Slide 1

Chapter 29

DNA: Genetic Information, Recombination, and Mutation

Slide 2

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.

Slide 3

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

Segregation and

Slide 4

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

Slide 5

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

Slide 6

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)

Slide 7

Recombination in Bacteria, con't.

- F factor integration into bacterial chromosome creases **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"

Slide 8

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"

Slide 9

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

Slide 10

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”.

Slide 11

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)

Slide 12

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.

Slide 13

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

Slide 14

Molecular Nature of Mutations

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

Slide 15

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

Slide 16

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

Slide 17

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

Slide 18

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

Slide 19

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

Slide 20

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

Slide 21

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