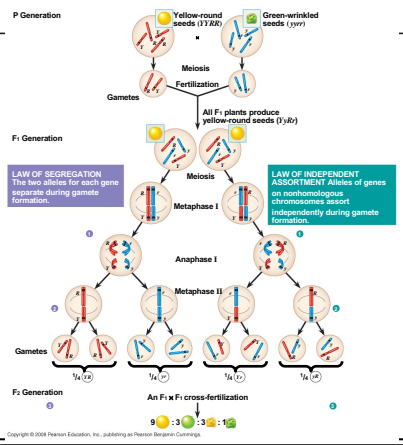
Ch. 15

The Chromosomal Basis of Inheritance

BIOL 221

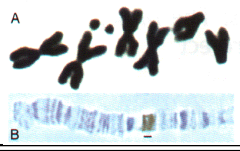
Overview: Locating Genes Along Chromosomes

- Mendel's "hereditary factors" were genes
  - Not known at the time
- Today we can show that genes are located on chromosomes
  - Location of a particular gene
    - Can be seen by tagging isolated chromosomes with a fluorescent dye that highlights the gene



Morgan's Choice of Experimental Organism

- Thomas Hunt Morgan - Embryologist
  - Showed genes are on chromosomes
  - Studied fruit flies
    - Convenient organism for genetic studies:
      - They breed at a high rate
      - A generation can be bred every two weeks
      - They have only four pairs of chromosomes

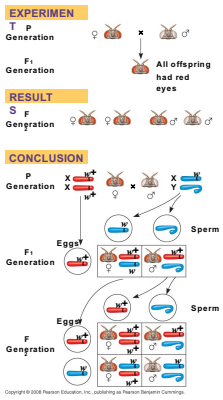


Morgan's Choice of Experimental Organism

- **Wild type**
  - Normal, phenotypes that were common in fly populations
- **Mutant phenotypes**
  - Traits alternative to the wild type

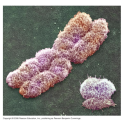
Alleles and Behavior of a Chromosome Pair

- Mated male flies with white eyes (mutant)
  - With female flies with red eyes (wild type)
    - The F_1 generation all had red eyes
    - The F_2 generation showed the 3:1 red:white eye ratio
      - But only males had white eyes
      - Therefore white-eyed mutant allele must be on X chromosome
      - Supported the chromosome theory of inheritance



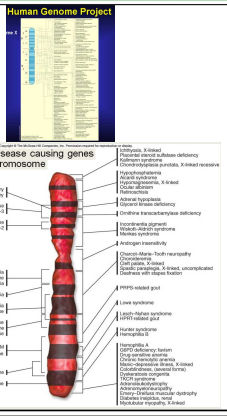
Sex-linked inheritance

- In mammals
  - two kinds of sex chromosomes - larger X, smaller Y chromosome
    - Regions on ends of Y chromosome are homologous with the X chromosome
- The *SRY* gene on the Y chromosome codes for the development of testes
  - Some other animals have different methods of sex determination
    - Birds, fish, some crustaceans, some insects
      - Female: ZW; Male ZZ



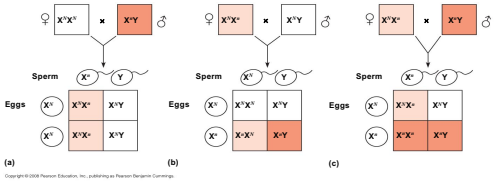
Inheritance of Sex-Linked Genes

- Sex chromosomes
  - Have genes for many characters unrelated to sex
  - **Sex-linked gene**
    - A gene located on either sex chromosome
    - In humans, sex-linked usually refers to a gene on the larger X chromosome
      - Called X-linked



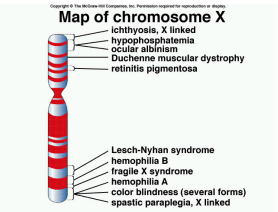
Sex-linked inheritance

- Sex-linked genes follow specific patterns of inheritance
- For a recessive sex-linked trait to be expressed
  - A female needs two copies of the allele
  - A male needs only one copy of the allele
- Sex-linked recessive disorders
  - Are much more common in males than in females



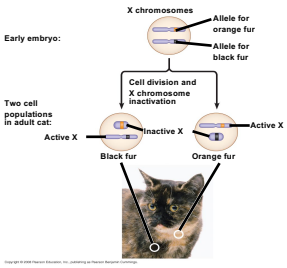
Sex-linked inheritance

- Common X-linked conditions - Due to recessive alleles
  - Color blindness
    - Red/green most common
    - May include 19 chromosomes and 56 genes
  - Duchenne muscular dystrophy
    - Mutant Dystrophin gene Xp21
  - Hemophilia - Failed blood clotting
    - Three types
      - Two found on X chromosome



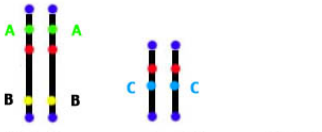
X Inactivation in Female Mammals

- Mammalian females
  - One of the two X chromosomes in each cell is randomly inactivated during embryonic development
    - **Barr body**
      - The condensed inactive X
- If a female is heterozygous for a particular gene located on the X chromosome
  - She will be a mosaic for that character



Linked Genes

- Each chromosome
  - has hundreds or thousands of genes
- **linked genes**
  - Genes located on the same chromosome that tend to be inherited together are called

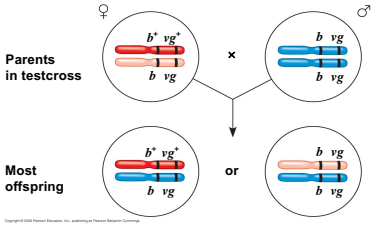


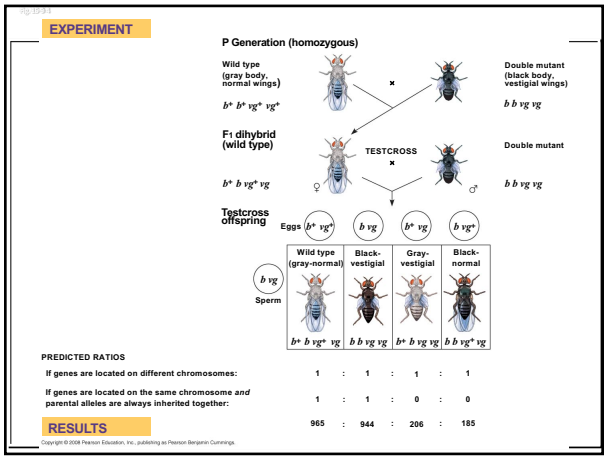
A and B are linked

A and C are not linked

How Linkage Affects Inheritance

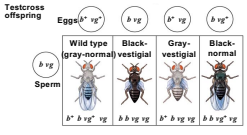
- Morgan did other experiments with fruit flies
  - To see how linkage affects inheritance of two characters
- Crossed flies
  - That differed in traits of body color and wing size





Linked inheritance

- Morgan found that
  - Body color and wing size
    - Are usually inherited together in specific combinations
- Failed Law of Segregation
  - Reasoned that they were on the same chromosome
    - Therefore linked
    - The closer together on chromosome
      - More likely to be inherited together

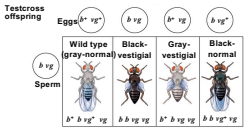


PREDICTED RATIOS

If genes are located on different chromosomes:	1	: 1 :	1	:	1
If genes are located on the same chromosome *and* parental alleles are always inherited together:	1	: 1 :	0	:	0
RESULTS	965	: 944 :	206	:	185

Linked inheritance

- A few non-parental phenotypes were also produced
- **Genetic recombination**
  - The production of offspring with combinations of traits
    - Differing from either parent
      - Ie not gray/normal or black/vestigial
        - But gray/vestigial or black/normal



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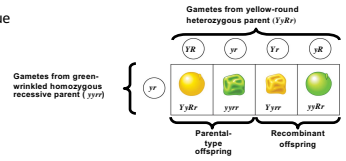
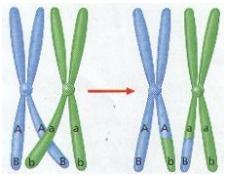
Independent Assortment of Chromosomes

- Mendel - Combinations of traits in some offspring differ from either parent
- **Parental types**
  - Offspring with a phenotype matching one of the parental phenotypes
- **Recombinants**
  - Offspring with nonparental phenotypes
    - new combinations of traits
  - A 50% frequency of recombination observed for any two genes on diff chromosomes
    - Due



Recombination of Linked Genes: Crossing Over

- Morgan discovered that genes can be linked
  - But the linkage was incomplete
    - Evident from recombinant phenotypes
  - Proposed that some process must sometimes break the physical connection between genes on the same chromosome
- **crossing over** of homologous chromosomes was that mechanism



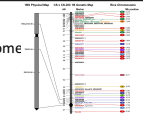
Mapping the Distance Between Genes

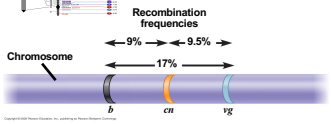
- Alfred Sturtevant
  - Student of Morgan
  - Constructed a **genetic map**
    - an ordered list of the genetic loci along a particular chromosome
  - Predicted that
    - *The farther apart two genes are*
      - *the higher the probability that a crossover will occur between them*
        - *and therefore the higher the recombination frequency*

Alfred Henry Sturtevant
Photo courtesy of Cold Spring Harbor Laboratory Archives.

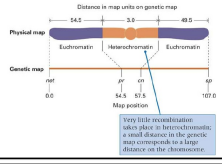
Linkage Map

- **Linkage map**
  - genetic map of a chromosome based on recombination frequencies
- **Map units**
  - Expression of distances between genes
    - one map unit, or centimorgan, represents a 1% recombination frequency
- Map units indicate relative distance and order, not precise locations of genes



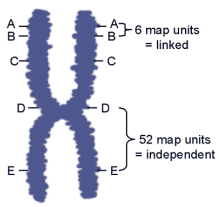


Genetic vs. Physical Distance



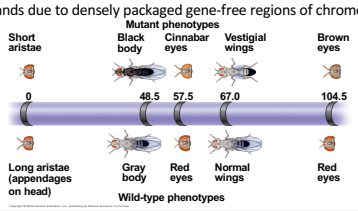
Linkage Map

- Genes that are far apart on the same chromosome
  - Can have a recombination frequency near 50%
- Such genes are physically linked, but genetically unlinked,
  - And behave as if found on different chromosomes



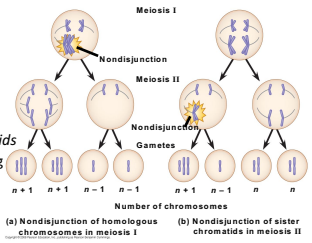
Gene Mapping

- Sturtevant - used recombination frequencies to make linkage maps of fruit fly genes
- Chromosomal banding
  - Staining method to identify regions of chromosomes
    - Geneticists can develop cytogenetic maps of chromosomes
- **Cytogenetic maps**
  - Indicate the positions of genes with respect to chromosomal features
  - Ie – bands due to densely packaged gene-free regions of chromosomes



Alterations of chromosome number or structure

- Large-scale chromosomal alterations
  - Often lead to spontaneous abortions (miscarriages)
    - Or cause a variety of developmental disorders
- **Nondisjunction**
  - Pairs of *homologous chromosomes* **or** *sister chromatids* do not separate normally during meiosis
  - As a result one gamete receives two of the same type of chromosome
    - And another gamete receives no copy

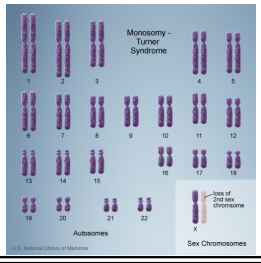


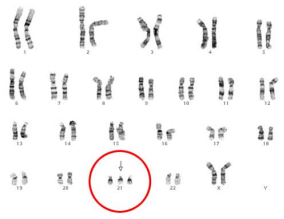
Abnormal Chromosome Number

- **Aneuploidy**
  - Results from the fertilization of gametes in which nondisjunction occurred
- Offspring with this condition have an abnormal number of a particular chromosome

Abnormal Chromosome Number

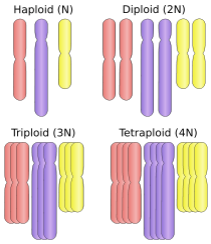
- **Monosomic** zygote
  - has only one copy of a particular chromosome
- **Trisomic** zygote
  - has three copies of a particular chromosome





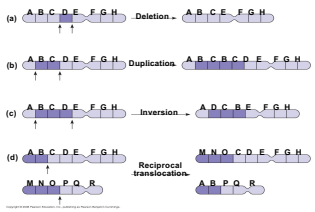
Chromosome Number

- **Polyploidy**
  - condition in which an organism has more than two complete sets of chromosomes
  - Triploidy (3*n*) is three sets of chromosomes
  - Tetraploidy (4*n*) is four sets of chromosomes
  - common in plants
    - but not animals
- Polyploids are more normal in appearance than aneuploids



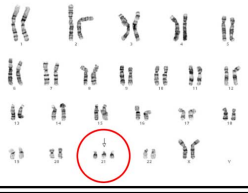
Alterations of Chromosome Structure

- Breakage of a chromosome can lead to four types of changes in chromosome structure:
  - **Deletion** removes a chromosomal segment
  - **Duplication** repeats a segment
  - **Inversion** reverses a segment within a chromosome
  - **Translocation** moves a segment from one chromosome to another



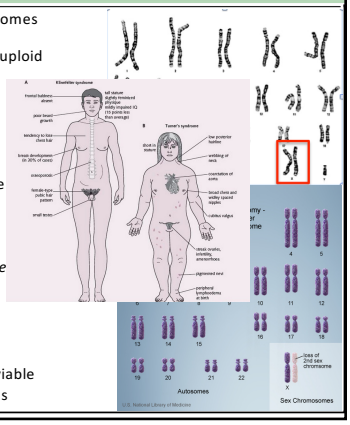
Aneuploidy Down Syndrome (Trisomy 21)

- **Down syndrome**
  - Aneuploid condition that results from three copies of chromosome 21
- Affects about one out of every 700 children
  - In the United States
- The frequency of Down syndrome increases with the age of the mother
  - A correlation that has not been explained



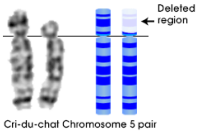
Aneuploidy of Sex Chromosomes

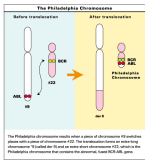
- Nondisjunction of sex chromosomes
  - Produces a variety of aneuploid conditions
- *Klinefelter syndrome*
  - XXY male
  - Sterile, small testes, some female secondary sexual characteristics
- Monosomy X, *Turner syndrome*
  - X0 female
    - sterile
    - it is the only known viable monosomy in humans

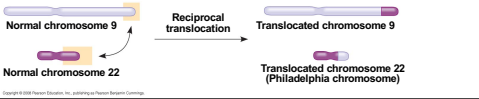


Structurally Altered Chromosomes

- *cri du chat* ("cry of the cat")
  - specific deletion in chromosome 5
  - mental retardation
  - catlike cry
  - usually die in infancy or early childhood
- Translocations of chromosomes
  - Certain cancers, including *chronic myelogenous leukemia* (CML)

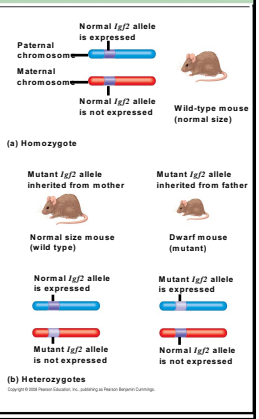






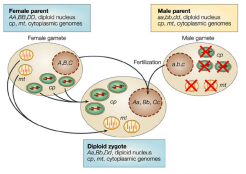
Genomic Imprinting

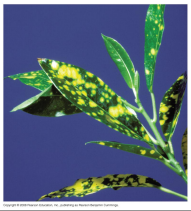
- **Genomic imprinting**
  - Variation in phenotype
    - depends on which parent passed along the alleles for those traits
  - Involves the silencing of certain genes
    - that are "stamped" with an imprint during gamete production
- Genomic Imprinting
  - One form of epigenetics
  - The result of the methylation (addition of $-CH_3$) of DNA
  - Thought to affect only a small fraction of mammalian genes
- Most imprinted genes are critical for embryonic development



Inheritance of Organelle Genes

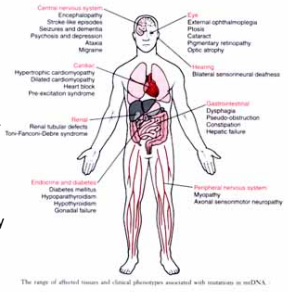
- *Extranuclear genes* (or *cytoplasmic genes*)
  - genes found in organelles in the cytoplasm
- Mitochondria, chloroplasts, and other plant plastids carry small circular DNA molecules
- Extranuclear genes
  - inherited maternally
    - zygote's cytoplasm comes from the egg
- The first evidence of extranuclear genes
  - came from studies on the inheritance of yellow or white patches on leaves
    - Variegation





Inheritance of Organelle Genes

- Some defects in mitochondrial genes
  - Prevent cells from making enough ATP
    - And result in diseases that affect the muscular and nervous systems
    - For example, mitochondrial myopathy and Leber's hereditary optic neuropathy
      - Failure of oxidative phosphorylation



You should now be able to:

1. Explain the chromosomal theory of inheritance and its discovery
2. Explain why sex-linked diseases are more common in human males than females
3. Distinguish between sex-linked genes and linked genes
4. Explain how meiosis accounts for recombinant phenotypes
5. Explain how linkage maps are constructed
6. Explain how nondisjunction can lead to aneuploidy
7. Define trisomy, triploidy, and polyploidy
8. Distinguish among deletions, duplications, inversions, and translocations
9. Explain genomic imprinting
10. Explain why extranuclear genes are not inherited in a Mendelian fashion