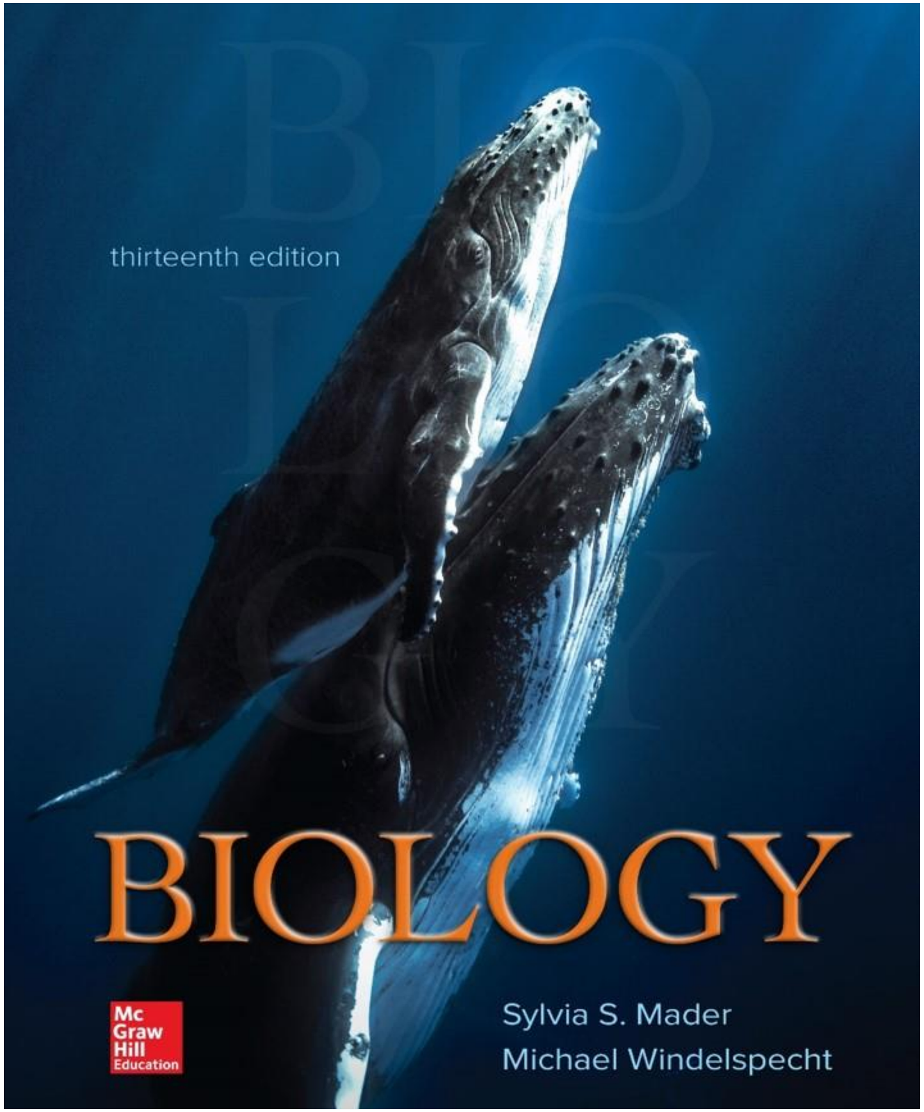

Biology

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Chapter 14
Biotechnology and Genomics
Lecture Outline

See separate FlexArt PowerPoint slides for all figures and tables pre-inserted into PowerPoint without notes.

Outline

14.1 DNA Technology

14.2 Biotechnology Products

14.3 Gene Therapy

14.4 Genomics

Tobacco Plants for Treatment of Dental Disease

Dental disease in dogs is a major concern of veterinarians.

- Toxins produced by oral cavity bacteria can be absorbed into the bloodstream, cause infections, and damage organs.
- Researchers have modified tobacco plants to produce vaccines against the bacterium *Streptococcus mutans*.
- They have also bioengineered the bacterium itself.
  - Using biotechnology, they have created strains of the bacterium that are harmless and wash away with saliva.
- Biotechnology can also be used to modify bacteria to make insulin or eat pollutants.
- Animals are also being genetically modified and cloned to produce specific proteins and crop plants altered for pest resistance or higher nutritive value.

14.1 DNA Technology

Cloning is the production of identical copies of DNA, cells, or organisms.

- Members of a bacterial colony on a petri dish are clones because they all came from division of the same cell.
- Identical twins are clones.
    - A single embryo separates to become two.

Gene cloning is the production of many identical copies of the same gene.

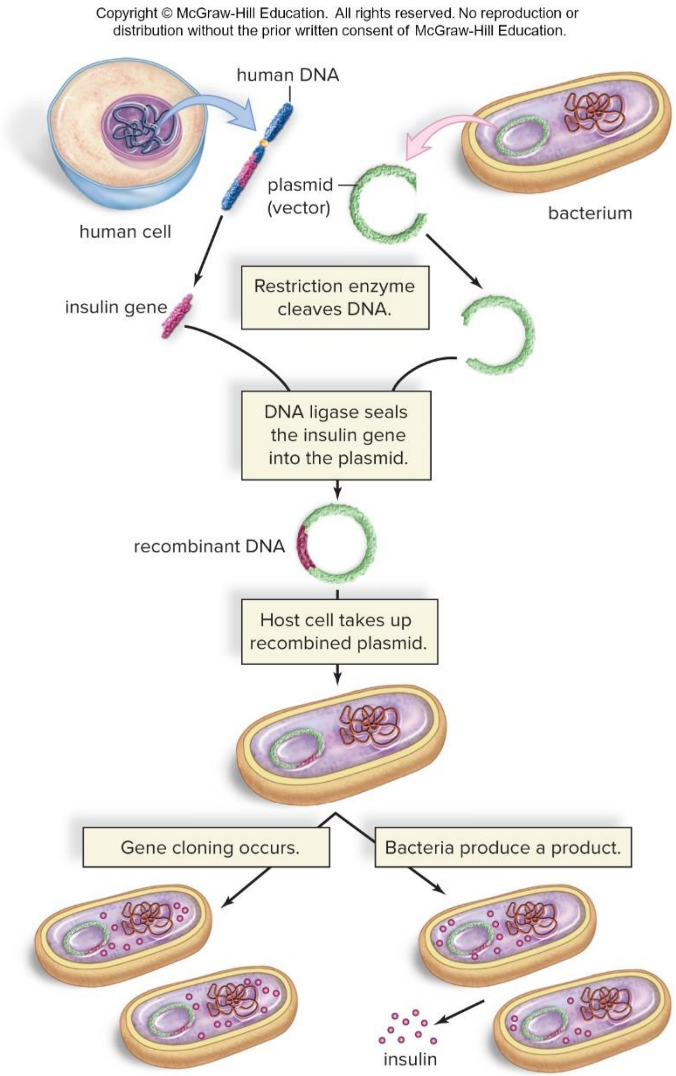
- If the inserted gene is replicated and expressed, we can recover the cloned gene or protein product.
- Cloned genes have many research purposes.
- Humans can be treated with **gene therapy**.

DNA Technology (1)

Recombinant DNA (rDNA) contains DNA from two or more different sources.

- Requires:
  - A **vector**
    - It introduces rDNA into host cell.
    - Plasmids (small accessory rings of DNA from bacteria) are common vectors.
  - Two enzymes are required to introduce foreign DNA into vector DNA.
    - **A restriction enzyme** cleaves DNA.
    - A **DNA ligase** enzyme seals DNA into an opening created by the restriction enzyme.

Cloning a Human Gene



Jump to Cloning a Human Gene Long Description

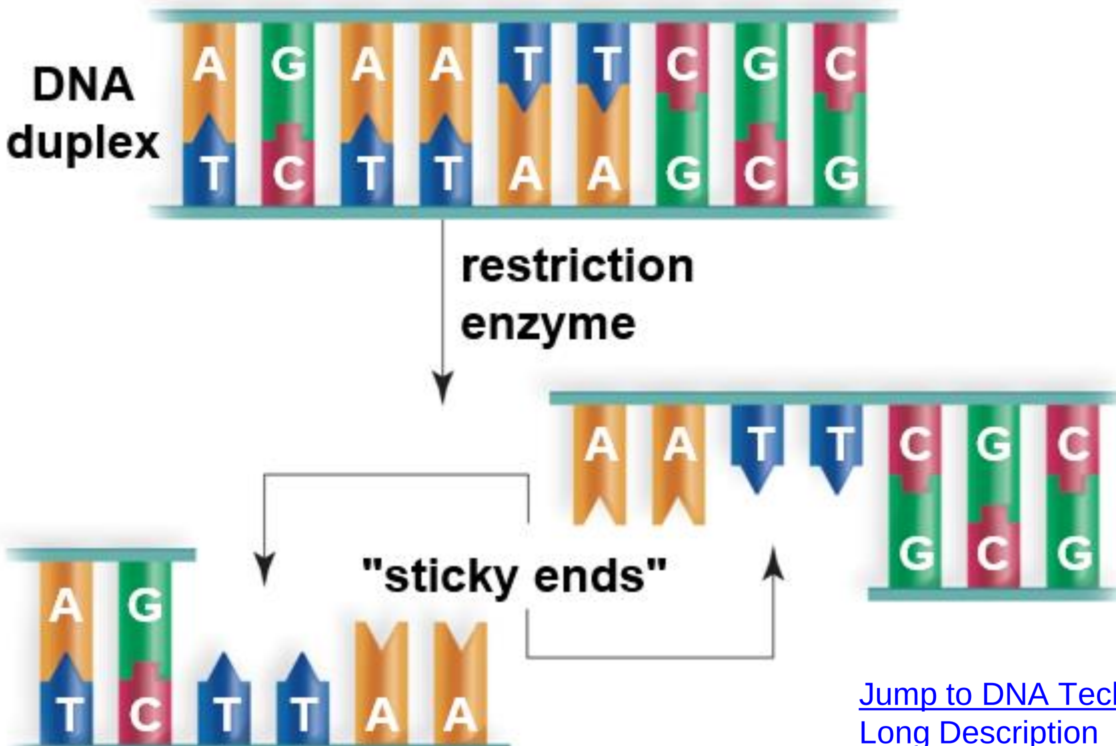
DNA Technology (2)

Restriction enzymes cut DNA at specific points.

It cleaves vector (plasmid) and foreign (human) DNA.

Cleaving DNA makes DNA fragments ending in short, single-stranded segments with “sticky ends.”

The “sticky ends” allow insertion of foreign DNA into vector DNA.



Jump to DNA Technology (2) Long Description

DNA Technology (3)

DNA Ligase

- It seals the foreign gene into the vector DNA.
  - An rDNA (recombinant DNA) molecule has been prepared.

Treated cells (bacteria) take up **plasmids**.

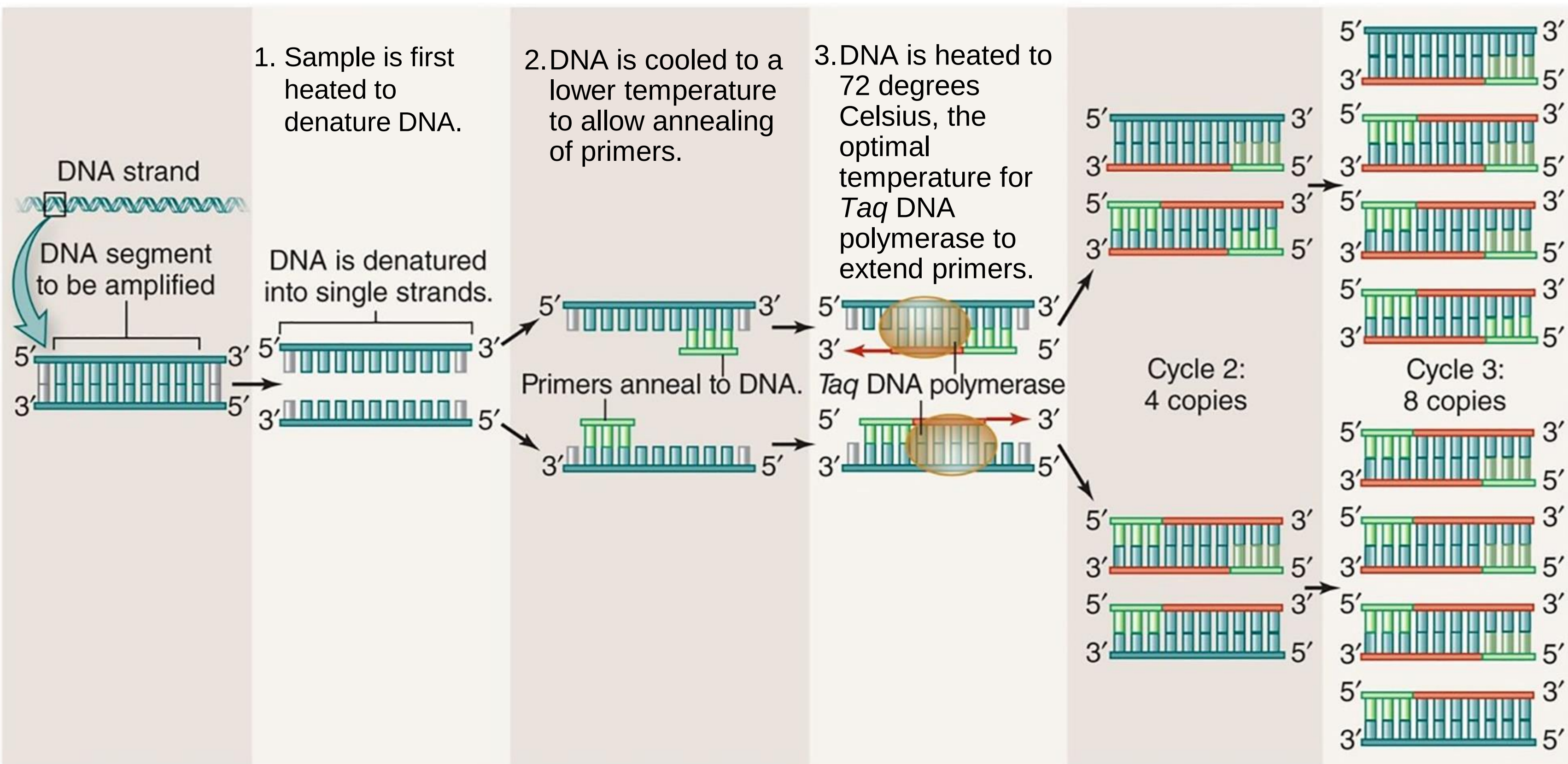
- Bacteria and plasmids reproduce.
- Many copies of the plasmid and many copies of the foreign gene are made.

DNA Technology (4)

The **Polymerase Chain Reaction (PCR)**

- It amplifies (copies) a targeted sequence of DNA.
  - It creates millions of copies of a single gene or a specific piece of DNA in a test tube.
- Requires
  - DNA polymerase
    - Withstands the temperature necessary to separate double-stranded DNA
  - A supply of nucleotides for the new, complementary strand
- The amount of DNA doubles with each replication cycle.

Polymerase Chain Reaction



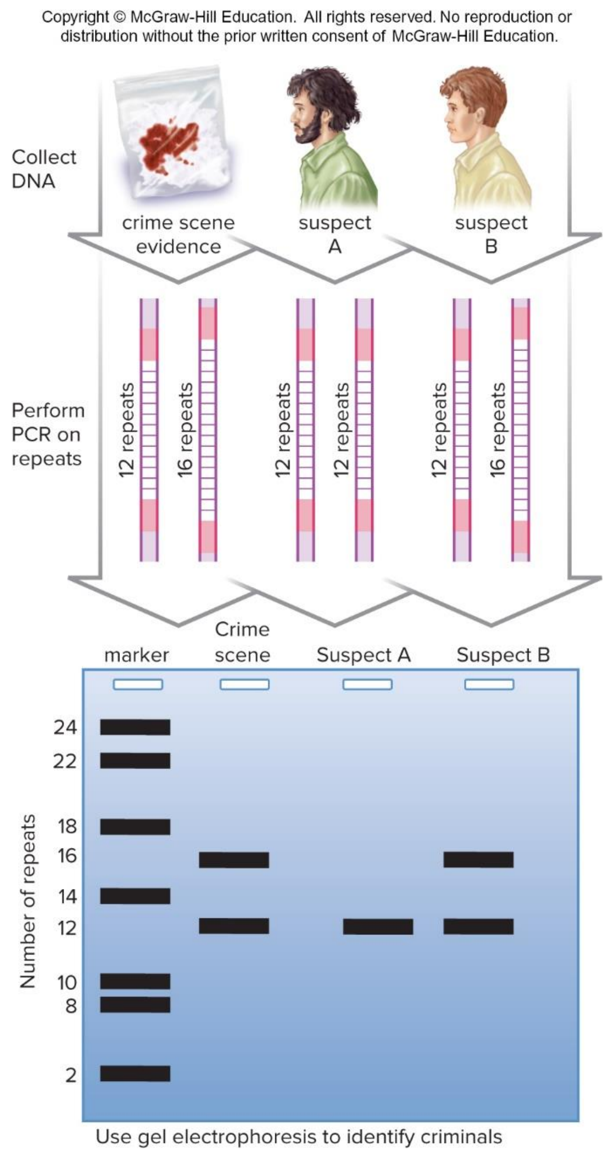
[Jump to Polymerase Chain Reaction Long Description](#)

DNA Technology (5)

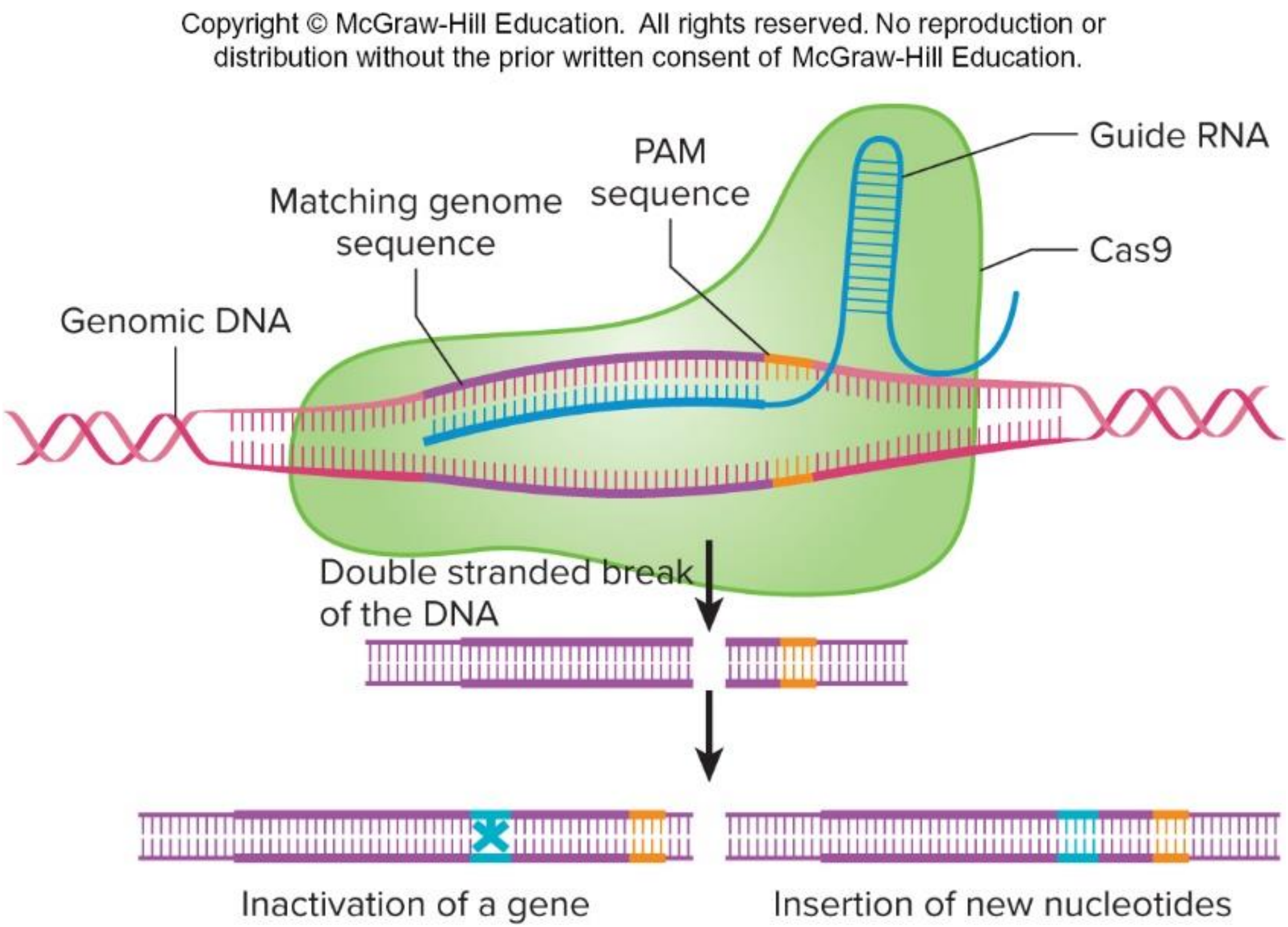
Applications of PCR – analyzing DNA segments

- **Short tandem repeat (STR) profiling** is a technique used to analyze DNA fragment lengths.
  - Treat DNA segment with restriction enzymes
    - A unique collection of different fragments is produced.
    - **Gel electrophoresis** separates the fragments according to their charge/size.
    - It produces a distinctive banding pattern called a **DNA fingerprint (also DNA profiling)**.
- It is usually used to measure the number of repeats of short sequences.
- Used in paternity suits, rape cases, corpse ID, etc.

DNA Fingerprinting



Genome Editing



14.2 Biotechnology Products

Genetically engineered organisms (GMOs) can produce biotechnology products.

Organisms that have had a foreign gene inserted into them are transgenic.

Biotechnology Products (1)

Transgenic bacteria

- A gene of interest is inserted into bacteria.
- Bacteria are grown in large vats called bioreactors and the gene product is harvested.
  - Products on the market include insulin, hepatitis B vaccine, t-PA, and human growth hormone.

Biotechnology Products (2)

Uses of transgenic bacteria

- Transgenic bacteria can produce chemical products.
- Transgenic bacteria promote plant health.
  - Frost-resistant strawberries
- Bioremediation is the process that uses transgenic microorganisms or other organisms such as plants to detoxify and degrade environmental pollutants.
  - Oil-eating bacteria can clean up beaches.
  - One strain was given genes to clean up toxins and a “suicide” gene to self-destruct after the job.

Biotechnology Products (3)

Genetically Modified Plants

- Foreign genes can be introduced into
  - Immature plant embryos or
  - Plant cells called protoplasts that have had the cell wall removed
- Agricultural Crops
  - Foreign genes now give cotton, corn, and potato strains the ability to produce an insect toxin.
  - Soybeans are now resistant to a common herbicide.
- Human Hormones
  - Plants are being engineered to produce human proteins including hormones, clotting factors, and antibodies in their seeds.

Biotechnology Products (4)

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Biotechnology Products (5)

Genetically Modified Animals

- Genes can be inserted into the eggs of animals by
  - Microinjection
  - Vortex Mixing
    - Eggs are placed in an agitator with DNA and silicon-carbide needles.
    - The needles make tiny holes through which the DNA can enter.
    - The fertilized eggs develop into transgenic animals.
    - This procedure has been used to introduce the gene for bovine growth hormone (bGH) into eggs for the purpose of producing larger fishes, cows, pigs, rabbits, and sheep.

Biotechnology Products (6)

Transgenic Animals

- **Gene Pharming**
  - It is the use of transgenic farm animals to produce pharmaceuticals.
  - Genes coded for therapeutic and diagnostic proteins are incorporated into an animal’s DNA.
  - The proteins appear in the animal’s milk.
  - Plans are to produce drugs to treat
    - Cystic fibrosis
    - Cancer
    - Blood diseases, etc.

Applications of Transgenic Animals

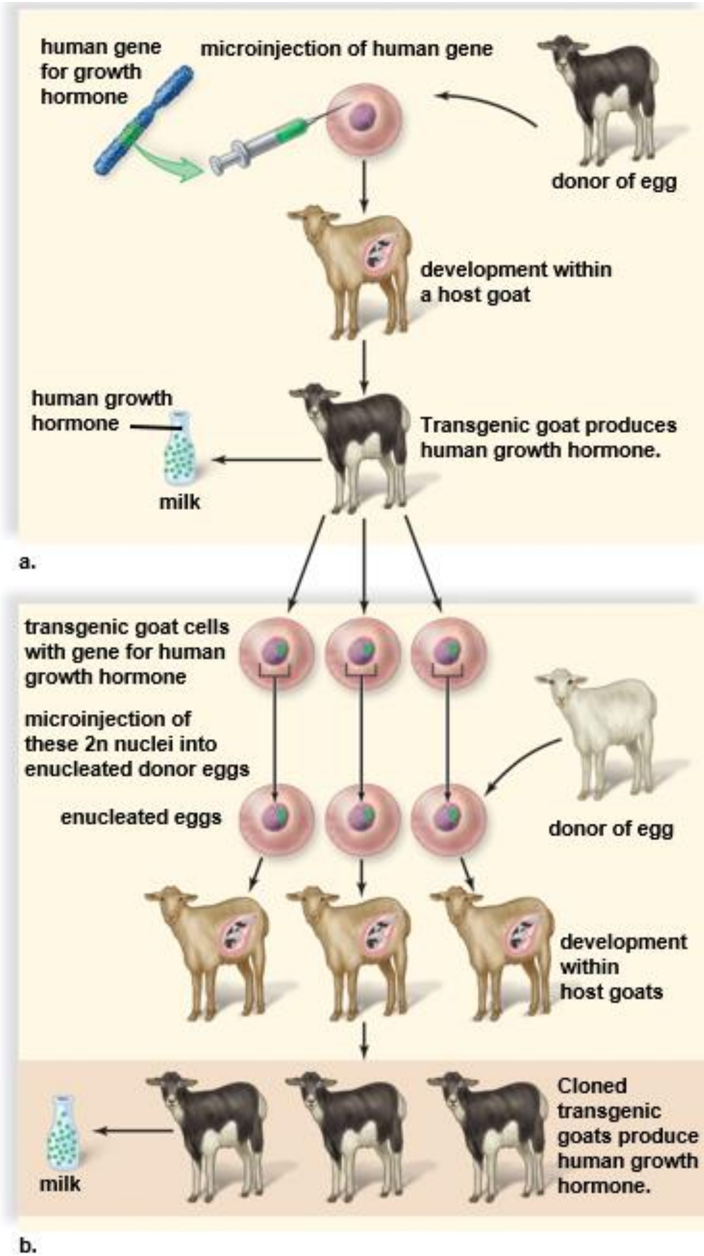
A section of DNA called *SRY* (sex determining region of the Y chromosome) produces a male animal.

- The *SRY* gene was cloned and a copy injected into single-celled mouse embryos, which only produced male embryos.

A knockout mouse has both alleles of a gene removed or made nonfunctional.

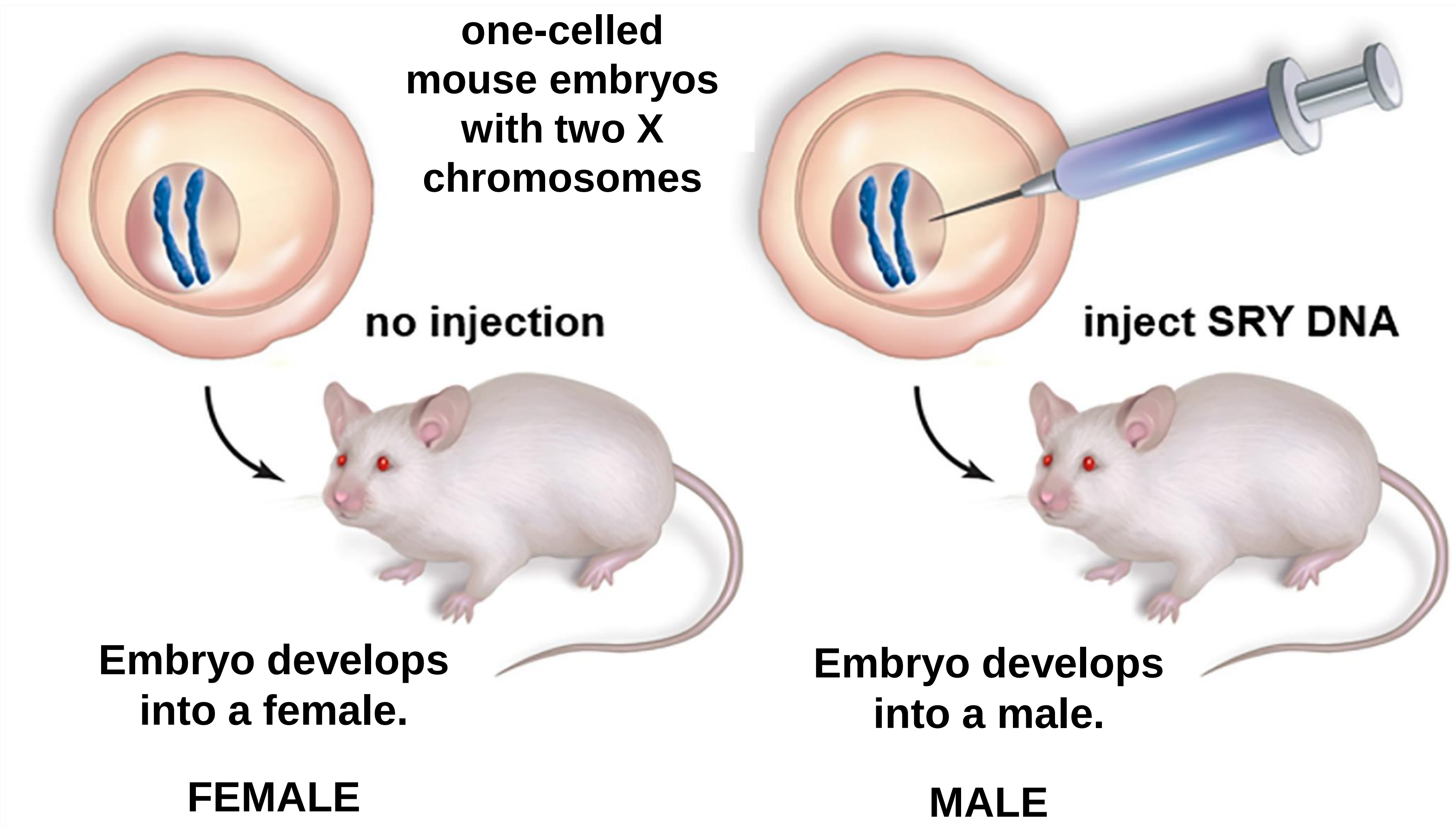
- Scientists made a knockout mouse without the *CTFR* gene, the gene that is mutated in cystic fibrosis.
  - The mutant mouse can be used to test new drug treatments for cystic fibrosis.

Transgenic Mammals Produce a Product



[Jump to Transgenic Mammals Produce a Product Long Description]

Experimental Use of Mice



14.3 Gene Therapy

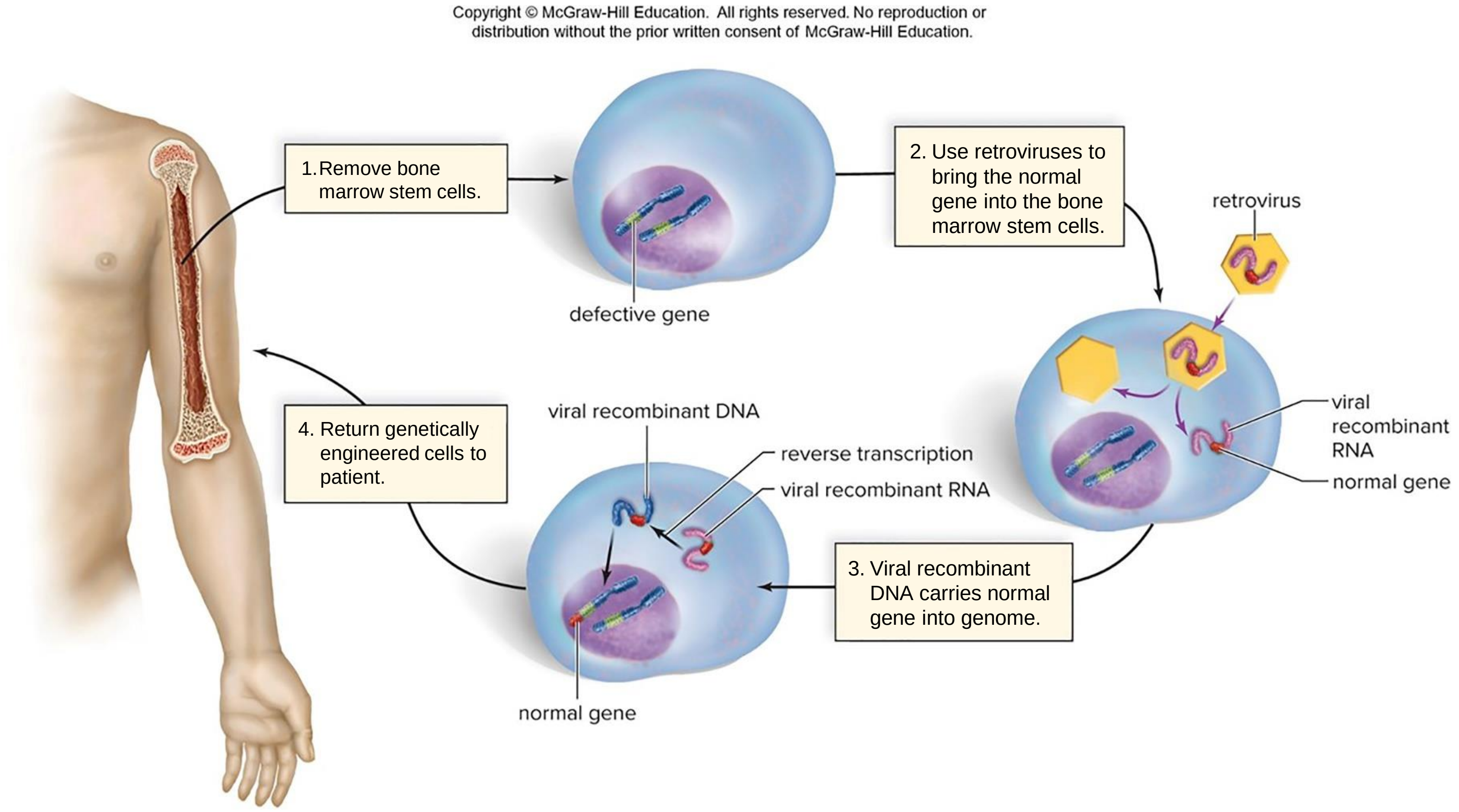
Gene therapy involves procedures to give patients healthy genes to make up for a faulty gene.

It also includes the use of genes to treat genetic disorders and various human illnesses.

There are *ex vivo* (outside body) and *in vivo* (inside body) methods of gene therapy.

- *Ex Vivo*
  - Children with severe combined immunodeficiency (SCID) lack the enzyme adenosine deaminase (ADA).
  - Bone marrow stem cells are infected with a virus carrying a normal gene for the ADA enzyme.
  - One of the earliest uses of ex vivo was for familial hypercholesterolemia.
- *In Vivo*
  - Cystic Fibrosis
  - Nasal/Respiratory Spray
  - Liposomes (lipid globules)
  - Lentiviral Vectors
  - Current research involves the insertion of the *p53* tumor suppressor gene into cancer cells to make tumors responsive to chemotherapy.

Gene Therapy



14.4 Genomics

Genomics is the study of the genomes of humans and other organisms.

Sequencing the Genome

- The **Human Genome Project (HGP)** produced a working draft of all the base pairs in all chromosomes.
- It took 13 years to sequence three billion base pairs along the length of chromosomes.
  - This project involved universities and private labs throughout the world.

Genomics (1)

Genome – All the genetic information of an individual (or species)

Goals of the Human Genome Project

- Determine the base pair sequence.
- Construct a map showing the sequences of genes on specific chromosomes.

Genomics (2)

Human Genome Project

- Humans have between 21,000 and 23,000 genes.
  - Most code for proteins
    - 95% of the average protein-coding gene in humans is introns.
  - Much of the human genome was formerly described as "junk."
    - It does not specify the order of amino acids in a polypeptide.
    - RNA molecules can have a regulatory effect in cells.
    - Polymorphisms were identified.
      - Most polymorphisms vary by only one nucleotide.
      - Certain SNP (single nucleotide polymorphisms) may change an individual's susceptibility to disease or response to treatment.

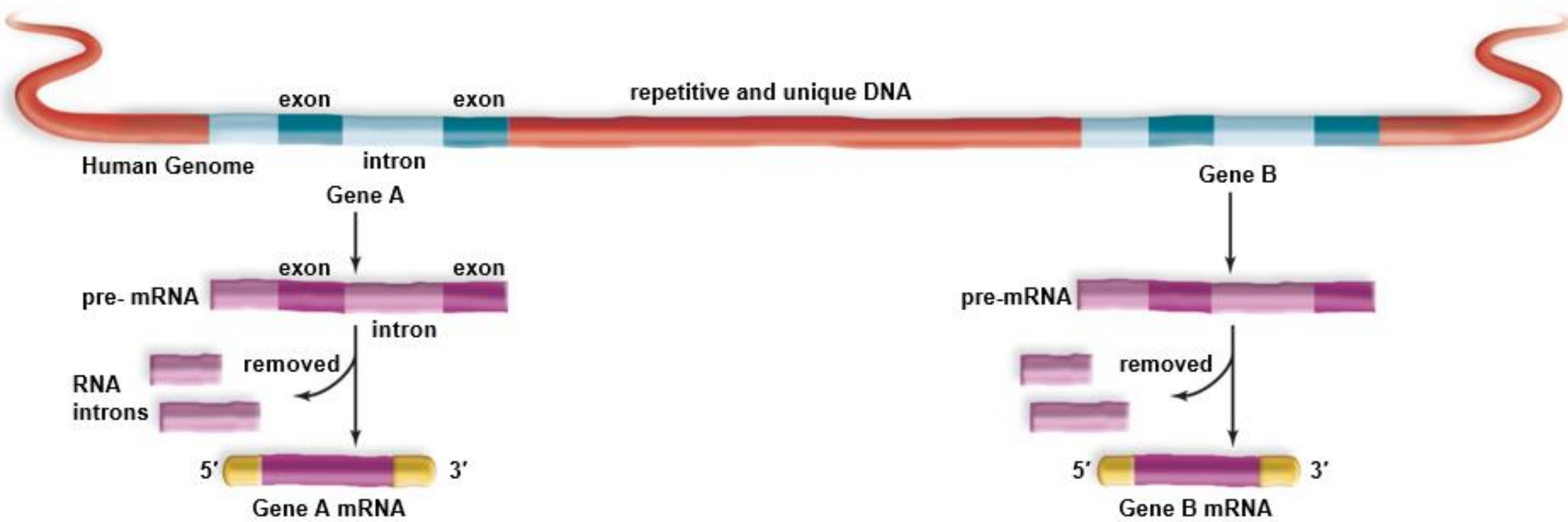
Structural genomics (knowing the base sequence) is being followed by functional genomics.

Genomics (3)

Structure of the Eukaryotic Genome

- Historically, genes were defined as discrete units of heredity that corresponded to a locus on a chromosome.
- Prokaryotes typically possess a single circular chromosome.
- Eukaryotic chromosomes are much more complex.
  - Genes are distributed along the length of a chromosome.
  - Genes are fragmented into exons.

Chromosomal DNA



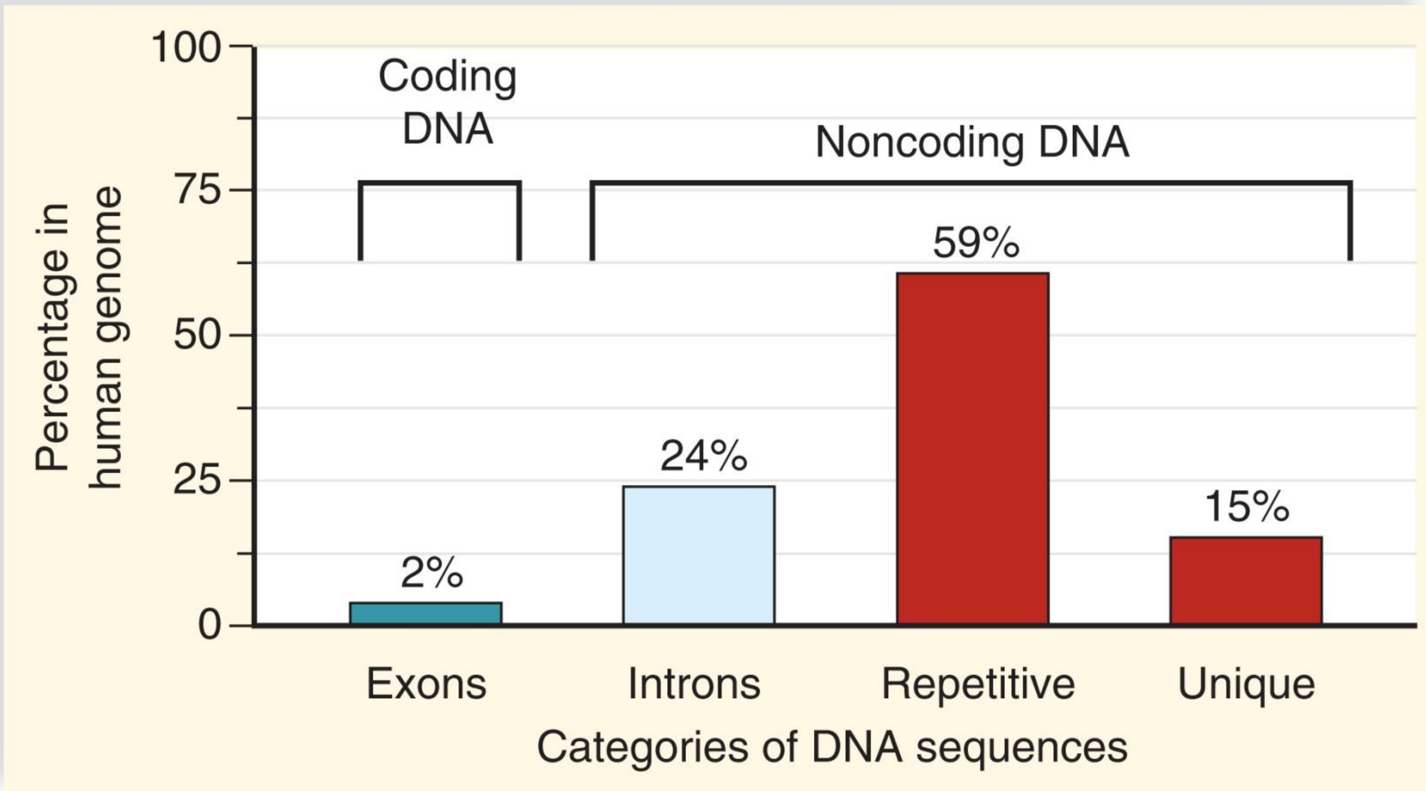
[Jump to Chromosomal DNA Long Description]

Genomics (4)

Eukaryotic Gene Structure

- **Intergenic sequences** are DNA sequences that occur between genes.
- **Repetitive DNA elements** occur when the same sequence of two or more nucleotides is repeated many times along the length of one or more chromosomes.
  - Interspersed repeats (a type of repetitive DNA element) are thought to play a role in the evolution of new genes.
- **Transposons** are specific DNA sequences that have the remarkable ability to move within and between chromosomes.
- **Unique noncoding** DNA (majority of intergenic sequences)

Genomics (5)



Percentage in human genome
100
75
50
25
0
Coding DNA
Noncoding DNA
2%
24%
59%
15%
Exons
Introns
Repetitive
Unique
Categories of DNA sequences

Transposons (1)

Transposons are specific DNA sequences that have the remarkable ability to move within and between chromosomes.

They can act as regulator genes.

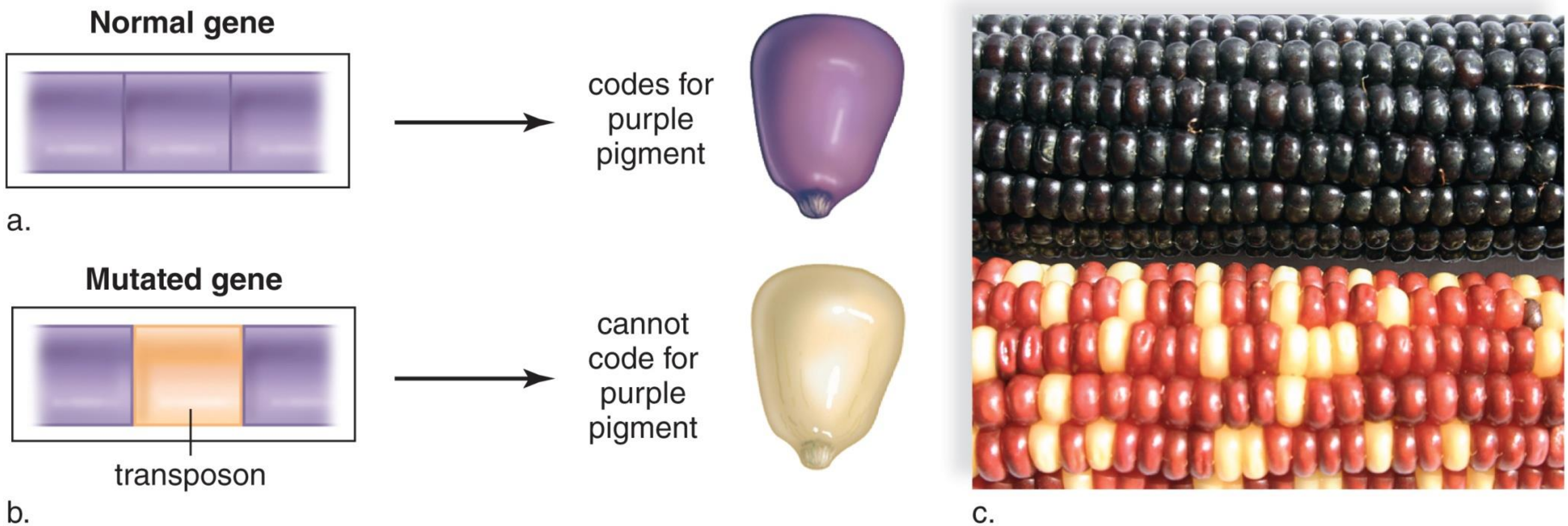
Movement of transposons throughout the genome is thought to be a driving force in evolution.

- Example: the *Alu* repetitive element

Barbara McClintock described transposable elements 60 years ago.

- Jumping genes were first identified in corn.
- They have since been discovered in flies, bacteria, and humans.

Transposons (2)



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Jump to Transposons (2) Long Description

Genomics (6)

Revising the Definition of a Gene

- The “new” definition of the gene should remove the emphasis from the chromosome and place it on the results of transcription.
- The central dogma of genetics has to be expanded.
- A gene product need not be a protein.
  - RNAs are also useful products.
- A gene need not be on one locus on a chromosome.
- Any DNA sequence can result in one or more products.
- In other words, the genetic material need not be DNA.

Genomics (7)

Functional Genomics

- Functional genomics aims to understand the role of the genome in cells or organisms.
- **DNA microarrays** can monitor the expression of thousands of genes simultaneously and tell us:
  - What genes are turned on
  - Environmental conditions that turn on the gene

Genomics (8)

Functional Genomics

- DNA microarrays contain microscopic amounts of known DNA fixed onto a small glass slide or silicon chip in known locations.
- mRNAs bind through to DNA sequences on the chip through complementary base pairing.
  - Allows identification of genes that are active in the cell
- It can be used to identify various mutations in the genome of an individual.
  - This is called the person’s **genetic profile**.
  - The genetic profile may indicate if any genetic illnesses are likely and what type of therapy might be most appropriate.

Genomics (9)

Comparative genomics compares the human genome to the genomes of other organisms.

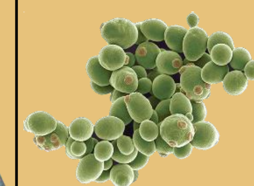
Model organisms have genetic mechanisms and cellular pathways in common with humans.

- Scientists inserted a human gene associated with early-onset Parkinson disease in *Drosophila melanogaster* (fruit flies), and the flies showed symptoms similar to humans with the disorder.
- This shows that flies might be used instead of mice to study therapies for early-onset Parkinson disease.

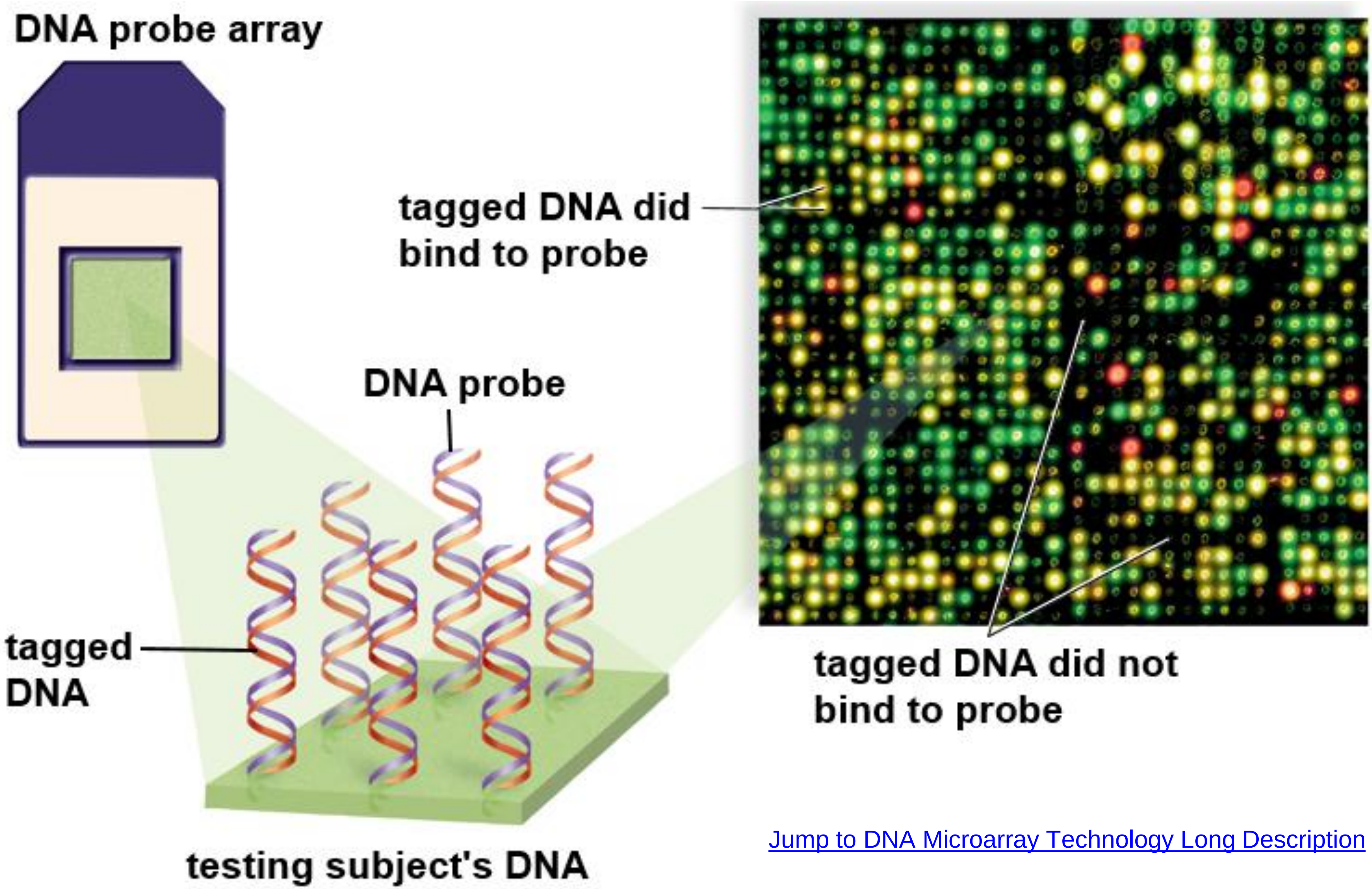
Comparative genomics offers a way to study changes in the genome over time.

Comparison of Sequenced Genomes

Table 14.1 Comparison of Sequenced Genomes

Organism	Homo sapiens (human) 	Mus musculus (mouse) 	Drosophila melanogaster (fruit fly) 	Arabidopsis thaliana (flowering plant) 	Caenorhabditis elegans (roundworm) 	Saccharomyces cerevisiae (yeast) 
Estimated Size	3,200 million bases	2,700 million bases	175 million bases	157 million bases	100 million bases	12 million bases
Estimated Number of Genes	Approximately 20,000	Approximately 20,000	13,600	25,500	19,000	6,200
Chromosome Number	46	40	8	10	12	32

DNA Microarray Technology



[Jump to DNA Microarray Technology Long Description]

Genomics (10)

Proteomics is the study of the structure, function, and interaction of cellular proteins.

The entire collection of a species' proteins is its proteome.

The proteome is larger than the genome.

- Mechanisms such as alternative pre-mRNA splicing increase the number of possible proteins.

Understanding protein function is essential to the development of better drugs.

- Correlate drug treatment to the particular genome
- Increase efficiency and decrease side effects

Once the primary structure of a protein is known

- It should be possible to predict its tertiary structure.
- Computer modeling of the tertiary structures of proteins is an important part of proteomics.

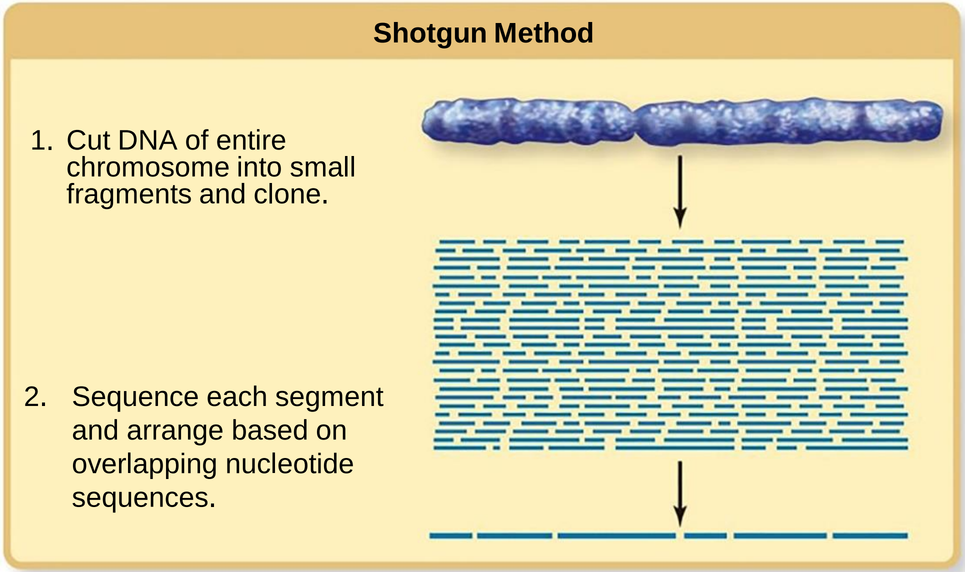
Genomics (11)

Bioinformatics is the application of computer technologies, software, and statistical techniques to the study of biological information.

- Genomics and proteomics produce raw data.
- These fields depend on computer analysis to find significant patterns in the data.
- Scientists hope to find relationships between genetic profiles and genetic disorders.
- BLAST searches identify homologous genes in model organisms.
  - Homologous genes are genes that code for the same proteins.

New computational tools will be needed to accomplish these goals.

Metagenomics



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Jump to Metagenomics Long Description