

## Genetics, after Mendel

- Mendel's work (1860's) not widely known until early 1900's
- Darwin published Origin of Species in 1859- trouble with blending vs particulate theory of inheritance
- 1900's- Chromosomal theory of inheritance: realization that the genes were on the chromosomes.



### T. H. Morgan Drosophila genetics

- very successful animal system for genetics
- Short generation time, convenient size, complex morphology
- early discovery: inheritance of a particular mutation (white eyes) was linked to inheritance of a particular chromosome (X)

Figure 15.2 Morgan's first mutant



## Linked genes

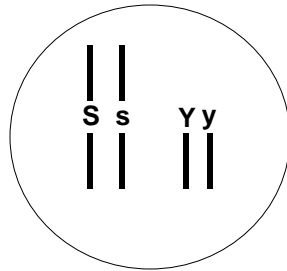
### Independent assortment

- Original combinations of alleles are not any more likely to occur than the others

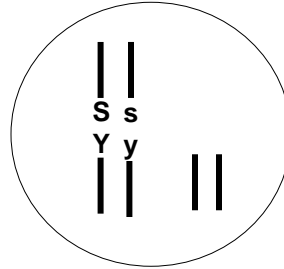
### Linkage

- alleles on the same chromosome tend to stay together during meiosis

## Loci can be on different chromosomes or on the same chromosome (linked)

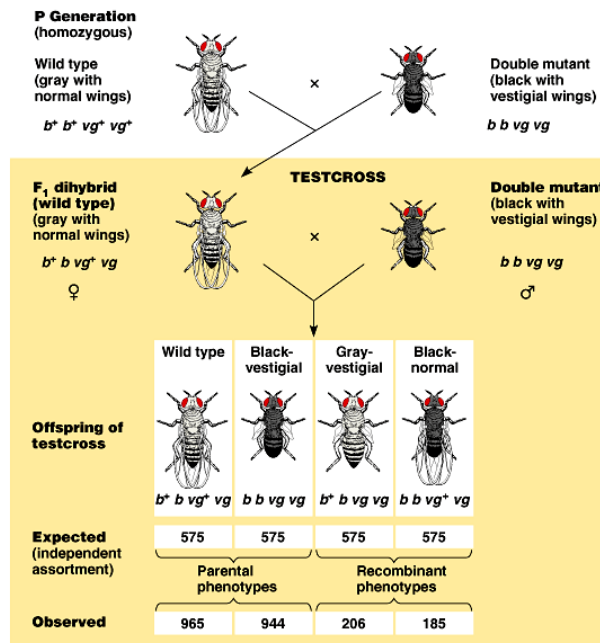


This cell can make SY, Sy, sY or sy gametes through independent assortment of the two pairs of chromosomes



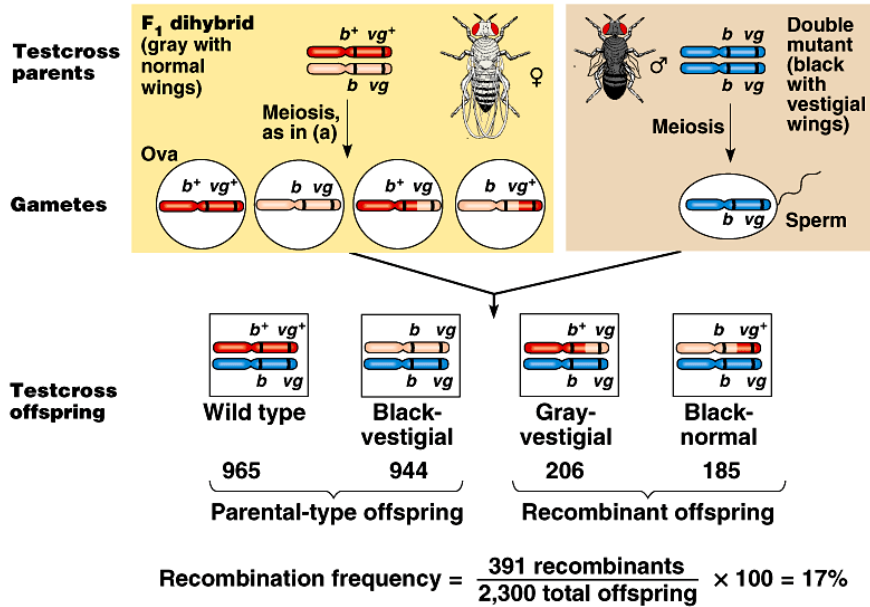
This cell can make only SY or sy gametes because the two loci are linked on the same chromosome

Figure 15.4 Evidence for linked genes in *Drosophila*



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Figure 15.5b Recombination due to crossing over



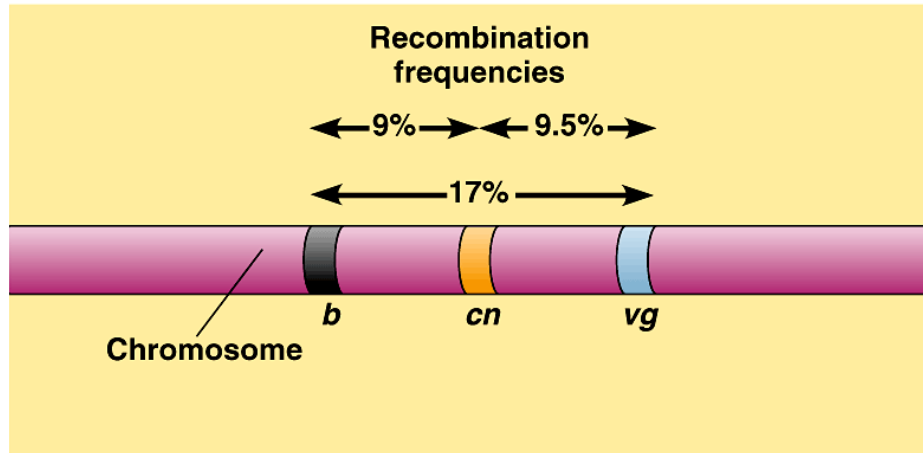
(b) Production of recombinant offspring

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## Crossing over can separate linked alleles

- Morgan found that recombinant phenotypes were less common than expected (expected = 50%) but not absent.
- Recombination occurs less frequently if loci are close together on a chromosome
- Recombination frequency used to map relative position of genes- “linkage maps”

Figure 15.6 Using recombination frequencies to construct a genetic map



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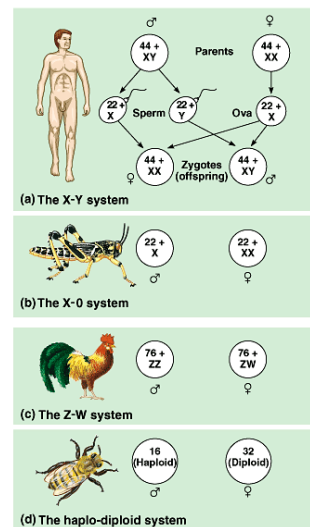
- Dihybrid cross data from many pairs of genes showed that there were 4 linkage groups.
- There are 4 chromosome pairs in *Drosophila*.
- Further supported the hypothesis that the genes are parts of the chromosomes.

# Sex determination

- anisogamy (eggs and sperm) vs isogamy
- Sexual vs asexual
  - Gonochorism (dioecy) vs hermaphroditism
- Sexual dimorphism
  - Primary (gonads) vs secondary (anatomy etc)
- Determination of sex
  - Primary signal
  - Developmental mechanisms

# Multiple mechanisms

- Genetic sex determination
  - Dual sex chromosomes
    - XY male, XX female (mammals)
    - ZZ male, ZW female (birds)
  - Sex chromosome “dosage”
    - X- male, XX female in grasshoppers
  - Haplodiploidy
    - Haploid males, diploid females (Hymenoptera)
- Environmental sex determination
  - Temperature (turtles)
  - Social cues (some fish)
  - Population density (some nematodes)



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## XY sex determination

- Y is smaller than X and lacks many loci
- Y causes male development
- males have only one copy of genes on X, because they only have one X chromosome
- One X inactivated in each cell of female (Barr bodies) which one in each cell is random

## Categories of disease

- infection- parasitic organisms live on or in a host and cause problems
- cancer- failure to control cell reproduction
- poisoning- damage caused by toxic substances
- birth defects- failure to develop properly due to injury or other factors
- genetic diseases: defective alleles or chromosomes cause disease or predisposition to disease.

## Defective alleles

- originate by mutation
- If present in gamete- all cells of the zygote will get copies
- Dominant harmful alleles likely to be culled by death or failure to reproduce.
- Recessive harmful alleles are not culled, because heterozygous "carrier" is unaffected.

## Biological reason for avoiding incest

- close relatives are more likely to have same alleles than are unrelated individuals- (why?)
- Offspring of heterozygotes have 25% chance of being homozygous.
- Children of close relatives are more likely to be homozygous for rare alleles, including harmful ones.

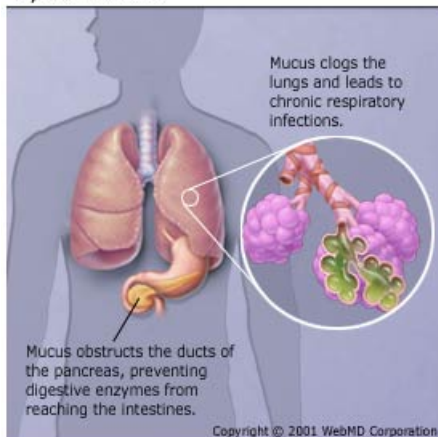


## Recessively inherited autosomal disorders

- The autosomes include all the chromosome pairs except the sex chromosomes (the XY pair).
- Some important inherited disorders of autosomal genes include cystic fibrosis, sickle cell anemia, and Tay Sachs disease

*“Woe to that child which when kissed on the forehead tastes salty. He is bewitched and soon must die.”* old European folklore

Cystic Fibrosis



## Cystic fibrosis (CF)

- Affects 1/2500 Caucasians in the U.S.
- symptoms: salty skin, difficulty breathing, lung infections, malnutrition, sterility
- affects mucus on epithelia of lungs, pancreas, intestine, other organs
- homozygotes used to die as children- heterozygotes are not significantly affected

## CFTR

- Cystic Fibrosis Transmembrane Conductance Regulator
- Mucus: mucopolysaccharides and water
- CFTR actively transports Cl<sup>-</sup> to produce the osmotic gradient for water transport
- CFTR is 1480 amino acids long.
- Most common mutation is “ΔF-508” a 3 base deletion, causes missing phenylalanine at position 508.

## How common is the allele?

- $P$  = frequency of the bad allele
- $Q$  = frequency of normal allele
- $P + Q = 1$
- $P^2 + 2PQ + Q^2 = 1$
- $P^2$  = probability of being homozygous for the bad allele
- $Q^2$  = probability of being homozygous for the normal allele

## Continued...

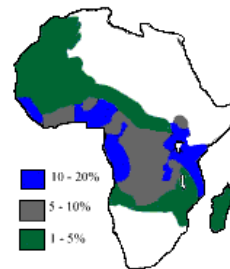
- $2PQ$  = probability of being heterozygous
- $P^2 = 1/2500 = 0.0004$
- $P = \sqrt{0.0004} = 0.02$
- $Q = 1 - 0.02 = 0.98$
- Probability of being heterozygous (carrier)  
 $2PQ = 0.0392$  (3.9%)

## Why is $\Delta F-508$ so common?

- Heterozygotes resistant to diseases that kill by causing severe diarrhea, e.g. cholera
- Epidemic disease in cities of medieval Europe may have selected for this allele.
- Evolution by natural selection- change in allele frequency through differential survival

## Sickle cell anemia

- Caused by an allele of hemoglobin
- Allele frequency up to 20% in some parts of Africa
- Most common in areas where malaria occurs
- Heterozygote advantage- resistance to malaria



## Tay-Sachs disease (TSD)

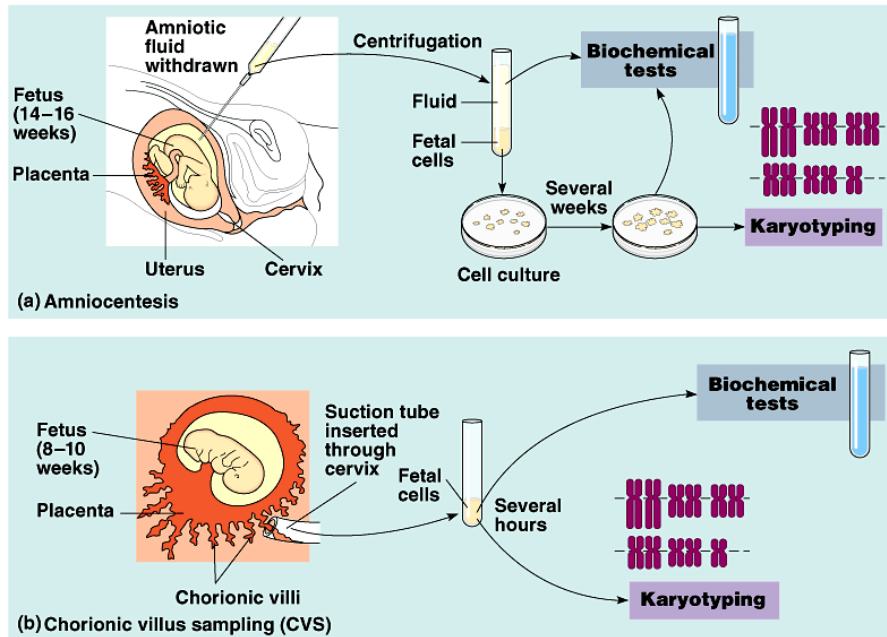
- Enzyme for metabolizing lipids in nervous system- homozygotes die in childhood
- Heterozygote frequency: 3.2% Eastern European Jewish, 1.9% Quebec French Canadian and Cajun ancestry.
- alleles run in families, and in larger related groups because of shared ancestors
- Marriage within descent group- more homozygotes

## Dominant autosomal genetic disorders

### Huntington's disease

- degenerative disease of nervous system
- symptoms develop at 35-45 years old
- 1/10,000 Caucasians is affected
- dominant allele- on average, 50% of a victim's children will get the allele and the disease.

Figure 14.17 Testing a fetus for genetic disorders



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## Sex linked inheritance

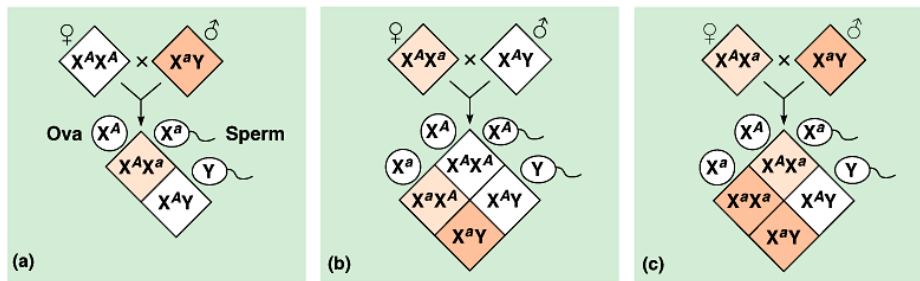
- X-linked genes are on X but not Y (many)
- Y-linked genes are on Y but not X (few)
- Many traits and several genetic diseases are X-linked

# Hemophilia A

- caused by allele for Factor VIII protein (important in blood clotting)
- blood loss, chronic joint problems, early disability or death
- Recessive X-linked. Mainly affects males (why?)

Figure 15.9

## Inheritance of sex-linked recessive traits



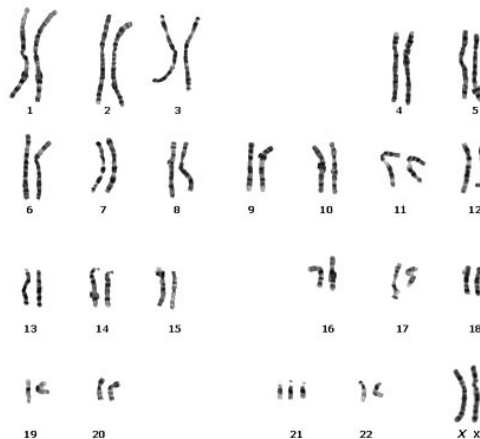
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## Aneuploidy- wrong number of chromosomes

- caused by nondisjunction - homologous chromosomes don't assort properly in meiosis
- Example: Down's syndrome (trisomy 21) extra chromosome #21

Figure 15.14 Down syndrome

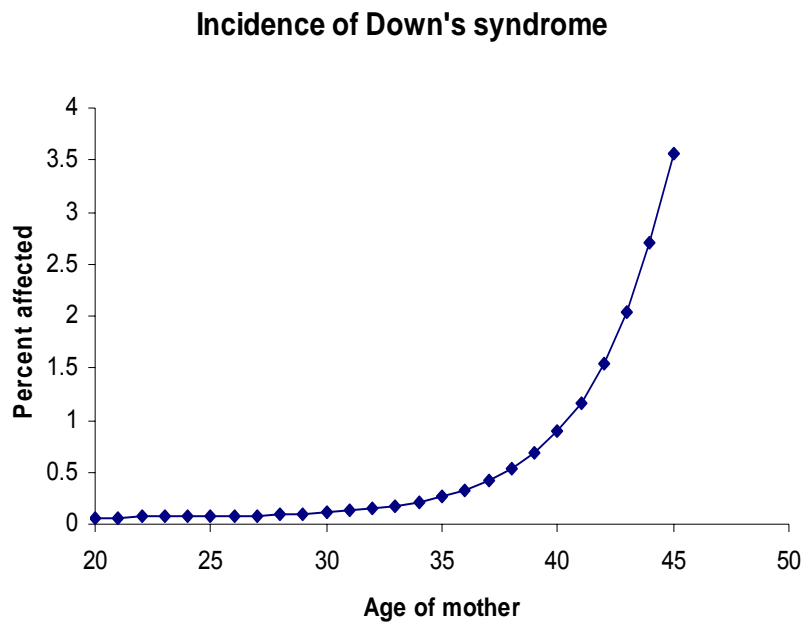
Trisomy 21





## Down syndrome, continued

- Symptoms....mild retardation, heart problems, characteristic phenotype
- Frequency increases with age of mother:  
3% of births at age 45, 8% at age 50



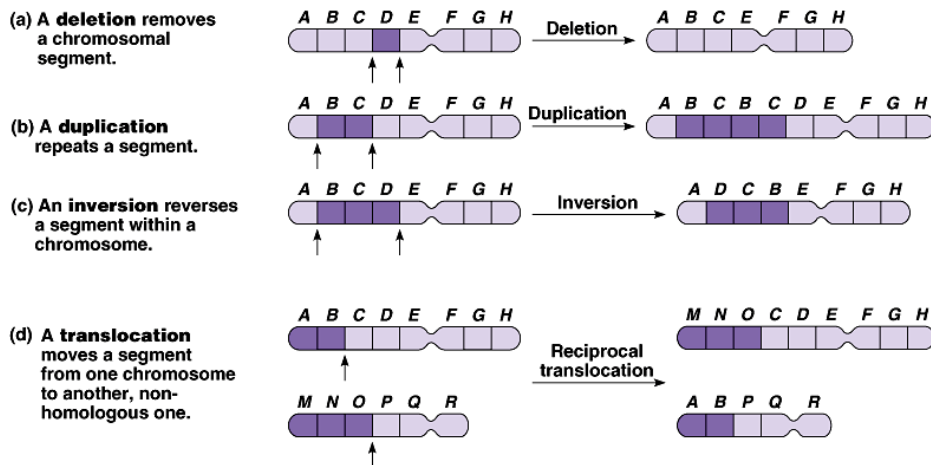
## Aneuploidies, continued

- Klinefelter syndrome
  - XXY individuals have male phenotype, but some degree of feminization occurs.
  - Occurs in about 1/2000 individuals (more common than cystic fibrosis)
  - Nondisjunction is more common in sex chromosomes than in autosomes

## Polyploidy

- Complete extra sets of chromosomes
- Rare event, but important evolutionarily
- Many groups of plant species and some animal species have different multiples of chromosomes than related species

Figure 15.13 A different kind of mutation:  
Alterations of chromosome structure



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## Genomic imprinting

- Certain genes are altered (imprinted) by DNA methylation in the gametes of one sex and not the other
- The effect may be activation or inactivation of that gene in one of the homologues in the zygote
- Helps explain inheritance of certain disorders- e.g. fragile X syndrome (p. 283)

## Extranuclear inheritance

- Mitochondrial or chloroplast DNA in eukaryotes
- Inherited maternally only (usually)
- No genetic recombination of these genes
- Mitochondria and chloroplast genes are often used to trace [genealogy](#) and evolutionary relationships