

# CONTENTS

CONTRIBUTORS

ix

PREFACE

xi

## 1. Genetic Tools

*Marc Ekker and Marie-Andrée Akimenko*

- |                                                             |    |
|-------------------------------------------------------------|----|
| 1. Introduction                                             | 2  |
| 2. Forward Genetics: From Large Screens to Targeted Screens | 3  |
| 3. Reverse Genetics: Morpholino Knockdowns                  | 4  |
| 4. Reverse Genetics: TILLING                                | 8  |
| 5. Reverse Genetics: Zinc Finger Nucleases                  | 10 |
| 6. Gain of Function: Targeted Misexpression of Genes        | 13 |
| 7. Genetic Ablation of Specific Cell Population             | 16 |
| 8. Concluding Remarks                                       | 18 |

## 2. Organization and Physiology of the Zebrafish Nervous System

*Laure Bally-Cuif and Philippe Vernier*

- |                                                                                          |    |
|------------------------------------------------------------------------------------------|----|
| 1. Introduction                                                                          | 26 |
| 2. Nervous System Development and General Organization                                   | 29 |
| 3. General Organization of the Zebrafish Nervous System, Subdivisions and Main Functions | 35 |
| 4. The Peripheral Nervous System                                                         | 44 |
| 5. Sensory Systems                                                                       | 47 |
| 6. Motor Systems and Integrative Centers                                                 | 50 |
| 7. Monoaminergic and Related Regulatory Systems                                          | 51 |
| 8. Emotions and Cognition                                                                | 55 |
| 9. Nervous System Plasticity                                                             | 62 |

## 3. Zebrafish Vision: Structure and Function of the Zebrafish Visual System

*Stephan C.F. Neuhauss*

- |                                   |    |
|-----------------------------------|----|
| 1. Visual Ecology                 | 82 |
| 2. Structure of the Visual System | 82 |

|      |                                                                           |     |
|------|---------------------------------------------------------------------------|-----|
| 3.   | Retinal Projections                                                       | 95  |
| 4.   | Optic Tectum                                                              | 97  |
| 5.   | Visual Behavior                                                           | 99  |
| 6.   | Complex Visual Behavior                                                   | 109 |
| 7.   | Concluding Remarks                                                        | 111 |
| <br> |                                                                           |     |
| 4.   | The Zebrafish Inner Ear                                                   |     |
|      | <i>Leila Abbas and Tanya T. Whitfield</i>                                 |     |
| 1.   | Introduction                                                              | 124 |
| 2.   | Development of the Inner Ear                                              | 127 |
| 3.   | Generation and Homeostasis of Endolymph in the Zebrafish Inner Ear        | 134 |
| 4.   | Zebrafish Sensory Hair Cells                                              | 137 |
| 5.   | Mechanotransduction                                                       | 141 |
| 6.   | Neural Activity                                                           | 144 |
| 7.   | Otoliths                                                                  | 147 |
| 8.   | Adult Hearing                                                             | 156 |
| 9.   | Concluding Remarks                                                        | 160 |
| <br> |                                                                           |     |
| 5.   | Endocrinology of Zebrafish: A Small Fish<br>with a Large Gene Pool        |     |
|      | <i>Ellen R. Busby, Graeme J. Roch and Nancy M. Sherwood</i>               |     |
| 1.   | Introduction                                                              | 174 |
| 2.   | Reproduction                                                              | 175 |
| 3.   | Stress: The Cortisol Stress Axis                                          | 212 |
| 4.   | Growth                                                                    | 214 |
| 5.   | Thyroidal Regulation                                                      | 221 |
| 6.   | Energy Homeostasis: Food Intake and Metabolism                            | 223 |
| 7.   | Osmoregulation                                                            | 229 |
| 8.   | Summary                                                                   | 232 |
| <br> |                                                                           |     |
| 6.   | Developmental Physiology of the Zebrafish<br>Cardiovascular System        |     |
|      | <i>John D. Mably and Sarah J. Childs</i>                                  |     |
| 1.   | Cardiovascular Disease: Models Wanted                                     | 250 |
| 2.   | Current Models for Cardiovascular System Studies                          | 251 |
| 3.   | Filling a Niche with Zebrafish                                            | 252 |
| 4.   | Unique Advantages of the Zebrafish for Cardiovascular Studies             | 252 |
| 5.   | Vertebrate Cardiac Development                                            | 253 |
| 6.   | Origin and Lineage of Cells in the Cardiovascular System                  | 253 |
| 7.   | Zebrafish Genetics and Development of the Cardiovascular System           | 254 |
| 8.   | Genetic Infrastructure and Tools for Zebrafish Studies                    | 255 |
| 9.   | Zebrafish Cardiovascular Mutants                                          | 255 |
| 10.  | Mutants Affecting Rate, Rhythm and Contractile<br>Properties of the Heart | 258 |
| 11.  | Relationship Between Cardiovascular Function and Form                     | 260 |
| 12.  | Endothelial Cell Specification and Differentiation                        | 261 |
| 13.  | Specification of Artery and Vein                                          | 261 |
| 14.  | Cell Migration of Angioblasts and Vascular Patterning                     | 263 |

|                                                                   |     |
|-------------------------------------------------------------------|-----|
| 15. Angiogenesis of the Intersegmental Vessels                    | 264 |
| 16. Lumenization of Vessels                                       | 264 |
| 17. Vascular Stabilization, Mural Cells, and Extracellular Matrix | 265 |
| 18. Angiogenesis of Organs                                        | 266 |
| 19. Chemical Biology Approaches to Study Cardiovascular Biology   | 268 |
| 20. Forces that Influence Cardiovascular Development              | 269 |
| 21. Endothelial Cell Survival                                     | 273 |
| 22. Zebrafish Models for Vascular Anomalies                       | 273 |
| 23. Tools for the Study of Cardiovascular Physiology              | 274 |
| 24. Vessel Regeneration                                           | 275 |
| 25. Cardiac Regeneration                                          | 276 |
| 26. Summary                                                       | 277 |
| <br>                                                              |     |
| 7. Respiration                                                    |     |
| <i>Bernd Pelster and Brian Bagatto</i>                            |     |
| 1. Introduction                                                   | 290 |
| 2. The Principles of Gas Exchange                                 | 291 |
| 3. The Site of Gas Exchange                                       | 293 |
| 4. Convective Transport                                           | 296 |
| 5. Metabolic Activity                                             | 299 |
| 6. Hypoxic Effects                                                | 301 |
| 7. Temperature Effects                                            | 303 |
| 8. Future Perspectives                                            | 305 |
| <br>                                                              |     |
| 8. Ionic and Acid-Base Regulation                                 |     |
| <i>Pung-Pung Hwang and Steve F. Perry</i>                         |     |
| 1. Introduction                                                   | 312 |
| 2. Identification of Ionocytes in Skin/gills                      | 313 |
| 3. Sodium Uptake and Acid Secretion by Skin/gills                 | 315 |
| 4. Chloride Uptake and Base Excretion                             | 320 |
| 5. Calcium Uptake                                                 | 322 |
| 6. Ammonia Excretion                                              | 323 |
| 7. Differentiation and Functional Regulation of Ionocytes         | 325 |
| 8. Neuroendocrine Control of Ion Uptake and Acid-Base Regulation  | 330 |
| 9. Renal Ionic and Acid-Base Regulation                           | 332 |
| 10. Conclusions and Perspectives                                  | 334 |
| <br>                                                              |     |
| 9. The Zebrafish as a Model for Human Disease                     |     |
| <i>Cong Xu and Leonard I. Zon</i>                                 |     |
| 1. Introduction                                                   | 346 |
| 2. Cancer                                                         | 347 |
| 3. Hematopoietic Disorders                                        | 352 |
| 4. Cardiovascular Diseases                                        | 357 |
| 5. Chemical Screening in Zebrafish                                | 359 |
| 6. Summary                                                        | 362 |

10. Perspectives on Zebrafish as a Model in Environmental Toxicology  
*John J. Stegeman, Jared V. Goldstone and Mark E. Hahn*

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| 1. Introduction                                                 | 368 |
| 2. Current Issues in Environmental Toxicology                   | 370 |
| 3. The Zebrafish Toxicology Landscape: Emergence of a New Model | 373 |
| 4. Molecular Environmental Toxicology: The Defensible Concept   | 375 |
| 5. Advances and Insights with Zebrafish                         | 394 |
| 6. Toxicity and Environmental Assessment with Zebrafish         | 406 |
| 7. Areas of Looming Significance and Promising Approaches       | 411 |
| 8. Some Conclusions                                             | 419 |

|       |     |
|-------|-----|
| INDEX | 441 |
|-------|-----|

|                                             |     |
|---------------------------------------------|-----|
| OTHER VOLUMES IN THE FISH PHYSIOLOGY SERIES | 453 |
|---------------------------------------------|-----|

|                     |  |
|---------------------|--|
| COLOR PLATE SECTION |  |
|---------------------|--|