

## Contents

|                 |  |             |
|-----------------|--|-------------|
|                 | <b>Foreword to <i>Parasitic Helminths: Targets, Screens, Drugs and Vaccines</i></b>  | <b>V</b>    |
|                 | <b>Preface</b>   | <b>XI</b>   |
|                 | <b>List of Contributors</b>  | <b>XIII</b> |
| <b>Part One</b> | <b>Targets</b>   | <b>1</b>    |
| <b>1</b>        | <b>Ligand-Gated Ion Channels as Targets for Anthelmintic Drugs: Past, Current, and Future Perspectives</b>                                       | <b>3</b>    |
|                 | <i>Kristin Lees*, Ann Sluder, Niroda Shannan, Lance Hammerland, and David Sattelle</i>   |             |
| <b>2</b>        | <b>How Relevant is <i>Caenorhabditis elegans</i> as a Model for the Analysis of Parasitic Nematode Biology?</b>                                  | <b>23</b>   |
|                 | <i>Lindy Holden-Dye* and Robert J. Walker</i>  |             |
| <b>3</b>        | <b>Integrating and Mining Helminth Genomes to Discover and Prioritize Novel Therapeutic Targets</b>  | <b>43</b>   |
|                 | <i>Dhanasekaran Shanmugam, Stuart A. Ralph, Santiago J. Carmona, Gregory J. Crowther, David S. Roos, and Fernán Agüero*</i>                      |             |
| <b>4</b>        | <b>Recent Progress in Transcriptomics of Key Gastrointestinal Nematodes of Animals – Fundamental Research Toward New Intervention Strategies</b> | <b>61</b>   |
|                 | <i>Cinzia Cantacessi, Bronwyn E. Campbell, Aaron R. Jex, Ross S. Hall, Neil D. Young, Matthew J. Nolan, and Robin B. Gasser*</i>                 |             |
| <b>5</b>        | <b>Harnessing Genomic Technologies to Explore the Molecular Biology of Liver Flukes-Major Implications for Fundamental and Applied Research</b>  | <b>73</b>   |
|                 | <i>Neil D. Young*, Aaron R. Jex, Cinzia Cantacessi, Bronwyn E. Campbell, and Robin B. Gasser</i>   |             |

- 6 RNA Interference: A Potential Discovery Tool for Therapeutic Targets of Parasitic Nematodes** 89  
*Collette Britton*
- 7 RNA Interference as a Tool for Drug Discovery in Parasitic Flatworms** 105  
*Akram A. Da'dara and Patrick J. Skelly\**
- Part Two Screens** 121
- 8 Mechanism-Based Screening Strategies for Anthelmintic Discovery** 123  
*Timothy G. Geary*
- 9 Identification and Profiling of Nematicidal Compounds in Veterinary Parasitology** 135  
*Andreas Rohwer, Jürgen Lutz, Christophe Chassaing, Manfred Uphoff, Anja R. Heckerroth, and Paul M. Selzer\**
- 10 Quantitative High-Content Screening-Based Drug Discovery against Helmintic Diseases** 159  
*Rahul Singh*
- 11 Use of Rodent Models in the Discovery of Novel Anthelmintics** 181  
*Rebecca Fankhauser, Linsey R. Cozzie, Bakela Nare, Kerrie Powell, Ann E. Sluder, and Lance G. Hammerland\**
- 12 To Kill a Mocking Worm: Strategies to Improve *Caenorhabditis elegans* as a Model System for use in Anthelmintic Discovery** 201  
*Andrew R. Burns and Peter J. Roy\**
- Part Three Drugs** 217
- 13 Anthelmintic Drugs: Tools and Shortcuts for the Long Road from Discovery to Product** 219  
*Eugenio L. de Hostos\* and Tue Nguyen*
- 14 Antinematodal Drugs – Modes of Action and Resistance: And Worms Will Not Come to Thee (Shakespeare: *Cymbeline*: IV, ii)** 233  
*Alan P. Robertson, Samuel K. Buxton, Sreekanth Puttachary, Sally M. Williamson, Adrian J. Wolstenholme, Cedric Neveu, Jacques Cabaret, Claude L. Charvet, and Richard J. Martin\**
- 15 Drugs and Targets to Perturb the Symbiosis of *Wolbachia* and Filarial Nematodes** 251  
*Mark J. Taylor\*, Louise Ford, Achim Hoerauf, Ken Pfarr, Jeremy M. Foster, Sanjay Kumar, and Barton E. Slatko*

- 16 Promise of *Bacillus thuringiensis* Crystal Proteins as Anthelmintics** 267  
*Yan Hu and Raffi V. Aroian\**
- 17 Monepantel: From Discovery to Mode of Action** 283  
*Ronald Kaminsky\* and Lucien Rufener*
- 18 Discovery, Mode of Action, and Commercialization of Derquantel** 297  
*Debra J. Woods\*, Steven J. Maeder, Alan P. Robertson, Richard J. Martin, Timothy G. Geary, David P. Thompson, Sandra S. Johnson, and George A. Conder*
- 19 Praziquantel: Too Good to be Replaced?** 309  
*Livia Pica-Mattoccia\* and Donato Cioli*
- 20 Drug Discovery for Trematodiasis: Challenges and Progress** 323  
*Conor R. Caffrey\*, Jürg Utzinger, and Jennifer Keiser*
- Part Four Vaccines** 341
- 21 Barefoot thru' the Valley of Darkness: Preclinical Development of a Human Hookworm Vaccine** 343  
*Jeffrey M. Bethony\*, Maria Victoria Periago, and Amar R. Jariwala*
- 22 Vaccines Linked to Chemotherapy: A New Approach to Control Helminth Infections** 357  
*Sara Lustigman\*, James H. McKerrow, and Maria Elena Bottazzi*
- 23 Antifilarial Vaccine Development: Present and Future Approaches** 377  
*Sara Lustigman\*, David Abraham, and Thomas R. Klei*
- 24 Proteases as Vaccines Against Gastrointestinal Nematode Parasites of Sheep and Cattle** 399  
*David Knox*
- 25 Schistosomiasis Vaccines – New Approaches to Antigen Discovery and Promising New Candidates** 421  
*Alex Loukas\*, Soraya Gaze, Mark Pearson, Denise Doolan, Philip Felgner, David Diemert, Donald P. McManus, Patrick Driguez, and Jeffrey Bethony*

- 26 Sm14 *Schistosoma mansoni* Fatty Acid-Binding Protein: Molecular Basis for an Antihelminth Vaccine** 435  
*Miriam Tendler\**, *Celso Raul Romero Ramos*,  
and *Andrew J.G. Simpson*
- 27 Mechanisms of Immune Modulation by *Fasciola hepatica*: Importance for Vaccine Development and for Novel Immunotherapeutics** 451  
*Mark W. Robinson\**, *John P. Dalton*, *Sandra M. O'Neill*,  
and *Sheila M. Donnelly*
- 28 Prospects for Immunoprophylaxis Against *Fasciola hepatica* (Liver Fluke)** 465  
*Terry W. Spithill\**, *Carlos Carmona*, *David Piedrafita*,  
and *Peter M. Smooker*
- 29 Vaccines Against Cestode Parasites** 485  
*Marshall W. Lightowers\**, *Charles G. Gauci*, *Abdul Jabbar*,  
and *Cristian Alvarez*
- Index** 505