LECTURE PRESENTATIONS
For CAMPBELL BIOLOGY, NINTH EDITION
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Chapter 17

From Gene to Protein

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Overview of gene expression

Central Dogma of Molecular Biology:

transcription translation

DNA → RNA → Protein

4-character alphabet → 20-character alphabet

- Questions:
  - A gene (DNA) is physically located on what molecule?
  - Where in a cell is DNA stored?

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Basic Principles of Transcription and Translation

- RNA is the bridge between genes and the proteins for which they code
- **Transcription** is the synthesis of RNA under the direction of DNA
- Transcription produces **messenger RNA (mRNA)**
- **Translation** is the synthesis of a polypeptide, using information in the mRNA
  - What are the building blocks of polypeptides?
- Where does translation occurs?

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- A **primary transcript** is the initial RNA transcript from any gene prior to processing
- The *central dogma* is the concept that cells are governed by a cellular chain of command: DNA → RNA → protein

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Figure 17.3

(a) Bacterial cell

(b) Eukaryotic cell

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Figure 17.3a-1

Transcription and Translation in Prokaryotes

- In prokaryotes, translation of mRNA can begin before transcription has finished

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Transcription and Translation in Eukaryotes

- In a eukaryotic cell, the nuclear envelope separates transcription from translation
- Eukaryotic RNA transcripts are modified through RNA processing to yield finished mRNA

The Genetic Code

- The genetic code refers to the code (rules) that governs how a DNA sequence is converted to a protein (amino acid) sequence
- There are 20 amino acids, but only four nucleotide bases in DNA (and RNA)
  - What is the minimum number of nucleotides that could code for an amino acid?

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- The genetic code is a triplet code where a 3-nucleotide DNA word codes for a 3-nucleotide mRNA word (a **codon**) which codes for an amino acid

- During transcription, one of the two DNA strands, called the **template strand,** provides a template for ordering the sequence of complementary nucleotides in an RNA transcript
- The template strand is always the same strand for a given gene
- During translation, the mRNA base triplets, called **codons**, are read in the 5′ to 3′ direction
- Each codon specifies the amino acid (one of 20) to be placed at the corresponding position along a polypeptide

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- Codons along an mRNA molecule are read by translation machinery in the 5′ to 3′ direction
- Each codon specifies the amino acid (one of 20) to be placed at the corresponding position along a polypeptide

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Cracking the Code

- All 64 codons were deciphered by the mid-1960s
- Of the 64 triplets, 61 code for amino acids; 3 triplets are “stop” signals to end translation
- The genetic code is redundant (more than one codon may specify a particular amino acid) but not ambiguous; no codon specifies more than one amino acid
- Codons must be read in the correct **reading frame** (correct groupings) in order for the specified polypeptide to be produced

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Properties of the Genetic Code

- 64 triplets
  - 61 code for amino acids
  - 3 triplets are "stop" codons
- The genetic code is redundant but not ambiguous

First mRNA base (5′ end of codon)	Second mRNA base: U	C	A	G	Third mRNA base (3′ end of codon)
U	UUU, UUC: Phe	UCU, UCC, UCA, UCG: Ser	UAU, UAC: Tyr	UGU, UGC: Cys	U
	UUA, UUG: Leu		UAA Stop	UGA Stop	C
			UAG Stop	UGG Trp	A
					G
C	CUU, CUC, CUA, CUG: Leu	CCU, CCC, CCA, CCG: Pro	CAU, CAC: His	CGU, CGC, CGA, CGG: Arg	U
			CAA, CAG: Gln		C
					A
					G
A	AUU, AUC, AUA: Ile	ACU, ACC, ACA, ACG: Thr	AAU, AAC: Asn	AGU, AGC: Ser	U
	AUG Met or start		AAA, AAG: Lys	AGA, AGG: Arg	C
					A
					G
G	GUU, GUC, GUA, GUG: Val	GCU, GCC, GCA, GCG: Ala	GAU, GAC: Asp	GGU, GGC, GGA, GGG: Gly	U
			GAA, GAG: Glu		C
					A
					G

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The Universality of the Genetic Code

- The genetic code is nearly universal, shared by the simplest bacteria to the most complex animals
- Genes can be transcribed and translated after being transplanted from one species to another
- Examples: http://blogs.scientificamerican.com/observations/2011/09/12/jellyfish-genes-make-glow-in-the-dark-cats/
- http://www.nature.com/nmeth/journal/vaop/ncurrent/full/nmeth.1703.html

Pig expressing a jellyfish gene

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Transcription is the DNA-directed synthesis of RNA: *a closer look*

- Transcription consists of three steps
  - Initiation
    - The DNA sequence where RNA polymerase attaches is called the **promoter**
  - Elongation
    - **RNA polymerase** pries the DNA strands apart and hooks together the RNA nucleotides
    - The RNA is complementary to the DNA template strand, but uracil replaces thymine
  - Termination
    - in bacteria, the sequence signaling the end of transcription is called the **terminator**

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RNA Polymerase Binding and Initiation of Transcription

- Promoters signal the transcriptional **start point** and usually extend several dozen nucleotide pairs upstream of the start point
- **Transcription factors** mediate the binding of RNA polymerase and the initiation of transcription
- The completed assembly of transcription factors and RNA polymerase II bound to a promoter is called a **transcription initiation complex**
- A promoter called a **TATA box** is crucial in forming the initiation complex in eukaryotes

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Figure 17.8

- Transcription in eukaryotes

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Elongation of the RNA Strand

- As RNA polymerase moves along the DNA, it untwists the double helix, 10 to 20 bases at a time
- Transcription progresses at a rate of 40 nucleotides per second in eukaryotes
- A gene can be transcribed simultaneously by several RNA polymerases
- Nucleotides are added to the 3′ end of the growing RNA molecule

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Figure 17.9

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Termination of Transcription

- The mechanisms of termination are different in bacteria and eukaryotes
- In bacteria, the polymerase stops transcription at the end of the terminator and the mRNA can be translated without further modification
- In eukaryotes, RNA polymerase II transcribes the polyadenylation signal sequence (AAUAAA); the RNA transcript is released 10–35 nucleotides past this polyadenylation sequence

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Eukaryotic cells modify RNA after transcription

- Enzymes in the eukaryotic nucleus modify pre-mRNA (**RNA processing**) before the genetic messages are dispatched to the cytoplasm
- During RNA processing, both ends of the primary transcript are usually altered
- Also, usually some interior parts of the molecule are cut out, and the other parts spliced together

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Alteration of mRNA Ends

- Each end of a pre-mRNA molecule is modified in a particular way
  - The 5′ end receives a modified nucleotide **5′ cap**
  - The 3′ end gets a **poly-A tail**
- These modifications share several functions
  - They seem to facilitate the export of mRNA
  - They protect mRNA from hydrolytic enzymes
  - They help ribosomes attach to the 5′ end

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mRNA in Eukaryotes

- Note that pre-mRNA
  - Does *not* contain the 5' Cap or Poly-A tail
  - Does contain introns which are spliced out

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Split Genes and RNA Splicing

- Most eukaryotic genes and their RNA transcripts have long noncoding stretches of nucleotides that lie between coding regions
- These noncoding regions are called intervening sequences, or **introns**
- The other regions are called **exons** because they are eventually expressed, usually translated into amino acid sequences
- **RNA splicing** removes introns and joins exons, creating an mRNA molecule with a continuous coding sequence

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Figure 17.11

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The Functional and Evolutionary Importance of Introns

- Some introns contain sequences that may regulate gene expression
- Some genes can encode more than one kind of polypeptide, depending on which segments are treated as exons during splicing
- This is called **alternative RNA splicing**
- Consequently, the number of different proteins an organism can produce is much greater than its number of genes

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- Proteins often have a modular architecture consisting of discrete regions called **domains**
- In many cases, different exons code for the different domains in a protein
- Exon shuffling may result in the evolution of new proteins

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Figure 17.13

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Concept 17.5: Mutations of one or a few nucleotides can affect protein structure and function

- **Mutations** are changes in the genetic material of a cell or virus
- **Point mutations** are chemical changes in just one base pair of a gene
- The change of a single nucleotide in a DNA template strand can lead to the production of an abnormal protein

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Types of Small-Scale Mutations

- Point mutations within a gene can be divided into two general categories
  - Nucleotide-pair substitutions
  - One or more nucleotide-pair insertions or deletions

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Substitutions

- A **nucleotide-pair substitution** replaces one nucleotide and its partner with another pair of nucleotides
- **Silent mutations** have no effect on the amino acid produced by a codon because of redundancy in the genetic code
- **Missense mutations** still code for an amino acid, but not the correct amino acid
- **Nonsense mutations** change an amino acid codon into a stop codon, nearly always leading to a nonfunctional protein

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Figure 17.24a

Wild type

(a) Nucleotide-pair substitution: silent

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Figure 17.24b

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Figure 17.24c

Wild type

(a) Nucleotide-pair substitution: nonsense

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Insertions and Deletions

- **Insertions** and **deletions** are additions or losses of nucleotide pairs in a gene
- These mutations have a disastrous effect on the resulting protein more often than substitutions do
- Insertion or deletion of nucleotides may alter the reading frame, producing a **frameshift mutation**

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Figure 17.24d

Wild type

(b) Nucleotide-pair insertion or deletion: frameshift causing immediate nonsense

1 nucleotide-pair insertion

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Figure 17.24e

Wild type

(b) Nucleotide-pair insertion or deletion: frameshift causing extensive missense

1 nucleotide-pair deletion

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Figure 17.24f

Wild type

(b) Nucleotide-pair insertion or deletion: no frameshift, but one amino acid missing

3 nucleotide-pair deletion

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Translation

- A cell translates a mRNA message into protein with the help of **transfer RNA (tRNA)**
- tRNA transfer amino acids to the growing polypeptide in a ribosome
- Translation is a complex process in terms of its biochemistry and mechanics

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tRNA structure

Figure 17.15

- Each carries a specific amino acid on one end
- Each has an **anticodon** on the other end; the anticodon base-pairs with a complementary codon on mRNA

(a) Two-dimensional structure

(b) Three-dimensional structure

(c) Symbol used in this book

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Ribosomes

- Ribosomes facilitate specific coupling of tRNA anticodons with mRNA codons in protein synthesis
- The two ribosomal subunits (large and small) are made of proteins and **ribosomal RNA (rRNA)**
- Bacterial and eukaryotic ribosomes are somewhat similar but have significant differences: some antibiotic drugs specifically target bacterial ribosomes without harming eukaryotic ribosomes

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Figure 17.17

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- A ribosome has three binding sites for tRNA
  - The **P site** holds the tRNA that carries the growing polypeptide chain
  - The **A site** holds the tRNA that carries the next amino acid to be added to the chain
  - The **E site** is the exit site, where discharged tRNAs leave the ribosome
- As with transcription, there are three steps to translation
  - Initiation
  - Elongation
  - Termination

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Initiation of Translation

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Elongation of the Polypeptide Chain

- During the elongation stage, amino acids are added one by one to the preceding amino acid at the C-terminus of the growing chain
- Each addition involves proteins called elongation factors and occurs in three steps: codon recognition, peptide bond formation, and translocation
- Translation proceeds along the mRNA in a 5′ to 3′ direction

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Termination of Translation

- Termination occurs when a stop codon in the mRNA reaches the A site of the ribosome
- The A site accepts a protein called a release factor
- The release factor causes the addition of a water molecule instead of an amino acid
- This reaction releases the polypeptide, and the translation assembly then comes apart

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Termination of Translation

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Polyribosomes

- A number of ribosomes can translate a single mRNA simultaneously, forming a **polyribosome** (or **polysome**)
- Polyribosomes enable a cell to make many copies of a polypeptide very quickly

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Completing and Targeting the Functional Protein

- Often translation is not sufficient to make a functional protein
- Polypeptide chains are modified after translation or targeted to specific sites in the cell
  - Proteins targeted to specific sites in the cell contain a **signal sequence**
  - What organelle functions as a "highway" within a cell?

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What is a gene?

- a region of DNA that can be expressed to produce a final functional product, either
  - a polypeptide or
  - an RNA molecule

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