BCH 4054 Chapter 29 Lecture Notes

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Chapter 29

DNA: Genetic Information, Recombination, and Mutation

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DNA as the Genetic Material

- Griffith Experiment on pneumococcal transformation (Fig 29.1)
  - Avery, MacLeod and McCarty showed the principle was DNA
- Hershey-Chase experiment on bacteriophage infection (Fig 29.3)
  - DNA and coat protein labeled differently.

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Recombination of DNA

- Mendel recognized how genes could rearrange in different combinations, with some genes being **linked** and sorting together
  - Explained by random sorting of chromosomes
- Some linkages weren't complete, with some rearrangement of pieces of chromosomes

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Recombination in Meiosis

- Sister chromatids pair duing meiosis
- Chromosome ends can exchange in a process called “crossing over”
- Occurs with equal probability along entire chromosome
- Frequency of recombination measures distance between genes, and is used for mapping

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Importance of Recombination

- Phenomenon seen in many different situations
- Provides a means for nature to “experiment”
- Probably important in evolution of new combinations of genes and pieces of genes
- Also important in salvaging damaged genes
- Lets look at some specific examples

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Recombination in Bacteria

- Lederberg-Tatum experiments on rearrangement of genes between strains of bacteria (Fig 29.4)
- Explanation comes from **sexual conjugation** followed by **genetic recombination**
  - F factor is plasmid carrying genes for conjugation (Fig 29.6)

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Recombination in Bacteria, con't.

- F factor integration into bacterial chromosome creates **Hfr cells**
- Integrated F factor plus part of chromosome is transferred.
  - Creates **diploid** condition for some genes.
  - **Recombination** exchanges portions of the diploid genes.
  - Can be used for **mapping** position of genes on chromosome. (Fig 29.7)

Hfr stands for "high frequency of recombination"

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Recombination in Bacteriophage

- Two strains of bacterial viruses infecting a bacterial cell can produce a diploid condition for the viral genes.
- Recombination between viral genes can occur to produce a **heteroduplex DNA**
  - See Fig 29.10
- Messelson and Weigle showed by ^{13}C and ^{15}N labeling that recombinant phage contained DNA from both "parents"

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Classification of Recombination Events

- General recombination
  - Occurs between **homologous** DNA regions
- Site-specific recombination
  - Insertion of bacterial virus genomes into bacterial chromosomes at specific sites
- Transposition
  - Insertion and removal of DNA

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Mechanism of Homologous Recombination

- Model proposed by Robin Holliday in 1964
- Duplex unwinding, strand invasion and ligation to create a Holliday junction
  - See Fig 29.11
- Resolution can produce either a “patch recombinant” heteroduplex, or a “splice recombinant heteroduplex”.

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Enzymes in Recombination

- Bacterial recombination requires a number of proteins
  - First analyzed as mutations lacking in ability to recombine, hence the proteins are referred to by the genetic identification: recA, recB, etc.
- RecBCD initiates the process (Fig 29.12)
- RecA forms filament that binds to single stranded DNA (Fig 29.13)

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Enzymes in Recombination, con’t.

- RecA-SSDNA complex binds to duplex DNA and searches for homologous sequences
- RecA catalyzes “strand invasion” at homologous sequence
  - See Fig’s 29.14 and 29.15
- RuvA, RuvB, and RuvC bind to “Holliday junction”, drive branch migration, and resolve the junction into recombination products.

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Other Recombination Phenomena

- Transposons—"jumping genes"
  - First recognized in corn genetics by Barbara McClintock
  - Many variation now known. For example, bacterial plasmids integrating at various places in bacterial chromosome
- DNA rearrangement in Immunoglobulin genes
  - Produces great diversity in IgG sequences.
  - Skip the details

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Molecular Nature of Mutations

- Point mutations
  - Tautomer mistake
  - Base analogue induced
  - Chemical mutagens
- Insertions and Deletions
  - Intercalating agents
  - Transposon insertion

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Point Mutations

- Transitions or Transversions
  - Wrong tautomer at replication
    - About one in 10^{-10} per base pair
  - Conformation shift syn to anti
  - Water mediated H bonding between pyrimidines
    - See Fig 29.24

Transition: Purine replaced by purine (A by G or G by A); pyrimidine replaced by pyrimidine (C by T or T by C)
Transversion: Purine replaced by pyrimidine or pyrimidine replaced by purine

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Point Mutations, con't.

- Base analog induced
  - 5-bromouracil and 2 amino purine
    - Fig 29.25 and 29.26
- Chemical mutagens
  - Nitrous acid (oxidative deamination)
    - Fig 29.28a
  - Alkylating agents alter H-bonding
    - Fig 29.28d

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Insertions and Deletions

- Acridine orange and other aromatic molecules
  - Intercalation between bases causes added or skipped bases during replication
- Transposons
  - Insertion of a transposon can shift reading frame

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UV, X-ray, and Radiation

- Not discussed in book at this point
- Causes DNA damage
  - Example, UV can cause thymine dimers
- Can lead to mispairing
- Also induces an enzyme system for repair of damage that is called "error prone repair"

We'll have more to say about these in discussing DNA repair mechanisms

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RNA as Genetic Material

- Most plant viruses, some animal and bacterial viruses, use RNA as genetic material
- Retroviruses make DNA from the RNA, and the DNA can be "recombined" into the genome of the host

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Transgenic animals

- Recombinant DNA technology now allows for genetic manipulation
  - Insertion of genes
    - Ex. Is growth hormone gene in mice
  - Destruction ("knock-out") of genes
    - Useful in determining the function of a gene

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Prions

- Protein infectious particle
- A seeming case of a protein causing a "genetic" change
- Protein can exist in two conformational forms, normal and "diseased" form
- Infection by "diseased" conformation can induce conformational change in normal form
  - See Fig and discussion, page 979

1997 Nobel Prize awarded to Stanley Prusiner for discovery of prions