The AAPS Advances in the Pharmaceutical Sciences Series, published in partnership with the American Association of Pharmaceutical Scientists, is designed to deliver well-written volumes authored by opinion leaders and authoritarians from around the globe, addressing innovations in drug research and development, and best practice for scientists and industry professionals in the pharma and biotech industries. For more details and to see a list of titles in the Series please visit http://www.springer.com/series/8825

**Series Editors**
Daan J. A. Crommelin
Robert A. Lipper
Gert Folkerts • Johan Garssen
Editors

Pharma-Nutrition

An Overview
# Contents

## Part I  General

1 **Pharma-Nutrition** ................................................................. 3  
   Seil Sagar, Gert Folkerts, and Johan Garssen

2 **New Developments in Food Safety Assessment: Innovations in Food Allergy and Toxicological Safety Assessment** ........... 9  
   Geert Houben, Marty Blom, Jolanda van Bilsen, and Lisette Krul

3 **Bridging a Pharma-Like Innovation Gap in Medical Nutrition** . . . 29  
   Tamar C. Weenen, Kenneth Fernald, Esther S. Pronker,  
   Harry Commandeur, and Eric Claassen

## Part II  Inflammation and Immunity

4 **Modulation of the Gut Ecosystem in Irritable Bowel Syndrome** . . 55  
   Julia König and Robert-Jan Brummer

5 **Role of Omega-6 and Omega-3 Fatty Acids in Inflammatory Bowel Disease** ................................................................. 75  
   Kevan Jacobson and Philip C. Calder

6 **N-3 Polyunsaturated Fatty Acid and Neuroinflammation in Aging: Role in Cognition** ................................................................. 91  
   Sophie Layé, Charlotte Madore, Jean-Christophe Delpech, Corinne Joffre,  
   and Agnès Nadjar

7 **Nutritional Programming of Immune Defense Against Infections in Early Life** ................................................................. 113  
   Alma J. Nauta and Johan Garssen

8 **Impact of Nondigestible Oligosaccharides on Gut-Associated Lymphoid Tissue and Oral Tolerance Induction** ...................... 127  
   Linette E.M. Willemsen
9 The Endocannabinoid System: A Dynamic Signalling System at the Crossroads Between Metabolism and Disease 155
Renger F. Witkamp

10 Effects of Natural Products on Pharmacokinetics and Pharmacodynamics of Drugs 189
Shizuo Yamada, Shingen Misaka, Yoshihiko Ito, Hiroshi Watanabe, and Keizo Umegaki

11 Nutrition and Gastrointestinal Health as Modulators of Parkinson’s Disease 213
Heather E. Rasmussen, Bryana R. Piazza, Christopher B. Forsyth, and Ali Keshavarzian

12 Eat to Heal: Natural Inducers of the Heme Oxygenase-1 System 243
Matheus Correa-Costa and Leo E. Otterbein

Part III Cancer and Cachexia

13 Recent Developments in Treatment of Cachexia 259
Josep M. Argilés, Francisco Javier López-Soriano, Britta Stemmler, and Silvia Busquets

14 Individualized Tumor Therapy: Biomarkers and Possibilities for Targeted Therapy with Natural Products 275
Thomas Efferth

15 Nutrition in Oncology: From Treating Cachexia to Targeting the Tumor 295
Alessandro Laviano, Chiara Gori, Martina Stronati, Alessia Mari, and Serena Rianda

16 Nutraceuticals in Preventive Oncology: Chemical Biology and Translational Pharmaceutical Science 305
Ruiwen Zhang and Subhasree Nag

Part IV Allergy

17 The Onset of Atopic Dermatitis: Underlying Mechanisms 345
Alma J. Nauta and Hugo van Bever

18 Cow’s Milk Allergy: Protein Hydrolysates or Amino Acid Formula? 359
Christophe Dupont

19 Allergen Avoidance Versus Tolerance Induction 373
Prescilla V. Jeurink, Laura A.P.D. Meulenbroek, Johan Garssen and Léon M.J. Knippels
## Contents

### Part V  Brain and Neuroimmunity

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>Nutrition and Cognitive Decline in Older Persons: Bridging the Gap Between Epidemiology and Intervention Studies</td>
<td>395</td>
</tr>
<tr>
<td></td>
<td>Pascale Barberger-Gateau, Cécilia Samieri, Catherine Feart, and Stephen C. Cunnane</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Nutraceutical Regulation of the Neuroimmunoendocrine Super-system</td>
<td>415</td>
</tr>
<tr>
<td></td>
<td>Paul Forsythe</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Targeting (Gut)-Immune-Brain Axis with Pharmaceutical and Nutritional Concepts: Relevance for Mental and Neurological Disorders</td>
<td>439</td>
</tr>
<tr>
<td></td>
<td>Aletta D. Kraneveld and Johan Garssen</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Nutritional Approaches for Healthy Aging of the Brain and the Prevention of Neurodegenerative Diseases</td>
<td>457</td>
</tr>
<tr>
<td></td>
<td>Heike Asseburg, Stephanie Hagl, and Gunter P. Eckert</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Index</td>
<td>481</td>
</tr>
</tbody>
</table>
List of Contributors

Josep M. Argilés Cancer Research Group, Department of Biochemistry and Molecular Biology, Faculty of Biology, and Institute of Biomedicine, University of Barcelona, Barcelona, Spain

Heike Asseburg Nutritional Neuroscience Group, Department of Pharmacology, Goethe University Frankfurt, Frankfurt, Germany

Pascale Barberger-Gateau Institute of Public Health, Epidemiology, and Development (ISPED), French Institute of Health and Medical Research (INSERM), U897-Epidemiologie-Biostatistique, University of Bordeaux, Bordeaux, France

Hugo van Bever Department of Pediatrics, National University Health System (NUHS), Singapore, Singapore

Jolanda van Bilsen TNO, Zeist, The Netherlands

Marty Blom TNO, Zeist, The Netherlands

Robert-Jan Brummer Faculty of Medicine and Health, School of Health and Medical Sciences, Örebro University, Örebro, Sweden

Sílvia Busquets Cancer Research Group, Department of Biochemistry and Molecular Biology, Faculty of Biology, and Institute of Biomedicine, University of Barcelona, Barcelona, Spain

Philip C. Calder Faculty of Medicine and National Institute for Health Research Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK

Eric Claassen Department of Virology, Erasmus Medical Center, Erasmus University, Rotterdam, The Netherlands

Harry Commandeur Erasmus School of Economics, Erasmus University, Rotterdam, The Netherlands
Matheus Correa-Costa  Transplant Institute, Department of Surgery, Harvard Medical School and Beth Israel Deaconess Medical Center, Boston, MA, USA  

Stephen C. Cunnane  Department of Medicine, Research Center on Aging, University of Sherbrooke, Sherbrooke, QC, Canada  

Jean-Christophe Delpech  Integrated Nutrition and Neurobiology, National Institute of Agronomic Research (INRA) 1286, Bordeaux Segalen University, Bordeaux, France  

University of Bordeaux, Bordeaux, France  

Christophe Dupont  Department of Functional Digestive Pediatric Explorations, Necker-Enfants Malades Hospital, Paris Descartes University, Paris, France  

Gunter P. Eckert  Nutritional Neuroscience Group, Department of Pharmacology, Goethe University Frankfurt, Frankfurt, Germany  

Thomas Efferth  Department of Pharmaceutical Biology, Institute of Pharmacy and Biochemistry, Johannes Gutenberg University, Mainz, Germany  

Catherine Feart  Institute of Public Health, Epidemiology, and Development (ISPED), French Institute of Health and Medical Research (INSERM), U897-Epidemiologie-Biostatistique, University of Bordeaux, Bordeaux, France  

Kenneth Fernald  Athena Institute, Vrije Universiteit, Amsterdam, The Netherlands  

Gert Folkerts  Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Faculty of Science, Utrecht University, Utrecht, The Netherlands  

Christopher B. Forsyth  Digestive Diseases Basic Research Laboratory, Section of Gastroenterology, Division of Digestive Diseases, Hepatology and Nutrition, Department of Internal Medicine, Rush University Medical Center, Chicago, IL, USA  

Paul Forsythe  Department of Medicine, The McMaster Brain-Body Institute and Firestone Institute for Respiratory Health, McMaster University, Hamilton, ON, Canada  

Johan Garssen  Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Faculty of Science, Utrecht University, Utrecht, The Netherlands  

Nutricia Research, Utrecht, The Netherlands  

Chiara Gori  Department of Clinical Medicine, Sapienza University, Rome, Italy  

Stephanie Hagi  Nutritional Neuroscience Group, Department of Pharmacology, Goethe University Frankfurt, Frankfurt, Germany
List of Contributors

Geert Houben  TNO, Zeist, The Netherlands

Yoshihiko Ito  Department of Pharmacokinetics and Pharmacodynamics, School of Pharmaceutical Sciences, University of Shizuoka, Shizuoka, Japan

Kevan Jacobson  Division of Gastroenterology, Hepatology and Nutrition, Child and Family Research Institute, British Columbia’s Children’s Hospital, University of British Columbia, Vancouver, BC, Canada

Corinne Joffre  Integrated Nutrition and Neurobiology, National Institute of Agronomic Research (INRA) 1286, Bordeaux Segalen University, Bordeaux, France

University of Bordeaux, Bordeaux, France

Prescilla V. Jeurink  Nutricia Research, Utrecht, The Netherlands

Ali Keshavarzian  Division of Digestive Diseases, Department of Internal Medicine, Rush University Medical Center, Chicago, IL, USA

Léon M.J. Knippels  Nutricia Research, Utrecht, The Netherlands

Julia König  Faculty of Medicine and Health, School of Health and Medical Sciences, Örebro University, Örebro, Sweden

Aletta D. Kraneveld  Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Faculty of Science, Utrecht University, Utrecht, The Netherlands

Lisette Krul  TNO, Zeist, The Netherlands

Alessandro Laviano  Department of Clinical Medicine, Sapienza University, Rome, Italy

Sophie Layé  Integrated Nutrition and Neurobiology, National Institute of Agronomic Research (INRA) 1286, Bordeaux Segalen University, Bordeaux, France

University of Bordeaux, Bordeaux, France

Francisco Javier López-Soriano  Cancer Research Group, Department of Biochemistry and Molecular Biology, Faculty of Biology, and Institute of Biomedicine, University of Barcelona, Barcelona, Spain

Charlotte Madore  Integrated Nutrition and Neurobiology, National Institute of Agronomic Research (INRA) 1286, Bordeaux Segalen University, Bordeaux, France

University of Bordeaux, Bordeaux, France

Alessia Mari  Department of Clinical Medicine, Sapienza University, Rome, Italy

Laura A. P. D. Meulenbroek  Nutricia Research, Utrecht, The Netherlands

Shingen Misaka  Department of Pharmacology, School of Medicine, Fukushima Medical University, Fukushima, Japan
List of Contributors

Agnès Nadjar  Integrated Nutrition and Neurobiology, National Institute of Agro-nomic Research (INRA) 1286, Bordeaux Segalen University, Bordeaux, France
University of Bordeaux, Bordeaux, France

Subhasree Nag  Department of Pharmaceutical Sciences, School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, TX, USA

Alma J. Nauta  Nutricia Research, Utrecht, The Netherlands
Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands

Leo E. Otterbein  Transplant Institute, Department of Surgery, Harvard Medical School and Beth Israel Deaconess Medical Center, Boston, MA, USA

Bryana R. Piazza  Rush University Medical Center, Chicago, IL, USA

Esther S. Pronker  Vironovative, Rotterdam, The Netherlands

Heather E. Rasmussen  Rush University Medical Center, Chicago, IL, USA

Serena Rianda  Department of Clinical Medicine, Sapienza University, Rome, Italy

Seil Sagar  Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Faculty of Science, Utrecht University, Utrecht, The Netherlands

Cécilia Samieri  Institute of Public Health, Epidemiology, and Development (ISPED), French Institute of Health and Medical Research (INSERM), U897-Epidemiologie-Biostatistique, University of Bordeaux, Bordeaux, France

Britta Stemmler  BSA Nutrition Centre, Barcelona, Spain

Martina Stronati  Department of Clinical Medicine, Sapienza University, Rome, Italy

Keizo Umegaki  Information Center, National Institute of Health and Nutrition, Tokyo, Japan

Hiroshi Watanabe  Departments of Clinical Pharmacology and Therapeutics, Hamamatsu University School of Medicine, Shizuoka, Japan

Tamar C. Weenen  Erasmus Medical Center and Erasmus School of Economics, Erasmus University, Rotterdam, The Netherlands

Linette E.M. Willemsen  Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands

Renger F. Witkamp  Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands
Shizuo Yamada Department of Pharmacokinetics and Pharmacodynamics, School of Pharmaceutical Sciences, University of Shizuoka, Shizuoka, Japan

Ruiwen Zhang Department of Pharmaceutical Sciences, School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, TX, USA