in a manner providing a critical evaluation of the current status of research. Many accepted ideas have changed during the last decade, such as the effect of aging on the innate immune system, antigen presentation, the cytokine imbalance and low grade inflammation. If not exactly a paradigm shift, the time seems ripe to present this critical evaluation and update of the state-of-the-art in these different areas. We perceive a great need to assemble this current knowledge in one volume by collecting contributions from the most eminent researchers in the field from all around the world. In this way, we aim to facilitate a synthesis of the different aspects of the disparate disciplines in ageing research to focus on immunosenescence for the first time (basic and clinical, molecular, cellular, biochemical, genetics). We hope this multidisciplinary approach from the aging, immunity and inflammation community will also be important for future innovative research in this domain.

Thus, this book will have as its main themes Aging, Immunity and Inflammation, with an emphasis on studies in humans. However, as data are not always available in this species, work in experimental animals will be also treated as appropriate. A large number of colleagues responded enthusiastically to our proposal and contributed with very high quality chapters. We begin with a description of Methods and models for studying immunosenescence. We continue with Cellular immunosenescence, treating most specifically T cells, B cells, neutrophils, antigen presenting cells

and NK cells. We then proceed to mechanisms. In this context, receptor signaling, the role of mitochondrial activity, the proteasome, cytokine status and the neuro-endocrine-immune netweork are treated. The important but very challenging area of the Clinical relevance of immunosenescence for disease states is covered next by the individual treatment of infections, autoimmunity, cancer, metabolic syndrome, neurodegeneration and frailty. Finally, and even more challengingly, the last part of the book is devoted to possibilities for eventual intervention and modulation. We particularly emphasise nutritional aspects, lipids and experimental interventions. In this way we feel that we cover the whole range of areas from models, through basic molecular mechanisms to the clinical relevance and finally eventual modulation.

One of the main objectives of this book is to present in a systematic way our current knowledge in the field of the immunology related to aging. So do we now know what immunosenescence is? It is still difficult at answer this question, but we hope even the most specialist investigator in the field will find concepts and ideas within the book which will help him or her to approach an answer to this important question more closely than before. We would therefore sincerely like to hope that we have created an authoritative, innovative and thought-provoking book dedicated for the first time to this topic alone. We also like to hope that this volume will help to attract a new generation of researchers to the field of immunosenescence as an expanding and vital research arena.

Tamas Fulop — Quebec, Canada
Claudio Franceschi — Bologna, Italy
Katsuiku Hirokawa — Tokyo, Japan
Graham Pawelec — Tübingen, Germany

Contents

Part I: Methods and Models for Studying Immunosenescence

1. The Immune Risk Profile and Associated Parameters in Late Life: Lessons from the OCTO and NONA Longitudinal Studies
Anders Wikby, Jan Strindhall and Boo Johansson 3

2. Lymphocytes Sub-Types and Functions in Centenarians as Models for Successful Ageing
Enrico Lugli, Leonarda Troiano, Marcello Pinti, Milena Nasi, Erika Roat, Roberta Ferraresi, Linda Bertoncelli, Lara Gibellini, Elisa Nemes and Andrea Cossarizza. 29

3. Mouse Models and Genetics of Immunosenescence
Qing Yu, Jyoti Misra Sen and Dennis Taub 63

4. Insect Models of Immunosenescence
Jeff Leips. 87

5. Clonal Culture Models of T-cell Senescence
Graham Pawelec, Jürgen Kempf and Anis Larbi 107

6. Mouse Models of Influenza
Ian C. Brett and Bert E. Johansson 117

7. A Transgenic Dwarf Rat Strain as a Tool for the Study of Immunosenescence in Aging Rats and the Effect of Calorie Restriction
Isao Shimokawa, Masanori Utsuyama, Toshimitsu Komatsu, Haruyoshi Yamaza and Takuya Chiba 131

8. Mathematical Modeling of Immunosenescence: Scenarios, Processes and Limitations
A. A. Romanyukha, S. G. Rudnev, T. A. Sannikova and A. I. Yashin 145

Part II: Cellular Immunosenescene - T Cells

9. Age, T-cell Homeostasis, and T-cell Diversity in Humans
David L. Lamar, Cornelia M. Weyand and Jörg J. Goronzy 167

10. The Role of T-regulatory Cells in Immune Senescence
Paul Moss 193

11. Age-related Changes in Subpopulations of Peripheral Blood Lymphocytes in Healthy Japanese Population
Masanori Utsuyama, Yuko Kikuchi, Masanobu Kitagawa and Katsuiku Hirokawa 203

12. Age-associated T-cell Clonal Expansions (TCE) in vivo—Implications for Pathogen Resistance: Cellular Immunosenescence – T cells
Janko Nikolich-Zugich and Anna Lang 219

13. T-cell Cycle and Immunosenescence: Role of Aging in the T-cell Proliferative Behaviour and Status Quo Maintenance
Jacek M. Witkowski 235

14. Mismatch Repair System and Aging: Microsatellite Instability in Peripheral Blood Cells of the Elderly and in the T-cell Clone Longitudinal Model
Simona Neri and Erminia Mariani 257

15. Activation-Induced Cell Death of T-Cells in Elderly
Ewa Sikora and Agnieszka Brzezińska 277

16. CD8 Clonal Expansions in Mice: An Age-associated Alteration of CD8 Memory T-cells
Eric T. Clambey, John W. Kappler and Philippa Marrack 291

17. Generation and Gene Expression of CD28-CD8 T-cells in Human
Nan-ping Weng 327

18. Role of Regulatory Subsets During Aging
Piotr Trzonkowski 343

Cellular Immunosenescence - B Cells

19. Transcription Factors in Mature B-Cells During Aging
Daniela Frasca, Richard L. Riley and Bonnie B. Blomberg 381

20. B-Cell Repertoire Changes in Mouse Models of Aging
Jean L. Scholz, William J. Quinn III and Michael P. Cancro 393

21. B-Cells and Antibodies in Old Humans
Kate L. Gibson and Deborah K. Dunn-Walters 415

Cellular Immunosenescence - Neutrophils

22. Neutrophil Granulocyte Functions in the Elderly
Peter Uciechowski and Lothar Rink 439

23. Signal Transduction Changes in fMLP, TLRs, TREM-1 and GM-CSF Receptors in PMN with Aging
Carl F. Fortin, Anis Larbi, Gilles Dupuis and Tamas Fulop 457

24. Synergistic Effects of Ageing and Stress on Neutrophil Function
Janet M. Lord, Anna C. Phillips and Wiebke Arlt. 475

Cellular Immunosenescence - Antigen Presenting Cells

25. Role of Dendritic Cells in Aging
Anshu Agrawal, Sudhanshu Agrawal and Sudhir Gupta 499

26. Phenotypic and Functional Changes of Circulating Monocytes in Elderly
Lia Ginaldi and Massimo De Martinis 511

Cellular Immunosenescence - NK and NKT Cells

27. NK Cells in Human Ageing
Raquel Tarazona, Inmaculada Gayoso, Corona Alonso, M. Luisa Pita, Esther Peralbo, Javier G. Casado, Beatriz Sánchez-Correa, Sara Morgado and Rafael Solana 529

28. Natural Killer Cells and Human Longevity
Hideto Tamura and Kiyoyuki Ogata 545

29. The Effects of Age on CD1d-restricted NKT-cells and Their Contribution to Peripheral T-cell Immunity
Douglas E. Faunce and Jessica L. Palmer 561

Cellular Immunosenescence - Stem Cells

30. Lympho-Hematopoietic Stem Cells and Their Aging
Hartmut Geiger and Gary Van Zant 573

31. Implications of Developmental Switches for Hematopoietic Stem Cell Aging
Jens M. Nygren and David Bryder 589

Cellular Immunosenescence - Genetics

32. Associations of Cytokine Polymorphisms with Immunosenescence
Elissaveta Naumova and Milena Ivanova 615

33. Cytokine Polymorphisms and Immunosenescence
Owen A. Ross, Kelly M. Hinkle and I. Maeve Rea 631

34. Role of TLR Polymorphisms in Immunosenescence
Carmela Rita Balistreri, Giuseppina Candore, Giuseppina Colonna-Romano, Maria Paola Grimaldi, Domenico Lio, Florinda Listì, Sonya Vasto, Letizia Scola and Calogero Caruso 659

Part III: Mechanisms - Receptors and Signal Transduction

35. Signal Transduction Changes in T-cells with Aging
Tamas Fulop, Gilles Dupuis, Carl Fortin and Anis Larbi 675

36. Molecular Signaling of CD95- and TNFR-Mediatedapoptosis in Naïve and Various Memory Subsets of T-Cells
Sudhir Gupta and Ankmalika Gupta 695

Mechanisms - Mitochondria

37. Mitochondria and Immunosenescence
Pazit Beckerman and Arie Ben Yehuda 713

Mechanism - Proteasome

38. Proteasome Activity and Immunosenescence
Bertrand Friguet 729

Mechanisms - Cytokines

39. Age-Related Changes in Type 1 and Type 2 Cytokine Production in Humans
Elizabeth M. Gardner and Donna M. Murasko 753

40. Cytokine Expression and Production Changes in Very Old Age
Susan E. McNerlan, Marilyn Armstrong, Owen A. Ross and I. Maeve Rea 771

Mechanisms - Neuro-Endocrine-Immune Network

41. Neuro-Endocrine-Immune Network and its Age-Related Changes
K. Hirokawa and M. Utsuyama 785

42. Sex Hormones and Immunosenescence
Christian R. Gomez, Vanessa Nomellini and Elizabeth J. Kovacs 799

43. Glucocorticoids and DHEA: Do They Have a Role in Immunosenescence?
Moisés E. Bauer, Cristina M. Moriguchi Jeckel, Cristina Bonorino, Flávia Ribeiro and Clarice Luz 833

Mechanisms- Thymus

44. Thymic Involution and Thymic Renewal
Frances T. Hakim 865

Mechanisms- Inflammation

45. Inflamm-Aging
L. Bucci, R. Ostan, M. Capri, S. Salvioli, E. Cevenini, L. Celani, D. Monti and C. Franceschi 893

46. Molecular and Cellular Aspects of Macrophage Aging
Carlos Sebastián, Jorge Lloberas and Antonio Celada 919

Part IV: Clinical Relevance in Disease States-Infection

47. Aging and HIV Disease: Synergistic Immunological Effects?
Rita B. Effros. 949

48. Role of Immunosenescence in Infections and Sepsis in the Elderly
Tamas Fulop, Steven Castle, Anis Larbi, Carl Fortin, Olivier Lesur and Graham Pawelec 965

49. Beneficial and Detrimental Manifestations of Age on CD8+ T-Cell Memory to Respiratory Pathogens
Jacob E. Kohlmeier, Kenneth H. Ely, Alan D. Roberts, Eric J. Yager, Marcia A. Blackman and David L. Woodland 979

50. HIV Infection as a Model of Accelerated Immunosenescence
Victor Appay and Delphine Sauce 997

Clinical Relevance in Disease States- Autoimmunity

51. Autoimmunity and Autoimmune Diseases in the Elderly
Ewa Bryl and Jacek M. Witkowski 1029

52. Autoimmunity—Aging Mouse Model for Autoimmune Diseases
Yoshio Hayashi and Naozumi Ishimaru 1053

53. Atherosclerosis—An Age-dependent Autoimmune Disease
B. Henderson, A. Rossmann, Ch. Mayerl, M. Wick and G. Wick 1063

54. Immuno-Inflammatory Athero-Arteriosclerosis Induced by Elastin Peptides. Effect of Age
L. Robert and A. M. Robert 1089

Clinical Relevance in Disease States- Cancer

55. Aging, Immunity and Cancer
Claude Sportès and Frances T. Hakim 1119

56. Breast Cancer and Immunosenescence
Mauro Provinciali, Alessia Donnini, Arianna Smorlesi and Cristina Gatti 1139

57. Aging, Cancer and Apoptosis in Animal Models and Clinical Settings
Masanobu Kitagawa and Katsuiku Hirokawa 1165

58. Her-2/neu Transgenic Mice for Evaluation of Immune and Antitumor Responses Against Self-Tumor Antigens in the Young and the Old
Joseph Lustgarten and Noweeda Mirza 1189

59. Cancer Immunotherapy and Aging: Lessons From the Mouse
Claudia Gravekamp. 1217

Clincal Relevance in Disease States- Metabolic Syndrome

60. Insulin Resistance, Chronic Inflammation and the Link with Immunosenescence
Dawn J. Mazzatti, Kavita Karnik, Radu C. Oita and Jonathan R. Powell. 1247

Clinical Relevance in Disease States- Neurodegenerative Diseases

61. Decline of Immune Responsiveness: A Pathogenetic Factor in Alzheimer's Disease?
Elke Richartz-Salzburger and Niklas Koehler 1275

Clinical Relevance in Disease States- Frailty

62. Inflammatory Markers and Frailty
Sean X. Leng and Linda P. Fried 1293

63. CMV Infection and Frailty: Immunologic Consequences and Disease Pathogenesis
George C. Wang and Jeremy Walston. 1305

Clinical Relevance in Disease States- Osteoporosis

64. Osteoporosis, Inflammation and Ageing
Lia Ginaldi, Lucia P. Mengoli and Massimo De Martinis 1329

Part V: Modulation- Nutrition

65. Protein-Energy Malnutrition as a Determinant for Immuno-Senescence
Anis Larbi, Bruno Lesourd and Tamas Fulop. 1355

66. Role of Zinc and Selenium in Oxidative Stress and Immunosenescence: Implications for Healthy Ageing and Longevity
Eugenio Mocchegiani and Marco Malavolta 1367

Modulation- Lipids

67. Immunomoduation by Polyunsaturated Fatty Acids: Impact on T-cell Functions and Signaling
Maximilian Zeyda and Thomas M. Stulnig 1399

68. Omega-3 Polyunsaturated Fatty Acids and Immunosenescence
Christopher A. Jolly and Sirisha Karri 1423

69. Effect of Intrinsic and Extrinsic Lipids on T-cell Signalling
Anis Larbi, Emilie Combet, Graham Pawelec and Tamas Fulop 1437

Modulation- Vaccination

70. Effect of Anti-influenza Vaccination on Immune System in the Elderly
Piotr Trzonkowski 1455

71. Immunosenescence Modulation by Vaccination
Janet E. McElhaney and Allan M. McGavin 1487

Modulation- Can Interventions to Influence Immunosenescence Succeed?

72. Interleukin -7 and Immunorejuvenation
Wayne A. Mitchell and Richard Aspinall 1515

73. Assessment of Age-related Decline of Immunological Function and Possible Methods for Immunological Restoration in Elderly
Katsuiku Hirokawa, Masanori Utsuyama, Yuko Kikuchi and Masanobu Kitagawa 1547

74. Thymic Regeneration in Mice and Humans Following Sex Steroid Ablation
Anne Fletcher, Jessica Reiseger, Katerina Vlahos, Natalie Seach, Jarrod Dudakov, Ann Chidgey and Richard Boyd 1571

75. Nutraceuticals and Immune Restoration in the Elderly
Barry W. Ritz and Elizabeth M. Gardner 1611

76. Gene Therapy and Immune Senescence
Jian Chen, Hui-Chen Hsu and John D. Mountz 1629

77. Perspectives: Is Immunosenescence Clinically Relevant?
Tamas Fulop, Claudio Franceschi, Katsuiku Hirokawa and Graham Pawelec 1647

Subject Index 1649

Contributors

A.I. Yashin
Center for Population Health and Aging, Duke University, Durham, USA

A.M. Robert
Université paris 5. Laboratoire de Recherche Ophtalmologique., 1 place du Parvis Notre Dame, 75181 Paris cedex 04, France

Agnieszka Brzezińska
Molecular Bases of Aging Laboratory, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Pasteura 3, Warsaw Poland

Alan D. Roberts
Trudeau Institute, Saranac Lake, NY 12983, USA

Alessia Donnini
Laboratory of Tumour Immunology, INRCA Res. Dept., Via Birarelli 8, 60121 Ancona, Italy

Alexey A. Romanyukha
Institute of Numerical Mathematics, Russian Academy of Sciences, Moscow, Russia

Anders Wikby
Department of Natural Science and Biomedicine, School of Health Sciences, Jönköping University, Box 1026, 551 11 Jönköping, Sweden

Andrea Cossarizza
Chair of Immunology, Department of Biomedical Sciences, University of Modena and Reggio Emilia, Via Campi 287, Modena, 41100, Italy

Andrea Rossmann
Division of Experimental Pathophysiology and Immunology, Laboratory of Autoimmunity, Biocenter, Innsbruck Medical University, Fritz-Pregl-Strasse 3, A-6020-Innsbruck, Austria

Anis Larbi
Center for Medical Research, Section for Transplant-Immunology and Immuno-Hematology, Tuebingen Aging and Tumor Immunology group, University of Tuebingen Medical School, Waldhörnlestr. 22, D-72072 Tübingen, Germany

Ankmalika Gupta
Division of Basic and Clinical Immunology, University of California, Irvine, California

Ann Chidgey
Monash Immunology and Stem Cell Laboratories, Monash University, Clayton, Australia

Anna C. Phillips
School of Sport and Exercise Science, Birmingham University Medical School, Birmingham B15 2TT, UK

Anna Lang
Vaccine and Gene Therapy Institute, Department of Molecular Microbiology and Immunology and the Oregon National Primate Research Center, Oregon Health & Science University, Beaverton, OR 97006, USA

Anne Fletcher
Monash Immunology and Stem Cell Laboratories, Monash University, Clayton, Australia

Anshu Agrawal
Division of Basic and Clinical Immunology, University of California, Irvine, CA 92697, USA

Antonio Celada
Institute for Research in Biomedicine-University of Barcelona, Josep Samitier 1-5, 08028 Barcelona, Spain

Arianna Smorlesi
Laboratory of Tumour Immunology, INRCA Res. Dept., Via Birarelli 8, 60121 Ancona, Italy

Arie Ben Yehuda
University Hospital Kerem, The Department of Medicine at the Hadassah Ein, Jerusalem, Isreal

Barry W. Ritz
Drexel University, Department of Bioscience & Biotechnology, 118 Stratton Hall, 32nd and Chestnut Streets, Philadelphia, PA 19104, USA

Beatriz Sánchez-Correa
Immunology Unit, Department of Physiology, University of Extremadura, Cáceres, Spain

Bert E. Johansson
Innovation Sciences, Armonk, NY 10504, USA

Bertrand Friguet
Laboratoire de Biologie Cellulaire du Vieillissement, UMR 7079, Université Pierre et Marie Curie, 4 Place Jussieu, 75005 Paris, France

Blair Henderson
Division of Experimental Pathophysiology and Immunology, Laboratory of Autoimmunity, Biocenter, Innsbruck Medical University, Fritz-Pregl-Strasse 3, A-6020-Innsbruck, Austria

Bonnie B. Blomberg
Department of Microbiology and Immunology, University of Miami Miller School of Medicine, P.O. Box 016960 (R-138), Miami, FL 33101, USA

Boo Johansson
Institute of Gerontology, School of Health Sciences, Jönköping University, Box 1026, 551 11 Jönköping, Sweden, and Department of Psychology, Göteborg University, Box 500, 405 30 Göteborg, Sweden

Bruno Lesourd
EA 2431, Faculté de Médecine, 28 Place Henri Dunant, 63001 Clermont-Ferrand and Hôpital Nord du CHU de Clermont-Ferrand, BP 36, 63118 Cebazat, France

Claudio Franceschi
Department of Experimental Pathology, University of Bologna, Via San Giacomo 12, I-40126 Bologna, Italy; CIG-Interdepartmental Center “L. Galvani”, University of Bologna, Via San Giacomo 12, I-40126 Bologna, Italy

Calogero Caruso
Gruppo di Studio sull’Immunosenescenza, Dipartimento di Biopatologia e Metodologie Biomediche, Università di Palermo, Corso Tukory 211, 90134 Palermo, Italy

Carl Fortin
Clinical research Center, Graduate Immunology Program, Division of Pulmonology, Department of Medicine, Faculty of Medicine, University of Sherbrooke, Sherbrooke, Quebec, Canada

Carlos Sebastián
Institute for Research in Biomedicine-University of Barcelona, Josep Samitier 1-5, 08028 Barcelona, Spain

Carmela Rita Balistreri
Gruppo di Studio sull’Immunosenescenza, Dipartimento di Biopatologia e Metodologie Biomediche, Università di Palermo, Corso Tukory 211, 90134 Palermo, Italy

Christina Mayerl
Division of Experimental Pathophysiology and Immunology, Laboratory of Autoimmunity, Biocenter, Innsbruck Medical University, Fritz-Pregl-Strasse 3, A-6020-Innsbruck, Austria

Christian R. Gomez
The Burn and Shock Trauma Institute and the Immunology and Aging Program; Department of Surgery; Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153, USA; Facultad de Ciencias de la Salud, Universidad Diego Portales, Ejército 141, Santiago, Chile

Christopher A. Jolly
Division of Nutritional Sciences, The University of Texas, Austin, TX 78712, USA

Clarice Luz
LabVitrus, Rua Garibaldi, 659/502, Porto Alegre, RS 90035-050, Brazil

Claude Sportès
Experimental Transplantation & Immunology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, DHHS, Bethesda, MD, USA

Claudia Gravekamp
California Pacific Medical Center Research Institute, 475 Brannan Street, San Francisco, CA 94107, USA

Cornelia M. Weyand
Kathleen B. and Mason I. Lowance Center for Human Immunology, Department of Medicine, Emory University School of Medicine, Room 1003 Woodruff Memorial Research Building, 101 Woodruff Circle, Atlanta, GA, USA

Corona Alonso
Department of Immunology, Reina Sofia University Hospital, University of Córdoba, Corodoba, Spain

Cristina Bonorino
Faculdade de Biociências and Instituto de Pesquisas Biomédicas, Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Av. Ipiranga 6690, 2º andar. P.O. Box 1429. Porto Alegre, RS 90.610-000, Brazil

Cristina Gatti
Laboratory of Tumour Immunology, INRCA Res. Dept., Via Birarelli 8, 60121 Ancona, Italy

Cristina M. Moriguchi Jeckel
Faculdade de Farmácia, PUCRS, Av. Ipiranga, 6681. Porto Alegre, RS 90619-900, Brazil

Daniela Frasca
Department of Microbiology and Immunology, University of Miami Miller School of Medicine, P.O. Box 016960 (R-138), Miami, FL 33101, USA; Graduate School of Cell Biology and Development, University of Rome La Sapienza, Rome, Italy

Daniela Monti
Department of Oncology and Experimental Pathology, University of Florence, Via Morgagni 50, Florence, Italy

David Bryder
Stem Cell Aging, Department of Experimental Medical Science, BMC D14, Lund University, 221 84 Lund, Sweden

David L. Lamar
Kathleen B. and Mason I. Lowance Center for Human Immunology, Department of Medicine, Emory University School of Medicine, Room 1003 Woodruff Memorial Research Building, 101 Woodruff Circle, Atlanta, GA, USA

David L. Woodland
Trudeau Institute, Saranac Lake, NY 12983, USA

Deborah K. Dunn-Walters
Department of Immunobiology, 2nd Floor, Borough Wing Guy's, King's and St. Thomas School of Medicine, King's College London, Guy's Hospital, Great Maze Pond, London SE1 9RT, UK

Delphine Sauce
Cellular Immunology laboratory, INSERM U543, Avenir Group, Hopital Pitie-Salpetriere, Université Pierre et Marie Curie-Paris, 91 Bd de l'Hopital, 75013 Paris, France

Dennis Taub
Clinical Immunology Section, Laboratory of Immunology, National Institute on Aging, National Institutes of Health, Baltimore MD 21224, USA

Domenico Lio
Gruppo di Studio sull'Immunosenescenza, Dipartimento di Biopatologia e Metodologie Biomediche, Università di Palermo, Corso Tukory 211, 90134 Palermo, Italy

Donna M. Murasko
Department of Bioscience and Biotechnology, Drexel University, Philadelphia, PA 19104, USA

Douglas E. Faunce
Department of Surgery and The Burn and Shock Trauma Institute; Department of Microbiology and Immunology; Loyola Aging and Immunology Program, Loyola University Medical Center, Stritch School of Medicine, Maywood, IL, USA

Elisa Cevenini
CIG-Interdepartmental Center “L. Galvani”, University of Bologna, Via San Giacomo 12, I-40126 Bologna, Italy

Elisa Nemes
Chair of Immunology, Department of Biomedical Sciences, University of Modena and Reggio Emilia, Via Campi 287, Modena, 41100, Italy

Elissaveta Naumova
Central Laboratory of Clinical Immunology, University Hospital “Alexandrovska”. 1. G. Sofiisky str., 1431 Sofia, Bulgaria

Elizabeth J. Kovacs
The Burn and Shock Trauma Institute and the Immunology and Aging Program; Department of Surgery; Stritch School of Medicine, Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153, USA

Elizabeth M. Gardner
Department of Bioscience and Biotechnology, Drexel University, Philadelphia, PA 19104, USA; Department of Food Science and Human Nutrition, Michigan State University, East Lansing, MI 48824, USA

Elke Richartz-Salzburger
Department of Psychiatry and Psychotherapy, University of Tübingen, Osiander-strasse 24, DE-72076 Tübingen, Germany

Emilie Combet
Section of Medicine and Therapeutics, Western Infirmary, University of Glasgow, Scotland

Enrico Lugli
Chair of Immunology, Department of Biomedical Sciences, University of Modena and Reggio Emilia, Via Campi 287, Modena, 41100, Italy

Eric J. Yager
Trudeau Institute, Saranac Lake, NY 12983, USA

Eric T. Clambey
Integrated Department of Immunology, University of Colorado Health Sciences Center, Denver, CO 80206, USA; Howard Hughes Medical Institute, National Jewish Research & Medical Center, University of Colorado Health Sciences Center, Denver, CO 80206, USA

Erika Roat
Chair of Immunology, Department of Biomedical Sciences, University of Modena and Reggio Emilia, Via Campi 287, Modena, 41100, Italy

Erminia Mariani
Laboratorio di Immunologia e Genetica, Istituto di Ricerca Codivilla-Putti, IOR, Via di Barbiano 1/10, 40136, Bologna, Italy

Esther Peralbo
Department of Immunology, Reina Sofia University Hospital, University of Córdoba, Spain

Eugenio Mocchegiani
Immunology Ctr., Section Nutrigenomic and Immunosenescence, Res. Dept. INRCA, Ancona, Italy

Ewa Bryl
Department of Pathophysiology, Medical University of Gdańsk, Poland

Ewa Sikora
Molecular Bases of Aging Laboratory, Nencki Institutew of Experimental Biology, Polish Academy of Sciences, Pasteura 3, Warsaw Poland

Flávia Ribeiro
Ageing and Tumour Immunology Group, University of Tübingen, Sektion Transplantionsimmunologie / Immunhämatologie, Waldhörnle Strasse 22, D- 72072 Tübingen, Germany

Florinda Listì
Gruppo di Studio sull'Immunosenescenza, Dipartimento di Biopatologia e Metodologie Biomediche, Università di Palermo, Corso Tukory 211, 90134 Palermo, Italy

Frances T. Hakim
Experimental Transplantation and Immunology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, DHHS, Bethesda, MD, USA

Gary Van Zant
Department of Internal Medicine, University of Kentucky, Lexington, Kentucky, USA

Georg Wick
Division of Experimental Pathophysiology and Immunology, Laboratory of Autoimmunity, Biocenter, Innsbruck Medical University, Fritz-Pregl-Strasse 3, A-6020-Innsbruck, Austria

George C. Wang
Division of Geriatric Medicine and Gerontology, Department of Medicine, Johns Hopkins University School of Medicine, 5505 Hopkins Bayview Circle, John R. Burton Pavilion, Baltimore, MD 21224, USA

Gilles Dupuis
Clinical research Center, Department of Biochemistry, Immunology Graduate Programme, Faculty of Medicine, University of Sherbrooke, Sherbrooke, Quebec, Canada

Giuseppina Candore
Gruppo di Studio sull'Immunosenescenza, Dipartimento di Biopatologia e Metodologie Biomediche, Università di Palermo, Corso Tukory 211, 90134 Palermo, Italy

Giuseppina Colonna-Romano
Gruppo di Studio sull'Immunosenescenza, Dipartimento di Biopatologia e Metodologie Biomediche, Università di Palermo, Corso Tukory 211, 90134 Palermo, Italy

Graham Pawelec
Center for Medical Research (ZMF); Tübingen Ageing and Tumour Immunology Group, Center for Medical Research, University of Tübingen Medical School, Waldhörnlestr. 22, D-72072 Tübingen, Germany

Hartmut Geiger
Division of Experimental Hematology and Cancer Biology, Cincinnati Children's Hospital Medical Center and University of Cincinnati College of Medicine, Cincinnati, Ohio, USA

Haruyoshi Yamaza
Department of Investigative Pathology, Unit of Basic Medical Science, Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, Japan

Hideto Tamura
Division of Hematology, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan

Hui-Chen Hsu
Department of Medicine, 1825 University Blvd, SHELB 310; The University of Alabama at Birmingham, Birmingham, Alabama 35294, USA

I. Maeve Rea
Department of Geriatric Medicine, Queens University of Belfast, Northern, Ireland

Ian C. Brett
State University of New York, Stony Brook School of Medicine, Health Sciences Center, L4, Stony Brook, NY 11794, USA

Inmaculada Gayoso
Department of Immunology, Reina Sofia University Hospital, University of Córdoba, Spain

Isao Shimokawa
Department of Investigative Pathology, Unit of Basic Medical Science, Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, Japan

Jacek M. Witkowski
Department of Pathophysiology, Medical University of Gdansk, Gdansk, Poland

Jacob E. Kohlmeier
Trudeau Institute, Saranac Lake, NY 12983, USA

Jan Strindhall
Department of Natural Science and Biomedicine, School of Health Sciences, Jönköping University, Box 1026, 551 11 Jönköping, Sweden

Janet E. McElhaney
Geriatrics Research, University of British Columbia, Vancouver, Canada, and Center for Immunotherapy of Cancer and Infectious Diseases, University of Connecticut School of Medicine, Farmington, CT

Janet M. Lord
MRC Centre for Immune Regulation, Division of Immunity and Infection, Birmingham University Medical School, Birmingham B15 2TT, UK

Janko Nikolich-Zugich
Vaccine and Gene Therapy Institute, Department of Molecular Microbiology and Immunology and the Oregon National Primate Research Center, Oregon Health & Science University, Beaverton, OR 97006, USA

Jarrod Dudakov
Monash Immunology and Stem Cell Laboratories, Monash University, Clayton, Australia

Javier G. Casado
Immunology Unit, Department of Physiology, University of Extremadura, Cáceres, Spain

Jean L. Scholz
Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, 36th and Hamilton Walk, Philadelphia, PA 19104-6082, USA

Jeff Leips
Department of Biological Sciences, 1000 Hilltop Circle, University of Maryland Baltimore County, Baltimore, MD, 21250, USA

Jens M. Nygren
Stem Cell Aging, Deptartment of Experimental Medical Science, BMC I13, Lund University, 221 84 Lund, Sweden

Jeremy Walston
Division of Geriatric Medicine and Gerontology, Department of Medicine, Johns Hopkins University School of Medicine, 5505 Hopkins Bayview Circle, John R. Burton Pavilion, Baltimore, MD 21224, USA

Jessica L. Palmer
Department of Surgery and The Burn and Shock Trauma Institute, Loyola University Medical Center, Stritch School of Medicine, Maywood, IL, USA

Jessica Reiseger
Monash Immunology and Stem Cell Laboratories, Monash University, Clayton, Australia

Jian Chen
Department of Medicine, 1825 University Blvd, SHELB 310; The University of Alabama at Birmingham, Birmingham, Alabama 35294, USA

John D. Mountz
Department of Medicine; Birmingham VA Medical Center, 1825 University Blvd, SHELB 310; The University of Alabama at Birmingham, Birmingham, Alabama 35294, USA

John W. Kappler
Integrated Department of Immunology, University of Colorado Health Sciences Center, Denver, CO 80206, USA; Howard Hughes Medical Institute, National Jewish Research & Medical Center, University of Colorado Health Sciences Center, Denver, CO 80206, USA; Departments of Medicine, University of Colorado Health Sciences Center, Denver, CO 80206, USA; Pharmacology, University of Colorado Health Sciences Center, Denver, CO 80206, USA

Jörg J. Goronzy
Kathleen B. and Mason I. Lowance Center for Human Immunology, Department of Medicine, Emory University School of Medicine, Room 1003 Woodruff Memorial Research Building, 101 Woodruff Circle, Atlanta, GA, USA

Jorge Lloberas
Institute for Research in Biomedicine-University of Barcelona, Josep Samitier 1-5, 08028 Barcelona, Spain

Joseph Lustgarten
Cancer Center Scottsdale, Mayo Clinic Arizona, 13400 East Shea Boulevard Scottsdale, AZ 85259, USA

Jürgen Kempf
Center for Medical Research (ZMF), University of Tübingen Medical School, Waldhörnlestr. 22, D-72072 Tübingen, Germany

Jyoti Misra Sen
Laboratory of Immunology, Clinical Immunology Section, National Institute on Aging, Intramural Research Program, National Institutes of Health, Baltimore, MD, USA

Kate L. Gibson
Department of Immunobiology, 2nd Floor, Borough Wing Guy's, King's and St. Thomas School of Medicine, King's College London, Guy's Hospital, Great Maze Pond, London SE1 9RT, UK

Katerina Vlahos
Monash Immunology and Stem Cell Laboratories, Monash University, Clayton, Australia

Katsuiku Hirokawa
Institute for Health and Life Sciences; Department of Comprehensive Pathology, Tokyo Medical & Dental University; Nakanosogo Hospital, Ascent Myogadani, Kohinata, Bunkyo-ku, Tokyo 112-0006, Japan

Kelly M. Hinkle
Department of Neuroscience, Mayo Clinic College of Medicine, Jacksonville, Florida, USA

Kenneth H. Ely
Trudeau Institute, Saranac Lake, NY 12983, USA

Kiyoyuki Ogata
Division of Hematology, Department of Medicine, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan

Ladislas Robert
Université paris 5. Laboratoire de Recherche Ophtalmologique., 1 place du Parvis Notre Dame, 75181 Paris cedex 04, France

Lara Gibellini
Chair of Immunology, Department of Biomedical Sciences, University of Modena and Reggio Emilia, Via Campi 287, Modena, 41100, Italy

Laura Bucci
Department of Experimental Pathology, University of Bologna, Via San Giacomo 12, I-40126 Bologna, Italy

Laura Celani
CIG-Interdepartmental Center “L. Galvani”, University of Bologna, Via San Giacomo 12, I-40126 Bologna, Italy

Leonarda Troiano
Chair of Immunology, Department of Biomedical Sciences, University of Modena and Reggio Emilia, Via Campi 287, Modena, 41100, Italy

Letizia Scola
Gruppo di Studio sull’Immunosenescenza, Dipartimento di Biopatologia e Metodologie Biomediche, Università di Palermo, Corso Tukory 211, 90134 Palermo, Italy

Lia Ginaldi
Department of Internal Medicine and Public Health, University of L’Aquila, L’Aquila, Italy

Linda Bertoncelli
Chair of Immunology, Department of Biomedical Sciences, University of Modena and Reggio Emilia, Via Campi 287, Modena, 41100, Italy

Linda P. Fried
Division of Geriatric Medicine and Gerontology and Center on Aging and Health, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Lothar Rink
Institute for Immunology, RWTH Aachen University Hospital, Pauwelsstr. 30, 52074 Aachen, Germany

Lucia P. Mengoli
Department of Internal Medicine and Public Health, University of L'Aquila, L'Aquila, Italy

M. Luisa Pita
Department of Immunology, Reina Sofia University Hospital, University of Córdoba, Spain

Marcello Pinti
Chair of Immunology, Department of Biomedical Sciences, University of Modena and Reggio Emilia, Via Campi 287, Modena, 41100, Italy

Marcia A. Blackman
Trudeau Institute, Saranac Lake, NY 12983, USA

Marco Malavolta
Immunology Ctr., Section Nutrigenomic and Immunosenescence, Res. Dept. INRCA, Ancona, Italy

Maria Paola Grimaldi
Gruppo di Studio sull'Immunosenescenza, Dipartimento di Biopatologia e Metodologie Biomediche, Università di Palermo, Corso Tukory 211, 90134 Palermo, Italy

Marilyn Armstrong
Department of Geriatric Medicine, Queens University Belfast, Belfast, Ireland, UK

Marius Wick
Department of Radiology, Innsbruck Medical University, Anichstrasse 35, A-6020 Innsbruck, Austria

Masanobu Kitagawa
Department of Comprehensive Pathology, Aging and Developmental Sciences, Graduate School, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519, Japan

Masanori Utsuyama
Institute for Health and Life Sciences; Department of Comprehensive Pathology, Tokyo Medical & Dental University, Ascent Myogadani 4F, 4-4-22, Kohinata, Bunkyo-ku, Tokyo 112-0006, Japan

Massimo De Martinis
Department of Internal Medicine and Public Health, University of L'Aquila, L'Aquila, Italy

Mauro Provinciali
Laboratory of Tumour Immunology, INRCA Res. Dept., Via Birarelli 8, 60121 Ancona, Italy

Maximilian Zeyda
Department Internal Medicine III, Medical University of Vienna, Währinger Gürtel 18-20, A-1090 Vienna, Austria

Michael P. Cancro
Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, 36th and Hamilton Walk, Philadelphia, PA 19104-6082, USA

Milena Ivanova
Central Laboratory of Clinical Immunology, University Hospital "Alexandrovska". 1. G. Sofiisky str., 1431 Sofia, Bulgaria

Milena Nasi
Chair of Immunology, Department of Biomedical Sciences, University of Modena and Reggio Emilia, Via Campi 287, Modena, 41100, Italy

Miriam Capri
Department of Experimental Pathology, University of Bologna, Via San Giacomo 12, I-40126 Bologna, Italy; CIG-Interdepartmental Center "L. Galvani", University of Bologna, Via San Giacomo 12, I-40126 Bologna, Italy

Moisés E. Bauer
Faculdade de Biociências and Instituto de Pesquisas Biomédicas, Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Av. Ipiranga 6690, 2º andar. P.O. Box 1429. Porto Alegre, RS 90.610-000, Brazil

Nan-Ping Weng
Laboratory of Immunology, National Institute on Aging, National Institutes of Health, Baltimore, MD, USA

Naozumi Ishimaru
Department of Oral Molecular Pathology, Institute of Health Biosciences, The University of Tokushima Graduate School, 3 Kuramotocho, Tokushima 770-8504, Japan

Natalie Seach
Monash Immunology and Stem Cell Laboratories, Monash University, Clayton, Australia

Niklas Koehler
Department of Psychiatry and Psychotherapy, University of Tübingen, Osiander-strasse 24, DE-72076 Tübingen, Germany

Noweeda Mirza
Cancer Center Scottsdale, Mayo Clinic Arizona, 13400 East Shea Boulevard Scottsdale, AZ 85259, USA

Olivier Lesur
Clinical research Center, Graduate Immunology Program, Division of Pulmonology, Department of Medicine, Faculty of Medicine, University of Sherbrooke, Sherbrooke, Quebec, Canada

Owen A. Ross
Department of Geriatric Medicine, Queens University Belfast, Belfast, Irelan d, UK; Department of Neuroscience, Mayo Clinic College of Medicine, Jacksonville, Florida, USA

Paul Moss
Institute for Cancer Studies, University of Birmingham, Vincent Drive, Birmingham B 15 2TT, UK

Pazit Beckerman
University Hospital Kerem, The Department of Medicine at the Hadassah Ein, Jerusalem, Isreal

Peter Uciechowski
Institute for Immunology, RWTH Aachen University Hospital, Pauwelsstr. 30, 52074 Aachen, Germany

Philippa Marrack
Integrated Department of Immunology, University of Colorado Health Sciences Center, Denver, CO 80206, USA; Howard Hughes Medical Institute, National Jewish Research & Medical Center, University of Colorado Health Sciences Center, Denver, CO 80206, USA; Departments of Medicine, University of Colorado Health Sciences Center, Denver, CO 80206, USA; Pharmacology, University of Colorado Health Sciences Center, Denver, CO 80206, USA; Biochemistry and Molecular Genetics, University of Colorado Health Sciences Center, Denver, CO 80206, USA

Piotr Trzonkowski
Laboratory of Experimental Transplantology, Department of Histology and Immunology, Medical University of Gdańsk, Ul. Dębinki 1, 80-211 Gdańsk, Poland

Qing Yu
Laboratory of Immunology, Clinical Immunology Section, National Institute on Aging, Intramural Research Program, National Institutes of Health, Baltimore, MD, USA

Rafael Solana
Department of Immunology, Reina Sofia University Hospital, University of Córdoba, Spain

Raquel Tarazona
Immunology Unit, Department of Physiology, University of Extremadura, Cáceres, Spain

Richard Aspinall
Department of Immunology, Imperial College London, Faculty of Investigative Sciences, Chelsea and Westminster Campus, 369 Fulham Road, London, UK

Richard Boyd
Monash Immunology and Stem Cell Laboratories, Monash University, Clayton, Australia

Richard L. Riley
Department of Microbiology and Immunology, University of Miami Miller School of Medicine, P.O. Box 016960 (R-138), Miami, FL 33101, USA

Rita B. Effros
Department of Pathology & Laboratory Medicine, David Geffen School of Medicine at UCLA, 10833 Le Conte Avenue, Los Angeles, CA 90095-1732, USA

Rita Ostan
Department of Oncology and Experimental Pathology, University of Florence, Via Morgagni 50, Florence, Italy

Roberta Ferraresi
Chair of Immunology, Department of Biomedical Sciences, University of Modena and Reggio Emilia, Via Campi 287, Modena, 41100, Italy

Sara Morgado
Immunology Unit, Department of Physiology, University of Extremadura, Cáceres, Spain

Sean X. Leng
Division of Geriatric Medicine and Gerontology and Center on Aging and Health, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Sergey G. Rudnev
Institute of Numerical Mathematics, Russian Academy of Sciences, Moscow, Russia

Simona Neri
Laboratorio di Immunologia e Genetica, Istituto di Ricerca Codivilla-Putti, IOR, Via di Barbiano 1/10, 40136, Bologna, Italy

Sirisha Karri
Division of Nutritional Sciences, The University of Texas, Austin, TX 78712, USA

Sonya Vasto
Gruppo di Studio sull'Immunosenescenza, Dipartimento di Biopatologia e Metodologie Biomediche, Università di Palermo, Corso Tukory 211, 90134 Palermo, Italy

Stefano Salvioli
Department of Experimental Pathology, University of Bologna, Via San Giacomo 12, I-40126 Bologna, Italy; CIG-Interdepartmental Center "L. Galvani", University of Bologna, Via San Giacomo 12, I-40126 Bologna, Italy

Steven Castle
Geriatric Research Education and Clinical Center (GRECC) VA Greater Los Angeles Healthcare system, UCLA School of Medicine, 11301 Wilshire Boulvard, Los Angeles, CA, 90073, USA

Sudhanshu Agrawal
Division of Basic and Clinical Immunology, University of California, Irvine, CA 92697, USA

Sudhir Gupta
Division of Basic and Clinical Immunology, University of California, Irvine, CA 92697, USA

Susan E. McNerlan
Department of Geriatric Medicine, Queens University Belfast, Belfast, Ireland, UK

Takuya Chiba
Department of Investigative Pathology, Unit of Basic Medical Science, Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, Japan

Tamas Fulop
Centre de recherche sur le vieillissement; Research Center on Aging, Department of Medicine, Immunology Graduate Programme, Faculty of Medicine, University of Sherbrooke, Sherbrooke, Quebec, Canada

Tatiana A. Sannikova
Institute of Numerical Mathematics, Russian Academy of Sciences, Moscow, Russia

Thomas M. Stulnig
Department Internal Medicine III, Medical University of Vienna, Währinger Gürtel 18-20, A-1090 Vienna, Austria

Toshimitsu Komatsu
Department of Investigative Pathology, Unit of Basic Medical Science, Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, Japan

Vanessa Nomellini
The Burn and Shock Trauma Institute and the Immunology and Aging Program; Stritch School of Medicine, Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153, USA

Victor Appay
Cellular Immunology laboratory, INSERM U543, Avenir Group, Hopital Pitie-Salpetriere, Université Pierre et Marie Curie-Paris, 91 Bd de l'Hopital, 75013 Paris, France

Wayne A. Mitchell
Department of Immunology, Imperial College London, Faculty of Investigative Sciences, Chelsea and Westminster Campus, 369 Fulham Road, London, UK

Wiebke Arlt
Division of Medical Sciences, University of Birmingham, Birmingham B15 2TT, UK

William J. Quinn III
Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, 36th and Hamilton Walk, Philadelphia, PA 19104-6082, USA

Yoshio Hayashi
Department of Oral Molecular Pathology, Institute of Health Biosciences, The University of Tokushima Graduate School, 3 Kuramotocho, Tokushima 770-8504, Japan

Yuko Kikuchi
Institute for Health and Life Sciences, Department of Comprehensive Pathology, Tokyo Medical & Dental University, Ascent Myogadani, Kohinata, Bunkyo-ku, Tokyo 112-0006, Japan