DNA, Genes and their Regulation

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Learning Objectives
After this talk, you should be able to

• Account for the structure of DNA and RNA including their similarities and differences, and how complementary base pairing can take place between two DNA strands or between a DNA and an RNA strand. Describe how DNA is packed into chromosomes.

• Describe the Central Dogma of Molecular Biology, in particular transcription. Deduce the sequence of a pre-mRNA molecule that has been transcribed from a given gene.

• Sketch the structure of a eukaryotic gene and explain the difference between exons and introns.

• Describe how gene expression is regulated in eukaryotes emphasizing the many different levels this can be achieved on.
DNA
Deoxyribose Nucleic Acid

- Deoxyribose, phosphate, base (Adenine, Thymine, Guanine, Cytosine)
- Double helix: Via hydrogen bonds, A pairs with T and C with G.
- The two strings are antiparallel.
RNA
Ribonucleic Acid

- **RNA** differs from DNA in three ways:
  - RNA is usually single-stranded
  - The sugar is ribose, not deoxyribose
  - RNA contains the base uracil (U) instead of thymin (T)

- **RNA** can basepair with single-stranded DNA (adenin pairs with uracil instead of with thymin)

- An **RNA**-strand can fold and basepair with itself (creating a secondary structure)
Genes are sequences of DNA

>gi|6007800:215-1075 Escherichia coli beta-lactamase variant TEM-1D (blaTEM-1D) gene, complete cds

5’ATGAGTATTCAACATTTCCGTGTCGCCCTTTATTCCTCTTTTTTGCGGCATTTTGCCTTCCTGTTTTTGCTC
ACCCAGAAACGCTGGTGAAAGTAAAGATGCTGAAGATCAGTTGGGTGCACGAGTGGGTTACATCGAGCT
GGATCTCAACAGCGGTAGATCCTTGAGAGTTTTCGCCCCGAAGAAGACGTTTTTCACAATGATGAGCACTTTT
AAAGTTCTGCTATGTGTCGGTATATTATTCCGTGTTGACGCCGGCCAGAGCAACTGCGTGCACATAC
ACTATTCTCAAGAATGACTTGGTTGAGTACTCAACCAGTCAACAGAAAGCATCATTACGGATGACATGACAGT
AAGAGAATTATGCGATGCTGCCATAACCATGAGTGATAAACAATGCGGCACACTTACTTCTGACAAACGATC
GGAGGACCGAAGGAGCTAACCAGCTTTTTTGCAAACACATGGGGGATCATGTAACCCGCCTTGATCGTGGG
AACCAGGAGCTGGAATGACGCATTACAAACGACGAGCGTGCACCCACAGATGCTGCAGCAATGGCAACAAC
GGTTCGCAAATATTACATTGCGGAACACTACTTACTCTAGCTTCCCGCAAACAAATTATAAGACTGGAATGAG
GCGGATAAAGTTGGAGACACACTTCTCGCTGCGCCCTTCCCGGGCTGGCTGTTATTGTCAATTCTGG
AGCGCGGTAGACGTGGATCCTCCGCGATCATTGCAGCACTGGGGCCAGATGTAAGCCCTCCCGATCGT
AGTTATCTACAGCAGCGGGAGTCAGCGCAACTATGGATGACAGATCGTGCAGATGATGGTGC
TCATGATTAAGCATTTGGTAA 3’
DNA is packed into chromosomes

1. A DNA molecule binds with histones, forming a vast number of nucleosomes.
2. Nucleosomes form "beads" on DNA "string."
3. Nucleosomes pack into a coil that twists into another larger coil, and so forth, producing condensed, supercoiled chromatin fibers.
4. The coils fold to form loops.
5. The loops coil even further, forming a chromosome.
Learning objective
Be able to account for the structure of DNA and RNA including their similarities and differences and how complementary base pairing can take place between two DNA strands or between a DNA and an RNA strand. Describe how DNA is packed into chromosomes.

Typical exam questions

Q: What is the chemical group called that is attached to the 5’ carbon atom in deoxyribose in DNA?

Q: Below is shown a single stranded DNA molecule. Which of the strands shown in a. - e. is the complementary DNA strand?

Single stranded DNA molecule: 5’ ATGCCCGGG 3’

a. 3’ ATGCCCGGG 5’
b. 5’ CCCGGGCAT 3’
c. 3’ CCCGGGCAT 5’
d. 3’ UACGGGCCC 5’
e. 5’ TACGGGCCC 3’
The Central Dogma of Molecular Biology

- Genetic information is transferred from DNA to RNA to protein. (Almost) never in the opposite direction (Francis Crick).
TRANSCRIPTION

INTRODUCTION

For a protein-coding gene to be expressed, it must first be transcribed. In transcription, the code in the gene’s DNA is converted into a complementary code in an RNA molecule. The RNA molecule then participates in the second phase of gene expression: translation. In translation, the code in the RNA is converted into an amino acid sequence in a protein. Transcription and translation are the main events of gene expression.

In the accompanying animation, we focus on transcription, which occurs in three phases: initiation, elongation, and termination.

Select NARRATED to view the animation with audio narration. Select STEP-THROUGH to view the tutorial as a series of discrete steps.

http://bcs.whfreeman.com/thelifewire9e/default.asp#542578__591301__
Template or Coding Strand?

>gi|6007800:215-1075 Escherichia coli beta-lactamase variant TEM-1D (blaTEM-1D) gene, complete cds
ATGAGTATTCAATTTGTCGCCCTTATTCCCTTTTTTGCCGGCATTTTTGCTC
ACCCAGAACGCTGTTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTCACGAGTGGGTTACATCGAGCT
GGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCCAATGATGAGACCTTT
AAAGTTCTGCTATGTGGTGCGGTATTATCCCGTGTTGACGCCGGCAAGGGAACAATCGGTCGCCGATAC
ACTATTTCTGAGATGACTTGGTGTAATCTACTACGACCATAGAAGGATATCGGATAGCTGACCAGT
AAGAGAATTATAGTGCAGTGCCTCAATAACCATGAGTAACACTGCGCCCAACTTACATTGACACAAGATC
GAGGGACGGAAGGACGTCAAACCGCTTTTTTGCAACAACATGGGGGTATGTAACCCGGCCCTTGTGATTC
AAACCCGGAGCTGTAATGAGGCCCATACCAAACGACGAGGCGTCGACACCACGAGATGCTGCAGCAATGGC
GAACGTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGTGCGGTATTATCCCGTGTTGACGCC
GGCAAGAGCAACTCGGTCGCCGCAUACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGA
AAAAGCATCTTACGAGCGGGGATCATGTAACCCGCCUUGAUCGUUGGG
AACCGGAGCTGAAUGAAGCCCAACCAAACGACGAGCGTGACACCACGATGCTGCAGCAATGGCAACAAC
GTTTGCGCAAAACTTAACTGGCAGAATCTTACTCTAAGTCTCCGGCAGAAATTAATAGACTTGAGAT
GCGGATAAAGGTGTCAGGACACTTCTCTGCGCTCGGCCTTTCCGGCTGGCTGGTTTATTGGCTGATAAAATCTG
GAGCCGGTGCAGCTGATCTCGGCTGCATATTGACACTGGGCGACATGTAACCCGCCCTTGATCTCGT
AGTTATCTACGACGCGGGGATCATGTAACCGCAGATCGCTGAGATAGGGTTC
TCACTGATTAAGCATTTGTTAA

>blaTEM-1D mRNA
AUGAGUAUUCAACAUUUCGUGUCGCCCUUAAUCUUUUUUGCGCAUUUUGCCUUUUUCGUGUCUC
ACCCAGAACGCTGTTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTCACGAGTGGGTTACATCGAGCT
GGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCCAATGATGAGACCTTT
AAAGTTCTGCTATGTGGTGCGGTATTATCCCGTGTTGACGCCGGCAAGGGAACAATCGGTCGCCGATAC
ACTATTTCTGAGATGACTTGGTGTAATCTACTACGACCATAGAAGGATATCGGATAGCTGACCAGT
AAGAGAATTATAGTGCAGTGCCTCAATAACCATGAGTAACACTGCGCCCAACTTACATTGACACAAGATC
GAGGGACGGAAGGACGTCAAACCGCTTTTTTGCAACAACATGGGGGTATGTAACCCGGCCCTTGTGATTC
AAACCCGGAGCTGTAATGAGGCCCATACCAAACGACGAGGCGTCGACACCACGAGATGCTGCAGCAATGGC
GAACGTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGTGCGGTATTATCCCGTGTTGACGCC
GGCAAGAGCAACTCGGTCGCCGCAUACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGA
AAAAGCATCTTACGAGCGGGGATCATGTAACCCGCCUUGAUCGUUGGG
AACCGGAGCTGAAUGAAGCCCAACCAAACGACGAGCGTGACACCACGATGCTGCAGCAATGGCAACAAC
GTTTGCGCAAAACTTAACTGGCAGAATCTTACTCTAAGTCTCCGGCAGAAATTAATAGACTTGAGAT
GCGGATAAAGGTGTCAGGACACTTCTCTGCGCTCGGCCTTTCCGGCTGGCTGGTTTATTGGCTGATAAAATCTG
GAGCCGGTGCAGCTGATCTCGGCTGCATATTGACACTGGGCGACATGTAACCCGCCCTTGATCTCGT
AGTTATCTACGACGCGGGGATCATGTAACCGCAGATCGCTGAGATAGGGTTC
TCACTGATTAAGCATTTGTTAA
Learning objective
Be able to describe the Central Dogma of Molecular Biology, in particular transcription. Deduce the sequence of a pre-mRNA molecule that have been transcribed from a given gene

Typical exam question

What is the name of the enzyme that transcribes DNA into RNA?

Q: Below, the **coding** strand of a DNA molecule is shown. The arrow indicates where, and in which direction transcription occurs. Write the resulting mRNA molecule

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5’ GGTCTATATATAAGCAGAGCTGGTTTATGAACCGTCAGATGAG 3’
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BREAK
Structure of eukaryotic protein-coding genes

- Start codon
- Exons: Code for amino acids
- Stop codon
- Introns: Code for nothing
- Promotor
  - Here the RNA polymerase binds
- Terminator
  - Signals to the RNA polymerase to stop transcribing

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Structure of eukaryotic protein-coding genes
Alternative splicing
**Learning objective**
Be able to sketch the structure of a eukaryotic gene and explain the difference between exons and introns

**Typical exam question**

The $RB$ gene contains 27 exons and 26 introns. Below, exon no. 17-19 and intron no. 17-19 are shown schematically. Sketch the mature mRNA molecule with regards to these exons/introns (you may assume that there is no alternative splicing).
Regulating gene expression in multi cellular organisms

Same genome – different expression at different stages

Same genome – different expression in different places
Chromatin (DNA+histones)

**Euchromatin:** Lightly packed chromatin. The genes are transcribed.

**Heterochromatin:** Tightly packed chromatin. The genes are normally not transcribed.
Barr body – One of the X chromosomes of women are inactivated as heterochromatin

During the development of a female embryo, one of the two X chromosomes are inactivated.

The female body is a mosaic, where some areas contain cells that have the one X chromosome inactivated, while cells in other areas have the other X chromosome inactivated.
Gene expression can be regulated here.
Gene expression can be regulated here
More on initiation of transcription

The same transcription factor can bind/regulate several genes!

Gene expression can be regulated here
**MicroRNA – regulation mRNA longevity**

- Small RNA molecules, ≈ 22 to 23 nucleotides
- Bind via basepairing to the 3’ end of the mRNA
- Binding inhibits translation and sometimes the mRNA is even degraded
- Computers predict that more than 1000 genes encode microRNA
- It is also predicted that microRNA molecules regulate the expression of more than 1/3 of all human genes

*Gene expression can be regulated here*
Post translational regulation of expression

Ubiquitination - or

The Kiss of Death

Gene expression can be regulated here
Learning objective
Describe how gene expression is regulated in eukaryotes emphasizing the many different levels this can be achieved on.

Typical exam question
What is the effect of deacetylation of histone proteins on the transcription rate of nearby genes?
INTRODUCTION

According to the recent data derived from sequencing the human genome, the human genome contains 20,000 to 25,000 genes. As biologists become deluged with this new data, they are inventing clever new technologies that allow them to analyze genes by the thousands, rather than the old-fashioned way, one by one.

A thumbnail-sized invention called a DNA chip is one of the most powerful new tools to emerge from genome studies. A DNA chip is made with thousands of nucleotide sequences attached to the chip in a grid pattern. The attached sequences act as probes and tell a researcher whether a test sample contains a particular DNA or RNA sequence.

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