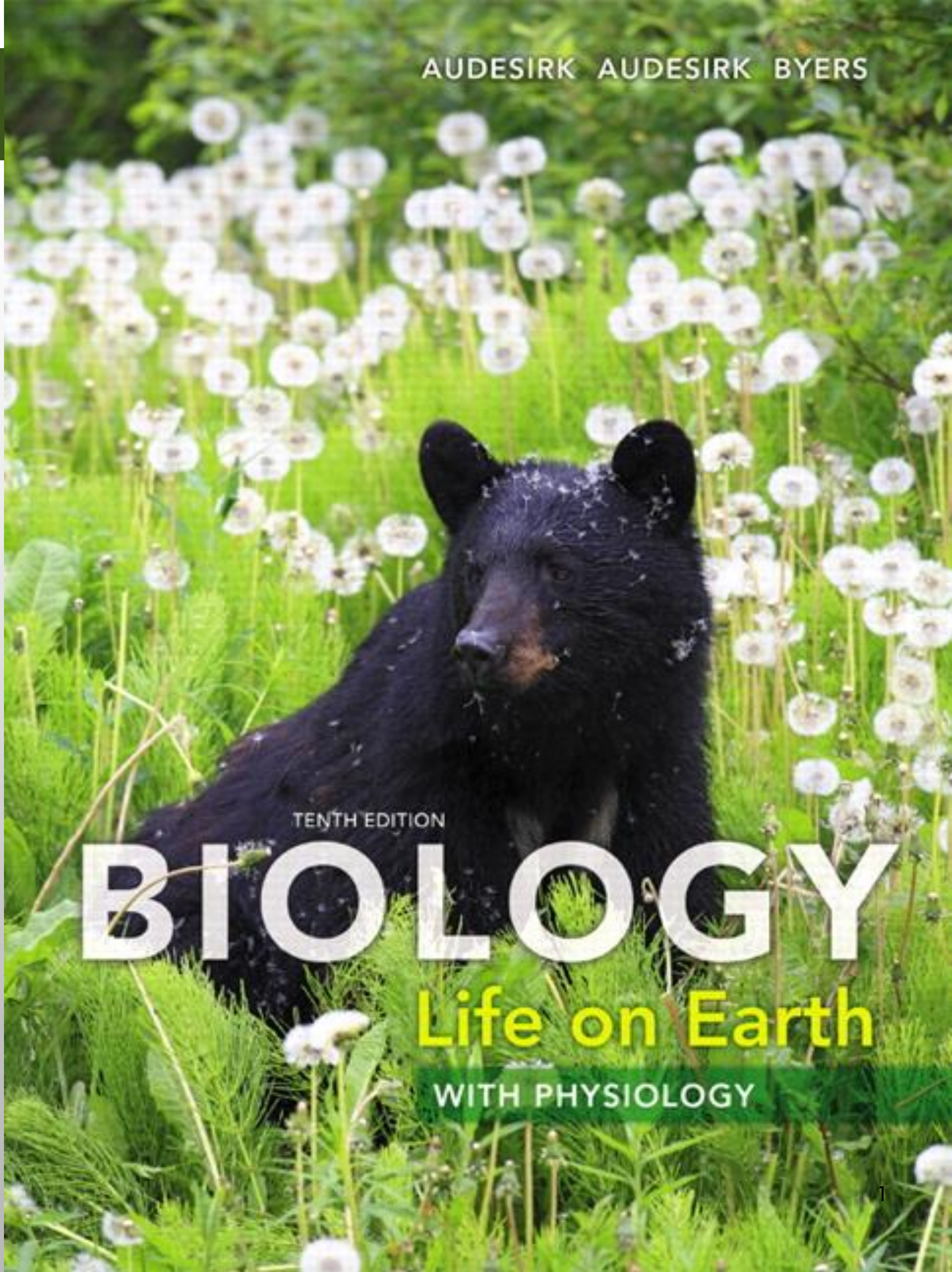
DNA: The Molecule of Heredity

Gene Expression and Regulation



Genes and DNA

- Hereditary information is found in discrete units called genes
  - Genes are segments of DNA located on chromosomes
  - Chromosomes are composed of DNA and proteins

Genes and DNA

- Transformed bacteria revealed the link between genes and DNA
- In the 1920s, Griffith worked with bacteria that caused pneumonia
  - He worked with two strains: R and S
    - R did not cause pneumonia in mice
    - S did cause pneumonia in mice
  - He mixed heat-killed S-strain and living R-strain
    - He tested to see if the mixture could cause pneumonia
    - He isolated living S-strain bacteria from infected mice
    - Some substance from dead S-strain transformed R-strain

Genes and DNA

- The transforming molecule is DNA
  - Avery, MacLeod, and McCarty showed DNA was the transforming material

- DNA, not protein, is the molecule of heredity

The Structure of DNA

- DNA is composed of four nucleotides
  - There are four kinds of nucleotides that differ depending on the nitrogen-containing base
  - Each nucleotide is composed of three parts
    - Phosphate
    - Deoxyribose sugar
    - Nitrogen-containing base

The Structure of DNA

- The four nitrogen-containing bases are:
  - Adenine (A)
  - Guanine (G)
  - Cytosine (C)
  - Thymine (T)
- The pairs of bases are held together by hydrogen bonds

- Chargaff's rule states that equal amounts of adenine and thymine, and guanine and cytosine are found in DNA

The Structure of DNA

- DNA is a double helix of two nucleotide strands
  - In 1952, Maurice Wilkins and Rosalind Franklin used X-ray diffraction in an attempt to determine the structure of DNA
  - James Watson and Francis Crick used Franklin's data to suggest that DNA was a double helix
    - The helix has two sugar–phosphate backbones
    - All of the nucleotides of one strand are oriented in the same direction

The Structure of DNA

- Hydrogen bonds between complementary bases hold two DNA strands together in a double helix
- The sugar – phosphate backbone forms the double helix
  - The backbones are antiparallel
    - Each strand is directional: free sugar on one end, phosphate on other
    - The directions of the two strands are opposite
      - Car headlight-taillight analogy
      - Traffic on two-lane road analogy

The Structure of DNA

- Nitrogen-containing bases from each backbone bond in the middle and are like rungs in a ladder
- Pairing rules:
  - A always pairs with T
  - G always pairs with C
    - This is called complementary base pairing
    - This pairing explains Chargaff's rules

DNA Encodes Genetic Information

- The small number of nucleotides (4) made many scientists skeptical that DNA was the hereditary molecule
- Scientists have learned that genetic information is encoded in the sequence of nucleotides

DNA Replication

- Replication of DNA is a critical event in the cell cycle
  - DNA replication produces identical DNA double helices that are passed on to cells during cell division
- DNA replication produces two DNA double helices, each with one original strand and one new strand
  - DNA replication is quite simple and needs the following:

1) Parental DNA strands
2) Free nucleotides
3) A variety of enzymes
   - DNA helicases
   - DNA polymerases

  - DNA replication is semiconservative

Mutations

- Mutations: changes in the base sequence of DNA
- Accurate replication, proofreading, and DNA repair produce almost error-free DNA
  - DNA replication is highly accurate due to complementary base pairing
  - DNA repair enzymes proofread each daughter strand of DNA after its synthesis and fix mistakes

Mutations

- Toxic chemicals, radiation, and occasional errors during DNA replication cause mutations
  - Certain chemicals and some types of radiation can cause mutations
    - Some of these mutations are fixed by repair enzymes, but some remain

Mutations

- Mutations range from changes in single nucleotide pairs to movements of large pieces of chromosomes
  - Nucleotide substitutions are called point mutations because individual nucleotides in the DNA sequence are changed
    - Insertion mutations occur when one or more nucleotide pairs are inserted into the DNA double helix
    - Deletion mutations occur when one or more nucleotide pairs are removed from the DNA double helix
  - Pieces of chromosomes ranging in size from a single nucleotide pair to massive pieces of DNA are occasionally rearranged
    - These include inversions and translocations

Using DNA Information in Cells

- Most genes contain the information needed to synthesize a protein
  - Genes provide information to make proteins
  - Proteins are the cell’s “molecular workers”

Using DNA Information in Cells

- DNA provides instructions for protein synthesis via RNA intermediaries
  - Ribonucleic acid (RNA) carries the information in DNA necessary for making proteins
- Structural differences between DNA and RNA

DNA	RNA
Double-stranded	Single-stranded
Sugar: deoxyribose	Sugar: ribose
Base – thymine (T)	Base – uracil (U)

Using DNA Information in Cells

- DNA codes for the synthesis of the three kinds of RNA
  - mRNA – messenger RNA
  - rRNA – ribosomal RNA
  - tRNA – transfer RNA

Using DNA Information in Cells

- Messenger RNA: carries the code for protein synthesis from DNA to ribosomes
  - mRNA takes genetic information from the nucleus to the cytoplasm
- Ribosomal RNA: and proteins form ribosomes
  - The small subunit of the ribosome has binding sites for mRNA
  - The large subunit of the ribosome has binding sites for tRNA
- Transfer RNA: carries amino acids to the ribosomes
  - Every cell synthesizes at least one tRNA for each amino acid
  - Complementary base pairs between the tRNA anticodon and the mRNA codon ensure that the correct amino acid is used to synthesize a protein

Using DNA Information in Cells

- Overview: genetic information is transcribed into RNA and then translated into protein
  - In transcription, the information contained in the DNA of a specific gene is copied into RNA
    - This process occurs in the nucleus
  - During translation, the mRNA base sequence is decoded into an amino acid sequence
    - tRNA molecules bring amino acids to the ribosome for assembly into proteins
  - Transcription is the process of copying DNA to RNA using the nucleotide "language"
    - Translation is the process of translating the nucleotide "language" into the "language" of amino acids

Using DNA Information in Cells

- The genetic code uses three bases to specify an amino acid
  - The genetic code translates the sequence of bases in nucleotides into a sequence of amino acids in a protein
  - Codons are sequences of three bases that code for specific amino acids
  - Stop and start codons act as the "punctuation" for an mRNA sequence
    - The start codon (AUG) signifies the start of the mRNA message
    - The three stop codons (UAG, UAA, and UGA) signify the end of the mRNA message
  - The genetic code is redundant
    - There is more than one codon for many amino acids
  - Anticodons in the tRNA are complementary to the codons in mRNA
    - The anticodons ensure that the correct amino acid is placed in the proper sequence in the protein

Transcribing Genetic Information to RNA

- Transcription has three steps: initiation, elongation, and termination

1) Transcription: begins when RNA polymerase binds to the promoter of a gene
   - RNA polymerase binds at the promoter region (TATAAA sequence)
   - The DNA begins to unwind

Transcribing Genetic Information to RNA

2) Elongation: generates a growing strand of RNA
   - RNA polymerase synthesizes RNA that is complementary to template strand of DNA
3) Termination: transcription stops when the RNA polymerase reaches the termination signal
   - RNA polymerase continues down the template strand of DNA until it reaches a sequence of bases called the termination signal
     - RNA polymerase then releases the completed RNA and detaches from the DNA

Translating mRNA into Protein

- Messenger RNA synthesis differs between prokaryotes and eukaryotes
- Messenger RNA synthesis in prokaryotes
  - Prokaryotes commonly transcribe a single, very long mRNA from a series of adjacent genes
  - Transcription and translation typically occur together

Translating mRNA into Protein

- In eukaryotes, a precursor RNA is processed to form mRNA that is translated into protein
- In eukaryotes, the genes that encode proteins are not clustered together as they are in prokaryotes
  - Exons: coding segments
  - Introns: noncoding segments
- Transcription of a eukaryotic gene produces a very long RNA strand
  - More nucleotides are added to the beginning and end of the RNA, forming a “cap” and a “tail”
  - The introns are removed from the RNA and the exons are spliced together, forming mRNA

Translating mRNA into Protein

- Functions of intron – exon gene structure
  - This structure appears to allow a cell to produce multiple proteins from a single gene
  - This structure may allow eukaryotes to evolve new proteins with new functions

Translating mRNA into Protein

- During translation, mRNA, tRNA, and ribosomes cooperate to synthesize proteins
- Like transcription, translation has three steps:

1) Initiation: translation begins when tRNA and mRNA bind to a ribosome
   - The preinitiation complex scans the mRNA for an initiation codon, AUG, which codes for methionine
   - The initiation complex forms
   - The large ribosomal subunit joins the complex

Translating mRNA into Protein

2) Elongation: amino acids are added one at a time to the growing protein chain
   - The ribosome holds two mRNA codons in both binding sites
     - A peptide bond forms between the two amino acids
   - The complex moves one codon along mRNA
     - This process repeats one codon at a time
3) Termination: a stop codon signals the end of translation
   - Translation stops when the stop codon is reached
   - Ribosome releases the complete protein
   - Ribosome and mRNA dissociate

Translating mRNA into Protein

- Decoding the sequence of bases in DNA into the sequence of amino acids in protein
  - With some exceptions, each gene codes for the amino acid sequence of a protein
  - Transcription of a protein-coding gene produces an mRNA that is complementary to DNA, and starting with AUG, each codon in mRNA is a sequence of three bases that specifies an amino acid or a “stop”
  - Enzymes in the cytoplasm attach the appropriate amino acid to tRNA
  - During translation, tRNAs carry their attached amino acid to the ribosome based on the tRNA anticodon
    - The amino acids are linked together to form a protein

Mutation Effect on Protein Structure and Function

- Mutation: a change in the DNA sequence of a gene
- The effects of mutations depend on how they alter the codons of mRNA
  - Inversions and Translocations
    - Inversions: mutations that occur when a piece of DNA is cut out of a chromosome, flipped around, and reinserted
    - Translocations: mutations that occur when a piece of DNA is removed from one chromosome and attached to another
    - These mutations can be benign or very serious

Mutation Effect on Protein Structure and Function

- The effects of mutations depend on how they alter the codons of mRNA
  - Deletions and insertions
    - The effects of deletions and insertions usually depend on how many nucleotides are removed or added
  - Substitutions
    - This type of mutation may cause four different effects
      - The amino acid sequence of a protein may be unchanged
      - Protein function may be unchanged
      - Protein function may be changed by an altered amino acid sequence
      - Protein function may be destroyed by a premature stop codon

Gene Expression Regulation

- Some genes are expressed in all cells
  - Other genes are expressed exclusively in certain cell types
  - Regulation may occur at the level of transcription, translation, or protein activity

Gene Expression Regulation

- In prokaryotes, gene expression is primarily regulated at the level of transcription
  - Prokaryotic DNA is organized into packages called operons, which contain various components
    - A regulatory gene
    - A promoter
    - An operator
    - Structural genes
  - The lactose operon is an example of gene regulation in prokaryotes

Gene Expression Regulation

- In eukaryotes, gene expression is regulated at many levels
  - Regulation of gene expression in eukaryotic cells can be controlled at any of a number of steps
    - Cells can control the frequency at which an individual gene is transcribed
    - The same gene may be used to produce different mRNAs and protein products
    - Cells can control the stability and translation of mRNAs
    - Proteins may require modification before they can carry out their functions
    - Cells can control the rate at which proteins are degraded
  - Regulatory proteins binding to a gene's promoter alter its rate of transcription
    - Many transcription factors require activation before they can affect gene transcription

Gene Expression Regulation

- In eukaryotes, gene expression is regulated at many levels
  - Epigenetic controls alter gene transcription and translation
    - Epigenetics is the study of gene expression
    - Epigenetic control works in three ways
      - Epigenetic modification of DNA may suppress transcription
      - Epigenetic modification of histones may enhance transcription
      - Changing transcription and translation through the actions of several types of RNA

Gene Expression Regulation

- In eukaryotes, gene expression is regulated at many levels
  - Noncoding RNA may alter transcription or translation
    - MicroRNA and RNA interferences
      - MicroRNA binds mRNA and interferes with translation
    - Altering transcription with noncoding RNA
      - Some noncoding RNAs bind to RNA polymerase, blocking transcription
      - Other noncoding RNAs alter DNA or histones on specific parts of a chromosome
      - The X chromosome may be condensed into a Barr body, and inactivated, preventing transcription and altering gene expression