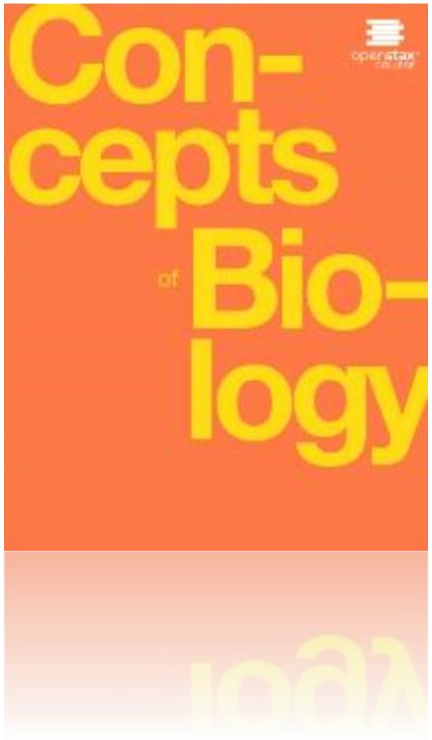
CONCEPTS OF BIOLOGY

Chapter 10 BIOTECHNOLOGY

PowerPoint Image Slideshow



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Introduction

- The latter half of the twentieth century began with the discovery of the structure of DNA, then progressed to the development of the basic tools used to study and manipulate DNA
- Some refer to the twenty-first century as the biotechnology century
- Many of these developments are expected to raise significant ethical and social questions that human societies have not yet had to consider

FIGURE 10.1

(a) (b)

(a) A thermal cycler, such as the one shown here, is a basic tool used to study DNA in a process called the polymerase chain reaction (PCR). The polymerase enzyme most often used with PCR comes from a strain of bacteria that lives in (b) the hot springs of Yellowstone National Park. (credit a: modification of work by Magnus Manske; credit b: modification of work by Jon Sullivan)

10.1: CLONING AND GENETIC ENGINEERING (1 of 2)

- **Biotechnology** is the use of artificial methods to modify the genetic material of living organisms or cells to produce novel compounds or to perform new functions
- Biotechnology has been used for improving livestock and crops since the beginning of agriculture through selective breeding
- Biotechnology has become synonymous with the manipulation of organisms' DNA at the molecular level

10.1: CLONING AND GENETIC ENGINEERING (2 of 2)

- The primary applications of this technology are in medicine (for the production of vaccines and antibiotics) and in agriculture (for the genetic modification of crops)
- Biotechnology also has many industrial applications, such as fermentation, the treatment of oil spills, and the production of biofuels, as well as many household applications such as the use of enzymes in laundry detergent

Manipulation of Genetic Material (1 of 2)

- To accomplish the applications described above, biotechnologists must be able to extract, manipulate, and analyze nucleic acids
- Remember that nucleic acids are macromolecules made of nucleotides (a sugar, a phosphate, and a nitrogenous base)
- The phosphate groups on these molecules each have a net negative charge

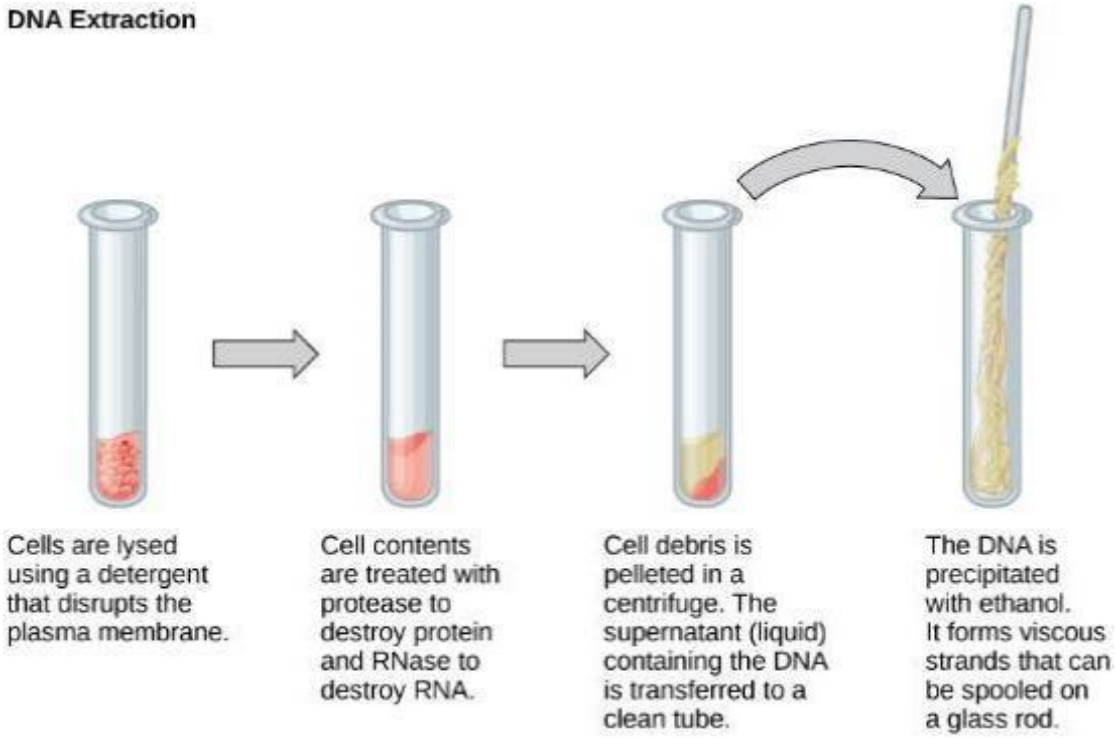
Manipulation of Genetic Material (2 of 2)

- **Genome** – an entire set of DNA molecules in the nucleus of eukaryotic organisms
- DNA has two complementary strands linked by hydrogen bonds between the paired bases
- Unlike DNA in eukaryotic cells, RNA molecules leave the nucleus
- Messenger RNA (mRNA) is analyzed most frequently because it represents the protein-coding genes that are being expressed in the cell

Isolation of Nucleic Acids (1 of 2)

- To study or manipulate nucleic acids, the DNA must first be extracted from cells
- Various techniques are used to extract different types of DNA (Figure10.2)
- Most nucleic acid extraction techniques involve steps to break open the cell, often by using a detergent solution containing buffering compounds
- The DNA is then brought out of solution using alcohol
- The resulting DNA, because it is made up of long polymers, forms a gelatinous mass

FIGURE 10.2



This diagram shows the basic method used for the extraction of DNA.

Isolation of Nucleic Acids (2 of 2)

- RNA is studied to understand gene expression patterns in cells
- RNA is naturally very unstable because enzymes that break down RNA are commonly present in nature, some are even secreted by our own skin and are very difficult to inactivate
- Similar to DNA extraction, RNA extraction involves the use of various buffers and enzymes to inactivate other macromolecules and preserve only the RNA

Gel Electrophoresis (1 of 3)

- Because nucleic acids are negatively charged ions at neutral or alkaline pH in an aqueous environment, they can be moved by an electric field
- **Gel electrophoresis** - a technique used to separate charged molecules on the basis of size and charge
- The nucleic acids can be separated as whole chromosomes or as fragments

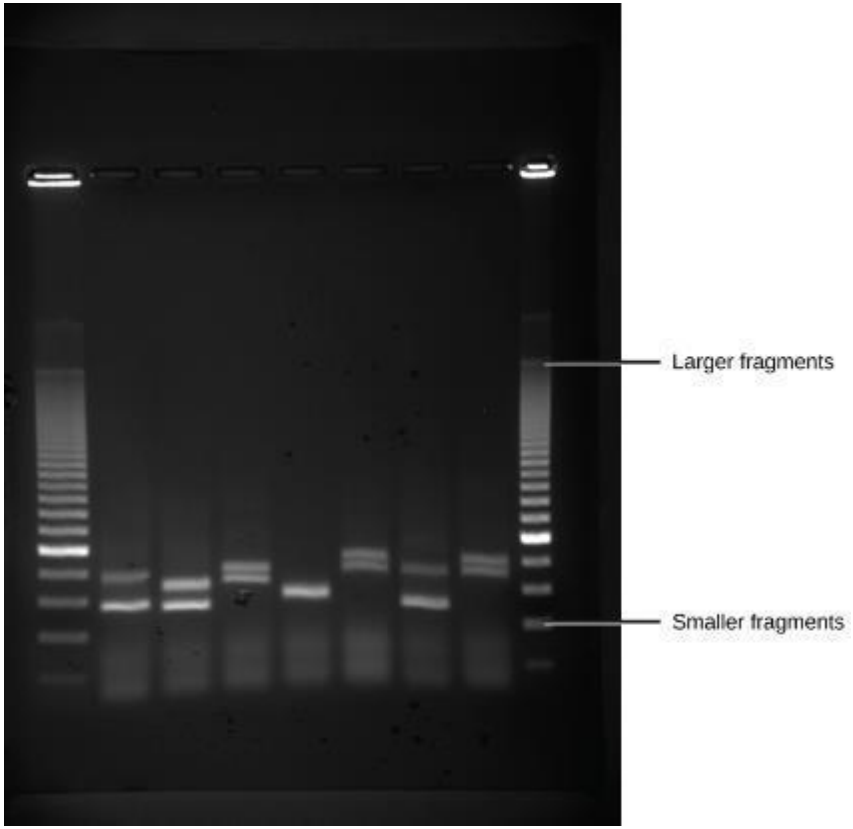
Gel Electrophoresis (2 of 3)

- The nucleic acids are loaded into a slot at one end of a gel matrix, an electric current is applied, and negatively charged molecules are pulled toward the opposite end of the gel (the end with the positive electrode)
- Smaller molecules move through the pores in the gel faster than larger molecules; this difference in the rate of migration separates the fragments on the basis of size

Gel Electrophoresis (3 of 3)

- The nucleic acids in a gel matrix are invisible until they are stained with a compound that allows them to be seen, such as a dye
- Distinct fragments of nucleic acids appear as bands at specific distances from the top of the gel (the negative electrode end) that are based on their size (Figure 10.3)
- A mixture of many fragments of varying sizes appear as a long smear, whereas uncut genomic DNA is usually too large to run through the gel and forms a single large band at the top of the gel

FIGURE 10.3



Shown are DNA fragments from six samples run on a gel, stained with a fluorescent dye and viewed under UV light. (credit: modification of work by James Jacob, Tompkins Cortland Community College)

Polymerase Chain Reaction (1 of 2)

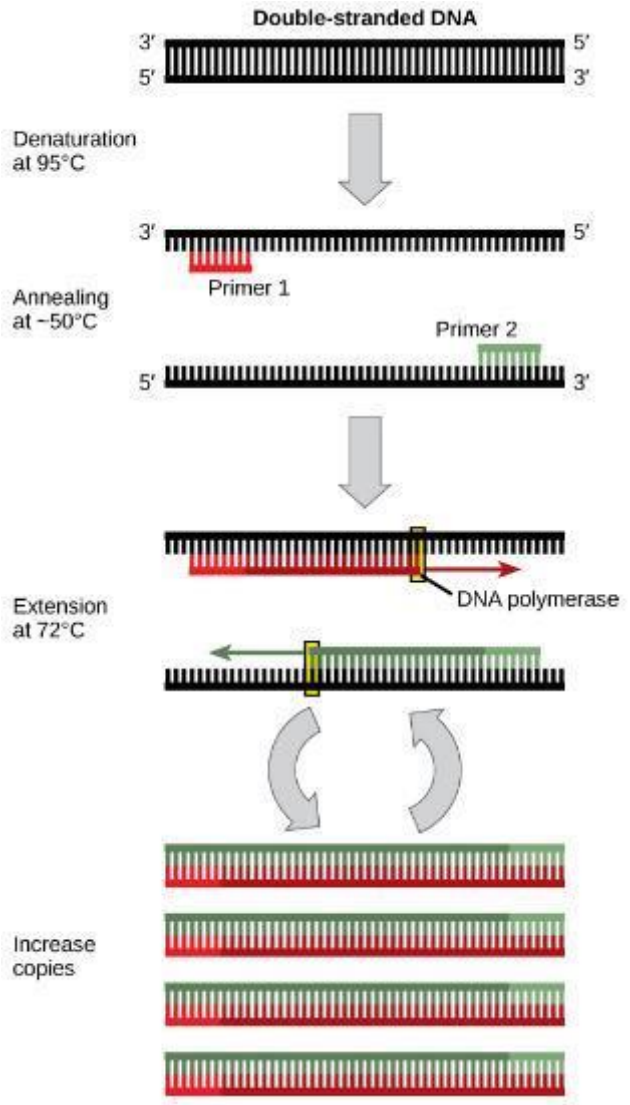
- DNA analysis often requires focusing on one or more specific regions of the genome
- It also frequently involves situations in which only one or a few copies of a DNA molecule are available for further analysis
- These amounts are insufficient for most procedures, such as gel electrophoresis
- **Polymerase chain reaction (PCR)** - a technique used to rapidly increase the number of copies of specific regions of DNA for further analyses (Figure 10.4)

Polymerase Chain Reaction (2 of 2)

- PCR uses a special form of DNA polymerase, the enzyme that replicates DNA, and other short nucleotide sequences called primers that base pair to a specific portion of the DNA being replicated
- PCR is used for many purposes in laboratories, including:
    1) the identification of a criminal
    2) paternity analysis
    3) the comparison ancient DNA to modern organisms
    4) determining the sequence of nucleotides in a specific region

FIGURE 10.4

Polymerase chain reaction, or PCR, is used to produce many copies of a specific sequence of DNA using a special form of DNA polymerase.



Cloning

- **Cloning** generally means the creation of a perfect replica
- Typically, the word is used to describe the creation of a genetically identical copy
- In biology, the re-creation of a whole organism is referred to as “reproductive cloning”

Molecular Cloning (1 of 6)

- Cloning allows for the creation of multiple copies of genes
- The DNA fragment is first inserted into a plasmid
- A **plasmid** (also called a vector in this context) is a small circular DNA molecule that replicates independently of the chromosomal DNA in bacteria

Molecular Cloning (2 of 6)

- As the bacteria divide, they copy their own DNA (including the plasmids)
- The inserted DNA fragment is copied along with the rest of the bacterial DNA
- In a bacterial cell, the fragment of DNA from the human genome (or another organism that is being studied) is referred to as foreign DNA to differentiate it from the DNA of the bacterium (the host DNA)

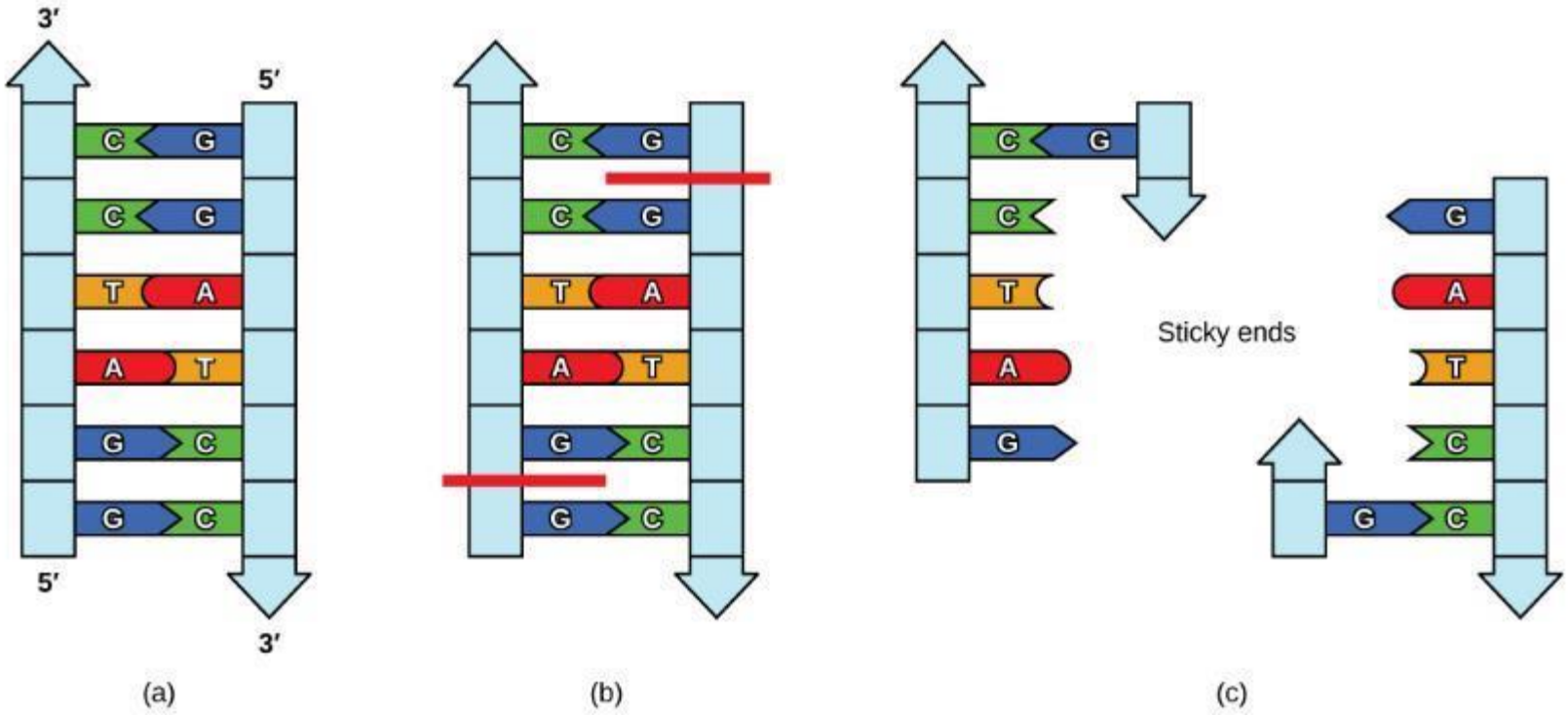
Molecular Cloning (3 of 6)

- Plasmids occur naturally in bacterial populations (such as Escherichia coli) and have genes that can contribute favorable traits to the organism, such as antibiotic resistance (the ability to be unaffected by antibiotics)
- A valuable characteristic of plasmid vectors is the ease with which a foreign DNA fragment can be introduced

Molecular Cloning (4 of 6)

- Restriction enzymes recognize specific DNA sequences and cut them in a predictable manner
- Many restriction enzymes make staggered cuts in the two strands of DNA, such that the cut ends have a 2- to 4-nucleotide single stranded overhang
- The sequence that is recognized by the restriction enzyme is a four- to eight-nucleotide sequence that is a palindrome, this means the sequence reads the same forward and backward

FIGURE 10.5

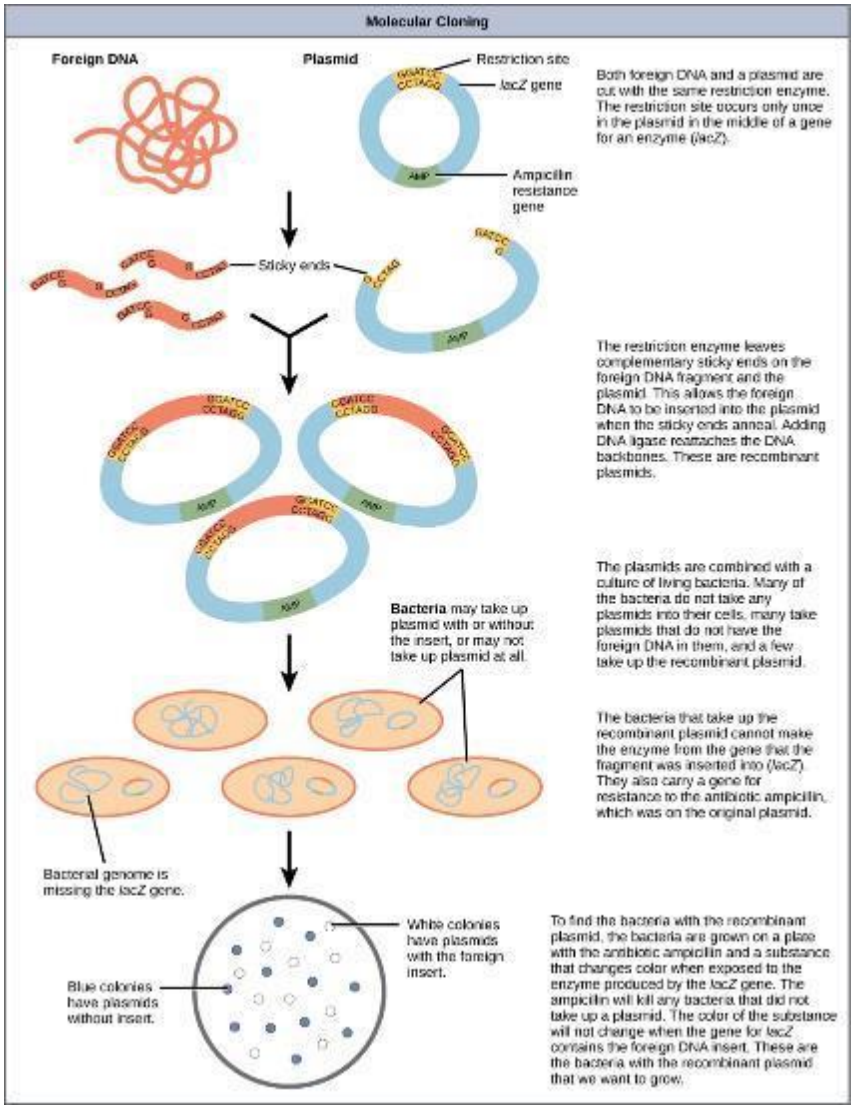


In this (a) six-nucleotide restriction enzyme recognition site, notice that the sequence of six nucleotides reads the same in the 5' to 3' direction on one strand as it does in the 5' to 3' direction on the complementary strand. This is known as a palindrome. (b) The restriction enzyme makes breaks in the DNA strands, and (c) the cut in the DNA results in “sticky ends”. Another piece of DNA cut on either end by the same restriction enzyme could attach to these sticky ends and be inserted into the gap made by this cut.

Molecular Cloning (5 of 6)

- When a staggered cut is made in a sequence like this, the overhangs are complementary (Figure 10.5)
- Because these overhangs are capable of coming back together by hydrogen bonding with complementary overhangs on a piece of DNA cut with the same restriction enzyme, these are called "**stickyends**"
- The process of forming hydrogen bonds between complementary sequences on single strands to form double-stranded DNA is called **annealing**
- DNA ligase permanently joins the DNA fragments when the sticky ends come together

FIGURE 10.6



This diagram shows the steps involved in molecular cloning.

Molecular Cloning (6 of 6)

- Plasmids with foreign DNA inserted into them are called **recombinant DNA molecules** because they contain new combinations of genetic material
- Proteins that are produced from recombinant DNA molecules are called **recombinant proteins**

Reproductive Cloning (1 of 5)

- **Reproductive cloning** - a method used to make a clone or an identical copy of an entire multicellular organism
- Recent advances in biotechnology have made it possible to reproductively clone mammals in the laboratory, therefore offspring are genetically identical to the one parent

Reproductive Cloning (2 of 5)

- The approach to producing an artificially cloned individual is to take the egg cell of one individual and to remove the haploid nucleus
- Then a diploid nucleus from a body cell of a second individual, the donor, is put into the egg cell
- The egg is then stimulated to divide so that development proceeds
- This isn’t as simple as it sounds

Reproductive Cloning (3 of 5)

- The first cloned agricultural animal was Dolly, a sheep who was born in 1996
- The success rate of reproductive cloning at the time was very low
- Dolly lived for six years and died of a lung tumor (Figure 10.7)
- There was speculation that because the cell DNA that gave rise to Dolly came from an older individual, the age of the DNA may have affected her life expectancy

Reproductive Cloning (4 of 5)

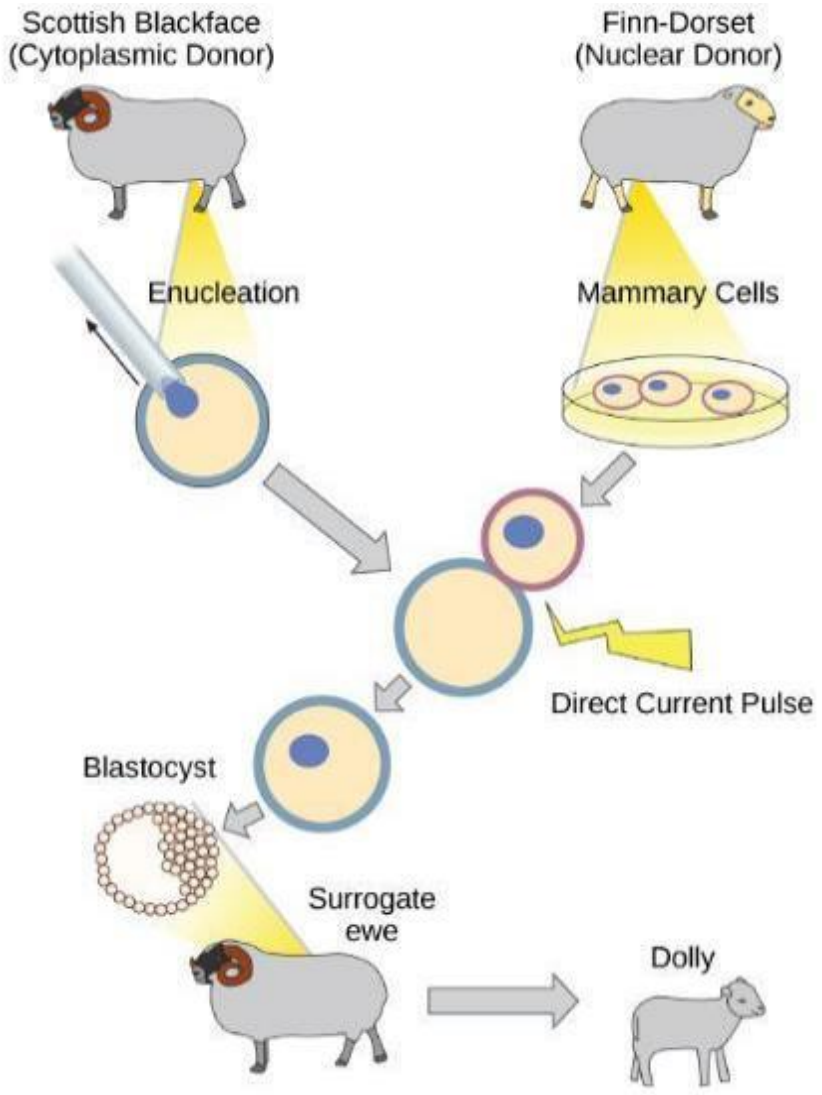
- Since Dolly, several species of animals (such as horses, bulls, and goats) have been successfully cloned
- There have been attempts at producing cloned human embryos as sources of embryonic stem cells
- In the procedure, the DNA from an adult human is introduced into a human egg cell, which is then stimulated to divide
- The technology is similar to the technology that was used to produce Dolly, but the embryo is never implanted into a surrogate mother

Reproductive Cloning (5 of 5)

- The cells produced are called **embryonic stem cells** because they have the capacity to develop into many different kinds of cells, such as muscle or nerve cells
- The stem cells could be used to research and ultimately provide therapeutic applications, such as replacing damaged tissues
- The benefit of cloning in this instance is that the cells used to regenerate new tissues would be a perfect match to the donor of the original DNA
- For example, a leukemia patient would not require a sibling with a tissue match for a bone-marrow transplant

FIGURE 10.7

Dolly the sheep was the first agricultural animal to be cloned. To create Dolly, the nucleus was removed from a donor egg cell. The enucleated egg was placed next to the other cell, then they were shocked to fuse. They were shocked again to start division. The cells were allowed to divide for several days until an early embryonic stage was reached, before being implanted in a surrogate mother.



Genetic Engineering (1 of 4)

- **Genetic Engineering** – Using recombinant DNA technology to modify an organism's DNA to achieve desirable traits
- Addition of foreign DNA in the form of recombinant DNA vectors that are generated by molecular cloning is the most common method of genetic engineering
- **Genetically Modified Organism (GMO)** – An organism that receives the recombinant DNA
- If the foreign DNA that is introduced comes from a different species, the host organism is called **transgenic**

Genetic Engineering (2 of 4)

- Bacteria, plants, and animals have been genetically modified since the early 1970s for academic, medical, agricultural, and industrial purposes
- Watch this short video (http://openstaxcollege.org/l/transgenic) explaining how scientists create a transgenic animal

Genetic Engineering (3 of 4)

- Modern techniques allow researchers to start at the DNA sequence level and ask: "What does this gene or DNA element do?"
- This technique, called **reverse genetics**, has resulted in reversing the classical genetic methodology
- One example of this method is analogous to damaging a body part to determine its function

Genetic Engineering (4 of 4)

- An insect that loses a wing cannot fly, which means that the wing's function is flight
- The classic genetic method compares insects that cannot fly with insects that can fly, and observes that the non-flying insects have lost wings
- Similarly in a reverse genetics approach, mutating or deleting genes provides researchers with clues about gene function
- Alternately, reverse genetics can be used to cause a gene to overexpress itself to determine what phenotypic effects may occur

10.2 BIOTECHNOLOGY IN MEDICINE AND AGRICUTURE

- Knowledge of the genetic makeup of our species, the genetic basis of heritable diseases, and the invention of technology to manipulate and fix mutant genes provides methods to treat diseases
- Biotechnology in agriculture can enhance resistance to disease, pests, and environmental stress to improve both crop yield and quality

Genetic Diagnosis and Gene Therapy (1 of 4)

- The process of testing for suspected genetic defects before administering treatment is called **genetic diagnosis** by **genetic testing**
- When a genetic disease is present in an individual's family, family members may be advised to undergo genetic testing

Genetic Diagnosis and Gene Therapy (2 of 4)

- For example, a woman with breast cancer can be screened for the BRCA mutations
- If one of the high-risk mutations is found, her female relatives can be screened for that particular mutation, or simply be more vigilant for the occurrence of cancers
- Genetic testing is also offered for fetuses (or embryos with in vitro fertilization) to determine the presence or absence of disease-causing genes in families with specific debilitating diseases

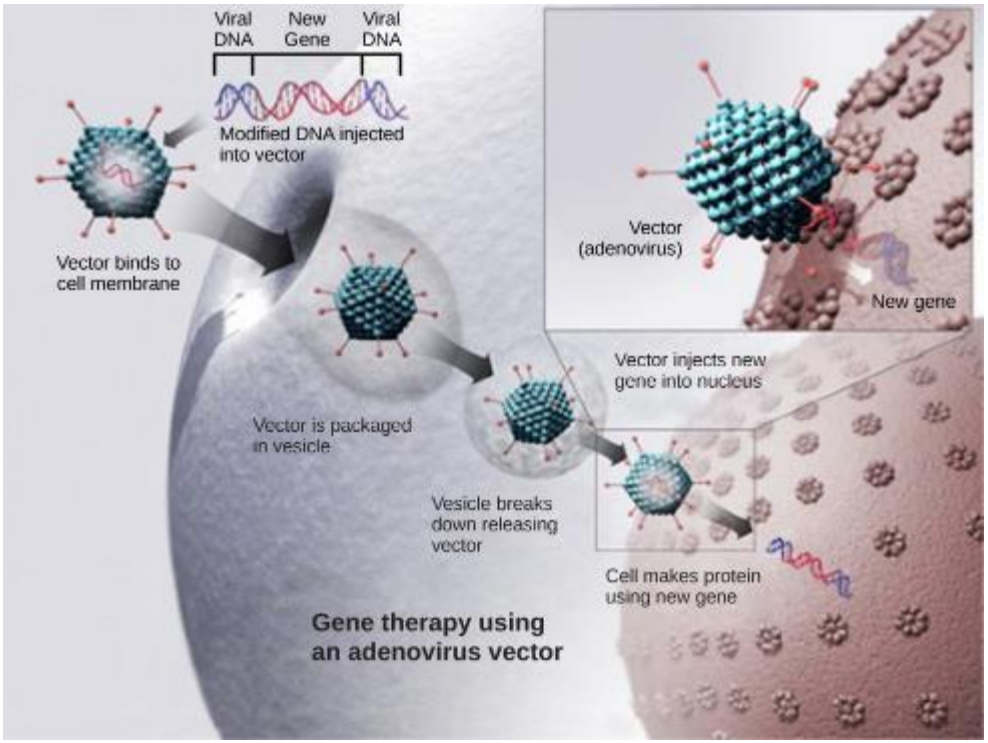
Genetic Diagnosis and Gene Therapy (3 of 4)

- **Gene therapy** - a genetic engineering technique that may one day be used to cure certain genetic diseases
- In its simplest form, it involves the introduction of a non-mutated gene at a random location in the genome to cure a disease by replacing a protein that may be absent in these individuals because of a genetic mutation

Genetic Diagnosis and Gene Therapy (4 of 4)

- The non-mutated gene is usually introduced into diseased cells as part of a vector transmitted by a virus, such as an adenovirus, that can infect the host cell and deliver the foreign DNA into the genome of the targeted cell (Figure 10.8)
- To date only a few of human experimental treatments have been successful, but the methods maybe important in the future as the factors limiting its success are resolved

FIGURE 10.8



This diagram shows the steps involved in curing disease with gene therapy using an adenovirus vector. (credit: modification of work by NIH)

Production of Vaccines, Antibiotics, and Hormones (1 of 3)

- Traditional vaccination strategies use weakened or inactive forms of microorganisms or viruses to stimulate the immune system
- Modern techniques use specific genes of microorganisms cloned into vectors and mass-produced in bacteria to make large quantities of specific substances to stimulate the immune system
- The substance is then used as a vaccine

Production of Vaccines, Antibiotics, and Hormones (2 of 3)

- Antibiotics kill bacteria and are naturally produced by microorganisms such as fungi; penicillin is perhaps the most well known example
- Antibiotics are produced on a large scale by cultivating and manipulating fungal cells

Production of Vaccines, Antibiotics, and Hormones (3 of 3)

- Recombinant DNA technology was used to produce large-scale quantities of the human hormone insulin in E. coli as early as1978; previously, pig insulin was used, which caused allergic reactions in many humans
- In children, the Human Growth Hormone (HGH) gene was cloned from a cDNA (complementary DNA) library and inserted into E. coli cells by cloning it into a bacterial vector

Transgenic Animals

- Some proteins need a eukaryotic animal host for proper processing
- For this reason, genes have been cloned and expressed in animals such as sheep, goats, chickens, and mice
- Animals that have been modified to express recombinant DNA are called **transgenic animals** (Figure 10.9)

FIGURE 10.9

It can be seen that two of these mice are transgenic because they have a gene that causes them to fluoresce under a UV light. The non-transgenic mouse does not have the gene that causes fluorescence. (credit: Ingrid Moen et al.)

Transgenic Plants (1 of 3)

- Manipulating the DNA of plants (creating genetically modified organisms, or GMOs) has helped to create desirable traits such as:
  - ✓ Disease Resistance
  - ✓ Herbicide
  - ✓ Pest Resistance
  - ✓ Better Nutritional Value
  - ✓ Better Shelf Life

FIGURE 10.10

Corn, a major agricultural crop used to create products for a variety of industries, is often modified through plant biotechnology. (credit: Keith Weller, USDA)

Transgenic Plants (2 of 3)

- Plants are the most important source of food for the human population
- Farmers developed ways to select for plant varieties with desirable traits long before modern-day biotechnology practices were established
- **Transgenic plants** have received DNA from other species

Transgenic Plants (3 of 3)

- GMOs are closely monitored by government agencies to ensure that they are fit for human consumption and do not endanger other plant and animal life
- Because foreign genes can spread to other species in the environment, particularly in the pollen and seeds of plants, extensive testing is required to ensure ecological stability
- Staples like corn, potatoes, and tomatoes were the first crop plants to be genetically engineered

10.3 GENOMICS AND PROTEOMICS

- **Genomics** - the study of entire genomes, including the complete set of genes, their nucleotide sequence and organization, and their interactions within a species and with other species
- The advances in genomics have been made possible by DNA sequencing technology
- Just as information technology has led to Google Maps that enable us to get detailed information about locations around the globe, genomic information is used to create similar maps of the DNA of different organisms

Mapping Genomes (1 of 4)

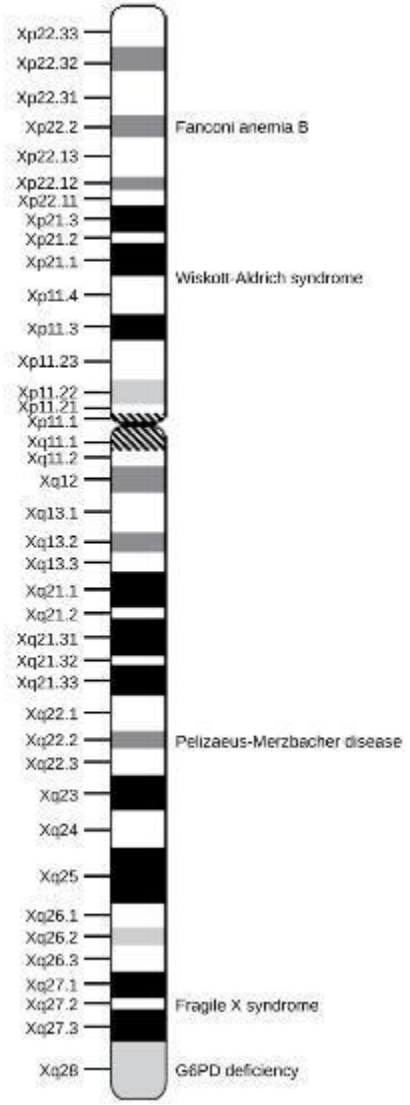
- **Genome mapping** - the process of finding the location of genes on each chromosome
- **Genetic map** - an illustration that lists genes and their location on a chromosome
- Genetic maps provide the big picture (similar to a map of interstate highways) and use genetic markers (similar to landmarks)
- **Genetic marker** - a gene or sequence on a chromosome that shows genetic linkage with a trait of interest

Mapping Genomes (2 of 4)

- The genetic marker tends to be inherited with the gene of interest, and one measure of distance between them is the recombination frequency during meiosis
- Early geneticists called this **linkage analysis**
- Physical maps get into the intimate details of smaller regions of the chromosomes (similar to a detailed road map)(Figure 10.11)
- **Physical map** - a representation of the physical distance, in nucleotides, between genes or genetic markers

FIGURE 10.11

This is a physical map of the human X chromosome. (credit: modification of work by NCBI, NIH)



Mapping Genomes (3 of 4)

- Human genome maps help researchers in their efforts to identify human disease-causing genes related to illnesses such as cancer, heart disease, and cystic fibrosis
- In addition, genome mapping can be used to help identify organisms with beneficial traits, such as microbes with the ability to clean up pollutants or even prevent pollution

Mapping Genomes (4 of 4)

- Genomic mapping is used with different model organisms that are used for research
- Genome mapping is similar to completing a complicated puzzle using every piece of available data
- Just as we use global positioning systems instead of paper maps to navigate through roadways, National Center for Biotechnology Information (NCBI) allows us to use a genome viewer tool to simplify the data mining process

Whole Genome Sequencing (1 of 5)

- **Whole genome sequencing** - a process that determines the DNA sequence of an entire genome
- Whole genome sequencing can provide answers to genetic diseases

Whole Genome Sequencing (2 of 5)

- In 2010, whole genome sequencing saved a young boy whose intestines had multiple mysterious abscesses, he had several colon operations with no relief; finally, a whole genome sequence revealed a defect in a pathway that controls apoptosis (programmed cell death)
- A bone marrow transplant cured his genetic disorder

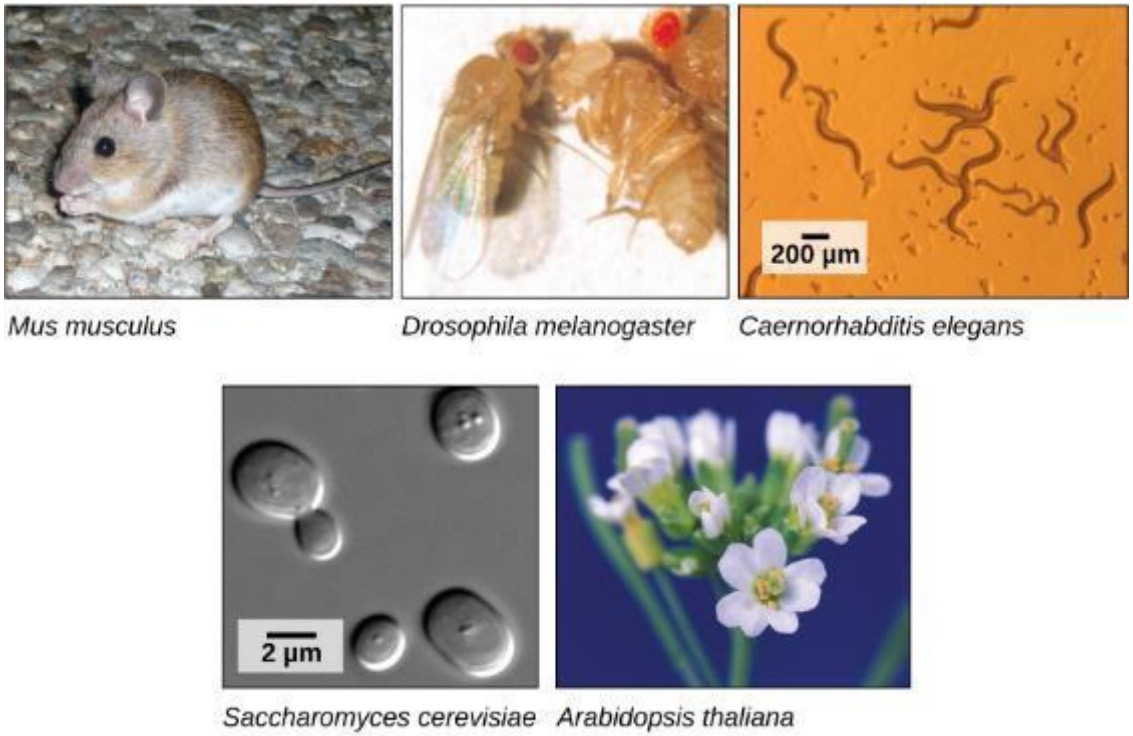
Whole Genome Sequencing (3 of 5)

- The first genomes to be sequenced (viruses, bacteria, and yeast) were smaller in terms of the number of nucleotides than the genomes of multicellular organisms
- The genomes of other model organisms, such as the mouse (Mus musculus), the fruit fly (Drosophila melanogaster), and the nematode (Caenorhabditis elegans) are now known

Whole Genome Sequencing (4 of 5)

- A great deal of basic research is performed in model organisms because the information can be applied to other organisms
- **Model organism** - a species that is studied as a model to understand the biological processes in other species that can be represented by the model organism
- For example, fruit flies are able to metabolize alcohol like humans, so the genes affecting sensitivity to alcohol have been studied in fruit flies in an effort to understand the variation in sensitivity to alcohol in humans

FIGURE 10.12



Much basic research is done with model organisms, such as the mouse, *Mus musculus*; the fruit fly, *Drosophila melanogaster*; the nematode *Caenorhabditis elegans*; the yeast *Saccharomyces cerevisiae*; and the common weed, *Arabidopsis thaliana*. (credit “mouse”: modification of work by Florean Fortescue; credit “nematodes”: modification of work by “snickclunk”/Flickr; credit “common weed”: modification of work by Peggy Greb, USDA; scale-bar data from Matt Russell)

Whole Genome Sequencing (5 of 5)

- The first human genome sequence was published in 2003
- The number of whole genomes that have been sequenced steadily increases and now includes hundreds of species and thousands of individual human genomes

Applying Genomics

- The introduction of DNA sequencing and whole genome sequencing projects, particularly the Human Genome Project, has expanded the applicability of DNA sequence information
- Genomics is now being used in a wide variety of fields, but the most commonly known application of genomics is to understand and find cures for diseases

Predicting Disease Risk at the Individual Level (1 of 4)

- Predicting the risk of disease involves screening and identifying currently healthy individuals by genome analysis at the individual level
- This approach is most applicable when the problem arises from a single gene mutation
- Such defects only account for about 5 percent of diseases found in developed countries

Predicting Disease Risk at the Individual Level (2 of 4)

- Most of the common diseases, such as heart disease, are multifactorial or polygenic (a phenotypic characteristic that is determined by two or more genes) and also environmental factors such as diet
- In April 2010, scientists at Stanford University published the genome analysis of a healthy individual (Stephen Quake, a scientist at Stanford University, who had his genome sequenced); the analysis predicted his propensity to acquire various diseases

Predicting Disease Risk at the Individual Level (3 of 4)

- A risk assessment was done to analyze Quake's percentage of risk for 55 different medical conditions
- A rare genetic mutation was found that showed him to be at risk for sudden heart attack
- He was also predicted to have a 23 percent risk of developing prostate cancer and a 1.4 percent risk of developing Alzheimer's disease

Predicting Disease Risk at the Individual Level (4 of 4)

- Genomic sequencing is becoming more affordable and analytical tools are becoming more reliable
- Ethical issues surrounding genomic analysis at a population level remain to be addressed
- For example, could such data be legitimately used to charge more or less for insurance or to affect credit ratings?

Genome-Wide Association Studies (1 of 10)

- Since 2005, it has been possible to conduct a type of study called a **genome-wide association study**, or **GWAS**
- GWAS is a method that identifies differences between individuals in single nucleotide polymorphisms (SNPs) that may be involved in causing diseases
- The method is particularly suited to diseases that may be affected by one or many genetic changes throughout the genome

Genome-Wide Association Studies (2 of 10)

- The GWAS method relies on a genetic database that has been in development since 2002 called the International HapMap Project
- The HapMap Project sequenced the genomes of several hundred individuals from around the world and identified groups of SNPs
- The groups include SNPs that are located near to each other on chromosomes so they tend to stay together throughout recombination

Genome-Wide Association Studies (3 of 10)

- The fact that the group stays together means that identifying one marker SNP is all that is needed to identify all the SNPs in the group
- There are several million SNPs identified, but identifying them in other individuals who have not had their complete genome sequenced is much easier because only the marker SNPs need to be identified

Genome-Wide Association Studies (4 of 10)

- In a common design for a GWAS, two groups of individuals are chosen: one group has the disease, and the other group does not
- The individuals in each group are matched in other characteristics to reduce the effect of confounding variables causing differences between the two groups
- For example, the genotypes may differ because the two groups are mostly taken from different parts of the world

Genome-Wide Association Studies (5 of 10)

- Once the individuals are chosen (typically, a thousand or more for the study to work) samples of their DNA are obtained
- The DNA is analyzed using automated systems to identify large differences in the percentage of particular SNPs between the two groups

Genome-Wide Association Studies (6 of 10)

- The results of GWAS can be used in two ways:
  - the genetic differences may be used as markers for susceptibility to the disease in undiagnosed individuals
  - the particular genes identified can be targets for research into the molecular pathway of the disease and potential therapies

Genome-Wide Association Studies (7 of 10)

- An offshoot of the discovery of gene associations with disease has been the formation of companies that provide so-called “personal genomics” that will identify risk levels for various diseases based on an individual’s SNP complement
- The science behind these services is controversial

Genome-Wide Association Studies (8 of 10)

- Because GWAS looks for associations between genes and disease, these studies provide data for other research into causes, rather than answering specific questions themselves
- An association between a gene difference and a disease does not necessarily mean there is a cause-and-effect relationship
- However, some studies have provided useful information about the genetic causes of diseases

Genome-Wide Association Studies (9 of 10)

- For example, three different studies in 2005 identified a gene for a protein involved in regulating inflammation in the body that is associated with a disease-causing blindness called age-related macular degeneration
- This opened up new possibilities for research into the cause of this disease

Genome-Wide Association Studies (10 of 10)

- A large number of genes have been identified to be associated with Crohn's disease using GWAS, and some of these have suggested new hypothetical mechanisms for the cause of the disease

Pharmacogenomics (1 of 2)

- **Pharmacogenomics** involves evaluating the effectiveness and safety of drugs on the basis of information from an individual's genomic sequence
- Personal genome sequence information can be used to prescribe medications that will be most effective and least toxic on the basis of the individual patient’s genotype
- Studying changes in gene expression could provide information about the gene transcription profile in the presence of the drug, which can be used as an early indicator of the potential for toxic effects

Pharmacogenomics (2 of 2)

- For example, genes involved in cellular growth and controlled cell death, when disturbed, could lead to the growth of cancerous cells
- Genome-wide studies can also help to find new genes involved in drug toxicity
- The gene signatures may not be completely accurate, but can be tested further before pathologic symptoms arise

Metagenomics (1 of 3)

- Traditionally, microbiology has been taught with the view that microorganisms are best studied under pure culture conditions, which involves isolating a single type of cell and culturing it in the laboratory
- Because microorganisms can go through several generations in a matter of hours, their gene expression profiles adapt to the new laboratory environment very quickly
- On the other hand, many species resist being cultured in isolation

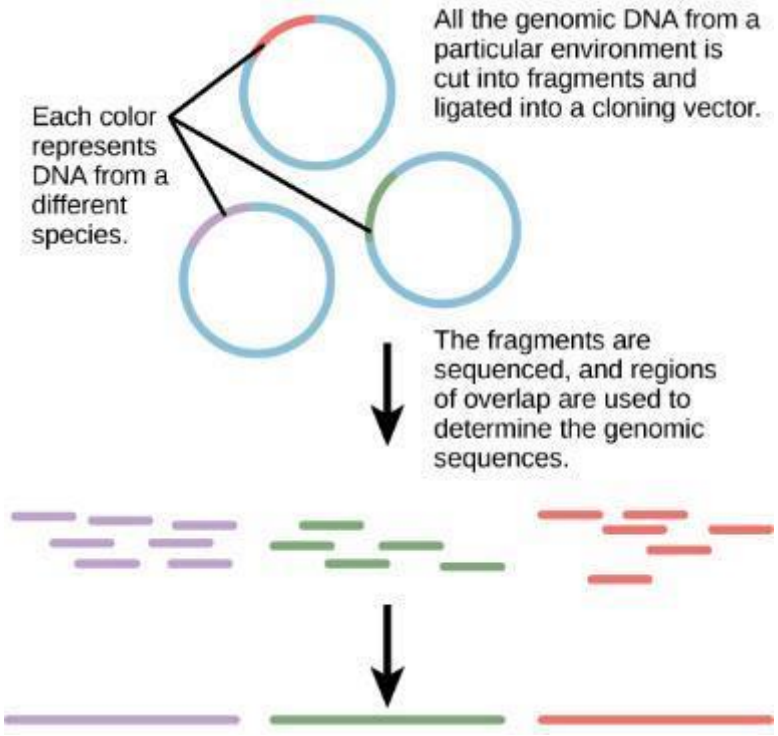
Metagenomics (2 of 3)

- Most microorganisms do not live as isolated entities, but in microbial communities known as **biofilms**
- For all of these reasons, pure culture is not always the best way to study microorganisms
- **Metagenomics** - the study of the collective genomes of multiple species that grow and interact in an environmental niche

Metagenomics (3 of 3)

- Metagenomics can be used to identify new species more rapidly and to analyze the effect of pollutants on the environment (Figure10.13)
- Metagenomics techniques can now also be applied to communities of higher eukaryotes, such as fish

FIGURE 10.13



Metagenomics involves isolating DNA from multiple species within an environmental niche. The DNA is cut up and sequenced, allowing entire genome sequences of multiple species to be reconstructed from the sequences of overlapping pieces.

Creation of New Biofuels

- Knowledge of the genomics of microorganisms is being used to find better ways to harness biofuels from algae and cyanobacteria
- The primary sources of fuel today are coal, oil, wood, and other plant products such as ethanol
- The microbial world is one of the largest resources for genes that encode new enzymes and produce new organic compounds, and it remains largely untapped
- This vast genetic resource holds the potential to provide new sources of biofuels (Figure 10.14)

FIGURE 10.14

Renewable fuels were tested in Navy ships and aircraft at the first Naval Energy Forum. (credit: modification of work by John F. Williams, US Navy)

Mitochondrial Genomics

- Mitochondria are intracellular organelles that contain their own DNA
- Mitochondrial DNA mutates at a rapid rate and is often used to study evolutionary relationships
- Another feature that makes studying the mitochondrial genome interesting is that in most multicellular organisms, the mitochondrial DNA is passed on from the mother during the process of fertilization
- For this reason, mitochondrial genomics is often used to trace genealogy

Genomics in Forensic Analysis (1 of 3)

- Information and clues obtained from DNA samples found at crime scenes have been used as evidence in court cases, and genetic markers have been used in forensic analysis
- In 2001, the first use of genomics in forensics was published

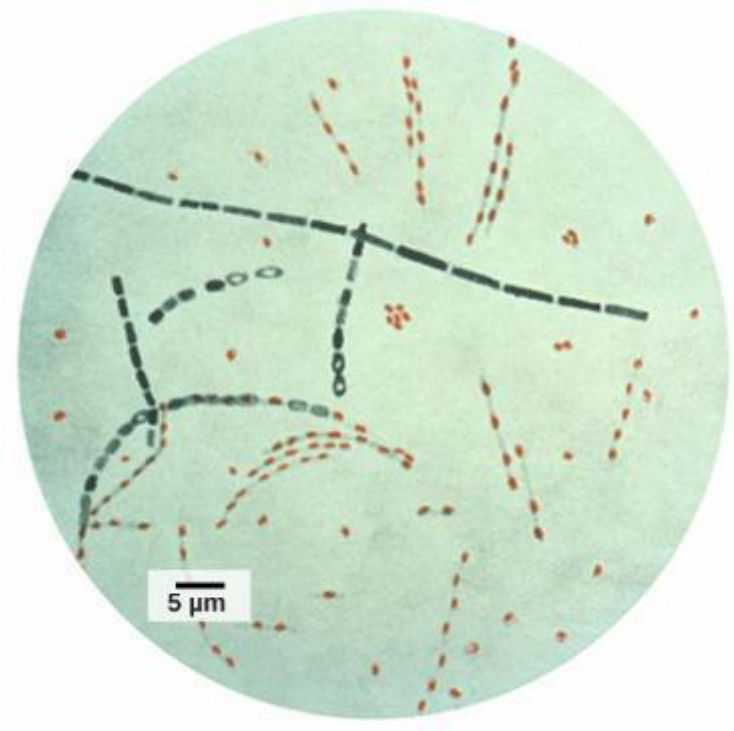
Genomics in Forensic Analysis (2 of 3)

- It was a collaborative effort between academic research institutions and the FBI to solve the mysterious cases of anthrax (Figure 10.15) that was transported by the US Postal Service
- Anthrax bacteria were made into an infectious powder and mailed to news media and two U.S. Senators
- The powder infected the administrative staff and postal workers who opened or handled the letters
- Five people died, and 17 were sickened from the bacteria

Genomics in Forensic Analysis (3 of 3)

- Using microbial genomics, researchers determined that a specific strain of anthrax was used in all the mailings; eventually, the source was traced to a scientist at a national biodefense laboratory in Maryland (Figure 10.15)

FIGURE 10.15



Bacillus anthracis is the organism that causes anthrax. (credit: modification of work by CDC; scale-bar data from Matt Russell)

Genomics in Agriculture (1 of 2)

- Genomics can reduce the trials and failures involved in scientific research to a certain extent, which could improve the quality and quantity of crop yields in agriculture (Figure10.16)
- Linking traits to genes or gene signatures helps to improve crop breeding to generate hybrids with the most desirable qualities
- Scientists use genomic data to identify desirable traits, and then transfer those traits to a different organism to create a new genetically modified organism, as described in the previous module

Genomics in Agriculture (2 of 2)

- Scientists are discovering how genomics can improve the quality and quantity of agricultural production
- For example, scientists could use desirable traits to create a useful product or enhance an existing product, such as making a drought-sensitive crop more tolerant of the dry season

FIGURE 10.16

Transgenic agricultural plants can be made to resist disease. These transgenic plums are resistant to the plum pox virus. (credit: Scott Bauer, USDA ARS)

Proteomics (1 of 9)

- Proteins are the final products of genes that perform the function encoded by the gene
- Proteins are composed of amino acids and play important roles in the cell
- All enzymes (except ribozymes) are proteins and act as catalysts, regulatory molecules, and hormones
- Transport proteins, such as hemoglobin, help transport oxygen to various organs
- Antibodies that defend against foreign particles are also proteins

Proteomics (2 of 9)

- In the diseased state, protein function can be impaired because of changes at the genetic level or because of direct impact on a specific protein
- **Proteome** - the entire set of proteins produced by a cell type
- Proteomes can be studied using the knowledge of genomes because genes code for mRNAs, and the mRNAs encode proteins
- The study of the function of proteomes is called **proteomics**

Proteomics (3 of 9)

- Proteomics complements genomics and is useful when scientists want to test their hypotheses that were based on genes
- Even though all cells in a multicellular organism have the same set of genes, the set of proteins produced in different tissues is different and dependent on gene expression
- Thus, the genome is constant, but the proteome varies and is dynamic within an organism

Proteomics (4 of 9)

- In addition, RNAs can be alternatively spliced (cut and pasted to create novel combinations and novel proteins), and many proteins are modified after translation
- Although the genome provides a blueprint, the final architecture depends on several factors that can change the progression of events that generate the proteome

Proteomics (5 of 9)

- Genomes and proteomes of patients suffering from specific diseases are being studied to understand the genetic basis of the disease
- The most prominent disease being studied with proteomic approaches is cancer (Figure 10.17)
- Proteomic approaches are being used to improve the screening and early detection of cancer; this is achieved by identifying proteins whose expression is affected by the disease process

Proteomics (6 of 9)

- An individual protein is called a **biomarker**, whereas a set of proteins with altered expression levels is called a **protein signature**
- For a biomarker or protein signature to be useful to a candidate for early screening and detection of a cancer, it must be secreted in body fluids such as sweat, blood, or urine, so that large-scale screenings can be performed in a noninvasive fashion

Proteomics (7 of 9)

- The current problem with using biomarkers for the early detection of cancer is the high rate of false-negative results
- A false-negative result is a negative test result that should have been positive
- In other words, many cases of cancer go undetected, which makes biomarkers unreliable

Proteomics (8 of 9)

- Some examples of protein biomarkers used in cancer detection are CA-125 for ovarian cancer and PSA for prostate cancer
- Protein signatures may be more reliable than biomarkers to detect cancer cells
- Proteomics is also being used to develop individualized treatment plans, which involves the prediction of whether or not an individual will respond to specific drugs and the side effects that the individual may have
- Proteomics is also being used to predict the possibility of disease recurrence

FIGURE 10.17

This machine is preparing to do a proteomic pattern analysis to identify specific cancers so that an accurate cancer prognosis can be made. (credit: Dorie Hightower, NCI, NIH)

Proteomics (9 of 9)

- The National Cancer Institute has developed programs to improve the detection and treatment of cancer
- The Clinical Proteomic Technologies for Cancer and the Early Detection Research Network are efforts to identify protein signatures specific to different types of cancers
- The Biomedical Proteomics Program is designed to identify protein signatures and design effective therapies for cancer patients