

# Contents

|                                                                                               |           |
|-----------------------------------------------------------------------------------------------|-----------|
| Acknowledgments .....                                                                         | xi        |
| Epigraph .....                                                                                | xiii      |
| <b>Chapter 1 Interacting with the environment receiving<br/>and interpreting signals.....</b> | <b>1</b>  |
| Sensory receptors .....                                                                       | 1         |
| Hearing .....                                                                                 | 6         |
| Hearing impairment and deafness.....                                                          | 12        |
| Usher syndrome .....                                                                          | 18        |
| Vision and the retina .....                                                                   | 19        |
| The visual cycle, retinal pigmentary epithelium and<br>photoreceptor interactions .....       | 21        |
| Newborn eye screening and retinopathy of prematurity.....                                     | 26        |
| References .....                                                                              | 28        |
| <b>Chapter 2 Environment as provider .....</b>                                                | <b>33</b> |
| Introduction .....                                                                            | 33        |
| Nutrients.....                                                                                | 33        |
| Nutrition and growth.....                                                                     | 37        |
| Requirement for specific minerals.....                                                        | 38        |
| Water.....                                                                                    | 49        |
| Air and oxygen.....                                                                           | 51        |
| References .....                                                                              | 52        |
| <b>Chapter 3 Evolution.....</b>                                                               | <b>55</b> |
| Connections between paleoclimate and evolution.....                                           | 55        |
| Modern humans and their relationship to archaic humans.....                                   | 55        |
| Population migrations.....                                                                    | 60        |
| Brain evolution: Primate and human divergence .....                                           | 61        |

|                                                                                                                                    |            |
|------------------------------------------------------------------------------------------------------------------------------------|------------|
| The advantages and disadvantages of extra-copies of genomic segments .....                                                         | 67         |
| Phenotypic plasticity and evolution .....                                                                                          | 70         |
| Mitochondrial DNA variations and population divergence .....                                                                       | 71         |
| Nutritional factors and genomic adaptations .....                                                                                  | 72         |
| Polygenic adaptations to changing environments .....                                                                               | 73         |
| References .....                                                                                                                   | 74         |
| <b>Chapter 4 Gene and environment interactions and phenotypes .....</b>                                                            | <b>79</b>  |
| Introduction .....                                                                                                                 | 79         |
| Skin pigmentation .....                                                                                                            | 79         |
| Recognizing non-self: The immune system .....                                                                                      | 87         |
| Trypanosome infection and adaptations .....                                                                                        | 97         |
| Immune response, pathogens and adaptations in different environments .....                                                         | 98         |
| Adaptation of organisms to different environments .....                                                                            | 101        |
| Human adaptations to high altitude .....                                                                                           | 102        |
| References .....                                                                                                                   | 104        |
| <b>Chapter 5 Signals, epigenetics, regulation of gene expression ....</b>                                                          | <b>109</b> |
| Conveying signals into cells to modify gene expression .....                                                                       | 109        |
| Epigenetics .....                                                                                                                  | 117        |
| RNA modifications .....                                                                                                            | 132        |
| References .....                                                                                                                   | 133        |
| <b>Chapter 6 Maintaining homeostasis and mitigating effects of harmful factors in the intrinsic or extrinsic environment .....</b> | <b>139</b> |
| Concepts of homeostasis .....                                                                                                      | 139        |
| Metabolism and homeostasis .....                                                                                                   | 139        |
| Harmful damaging factors, endogenous or exogenous .....                                                                            | 154        |
| DNA damage detection, consequences, and repair .....                                                                               | 158        |
| References .....                                                                                                                   | 171        |

|                                                                                                                                |            |
|--------------------------------------------------------------------------------------------------------------------------------|------------|
| <b>Chapter 7 Microorganisms and microbiome</b>                                                                                 | <b>177</b> |
| Microorganisms in soil                                                                                                         | 177        |
| Antibiotic resistance                                                                                                          | 179        |
| New techniques for identifying anti-microbial agents                                                                           | 183        |
| The search for anti-microbial medicines in plants                                                                              | 184        |
| Phage therapy                                                                                                                  | 184        |
| Microbiome                                                                                                                     | 186        |
| References                                                                                                                     | 198        |
| <b>Chapter 8 Genomic changes and environmental factors in causation of birth defects and neurodevelopmental disorders</b>      | <b>205</b> |
| Birth defects                                                                                                                  | 205        |
| Neurodevelopmental disorders: Genetic and environmental factors                                                                | 211        |
| Infant and child development, environment, genes and their interactions                                                        | 213        |
| Epilepsy                                                                                                                       | 220        |
| References                                                                                                                     | 222        |
| <b>Chapter 9A Personalized precision medicine—Part A: Concepts and relevance in Mendelian disorders</b>                        | <b>227</b> |
| Concepts                                                                                                                       | 227        |
| Personalized precision medicine in individuals with Mendelian disorders                                                        | 237        |
| References                                                                                                                     | 253        |
| <b>Chapter 9B Personalized medicine. Precision medicine: PART B multifactorial diseases, genes, environments, interactions</b> | <b>259</b> |
| Cardiac conditions                                                                                                             | 259        |
| Cardio-vascular diseases and precision medicine                                                                                | 265        |

|                                                                                            |     |
|--------------------------------------------------------------------------------------------|-----|
| Age related macular degeneration: Gene variants and environmental interactions.....        | 267 |
| Age related neurodegenerative disorders.....                                               | 268 |
| Amyotrophic lateral sclerosis also known as Lou Gehrig disease, motor neuron disease ..... | 272 |
| Parkinson's disease (PD) .....                                                             | 275 |
| Traumatic brain injury and consequences.....                                               | 277 |
| Psychiatric disorders.....                                                                 | 278 |
| Personalized medicine and Cancer prevention.....                                           | 278 |
| DNA mismatch repair and its role in cancer .....                                           | 283 |
| References .....                                                                           | 286 |

## **Chapter 10 Integrating genetic, epigenetic and environmental information to improve health and well-being ..... 291**

|                                                                                                                |     |
|----------------------------------------------------------------------------------------------------------------|-----|
| Integrating information on genetic variants and environmental factors in analyses of disease risk factors..... | 291 |
| Rare genetic defects that increase the impact of specific environmental factors.....                           | 312 |
| Adjusting the environment particularly nutrition to compensate for inborn errors of metabolism.....            | 314 |
| Genes, networks, society and patients .....                                                                    | 324 |
| References .....                                                                                               | 326 |

## **Chapter 11 Environments, resources, and health ..... 333**

|                                                                                      |     |
|--------------------------------------------------------------------------------------|-----|
| Green-house gas production and climate change problems and potential solutions ..... | 333 |
| Climate change, questions relating to sustainability and human health.....           | 337 |
| Efforts to counteract climate change and associated devastations.....                | 362 |
| Celebrations of nature in human endeavors.....                                       | 367 |
| References .....                                                                     | 369 |

|                                                                                                                                |            |
|--------------------------------------------------------------------------------------------------------------------------------|------------|
| <b>Chapter 12 Summary chapter epilogue .....</b>                                                                               | <b>375</b> |
| Chapter 1 Interacting with the environment receiving<br>and interpreting signals .....                                         | 375        |
| Chapter 2 Environment as provider .....                                                                                        | 376        |
| Chapter 3 Evolution .....                                                                                                      | 378        |
| Chapter 4 Gene and environment interactions and phenotypes. . .                                                                | 380        |
| Chapter 5 Signals, epigenetics, regulation of gene<br>expression .....                                                         | 381        |
| Chapter 6 Maintaining homeostasis and mitigating effects<br>of harmful factors in the intrinsic or extrinsic environment ..... | 383        |
| Chapter 7 Microorganisms and microbiome .....                                                                                  | 386        |
| Chapter 9 Precision medicine and personalized medicine .....                                                                   | 388        |
| Chapter 10 Integrating genetic, epigenetic and environmental<br>information to improve health and well-being .....             | 392        |
| Chapter 11 Environments, resources, and health .....                                                                           | 395        |
| Index .....                                                                                                                    | 397        |