Molecular Diagnostics: Promises and Possibilities
Molecular Diagnostics: Promises and Possibilities
Molecular diagnostics represents a revolution postponed, perhaps, but one that is now clearly underway. Early and accurate diagnosis in medicine goes big way in prevention and treatment of communicable as well as non-communicable disorders. Traditional tests typically screen for a biochemical constituent or specific antibody or antigen derived from infectious agent to a particular disease. Molecular diagnostic tests typically analyze key DNA, RNA, or protein biomarkers (analytes) to identify a disease, determine its course, evaluate response to therapy, or predict individual predisposition to a disease. The techniques applied involve analysis of DNA sequences, DNA methylation patterns, gene expression profiles, proteins, protein expression, or combinations of these biomarkers. Such biomarkers provide direct information about genotypic and/or phenotypic changes associated with specific diseases or responses to treatment. Biomarker analysis has also become an important tool in drug discovery, preclinical drug development, and patient monitoring during clinical trials. The first few chapters of the book deals with the concepts of genomics and molecular biology.

Specificity and sensitivity of DNA based tests are much higher, and the test is quicker than identification by traditional laboratory methods. In the case of human immunodeficiency virus (HIV), the initial detection limit in the late 1980s was 22 days post infection. However, the advent of nucleic acid testing for HIV RNA shortened this time to 11 days post infection. This highlights another distinct advantage offered by molecular diagnostics over immunoassays – amplification. The polymerase chain reaction (PCR) allows for the billion-fold amplification of available genetic material, thereby allowing the detection of minute amounts of genetic material and greatly increasing the sensitivity of the assay. No such amplification technique exists for proteins.

A series of technologies developed over the years to address the challenges of molecular diagnostics include eight major areas: amplification technologies (gene and signal), blotting technologies, electrophoretic technologies, microarray technologies, probe technologies, restriction fragment-length polymorphism (RFLP) analysis, RNA inhibition analysis, and single nucleotide polymorphism (SNP) analysis and software. These developments have set the stage for excellent growth potential in molecular diagnostics.
Current molecular diagnostics are primarily single-analyte tests involving the detection of a single gene or protein. However, many disease-related processes are multifactorial, involving the abnormal expression of multiple genes or proteins. Second-generation molecular diagnostics are anticipated to utilize novel detection technologies and multiplexing platforms to allow the measurement of a large number of analytes simultaneously. These innovations will increasingly utilize multiplexing platforms such as DNA microarrays that perform parallel biomarker analyses.

Molecular diagnostics also has an additional ace up its sleeve – the capability to multiplex. A single assay can be used for the detection of multiple genetic targets. An example of this would be the simultaneous detection of HIV, hepatitis C and hepatitis B. This multiplexing capability helps save time, costs and represents a more effective diagnostic tool than an immunoassay for a single analyte. The next few chapters is focused on development of various nucleic acid technologies starting from PCR to microarrays.

Molecular diagnostics got its big break following the successful sequencing of the human genome in 2003. DNA Testing has emerged fully from research into clinical practice and becoming a dominant platform in clinical medicine. This allowed the identification of portions of host or infectious agent genome that are responsible for disorder, as well as those that could be used as a marker to predict adverse reaction, dosing and efficacy to a particular drug. Applications in molecular diagnostics currently range from screening for infectious diseases and genetic disorders. It could test for genetic mutations and genome changes associated with cancers, or for the sequence or biomarker associated with a type of cancer. It has been particularly successful in diagnosing colorectal cancer, Methicillin-resistant *Staphylococcus aureus* (MRSA), breast cancer, respiratory viruses, prostate cancer and human papillomavirus (HPV). It could also be used to sequence individual genomes to identify a predisposition to developing disorders such as Alzheimer’s disease, Parkinson’s disease, diabetes and alcoholism. The molecular diagnostics is going to play an important role in pharmacogenomics, or personalized medicine. These methods allows to test an individual’s genetic disposition to a specific drug for most effective dosage and also helps to detect if the patient would show side effects. Molecular diagnosis aids in determining the right dosage of the right drug and at the right time for each patient. Molecular diagnostics is considered to work faster than traditional microbiology and more sensitive than traditional immunoassay testing. The capabilities of molecular diagnostics are increasingly being recognized due to global trends in emerging infectious diseases. Molecular assays have the capability to differentiate viral subtypes, detect genetic predispositions to a disease and monitor the course of a disease. The severe acute respiratory syndrome (SARS) corona virus and avian influenza outbreak in the recent past created an increasing awareness for this technology. The next few chapters of the book deals with the applications of molecular diagnostics in infectious, non-infectious and metabolic disorders.

Semi and fully automated molecular testing platforms are being developed that address the issues of pre-analytical sample preparation and cross contamination. This will eventually allow molecular diagnostics to capture a larger segment of the
infectious disease diagnostics market and achieve wider penetration in clinical diagnostics. The last chapter of the book deals with molecular diagnostics, its segments, market potential and current and future trends. The major shortcoming of molecular diagnostics lies in its high cost and the high level of technical skill needed to run complex assays. However, there is no match for the specificity and sensitivity of molecular assays. The adoption of the technology is increasing globally and the costs of molecular assays are expected to drop following the expiration of various PCR patents. Despite these obstacles, the speed and sensitivity of molecular diagnostics would gain more market share from traditional immunoassay testing, especially as costs come down.

We thank Mr. Devendra Singh, Mr. Gulab Singh Thakur, Mr. Bhagwan S. Sanodiya, Mr. Vikas Dubey for their valuable assistance in preparation of this book. We are particularly indebted to Mr. Vikas Dubey, Web Designer, Vikrant Institute of Technology and Management, Gwalior for front cover image design. Finally we owe an unquantifiable debt to our families, who has seen the book built sentence by sentence and whose encouragement has never flagged.

Jaipur, India
Gwalior, India
Gwalior, India

Mousumi Debnath
Godavarthi B.K.S. Prasad
Prakash S. Bisen
Contents

1 Introduction to Molecular Diagnostics ........................................... 1
  1.1 Prologue ................................................................................. 1
  1.2 Clinical Diagnostics Entering a New Phase ............................. 2
  1.3 Concept of Molecular Diagnostics .......................................... 3
  1.4 Molecular Diagnostic Technology and Health Care Industries .... 4
  1.5 Molecular Diagnostic Approaches ........................................... 6
    1.5.1 Nucleic Acid Test Systems ............................................ 7
    1.5.2 Gene-Based Diagnostics ............................................... 8
  1.6 Conclusion ............................................................................ 10
  References .................................................................................. 10

2 Omics Technology ......................................................................... 11
  2.1 Prologue ................................................................................ 11
  2.2 Concept of Omics .................................................................. 12
  2.3 Genome and Genomics .......................................................... 13
  2.4 Transcriptome and Transcriptomics ........................................ 15
  2.5 Proteome and Proteomics ...................................................... 17
  2.6 Metabolome and Metabolomics ............................................. 21
  2.7 Integration of Omics ............................................................. 23
  2.8 Conclusion ............................................................................ 27
  References .................................................................................. 29

3 Recombinant DNA Pharmaceuticals .............................................. 33
  3.1 Prologue ................................................................................ 34
  3.2 Concept ................................................................................ 34
  3.3 Tools of Recombinant DNA Technology ................................. 35
    3.3.1 Common Enzymes Used in Recombinant DNA Technology ... 36
    3.3.2 Vectors ........................................................................... 38
    3.3.3 Hosts .............................................................................. 38
    3.3.4 DNA Libraries ............................................................... 42
    3.3.5 Library Screening ........................................................... 43
    3.3.6 Polymerase Chain Reaction ............................................ 44
6.3 Goals and Issues of HGP
6.4 The Human Genome and Genetic Variation
6.5 Human Genome Project and Health Services
6.6 Single Gene Disease
6.7 New and Individualised Drug Treatments
6.8 The Achievements and Challenges of the HGP
6.9 Information Transfer
6.10 Impact of the Human Genome Project on Epidemiologic Research
6.11 Impact of the Human Genome Project on Our Genomic Makeup
6.12 Conclusion

References

7 Molecular Diagnosis in the Post Genomic and Proteomic Era
7.1 Prologue
7.2 The Genomic Era
7.3 Concept
7.4 The Post Genomic Era
7.5 Advantages of Combining Multiple Types of Data
7.6 Biomedical Research in the Postgenomic Era
7.7 Conclusion

References

8 Ethics, Patents and Regulations
8.1 Prologue
8.2 Concept of Ethical, Legal, and Social Issues
8.3 Ethical and Social Issues in Diagnostic Molecular Genetics
8.4 Confronting the Ethical, Legal and Social Issues
8.5 Genes and Disease
8.6 The Existence of Genetic Information
8.6.1 Genetic Treatment of Disease
8.6.2 Genetic Testing
8.6.3 Discrimination
8.7 Impact of the Human Genome Project at the Interface Between Patent and FDA Law
8.8 Regulatory Process
8.9 Conclusion

References

9 Polymerase Chain Reaction
9.1 Prologue
9.2 The Concept of Polymerase Chain Reaction
9.3 PCR Optimisation
9.3.1 Magnesium Concentration
9.3.2 Buffer Concentration
9.3.3 Enzyme Concentration ........................................... 133
9.3.4 PCR Primer Design .............................................. 133
9.3.5 Template Quality ................................................ 133
9.3.6 Template Quantity ............................................... 134
9.3.7 Cycling Parameter ............................................... 134
9.3.8 PCR Enhancers and Additives ................................. 135
9.3.9 Nucleic Acid Cross-Contamination ............................ 135
9.4 Advances in the PCR Technique ................................. 136
  9.4.1 RT-PCR ........................................................ 137
  9.4.2 “Hot Start” PCR ................................................ 137
  9.4.3 Long Range PCR ............................................... 138
  9.4.4 Inverse PCR .................................................... 138
  9.4.5 Anchored PCR .................................................. 138
  9.4.6 Nested Primer PCR ............................................. 139
  9.4.7 Colony PCR ..................................................... 139
  9.4.8 Quantitative PCR ............................................... 139
  9.4.9 Real-Time PCR ................................................. 140
  9.4.10 Rapid Amplification of cDNA Ends (RACE) ............... 141
  9.4.11 AFLP .......................................................... 141
  9.4.12 In Situ PCR ..................................................... 142
9.5 Cloning PCR Products .............................................. 142
  9.5.1 T-A Cloning Strategy .......................................... 142
  9.5.2 Incorporation of Restriction Sites in Primers ............... 143
9.6 PCR as a Diagnostic Tool ......................................... 143
9.7 Conclusion .......................................................... 147
References ..................................................................... 148

10 In Situ Hybridization ................................................. 153
  10.1 Prologue ............................................................ 153
  10.2 The Concept of In Situ Hybridization ......................... 154
    10.2.1 The Process .................................................. 154
  10.3 Disadvantages of Radioactive Probes ........................... 156
  10.4 Solving the Problem: Advent of FISH Technique ............. 156
    10.4.1 Fluorescence In Situ Hybridization ....................... 157
    10.4.2 FISH in Action ................................................ 159
  10.5 Applications of FISH as a Diagnostic Tool for Research .... 160
    10.5.1 To Analyze the Onset of Specific Gene Expression ....... 161
    10.5.2 Analysis of the Chromosome Structure .................... 161
    10.5.3 Localisation of RNA Transcripts ............................ 162
    10.5.4 FISH as a Molecular Cytogenetic Technique to Understand Diseases ........................................ 162
    10.5.5 FISH for Detection of Pathogens ............................ 165
  10.6 Recent Advances of In Situ Hybridisation Technology ...... 165
  10.7 Conclusion .......................................................... 166
References ..................................................................... 167
11 Immunoassay .................................................. 171
   11.1 Prologue .............................................. 171
   11.2 Concept .............................................. 172
   11.3 Types of Immunoassay ............................... 172
   11.4 Recent Advances in the Field of Immunodiagnostics .. 174
   11.5 Clinical Applications of Immunoassay ............... 175
   11.6 Utilization and Interpretation of Immunological Tests .. 177
   11.7 Conclusion .......................................... 178
References .................................................. 178

12 Phage Display ............................................. 181
   12.1 Prologue .............................................. 181
   12.2 Concept .............................................. 181
   12.3 Phage-Display Libraries as Populations of Replicable, Mutable Chemicals .............. 182
   12.4 Practical Applications of Phage Display .......... 184
      12.4.1 Target Receptors Used in Affinity Selection .. 184
      12.4.2 Epitope Mapping and Mimicking ................ 185
      12.4.3 Identifying New Receptors and Natural Ligands . 186
      12.4.4 Drug Discovery .................................. 186
      12.4.5 Epitope Discovery – A New Route to Vaccines and Diagnostics ...................... 187
      12.4.6 Selection of DNA-Binding Proteins .......... 188
      12.4.7 Landscape Libraries as a Source of New Materials ... 189
      12.4.8 Phage Display-Combinatorial Chemistry on the Cheap ................................. 190
      12.4.9 Cloning Allergens by Phage Display ......... 190
   12.5 Conclusion .......................................... 191
References .................................................. 192

13 Microarray .................................................. 193
   13.1 Prologue .............................................. 193
   13.2 The Concept of Microarray ........................... 195
   13.3 Current Challenges of Microarrays ................. 198
      13.3.1 Gene Discovery .................................. 199
      13.3.2 Gene Expression Profiling ....................... 200
      13.3.3 Pharmacogenomics and Microarray .......... 202
      13.3.4 Molecular Diagnostic Research ............... 204
   13.4 Conclusion .......................................... 205
References .................................................. 206

14 DNA Biosensors ............................................ 209
   14.1 Prologue .............................................. 209
   14.2 The Concept of DNA Biosensor .................... 210
   14.3 Applications of Biosensors ......................... 211
   14.4 Advantages of Biosensors ......................... 212
14.5 Development of DNA Hybridization Biosensor ........ 213
14.6 DNA Biosensor for Molecular Detection of Pathogens .... 217
14.7 Biosensors as Analytical Tools in the Food and Drink Industries 218
14.8 Potential of Biosensor for Environmental Monitoring .... 220
14.9 Conclusions & Future Challenges ....................... 221
References .......................................................... 223

15 Molecular Microbiological Testing ............................... 227
15.1 Prologue .................................................. 227
15.2 Concept ................................................ 228
15.3 Advent of Improved Diagnostics ........................... 229
15.4 Traditional Microbial Typing ............................... 230
  15.4.1 Biotyping ........................................... 230
  15.4.2 Antibiograms, Resistograms, and Bacteriocin Typing 231
  15.4.3 Protein Analysis .................................... 231
  15.4.4 Phage Analysis ...................................... 231
  15.4.5 Chromatographic Analysis ........................... 231
15.5 Nucleic Acid-Based Typing Systems ......................... 232
  15.5.1 Plasmid Analysis .................................... 232
  15.5.2 Restriction Enzyme Pattern .......................... 232
  15.5.3 Ribotyping ........................................... 232
  15.5.4 Random Amplified Polymorphic DNA (RAPD) ........ 232
  15.5.5 Nucleic Acid Probes .................................. 233
  15.5.6 Polymerase Chain Reaction ......................... 233
15.6 Current Application of Molecular Diagnostics ............. 234
  15.6.1 Clinical Microbiology ................................ 234
  15.6.2 Clinical Epidemiology and Infection Control .......... 237
15.7 Promise of Molecular Testing .............................. 238
15.8 Assay Validation-Analytic Sensitivity and Specificity .... 239
15.9 Conclusion ................................................. 241
References .......................................................... 241

16 Proteomic Technology ................................................. 245
16.1 Prologue .................................................. 245
16.2 Concept ................................................ 246
16.3 Methods to Perform Proteomic Analysis ..................... 247
16.4 Functional Proteomics .................................... 249
16.5 Implications of the Human Genome Project ................ 249
16.6 Measurement Using a Proteomic Approach ................. 251
16.7 Use of Mass Spectrometry in Proteomics ................... 252
16.8 Proteomics: From Basic Research to Diagnostic Application ........................................ 253
16.9 Role of In Vitro Diagnostics (IVD) in Health Care ......... 254
16.10 Goals of Proteomics ..................................... 257
16.11 Conclusion ................................................. 258
References .......................................................... 259
## 19 Diagnosis and Monitoring of Infections

19.1 Prologue ........................................... 309
19.2 Concept of Diagnosis and Monitoring of Infections ........ 310
19.2.1 Detection and Identification of Pathogens Without Target Amplification .......... 311
19.2.2 Nucleic Acid Amplification ................. 312
19.2.3 Detecting Antimicrobial-Drug Resistance .......... 314
19.3 Molecular Diagnostics of Infections .................. 316
19.3.1 Sexually Transmitted Infections ............... 316
19.3.2 Vector Borne Disease ....................... 318
19.3.3 Viral Infections ................................ 318
19.3.4 Bacterial Infections ......................... 321
19.3.5 Fungal Infections ............................ 323
19.3.6 Practical Applications of Molecular Methods in the Clinical Microbiology Laboratory .... 323
19.4 Conclusion ..................................... 327
References ............................................ 328

## 20 Diagnosis of Mutation and Genetic Disorders

20.1 Prologue ........................................... 331
20.2 Concept ........................................... 332
20.3 Factors Regulating a Genetic Disease .................. 333
20.4 Genetic Testing ................................... 334
20.4.1 Cytogenetic Testing ............................ 334
20.4.2 Biochemical Testing ............................ 335
20.4.3 Molecular Testing ............................ 336
20.5 Current Status of Molecular Diagnosis of Some Common Genetic Diseases .................. 336
20.5.1 Cystic Fibrosis ................................. 337
20.5.2 Duchenne Muscular Dystrophy .................. 338
20.5.3 Haemophilia A .................................. 338
20.5.4 Haemophilia B .................................. 338
20.5.5 Phenylketonuria ............................... 339
20.5.6 \( \beta \) Thalassaemia ............................ 339
20.5.7 Wilson’s Disease (Hepatolenticular Degeneration) ... 339
20.5.8 \( \alpha \) Antitrypsin Deficiency .................. 340
20.5.9 Familial Hypercholesterolaemia and Other Lipoprotein Disorders .................. 340
20.5.10 Huntington’s Disease Gene .................... 340
20.5.11 Multiple Endocrine Neoplasia .................. 341
20.5.12 Factor V (Leiden) Mutation ................... 342
20.5.13 Hemochromatosis Gene, HFE .................. 342
20.5.14 Colon Cancer Gene, APC ..................... 343
20.6 Microarray Analysis for Detection of Complex Pattern of Genes .......................... 343
## Contents

---

<table>
<thead>
<tr>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.7 Conclusion</td>
</tr>
<tr>
<td>References</td>
</tr>
<tr>
<td>21 Diagnosis of Complex Diseases</td>
</tr>
<tr>
<td>21.1 Prologue</td>
</tr>
<tr>
<td>21.2 Concept</td>
</tr>
<tr>
<td>21.3 Background Information</td>
</tr>
<tr>
<td>21.4 Detecting New Metabolic Disease Pathways</td>
</tr>
<tr>
<td>21.5 Phenotypic Variations in Simplex Diseases</td>
</tr>
<tr>
<td>21.6 The Genetic Background of Complex Disorders</td>
</tr>
<tr>
<td>21.7 Dissecting Interactions Between Genes and Environment</td>
</tr>
<tr>
<td>21.7.1 Alzheimer Disease</td>
</tr>
<tr>
<td>21.7.2 Cancer</td>
</tr>
<tr>
<td>21.7.3 Multiple Sclerosis</td>
</tr>
<tr>
<td>21.7.4 Diabetes</td>
</tr>
<tr>
<td>21.7.5 Hemophilia</td>
</tr>
<tr>
<td>21.7.6 Obesity</td>
</tr>
<tr>
<td>21.7.7 Schizophrenia</td>
</tr>
<tr>
<td>21.8 Conclusion</td>
</tr>
<tr>
<td>References</td>
</tr>
<tr>
<td>22 Biochips</td>
</tr>
<tr>
<td>22.1 Prologue</td>
</tr>
<tr>
<td>22.2 Concept</td>
</tr>
<tr>
<td>22.3 Design of Biochip</td>
</tr>
<tr>
<td>22.4 Applications of Biochips</td>
</tr>
<tr>
<td>22.4.1 Biochip and Clinical Medicine</td>
</tr>
<tr>
<td>22.4.2 Biochips and Biosensors</td>
</tr>
<tr>
<td>22.4.3 Biochip and Pharmacogenetics</td>
</tr>
<tr>
<td>22.4.4 Biochip and Biowarfare</td>
</tr>
<tr>
<td>22.4.5 Biochip and Diagnostics</td>
</tr>
<tr>
<td>22.4.6 Biochip and Cancer</td>
</tr>
<tr>
<td>22.4.7 Biochip Department of Defense</td>
</tr>
<tr>
<td>22.5 Biochip Market</td>
</tr>
<tr>
<td>22.6 Future of Biochips</td>
</tr>
<tr>
<td>References</td>
</tr>
<tr>
<td>23 Personalised Medicine</td>
</tr>
<tr>
<td>23.1 Prologue</td>
</tr>
<tr>
<td>23.2 Concept</td>
</tr>
<tr>
<td>23.3 Practice of Medicine in the Twenty-First Century</td>
</tr>
<tr>
<td>23.4 Role of Personalized Medicine in Drug Discovery</td>
</tr>
<tr>
<td>23.5 Molecular Diagnosis Will Determine Prognosis and Therapy</td>
</tr>
<tr>
<td>23.6 Personalized Medicine and Genetic Markers</td>
</tr>
<tr>
<td>23.7 Challenges of Realizing the Promise of Personalized Medicine</td>
</tr>
</tbody>
</table>
### Contents

#### 23.8 Personalised Medicine and Pharmacogenomics

#### 23.9 Personalized Medicine and Diseases

#### 23.10 Personalized Medicine and Diagnostics Industry

#### 23.11 Impact of the US Patent System on the Promise of Personalized Medicine

#### 23.12 Ethical Legal and Social Issues of Personalised Medicine

#### 23.13 Conclusion

#### References

---

#### 24 Biopharmaceutical Industry and Health Care

#### 24.1 Prologue

#### 24.2 Concept

#### 24.3 Biopharmaceutical Research

#### 24.4 Opportunities in Healthcare

#### 24.5 Molecular Diagnostics and Health Care

#### 24.6 Global Context

#### 24.7 Emerging Biopharmaceuticals

#### 24.8 Challenges of the Biopharmaceutical Industry

#### References

---

#### 25 Forensic Medicine

#### 25.1 Prologue

#### 25.2 Concept

#### 25.3 Forensic Medicine and DNA Fingerprinting

#### 25.4 Applications of DNA Methylation Markers in Forensic Medicine

#### 25.5 Forensic Medicine and Anthropometry

#### 25.6 Clinical Forensic Medicine

#### 25.7 Conclusion

#### References

---

#### 26 Pharmacogenomics

#### 26.1 Prologue

#### 26.2 Concept

#### 26.3 Predicting Drug Response on Gene Variation

#### 26.4 Drug Development and Testing Benefit from Pharmacogenomics

#### 26.5 Applications and Benefits of Pharmacogenomics

#### 26.5.1 Better, Safer Drugs the First Time

#### 26.5.2 More Accurate Methods of Determining Appropriate Drug Dosages

#### 26.6 Benefits of Pharmacogenomic Testing

#### 26.6.1 Patient’s Ability to Metabolize Drugs

#### 26.6.2 Age-Related Genetic Variations

#### 26.7 Recent Reports of Pharmacogenomics Use

#### 26.8 Interpreting Pharmacogenomic Tests

#### 26.9 Barriers to Pharmacogenomics Progress

#### References
29.3.1 Anthrax ........................................ 487
29.3.2 Plague ........................................ 487
29.3.3 Tularemia ...................................... 487
29.3.4 Melioidosis .................................... 488
29.3.5 Viral Hemorrhagic Fevers ................. 488
29.3.6 Other Viral Fevers ............................ 488
29.3.7 Trichothecene Mycotoxins .................. 488
29.3.8 Aflatoxin ..................................... 489
29.4 Biodefense ....................................... 489
29.4.1 Viral Agents – Poxviridae ................... 490
29.4.2 Botulinal Toxins .............................. 490
29.4.3 Mycotoxins ................................... 491
29.5 Combating Detection of Biowarfare Agents .... 491
29.5.1 Prophylatic & Therapeutic Approaches .... 491
29.5.2 Detection Methods ............................ 495
29.6 Impact of Biological Weapons ................... 495
29.7 Tools for Self Defence Against Bioweapons .... 496
29.8 Genetic Engineering and Biological Warfare ... 497
29.9 Impact of Genomics and Genetic Technology ... 499
29.10 Conclusion ........................................ 500
References ............................................. 500

30 Segments of Molecular Diagnostics – Market Place 503
30.1 Prologue .......................................... 504
30.2 Concept .......................................... 504
30.3 Market Drivers .................................... 506
30.4 Trends in Infectious Diseases Testing Market .... 507
30.5 Trends in Cancer Diagnostic Testing World Markets ... 507
30.6 Trends in Cardiac Marker Diagnostic Testing Markets ... 508
30.7 Point of Care Diagnostic Testing World Markets .... 508
30.8 Next Generation Molecular Diagnostics ........... 509
30.9 The Rise of Companion Diagnostics ............. 510
30.10 Market Considerations and Forecasts .......... 510
References ............................................. 513

Index ..................................................... 515