

SIXTH EDITION

Molecular **Biotechnology**

Principles and Applications
of Recombinant DNA

Bernard R. Glick and Cheryl L. Patten

The cover features a dark blue background with a glowing DNA double helix in shades of red and blue, spiraling downwards from the top left. At the bottom center, a glowing yellow circular plasmid is shown. To the right, several smaller molecular structures, including what appear to be protein chains and clusters of red spheres, are scattered. The overall aesthetic is scientific and futuristic.

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*B. R. Glick
C. L. Patten*

About the Companion Website

This book is accompanied by a companion website for instructors.

www.wiley.com/go/glick/molbiotech6

This website includes:

- Powerpoints of Figures and Tables from the book

Contents

Preface to the Sixth Edition xvii

1 The Development of Molecular Biotechnology 1

Emergence of Molecular Biotechnology 1

Recombinant DNA Technology 3

Commercialization of Molecular Biotechnology 6

Concerns and Consequences 8

SUMMARY 10

REFERENCES 10

REVIEW QUESTIONS 11

2 Fundamental Technologies 13

Molecular Cloning 13

Preparation of DNA for Cloning 13

Insertion of Target DNA into a Plasmid Vector 18

Transformation and Selection of Cloned DNA in a Bacterial Host 21

Cloning Eukaryotic Genes 26

Recombinational Cloning 30

Genomic Libraries 32

Genome Engineering Using CRISPR Technology 36

Polymerase Chain Reaction 39

Amplification of DNA by PCR 39

Cloning PCR Products 42

Quantitative PCR 44

Chemical Synthesis of Genes 46

Assembling Oligonucleotides into Genes 46

Assembling PCR Products into Genes 46

DNA Sequencing Technologies 48

- Dideoxynucleotide Sequencing 50
- Sequencing Using Reversible Chain Terminators 53
- Single-Molecule Real-Time Sequencing 55
- Nanopore Sequencing 56

Sequencing Whole Genomes 56

- Preparation of Genomic DNA Sequencing Libraries 57
- High-Throughput Next-Generation Sequencing 59
- Genome Sequence Assembly 60
- Sequencing Metagenomes 61

Genomics 62

- Transcriptomics 65
- Proteomics 70
- Metabolomics 84

SUMMARY 86**REFERENCES 87****REVIEW QUESTIONS 89**

3 Production of Recombinant Proteins 91

Protein Production in Prokaryotic Hosts 91

- Regulating Transcription 92
- Increasing Translation Efficiency 96
- Increasing Protein Stability 100
- Increasing Protein Secretion 105
- Facilitating Protein Purification 111
- Integrating DNA into the Host Chromosome 114

Heterologous Protein Production in Eukaryotic Cells 119

- Posttranslational Modification of Eukaryotic Proteins 120
- General Features of Eukaryotic Expression Systems 123
- Yeast Expression Systems 123
- Baculovirus–Insect Cell Expression Systems 137
- Mammalian Cell Expression Systems 145

Protein Engineering 156

- Directed Mutagenesis 156
- Random Mutagenesis 161
- Examples of Protein Engineering 164

SUMMARY 173**REFERENCES 174****REVIEW QUESTIONS 176**

4 Molecular Diagnostics 179

Immunological Approaches To Detect Protein Biomarkers 180

- Antibodies 180
- Agglutination 185
- Enzyme-Linked Immunosorbent Assays 186
- Protein Arrays To Detect Polygenic Diseases 194
- Immunoassays for Protein Conformation-Specific Disorders 197

DNA-Based Diagnostic Approaches 199

- Hybridization Probes 199
- PCR-Based Detection Methods 207
- CRISPR-Cas-Based Diagnostic Assays 218
- DNA Microarrays 219
- Whole-Genome Sequencing To Assess Genetic Disease Risk 225

Detecting RNA Signatures of Disease 226

- Detection of Disease-Associated Changes in Gene Expression 227
- Detection of RNA Signatures of Antibiotic Resistance in Bacteria 228
- Detection of miRNA Signatures of Disease 230

Biofluorescent and Bioluminescent Systems 233

- Fluorescent Proteins 233
- Luciferase 234
- Microbial Biosensors 235

SUMMARY 238**REFERENCES 239****REVIEW QUESTIONS 241**

5 Protein Therapeutics 243

Pharmaceuticals 244

- Human Interferons 244
- Human Growth Hormone 248
- Tumor Necrosis Factor Alpha 251
- Extending Protein Half-Life 252

Enzymes 253

- DNase I 253
- Alginate Lyase 254
- Phenylalanine Ammonia Lyase 258
- α_1 -Antitrypsin 259
- Glycosidases 261
- Masking Nonhuman Epitopes 263
- Toxin-Intein Fusions 264
- Targeting Mitochondria 265

Bacteria and Therapeutics 267

- Interleukin-10 270
- Leptin 272
- An HIV Inhibitor 274
- Insulin 276
- Parkinson's Disease 279
- Cancer and Bacteria 279

Recombinant Antibodies 280

- Hybrid Human–Mouse Monoclonal Antibodies 284
- Human Monoclonal Antibodies 287
- Antibody Fragments 289
- Combinatorial Libraries of Antibody Fragments 294
- A Combinatorial Library of Full-Length Antibodies 297
- Shuffling CDR Sequences 298
- Dual-Variable-Domain Antibodies 298

- Bispecific Antibodies against Hemophilia 300
- Anti-HIV Antibodies 300
- Anticancer Antibodies 302
- Antibodies against Various Diseases 309
- Antiobesity Antibodies 313
- Enhanced Antibody Half-Life 315

Affibody Molecules 315

SUMMARY 318

REFERENCES 318

REVIEW QUESTIONS 322

6 Nucleic Acids as Therapeutic Agents 325

Targeting Specific mRNA and DNA Sequences 327

- Antisense RNA 327
- Aptamers 331
- Ribozymes and DNAzymes 338
- Interfering RNA 341
- Zinc Finger Nucleases 348
- CRISPR-Cas System 349
- Nanozymes 351
- Nanoparticles 352
- Engineering Bacteriophages 352

Viral Delivery Systems 357

Nonviral Delivery Systems 365

- Direct Injection 365
- Lipids 367
- Bacteria 369
- Dendrimers 372
- Antibodies 373
- Aptamers 373
- Transposons 374

Gene Therapy 376

- Mitochondrial Diseases 378
- Prodrug Activation Therapy 378
- Promoterless Gene Targeting 379

SUMMARY 382

REFERENCES 382

REVIEW QUESTIONS 386

7 Vaccines 387

Vaccination 387

Current and Future Vaccines 389

Subunit and Peptide Vaccines 392

- Herpes Simplex Virus 393
- Bovine Herpes Virus-1 394
- Cholera 396
- Influenza 396
- SARS 397
- COVID-19 399

Staphylococcus aureus 401
Human Papillomavirus 402
Foot-and-Mouth Virus 404
Streptococcus 405
Peptides 407
Malaria 408
Delivery 411

Genetic Immunization: DNA Vaccines 414

Delivery 414
Cancer 422
Zika Virus 422
Dental Caries 423

Engineered Attenuated Vaccines 424

Herpes Simplex Virus 425
Cholera 426
Salmonella Species 428
Leishmania Species 430

Vector Vaccines 430

Vaccines Directed against Viruses 430
Vaccines Directed against Bacteria 441
Bacteria as Antigen Delivery Systems 444

Monoclonal Antibody Passive Immunity 449

Influenza Virus 450

SUMMARY 452

REFERENCES 452

REVIEW QUESTIONS 456

8 Industrial and Environmental Uses of Recombinant Microorganisms 459

Restriction Endonucleases 459

Small Biological Molecules 461

L-Ascorbic Acid 463
Indigo 467
Amino Acids 468
Lycopene 473
Antibiotics 474
Biopolymers 487
Solvent Tolerance 493
Systems Metabolic Engineering To Optimize Product Yield 494

Microbial Degradation of Xenobiotics 496

Genetic Engineering of Biodegradative Pathways 497
Plastics 507

Utilization of Starch and Sugars 508

Commercial Production of Fructose and Alcohol 508
Increasing Alcohol Production 510
Improving Fructose Production 517

Utilization of Cellulose and Hemicellulose 518

Lignocellulosics 519
Cellulase Genes 522

Direct Conversion of Biomass to Ethanol 530
Alcohol Production by *Zymomonas mobilis* 531

Lipids from Cyanobacteria 534

Hydrogen Production 535

SUMMARY 538

REFERENCES 539

REVIEW QUESTIONS 542

9 Large-Scale Production of Proteins and Nucleic Acids from Recombinant Microorganisms 545

Principles of Microbial Growth 547

Batch Fermentation 548

Fed-Batch Fermentation 549

Continuous Fermentation 550

Maximizing the Efficiency of the Fermentation Process 551

High-Density Cell Cultures 552

Increasing Plasmid Stability 555

Quiescent *E. coli* Cells 555

Protein Secretion 558

Reducing Acetate 558

Improving Antibody Production in *E. coli* 561

Bioreactors 561

Typical Large-Scale Fermentation Systems 565

Two-Stage Fermentation in Tandem Airlift Reactors 566

Two-Stage Fermentation in a Single Stirred-Tank Reactor 568

Batch versus Fed-Batch Fermentation 569

Harvesting Microbial Cells 574

Disrupting Microbial Cells 576

Downstream Processing 578

Inclusion Bodies 579

Utilizing an Immobilized Enzyme 582

Magnetic Separation of Proteins 582

Large-Scale Production of DNA and RNA 583

Plasmid DNA 583

mRNA 586

SUMMARY 587

REFERENCES 587

REVIEW QUESTIONS 590

10 Genetic Engineering of Plants: Methodology 591

Plant Transformation with the Ti Plasmid of *A. tumefaciens* 595

Ti Plasmid-Derived Vector Systems 597

Increasing Transformation Efficiency 601

Microprojectile Bombardment 603**Chloroplast Engineering 604**

Very-High-Level Protein Expression 607

Use of Reporter Genes in Transformed Plant Cells 610**Manipulation of Gene Expression in Plants 611**

Transient Gene Expression 611

Plant Promoters 616

Manipulation of Genes in Plants 617

Facilitating Protein Purification 621

Protein Glycosylation 623

Gene Stacking 624

CRISPR-Based Directed Evolution 625

Polycistronic Gene Expression 626

Production of Marker-Free Transgenic Plants 626

Removing Marker Genes from Nuclear DNA 627

Removing Marker Genes from Chloroplast DNA 632

SUMMARY 633**REFERENCES 634****REVIEW QUESTIONS 636****11 Transgenic Plants 637****Insect Resistance 637***Bacillus thuringiensis* Insecticidal Toxin 637Increasing Expression of the *B. thuringiensis* Protoxin 642

Other Strategies for Protecting Plants against Insects 645

Preventing the Development of *B. thuringiensis*-Resistant Insects 652

Targeting Aphids 657

Virus Resistance 658

Viral Coat Protein-Mediated Protection 658

Protection by Expression of Other Genes 663

Herbicide Resistance 668

Glyphosate 669

Dicamba 672

Other Herbicides 673

Fungus and Bacterium Resistance 674

Transgenic Plants 675

RNAi and CRISPR/Cas 681

Salt and Drought Stress 682

Increasing Trehalose Production 683

Sequestering Sodium Ions 684

Delaying Drought-Induced Senescence 685

Phytoremediation 686**Fruits and Flowers 688**

Flavr Savr Tomato 688

Lowering Ethylene Levels 688

CRISPR Mutants 690

Modification of Plant Nutritional Content 690

- Amino Acids 690
- Lipids 692
- Vitamins 695
- Iron 698
- Gluten 700

Modification of Food Plant Taste and Appearance 701

- Preventing Discoloration 701
- Starch 703

Plants as Bioreactors 706

- Antibodies 706
- Pharmaceuticals and Vaccines 709
- Poly(3-Hydroxybutyric Acid) 710

Edible Vaccines 711

- Edible Cholera Vaccines 712
- Edible *E. coli* Vaccines 714

Plant Yield 716

- Increasing Grain Yield 716
- Increasing Harvest Index 716
- Decreasing Lignin Content 717
- Decreasing Pectin Content 720
- Increasing Oxygen Content 722

SUMMARY 723**REFERENCES 724****REVIEW QUESTIONS 729**

12 Transgenic Animals 731

Transgenic Animal Methodologies 733

- DNA Microinjection Method 733
- Retroviral Vector Method 736
- Engineered Embryonic Stem Cell Method 737
- Somatic Cell Nuclear Transfer for Transgenic Livestock 743
- Genome Editing with the CRISPR-Cas System 744
- Conditional Gene Modification with the Cre-*loxP* Recombination System 747
- Control of Transgene Expression with the Tetracycline-Inducible System 749
- Gene Knockdown by RNA Interference 754

Transgenic Animal Models of Human Diseases 756

- Mouse Models of Alzheimer's Disease 756
- Mouse Model of Duchenne Muscular Dystrophy 759
- Rabbit Models of Cardiovascular Disease 761
- Zebrafish Melanoma Model 763
- Nonhuman Primate Models of Neurodevelopmental Disorders 766

Animal Bioreactors for Production of Recombinant Therapeutic Proteins 767

- Production of Recombinant Antithrombin in Goat Milk 768
- Production of a Human Protease Inhibitor in Rabbits 770
- Production of Therapeutic Proteins in Chicken Eggs 771
- Production of Donor Organs in Pigs 773

Enhancing Production Traits of Food Animals 774

- Disease-Resistant Livestock 774
- Improving Milk Quality 781
- Increasing Muscle Mass in Cattle 782
- Enhancing Growth of Salmon 786

Gene Drives To Eradicate Vector-Transmitted Diseases 787

- Malaria Vector Population Suppression 789
- Dengue Fever Virus-Resistant Mosquitoes 791
- Reversal Drives 792

SUMMARY 795**REFERENCES 796****REVIEW QUESTIONS 797**

13

Molecular Biotechnology and Society 799**Development of Guidelines for Recombinant DNA Research 800****Deliberate Release of Genetically Modified Microorganisms 802**

- Environmental Concerns 802
- Regulations 803

Regulation of Genetically Modified Foods 804

- Food Ingredients Produced by Genetically Engineered Microorganisms 804
- Genetically Modified Crops 807
- Genetically Engineered Livestock 810

Societal Concerns about Genetically Modified Foods 812

- Alteration of Nutritional Content of Food 812
- Potential for Introducing Toxins or Allergens into Food 816
- Potential for Transferring Transgenes from Food to Humans or Intestinal Microorganisms 819
- Controversy about the Labeling of Genetically Modified Foods 820
- Impact of Genetically Engineered Crops on Biodiversity 822
- Who Benefits from the Production of Genetically Modified Foods? 824
- Environmental Benefits of Genetically Modified Crops 825
- How Do Views about Genetically Engineered Organisms Impact Trade? 827

Regulation and Safety of Medical Products of Biotechnology 827

- New Biological Drugs 828
- Genetic and Genomic Testing 832
- Economic Issues 835

Patenting Biotechnology 837

Patenting 838

Patenting in Different Countries 839

Patenting Nucleic Acid Sequences 841

Patenting Living Organisms 842

Patenting and Fundamental Research 844

SUMMARY 845

REFERENCES 846

REVIEW QUESTIONS 848

Amino Acids of Proteins and Their Designations 851

Index 853

Preface to the Sixth Edition

When the first edition of *Molecular Biotechnology: Principles and Applications of Recombinant DNA* was published in 1994, nearly all of the transgenic organisms that were produced included only a single foreign gene or cDNA. Now, nearly 30 years later it is common for scientific researchers to genetically engineer organisms by modifying both the activity and regulation of one or more existing genes or by introducing entire new pathways. Genetic engineering is no longer limited to only a small number of common bacterial strains using recombinant DNA technology. Scientists now routinely modify many different microorganisms, animals, and plants using the techniques of PCR, chemical DNA synthesis, directed mutagenesis, and genome editing. This progress has been greatly facilitated by advances in DNA and RNA sequencing, monoclonal antibody production, genomics, proteomics, and metabolomics. Scientists worldwide can understand and purposefully manipulate the biological world as never before.

In 1994, only a very few products produced by recombinant DNA technology had been commercialized. Today, as a consequence of molecular biotechnology hundreds of new therapeutic agents, diagnostics tests, and vaccines are available in the marketplace with many more in the pipeline. At the time of this writing, RNA vaccines have been produced in record time and approved for the first time by regulatory authorities worldwide to control the devastating COVID-19 global pandemic, which has also spurred advances in molecular diagnostics. Scientists have also genetically modified hundreds of different plants to improve crop yields and traits, with dozens of these transgenic plants already commercialized, and many more in the works. DNA technologies have become a cornerstone of modern forensics, paternity testing, and ancestry determination. The list goes on and on. Molecular biotechnology has clearly lived up to its promise and all of the original hype that has existed since the late 1970s. Worldwide there are several thousand biotechnology companies and research institutes, operating in virtually every corner of the globe, employing hundreds of thousands of highly skilled scientists. In addition to all of the scientific studies with commercial potential that are being conducted, there is also an enormous amount of exciting and innovative

fundamental biological research, using the many techniques of molecular biotechnology, being done at universities and government labs around the world. Never before in recorded history has the world witnessed such a vast amount of discovery and fundamental change in the biological sciences, and there is every indication that there is still much more to come. This sixth edition of *Molecular Biotechnology* builds upon the fundamentals that were established in the previous five editions, and endeavors to provide readers with a window on many of the major developments in this ever growing and ever important field. Given the enormity of the field of molecular biotechnology, we have had to be highly selective in choosing the material that we have included in this edition. Moreover, the window that we are looking through is continually moving. With the many changes in this field that have occurred since the first edition of *Molecular Biotechnology*, we both expect and look forward to a considerable amount of additional change in the coming years, including the implementation and commercialization of many of the discoveries that are discussed here.

We have throughout endeavored to make the text as reader-friendly as possible by minimizing the use of technical jargon and unnecessary abbreviations. When an important term appears for the first time in the text, it is generally followed in parentheses with a synonym or brief explanation. The figures and tables are not just restatements of the data from the original literature; rather, we have made an effort to conceptualize the experimenters' thinking and rationale. We have endeavored to be as up-to-date as possible, expanding on some previous discussions and providing large numbers of practical examples.

Each chapter opens with an outline of topics and concludes with a summary and list of review questions to sharpen students' critical thinking skills. All of the key ideas in the book are illustrated by the more than 585 full-color figures and elaborated in nearly 100 tables. After introducing molecular biotechnology as a scientific and economic venture in Chapter 1, the next two chapters explain the detailed methodologies of molecular biotechnology. These chapters provide a solid scientific base for the remainder of the book. Chapters 4 to 8 present examples of applications for microbial molecular biotechnology covering such topics as diagnostic techniques, both protein and nucleic acid therapeutic agents, vaccines, bioremediation of pollutants, the production of metabolites, and biomass utilization by industry. Chapter 9 describes some of the key components of large-scale fermentation processes using recombinant microorganisms. Chapters 10 to 12 describe the molecular manipulation of plants and animals addressing both fundamental approaches and a wide range of applications, with a particular emphasis on agricultural improvements. The book concludes in Chapter 13 with a discussion of the interaction of molecular biotechnology with society including some discussion of controversies that have occurred as a consequence of this technology, coverage of the regulation of molecular biotechnology, and patents.

Throughout the text we have relied extensively upon the recent published work of many researchers. In all cases, although not cited directly in the body of a chapter, the original published articles are cited in the references section of the appropriate chapter. In some cases, we have taken "pedagogic license" and either extracted or reformulated data from the original publications. Clearly, we are responsible for any distortions or

misrepresentations from these simplifications, although we hope that none have occurred. The references section also contains other sources that we used in a general way, which might, if consulted, bring the readers closer to a particular subject.

BERNARD R. GLICK
CHERYL L. PATTEN

The Development of Molecular Biotechnology



**Emergence of Molecular
Biotechnology**
Recombinant DNA Technology
**Commercialization of Molecular
Biotechnology**
Concerns and Consequences
SUMMARY
REFERENCES
REVIEW QUESTIONS

Emergence of Molecular Biotechnology

Long before we knew that microorganisms existed or that genes were the units of inheritance, humans looked to the natural world to develop methods to increase food production, preserve food, and heal the sick. Our ancestors discovered that grains could be preserved through fermentation into beer, that storing horse saddles in a warm, damp corner of the stable resulted in the growth of a saddle mold that could heal infected saddle sores, that intentional exposure to a “contagion” could somehow provide protection from an infectious disease on subsequent exposures, and that plants and animals with enhanced production traits could be developed through crossbreeding. Following the discovery of the microscopic world in the 17th century, microorganisms have been employed in the development of numerous useful processes and products. Many of these are found in our households and backyards. Lactic acid bacteria are used to prepare yogurts and probiotics, insecticide-producing bacteria are sprayed on many of the plants from which the vegetables in our refrigerator are harvested, nitrogen-fixing bacteria are added in the soil used for cultivation of legumes, the enzymatic stain removers in laundry detergent come from a microorganism, and antibiotics that are derived from common soil microbes are used to treat infectious diseases. These are just a few examples of traditional biotechnologies that have improved our lives. Up to the early 1970s, however, biotechnology was not a well-recognized scientific discipline, and research in this area was centered in departments of chemical engineering and occasionally in specialized microbiology programs.

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In a broad sense, biotechnology is concerned with the manipulation of organisms to develop and manufacture useful products. The term “biotechnology” was first used in 1917 by a Hungarian engineer, Karl Ereky, to describe an integrated process for the large-scale production of pigs by using sugar beets as the source of food. According to Ereky, biotechnology was “all lines of work by which products are produced from raw materials with the aid of living things.” This fairly precise definition was more or less ignored. For a number of years, biotechnology was used to describe two very different engineering disciplines. On one hand, it referred to industrial fermentation. On the other, it was used for the study of efficiency in the workplace—what is now called ergonomics. This ambiguity ended in 1961 when the Swedish microbiologist Carl Göran Hedén recommended that the title of a scientific journal dedicated to publishing research in the fields of applied microbiology and industrial fermentation be changed from the *Journal of Microbiological and Biochemical Engineering and Technology* to *Biotechnology and Bioengineering*. From that time on, biotechnology has been defined as the application of scientific and engineering principles to the processing of material by biological agents to provide goods and services. It is grounded on expertise in microbiology, genetics, biochemistry, immunology, cell biology, and chemical engineering.

Large-scale production of commodities from natural organisms is often considerably less than optimal. Initial efforts to enhance yields of microbial products focused on creating variants (mutants) using chemical mutagens or radiation to induce changes in the genetic constitution of existing strains. The level of improvement that could be achieved in this way was usually limited biologically. If, for example, a bacterium was mutated to produce high levels of a compound, other metabolic functions often were impaired, thereby causing the bacterium’s growth during large-scale fermentation to be less than desired. Despite this constraint, the traditional “induced mutagenesis and selection” strategies of strain improvement were extremely successful for a number of processes, such as the production of increased levels of antibiotics.

The traditional genetic improvement regimens were tedious, time-consuming, and costly because of the large numbers of microbial cells that had to be screened and tested. The best result that could be expected with this approach was the improvement of an existing inherited property of a microorganism rather than the expansion of its genetic capabilities. Despite these limitations, by the late 1970s, effective processes for the mass production of a wide range of commercial products from microorganisms had been perfected.

Today we have acquired sufficient knowledge of the biochemistry, genetics, and molecular biology of microbes and other organisms to significantly accelerate the development of useful and improved biological products and processes and to create new products that would not otherwise occur. Distinct from traditional biotechnology, the modern methods require knowledge of and manipulation of genes, the functional units of inheritance, and the discipline that is concerned with the manipulation of genes for the purpose of producing useful goods and services using living organisms is known as molecular biotechnology. The pivotal developments that enabled this technology were the establishment of techniques to isolate genes and to transfer them from one organism to another. The joining of DNA molecules from different sources was first demonstrated in 1971 by biochemist Paul Berg at Stanford University, who inserted genes from the bacterial

virus (bacteriophage) lambda into simian virus 40 DNA. This technology is known as recombinant DNA technology, and it was further developed by two scientists working in different fields who met at a scientific conference in 1972. In his laboratory at Stanford University in California, Stanley Cohen had been developing methods to transfer plasmids, small circular DNA molecules that replicate independently of chromosomal DNA, into bacterial cells. Meanwhile, Herbert Boyer at the University of California at San Francisco was working with enzymes that cut DNA at specific nucleotide sequences. Over lunch at a scientific meeting in Hawaii, they reasoned that Boyer's enzyme could be used to splice a specific segment of DNA into a plasmid and then the modified (recombinant) plasmid could be introduced into a host bacterium using Cohen's method.

Recombinant DNA Technology

It was clear to Cohen and Boyer, and others, that recombinant DNA technology had far-reaching possibilities. As Cohen noted at the time, "It may be possible to introduce in *E. coli*, genes specifying metabolic or synthetic functions such as photosynthesis or antibiotic production indigenous to other biological classes." The first commercial product produced using recombinant DNA technology was human insulin, which is used in the treatment of diabetes. The DNA sequence that encodes human insulin was synthesized, a remarkable feat in itself at the time, and was inserted into a plasmid that could be maintained in a nonpathogenic strain of the bacterium *Escherichia coli*. The bacterial host cells acted as biological factories for the production of the two peptide chains of human insulin that could be purified and combined and used to treat diabetics who were allergic to the commercially available porcine (pig) insulin. Today, this type of genetic engineering is commonplace.

The nature of biotechnology was changed forever by the development of recombinant DNA technology. Genetic engineering provided the means to create, rather than merely isolate, highly productive microbes and other organisms. Not long after the production of the first commercial preparation of recombinant human insulin in 1982, bacteria and then eukaryotic cells were used for the production of other therapeutic proteins, such as interferon, growth hormone, and viral antigens. Recombinant DNA technology also facilitated the biological production of large amounts of useful low-molecular-weight compounds and macromolecules that occur naturally in minuscule quantities. Plants and animals became natural bioreactors for producing new or altered gene products that could never have been created either by mutagenesis and selection or by crossbreeding. From its modest beginnings, around 50 years ago, molecular biotechnology has become the standard method for developing living systems with novel functions and capabilities for the synthesis of thousands of important commercial products.

Most new scientific disciplines do not arise solely on their own. They are often formed by the synthesis of knowledge from different areas of research. For molecular biotechnology, the biotechnology component was perfected by industrial microbiologists and chemical engineers, whereas the recombinant DNA technology portion owes much to discoveries in molecular biology, bacterial genetics, and nucleic acid enzymology (Table 1.1). In a broad sense, molecular biotechnology draws on knowledge from a diverse set of fundamental scientific disciplines to create products that are useful in a wide range of applications (Fig. 1.1).

Table 1.1 Selected developments in the history of molecular biotechnology^a

Date	Event
1917	Hungarian agricultural engineer Karl Ereky coins the term “biotechnology”
1940	Danish microbiologist A. Jost coins the term “genetic engineering” in a lecture on sexual reproduction in yeast
1943	Penicillin is produced on an industrial scale
1944	Avery, MacLeod, and McCarty demonstrate that DNA is the genetic material
1953	Watson and Crick determine the structure of DNA
1961–1966	Entire genetic code deciphered
1970	First restriction endonuclease isolated
1972	Khorana and coworkers synthesize an entire tRNA gene
1973	Boyer and Cohen establish recombinant DNA technology
1975	Kohler and Milstein describe the production of monoclonal antibodies
1976	First guidelines for the conduct of recombinant DNA research are issued
1976	Techniques are developed to determine the sequence of DNA
1978	Genentech produces human insulin in <i>E. coli</i>
1980	U.S. Supreme Court rules in the case of <i>Diamond vs Chakrabarty</i> that genetically manipulated microorganisms can be patented
1981	First commercial, automated DNA synthesizers are sold
1981	First monoclonal antibody-based diagnostic kit is approved for use in the United States
1982	First animal vaccine produced by recombinant DNA methodologies is approved for use in Europe
1983	Engineered Ti plasmids are used to transform plants
1988	U.S. patent is granted for a genetically engineered mouse susceptible to cancer
1988	PCR method is published
1990	Approval is granted in the United States for a trial of human somatic cell gene therapy
1990	Recombinant chymosin is used for cheese making in the United States
1994–1995	Detailed genetic and physical maps of human chromosomes are published
1994	FDA announces that genetically engineered tomatoes are as safe as conventionally bred tomatoes
1995	First genome of a cellular organism, the bacterium <i>Haemophilus influenzae</i> , is sequenced
1996	Recombinant protein erythropoietin exceeds \$1 billion in annual sales
1996	Complete DNA sequence of all the chromosomes of a eukaryotic organism, the yeast <i>Saccharomyces cerevisiae</i> , is determined
1996	Commercial planting of genetically modified crops
1997	A sheep is cloned by somatic cell nuclear transfer
1998	FDA approves first antisense drug
1999	FDA approves recombinant fusion protein (diphtheria toxin–interleukin-2) to treat cutaneous T-cell lymphoma
2000	<i>Arabidopsis</i> genome is sequenced
2000	Monoclonal antibodies exceed \$2 billion in annual sales
2000	Development of “Golden Rice” (provitamin-A-producing rice) is announced
2001	Human genome sequence is published
2002	Complete human gene microarrays are commercially available
2002	FDA approves first nucleic acid test to screen whole blood from donors for HIV and HCV
2004	Large-scale sequencing of the Sargasso Sea metagenome
2005	NCBI announces 100 gigabases of nucleotides in GenBank sequence database
2006	Recombinant cancer vaccine (Gardasil) is available to protect against cervical cancer
2009	FDA approves first drug produced in a genetically engineered animal (goat)

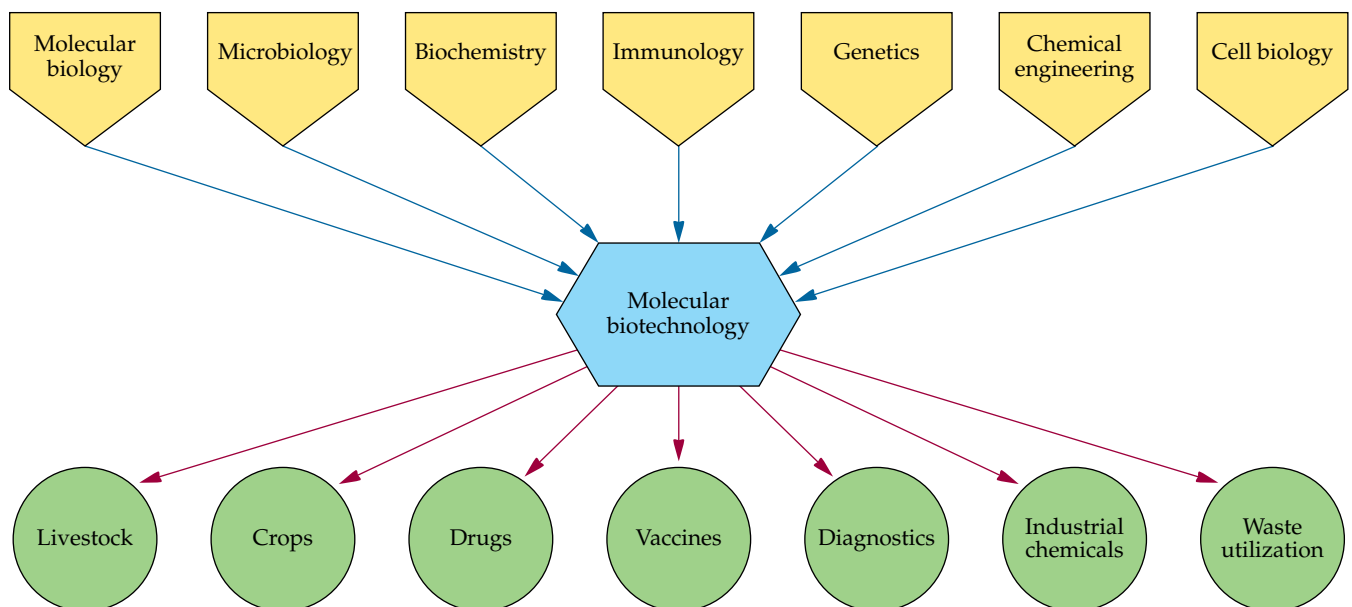
(continued)

Table 1.1 (continued)

Date	Event
2009	First clinical trial using embryonic stem cells
2010	Researchers create the first synthetic cell
2012	Doudna and Charpentier demonstrate targeted cleavage of DNA by CRISPR-Cas system
2013	U.S. Supreme Court rules that isolated genes are not eligible for patenting
2014	Patent granted for CRISPR-Cas systems and methods for altering expression of gene products
2015	FDA approves first transgenic animal (salmon) for human consumption
2016	National Bioengineered Food Disclosure Law is passed by the U.S. Congress requiring labeling of genetically engineered food
2017	FDA approves <i>in vivo</i> gene therapy for treatment of an inherited form of retinal dystrophy
2018	First RNA interference therapy (to treat hereditary transthyretin amyloidosis) approved in the United States and Europe
2018	Birth of genome-edited babies in China triggers widespread criticism
2019	Genetically engineered crops are grown in 29 countries on 190 million hectares
2019	Clinical trials begin to test the safety and efficacy of CRISPR-Cas genome editing to treat two blood disorders, β -thalassemia and sickle cell anemia
2019	Philippines is first Asian country to receive safety approval for genetically modified Golden Rice
2020	Results from the first CRISPR clinical trial indicate that the technique is safe
2020	First report of genome-edited mitochondria
2020	COVID-19 pandemic impels development of innovative molecular diagnostic tests, treatments, and vaccines
2021	Trial release of genetically modified mosquitoes in the United States

^aFDA, Food and Drug Administration; HCV, hepatitis C virus; HIV, human immunodeficiency virus; NCBI, National Center for Biotechnology Information; NIH, National Institutes of Health; PCR, polymerase chain reaction; tRNA, transfer ribonucleic acid; CRISPR, clustered regularly interspaced short palindromic repeats.

Figure 1.1 Many scientific disciplines contribute to molecular biotechnology, which generates a wide range of commercial products.



Construction of Biologically Functional Bacterial Plasmids *In Vitro*

S. N. Cohen, A. C. Y. Chang, H. W. Boyer, and R. B. Helling
Proc. Natl. Acad. Sci. USA **70**:3240–3244, 1973

The landmark study of Cohen et al. established the scientific foundation for recombinant DNA technology by showing how genetic information from different sources could be joined to create a novel, replicable genetic structure. In this case, the new genetic entities were derived from bacterial autonomously replicating extrachromosomal DNA structures called plasmids. In a previous study, Cohen and Chang (*Proc. Natl. Acad. Sci. USA* **70**:1293–1297, 1973) produced a small plasmid from a large naturally occurring plasmid by shearing the larger plasmid into smaller random pieces and introducing the mixture of pieces into a host cell, the bacterium *E. coli*. One of the fragments that was about 1/10 the size of the original plasmid was perpetuated as a functional plasmid. To overcome the randomness of this approach and to make the genetic manipulation of plasmids more manageable, Cohen and his coworkers used an enzyme

(restriction endonuclease) that cuts a DNA molecule at a specific nucleotide sequence and produces a short single-stranded extension at each end. The extensions of the cut ends of a restriction endonuclease-treated DNA molecule can combine (due to complementarity of the nitrogenous bases) with the extensions of another DNA molecule that has been cleaved with the same restriction endonuclease. Consequently, when DNA molecules from different sources are treated with the same restriction endonuclease and mixed together, new DNA combinations (recombinant DNA) that never existed before can be formed. In this way, Cohen et al. not only introduced a gene from one plasmid into another plasmid but also demonstrated that the introduced gene was biologically active. To their credit, these authors fully appreciated that their strategy was “potentially useful for insertion of specific sequences from prokaryotic

or eukaryotic chromosomes or extrachromosomal DNA into independently replicating bacterial plasmids.” In other words, any gene from any organism could theoretically be cloned into a plasmid which, after introduction into a host cell, would be maintained indefinitely and, perhaps, produce the protein encoded by the cloned gene. By demonstrating the feasibility of gene cloning, Cohen et al. provided the experimental basis for recombinant DNA technology and established that plasmids could act as vehicles (vectors) for maintaining cloned genes. This motivated others to pursue research in this area that rapidly led to the development of more sophisticated vectors and gene cloning strategies. It also engendered concerns about the safety and ethics of this kind of research that, in turn, were responsible for the establishment of official guidelines and governmental agencies for conducting and regulating recombinant DNA research, respectively, and contributed to the formation of the molecular biotechnology industry.

milestone



The Cohen and Boyer strategy for gene cloning was an experiment “heard round the world” (see Milestone). Once their concept was made public, many other researchers immediately appreciated the power of its potential. Consequently, scientists created a large variety of experimental protocols that made identifying, isolating, characterizing, and utilizing genes more efficient and relatively easy. These technological developments have had an enormous impact on generating new knowledge in practically all biological disciplines. Indeed, the emergence of the field of genomics was dependent on the ability to clone large fragments of DNA into plasmids in preparation for sequence determination.

Commercialization of Molecular Biotechnology

The potential of recombinant DNA technology reached the public with a frenzy of excitement, and many people became rich on its promise. Indeed, within 20 minutes of the start of trading on the New York Stock Exchange on 14 October 1980, the price of shares in Genentech, the company founded

by Boyer with chemist and entrepreneur Robert Swanson that produced recombinant human insulin, went from \$35 to \$89. This was the fastest increase in the value of any initial public offering in the history of the market up to that time. It was predicted that some genetically engineered microorganisms would replace chemical fertilizers and others would eat up oil spills; plants with inherited resistance to a variety of pests and exceptional nutritional content would be created; and livestock would have faster growing times, more efficient feed utilization, and meat with low fat content. Many were convinced that as long as a biological characteristic was genetically determined by one or a few genes, organisms with novel genetic constitutions could be readily created. Today, in many cases, the promise of recombinant DNA technology has become a reality.

Since the commercial production of recombinant human insulin, hundreds of drugs produced by recombinant DNA technology have been developed to treat diseases such as cancer, multiple sclerosis, rheumatoid arthritis, cystic fibrosis, and strokes, and to provide protection against numerous infectious diseases. The majority of these are therapeutic monoclonal antibodies, hormones, and growth factors, many of which are more effective and have fewer side effects than other therapies. Very recently, a small number of nucleic acid therapies have been approved to target diseases caused by specific mutations, including gene therapies to replace defective genes that cause blindness and spinal muscular atrophy, and RNA therapies to treat an inherited form of amyloidosis and Duchenne muscular dystrophy. Hundreds more new biological drugs and therapies are in the process of being tested in human clinical trials, most to treat various cancers and also genetic, neurological, autoimmune, and infectious diseases. Beyond medical applications, many molecular biotechnology products are available to enhance crop and livestock yields, decrease pesticide use, and improve industrial processes such as the manufacture of pulp and paper, food, energy, and textiles.

The impact on agriculture has been tremendous. While the global population is expanding rapidly, yield increases of all major crops have decreased due to poor agricultural management practices, decreased acreage of arable land, and increased reliance on fertilizers and pesticides that diminish soil quality. To produce more food on less land, in 2019, 17 million farmers in 29 countries planted genetically engineered crops on 190 million hectares of land. These crops are predominantly soybeans, corn, cotton, and canola that are resistant to herbicides and insects, although many others such as drought-resistant sugarcane and nonbrowning potatoes and apples are produced. The global market value of genetically modified crops is currently around \$20 billion. Small resource-poor farmers benefit substantially from agricultural biotechnology. In a comparative study of small cotton farms in South Africa, it was found, over three seasons, that the yield of cotton from plants that were genetically engineered to produce a bacterial insecticide was on average about 70% greater than those from non-genetically modified plants. Higher yields and reduced pesticide and labor costs translated into doubled revenues despite the slightly higher costs of the transgenic seeds. In a recent 2-year study in Bangladesh, the net returns per hectare for insect-resistant eggplant were six times higher than that for conventional eggplant.

The ultimate objective of all biotechnology research is the development of commercial products. Consequently, molecular biotechnology is driven

to a great extent by the prospect of financial gain. By nightfall on 14 October 1980, the principal shareholders of Genentech stock were worth millions of dollars. The unprecedented enthusiastic public response to Genentech encouraged others to follow. Between 1980 and 1983, about 200 small biotechnology companies were founded in the United States with the help of tax incentives and funding from both stock market speculation and private investment. Like Herbert Boyer, who was first a research scientist at the University of California at San Francisco and then a vice president of Genentech, university professors started many of the early companies.

Today, there are about 8,000 biotechnology companies worldwide, most in the United States and Europe, with annual earnings in the hundreds of billions of dollars. The biotechnology industry in these regions employs more than 200,000 people. Large multinational chemical and pharmaceutical companies, such as Bayer, DuPont, Pfizer, GlaxoSmithKline, Merck, Novartis, Hoffmann-LaRoche, Gilead Sciences, and Amgen, to name but a few, have made significant research commitments to molecular biotechnology. The roster of biotechnology companies is extensive and includes those focused on vaccines, protein and nucleic acid therapeutics, drug delivery, molecular diagnostics, genomics, industrial processing, and agricultural biotechnology.

Concerns and Consequences

While many people appreciate the potential of molecular biotechnology to solve important problems in agriculture, medicine, and industry, they recognize the need to be cautious about its widespread application. Indeed, one of the first scientific responses to recombinant DNA technology was a voluntary moratorium on certain experiments that were thought to be potentially hazardous. This research ban was self-imposed by a group of molecular biologists, including Cohen and Boyer. They were concerned that combining genes from two different organisms might unintentionally create a novel organism with undesirable or even dangerous properties. Within a few years, however, these apprehensions were allayed as scientists gained laboratory experience with the technology and safety guidelines were formulated for recombinant DNA research. The temporary cessation of some recombinant DNA research projects did not dampen the enthusiasm for genetic engineering. In fact, the new technology continued to receive unprecedented attention from both the public and the scientific community.

Molecular biotechnology can benefit humanity by

- Providing opportunities to accurately diagnose, prevent, treat, or cure a wide range of infectious and genetic diseases
- Increasing crop yields by creating plants that are resistant to insect predation, fungal and viral diseases, and environmental stresses such as short-term drought and excessive heat and at the same time reducing applications of hazardous agrichemicals
- Creating microorganisms that will produce metabolites (products of metabolism), polymers, amino acids, enzymes, and additives that are important for food production and other industries

- Developing livestock and other animals that have genetically enhanced attributes
- Facilitating the removal of pollutants and waste materials from the environment

Although it is exciting and important to emphasize the positive aspects of new advances, there are also social concerns and consequences that must be addressed. For example,

- Will some genetically engineered organisms, or their products, be harmful to humans or other organisms, or to the environment?
- Will the development and use of genetically engineered organisms reduce natural biological diversity?
- Should humans be genetically manipulated?
- Will new diagnostic procedures, especially those based on genome sequencing, undermine individual privacy?
- Will the emphasis on commercial success mean that the benefits of molecular biotechnology will be available only to wealthy individuals or nations?
- Will agricultural molecular biotechnology undermine traditional farming practices and limit food choices?
- Will medical therapies based on molecular biotechnology supersede equally effective traditional treatments?
- Will the quest for patents inhibit the free exchange of ideas among research scientists?

These and many other issues have been considered by government commissions, discussed extensively at conferences, and thoughtfully debated and analyzed by individuals in both popular and academic publications. On this basis, regulations have been formulated, guidelines have been established, and policies have been created. There has been active and extensive participation by both scientists and the general public in deciding how molecular biotechnology should proceed, although some controversies still remain.

Molecular biotechnology, with much fuss and fanfare, became a comprehensive scientific and commercial venture in a remarkably short period of time. Many scientific and business publications are now devoted to molecular biotechnology, and graduate and undergraduate programs and courses are available at universities throughout the world to teach molecular biotechnology. It could be debated whether the early promise of biotechnology has been fulfilled as it was predicted to in a 1987 document published by the U.S. Office of Technology Assessment, which declared that molecular biotechnology is "a new scientific revolution that could change the lives and futures of . . . citizens as dramatically as did the Industrial Revolution two centuries ago and the computer revolution today. The ability to manipulate genetic material to achieve specified outcomes in living organisms . . . promises major changes in many aspects of modern life." It does offer solutions to some serious global problems, including the spread of infectious diseases, the burden of waste accumulation, and food shortages that may become increasingly dire as the climate changes. The potential of molecular biotechnology to solve some of these imminent problems is the subject of this book.