Lecture Notes

NOTE: These notes are only some of the material that is printed on the slides. By providing these notes, it is intended that you will use them to follow along with the lecture, not replace viewing the lecture. If you only look at these notes, you will miss a great deal between material that is not written on the slides and given orally plus the illustrations with their explanations.

1 **The Gene Revolution**

Nucleic Acids:
Structure and Function,
Control and Manipulation,
Science and Technology

2 **I. Role of Nucleic Acids**

- Information storage and processing
- DNA = deoxyribonucleic acid
  - information storage
    - cellular control
    - heredity
- RNA = ribonucleic acid
  - information processing
    - uses stored information to control cell

3 **Gene**

- basic information storage unit
- segment of DNA
- types
  - structural gene
    - controls the synthesis of a specific protein
  - regulatory gene
    - controls other genes
- concept recognized in 1860's but ignored until around 1900

4 **Historical Development**

- early 1900's
  - DNA thought to be a binder and stabilizer in the nucleus
  - proteins thought to be the hereditary substance
  - reasons:
    - DNA shows less variability in structure than protein
      - less apparent information content
    - DNA in small amounts in cell
  - How could a relatively rare, invariable molecule carry complex hereditary information

5 **Recognition of DNA's Significance**

- critical experiments
- bacteria - 1920's to 1940's
  - harmless bacteria become pathogenic when mixed with killed pathogenic virus
  - DNA from pathogens had entered and transformed the harmless bacteria into pathogens

6 **Significance, con't**

- viruses
  - consist of outer coat of protein and inner core of nucleic acid
  - take over the functions of a cell for viral reproduction
  - experiments using radioactive protein and radioactive nucleic acids in viruses

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8 **Significance - con't**

- protein did <u>not</u> enter the cell
  - radioactivity showed protein in surrounding liquid, not cells
  - How can a hereditary material affect a cell if it does not enter the cell??? IT CAN'T!!!
- DNA <u>did</u> enter the cell
  - radioactivity showed nucleic acid in the cells, not the surrounding liquid
  - Therefore, DNA is the hereditary molecule!

9 **Race for discovery of DNA structure**

- several tries
- knew:
  - deoxyribose sugar and phosphate
  - nitrogen bases of 4 kind
    - Chargraff's rule for DNA
      - amount of A = amount of T

- amount of G = amount of C
- but ratio of A/T to C/G in various organisms varies
- example:
  - –species A 20% A, 20% T, 30% C, 30% G
  - –species B 10% A, 10%T, 40% C, 40% G

10 **The Race heats up**

- several tries
  - Linus Pauling - incorrect model
- James Watson and Francis Crick
  - JW, American, FC, British, at Cambridge
  - used data from Maurice Wilkins and Rosalind Franklin and constructed models
  - used Chargraff's Rule
  - 1953-1 pg.. paper in Nature
  - Nobel Prize with Maurice Wilkins in 1962

11 **II. Nucleic Acid Structure**

- polymers of nucleotides
- nucleotide structure:

12 **Bases**

- 5 bases:
  - both DNA and RNA (3)
    - A = adenine
    - C = cytosine
    - G = Guanine
  - RNA only (1)
    - U = uracil
  - DNA only (1)
    - T = thymine

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14 **DNA Structure**

- nucleotides form a polymer by synthesis

■sugar and phosphate “backbone”

15 **DNA Structure**

■double stranded

16 **DNA Structure**

■strand held together by hydrogen bonds
- ◆weaker
- ◆allow the molecule to more easily come apart
- ◆essential to the function of this molecule

■bases are complementary paired
- ◆A pairs with T -form 2 hydrogen bonds
- ◆C pairs with G -form 3 hydrogen bonds
  - ✦explains Chargraff’s Rule

17 **DNA Structure**

18 **DNA Structure**

■ladder twisted ==> double helix

■James Watson, The Double Helix
- ◆story of the discovery of DNA structure
- ◆good read
- ◆not a lot about science, lots about how science and scientists work

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20 **RNA Structure**

■single stranded

■U in place of T

■ribose instead of deoxyribose

21 **III. DNA Duplication**

■DNA splits apart (“unzips”)

■nucleotides already in cell complementary pair with each

strand
- forms a new half for each strand
- ==> 2 IDENTICAL DNA strands

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24 **IV. Protein Synthesis**

- Proteins
  - string of amino acids
  - order of amino acids determines function
    - structural
    - enzymes -moderate virtually all cellular activity

25 **Role and Significance of Nucleic Acids in Protein Synthesis**

- control of enzymes => control of cellular activity
- enzymes are proteins with specific amino acid sequences
- DNA and RNA determine the order of amino acids in proteins
- =>determines types of enzymes and structures in cells

26 **Protein Synthesis - Step 1: Transcription**

- DNA-stored information is copied to RNA
- TRANSCRIPTION
  - transcribe = “to copy”

27 **RNA Synthesis - Transcription**

❶ DNA unzips

❷ RNA forms by complementary base pairing to ONE strand of the DNA molecule

❸RNA becomes free of DNA
❹DNA re-zips
❺RNA travels to cytoplasm

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33 **Protein Synthesis - Step 2**

■RNA moves into cytoplasm through nuclear pores

34 **Protein Synthesis - Step 3**

■RNA attaches to a ribosome

35 **Protein Synthesis - Step 4: Translation**

■RNA information “read” to form the protein by bringing in appropriate amino acids one by one

■TRANSLATION

◆translated from “nucleic acid” language to “protein” language

36 **Summary of Protein Synthesis**

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■3 base sequence on RNA (codon)

◆code for 1 amino acid

38 **Translation**

- codons read three bases at a time in sequence
- no spacing between codons
  - likereadingwordswithoutspacesbetween
  - SUESAWTHEDOGSIT
  - SUE SAW THE DOG SIT

  - SUERANERESHESAT
  - SUE RAN ERE SHE SAT

39 **V. Genetic Code**

- codes for amino acids in protein synthesis
- each codon (3-base sequence) codes for a specific amino acid
  - examples: UGG = valine; GUC = glycine
- redundant: an amino acid may be coded for by more than one codon
  - CUU, CUC, CUA, CUG -all code for leucine
- start = AUG (methionine)
- stop = UAA, UGA, UAG

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42 **Genetic Code**

- 64 codons, each 3 bases long
  - 4 nucleotides
  - $4^3 = 64$
- why? 20 amino acids
  - 1 base = code for 4 (4^1)
  - 2 bases = codes for 16 (4^2)
  - neither is long enough to 20 amino acids

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44 **VI. Mutations**

■a change in DNA base sequence
■base changed => possible change in amino acid sequence in protein product
■can change or destroy that protein's function

45 **Mutations**

■3 outcomes:
❶no effect
◆CUU -> CUG both leucine, no effect
❷harmful - protein function destroyed or altered to detriment of organism
◆cancers caused by mutagens
❸beneficial - new or better protein function
◆bacteria able to exploit a new food source

46 **Types of Mutations:**
Point Mutations

■change in 1 base in DNA sequence
■examples
◆herbicide resistance in some plants
◆sickle cell anemia

47 **Sickle-cell Anemia**

■normal:

B - B - B - G - A - A - B - B - B RNA
glutamine

normal hemoglobin -->rounded cells

■sickle-cell:

B - B - B - G - U - A - B - B - B RNA
valine

altered hemoglobin-->sickle-shaped cells
- clog vessels => tissue destruction
-resistance to malaria

48 **Types of Mutations:**
Frameshift Mutation

■delete one or more bases
■changes 3-base reading frame for synthesis
■SUE SAW THE DOG SIT
■UES AWT HED OGS IT_
◆often nonsense
◆may evolve into a useful gene

49 **Frameshift Mutation**

■nucleic acid sequence:
U - G - U - A - C - C - A - A - G - C
cysteine threonine lysine

■remove first U:
U - G - U - A - C - C - A - A - G - C
valine proline serine
★completely different protein due to frameshift - totally alters protein function

50 **VII. The Gene Revolution**

■Manipulation of DNA and genes
■In the past, selective breeding
■Today, selective breeding and direct manipulation of DNA
◆genetic engineering
◆DNA “fingerprinting”

51 **A. Genetic Engineering**

■genetic code universal
◆same in all organisms
■human (or other) genes can be transferred to bacteria to make human proteins
◆“recombinant DNA” - any interspecies transfer
◆human insulin produced by bacteria for diabetics
✦“humulin”
◆other drugs and products

52 **Methods of Genetic Engineering**

- Obtain sample of DNA from an organism
- Cut into pieces
- Uptake and integration by bacteria
- Select and grow bacteria with desired gene
- harvest protein product

53 **B. DNA Analysis**

- RFLP ("rif-lip")
  - Restriction Fragment Length Polymorphism
- use restriction enzymes
  - from bacteria; function: digest DNA
  - cut DNA at specific base sequences
    - sequence cut varies with different enzymes

---AATT-- --CCGG--
---TTAA-- --GGCC--

54 **Restriction Sites on DNA**

- restriction sites vary from individual to individual because everyone has a unique mix of DNA
  - unique mix due to:
    - mutations
    - different alleles

55 **Restriction Site Example**

- variations --> different lengths of cut DNA
  - restriction fragments

56 **Study of the Restriction Fragments**

- sort by length in gel
  - place in gel (like jello or agar)
  - apply electricity across gel - attracts fragments through the gel
  - large fragments travel slower
  - separates
- stain gel
- produces a series of lines in gel

- ◆similar to bar code

57 **Electrophoresis**

- ■Process of separating the DNA fragments in a gel

58 **Forensic Use**

- ■match profiles of RFLP's

- ■Which suspect is the perpetrator?
- ■Can you be sure?

59 **C. Gene Therapy**

- ■Transfer of genetic information to cure a genetic condition
  - ◆Sickle cell anemia
  - ◆Cystic fibrosis
- ■Insert "normal" gene into the individual
- ■Normal gene replaces function of defective gene
- ■Has not yet been used effectively in humans

60 **Summary**

- ■Nucleic Acids:
  - ◆DNA - information storage
  - ◆RNA - information processing
- ■DNA Duplication
- ■Protein synthesis
  - ◆Transcription: DNA information copied to RNA
  - ◆Translation: RNA information used to form protein
- ■Mutation - change in DNA sequence
- ■Genetic Technology
  - ◆Genetic Engineering, Genetic Analysis, Gene Therapy