Topics

- Gene inheritance
  - Genetic variation
  - Genetic probabilities
  - Dominance varieties
  - Genetic disorders

In the 1800s, two basic theories explained natural variation between species:

- Blending inheritance
- Particulate inheritance

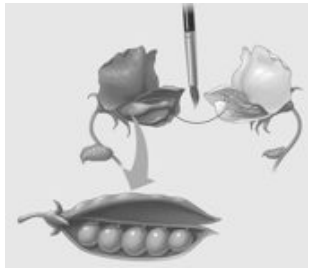
Gregor Mendel

Gregor Mendel, the father of modern **genetics** discovered the properties of inheritance by studying characteristics of pea plants.

Mendel used the Scientific Method

- Why peas? Easy to grow, easy to cross-pollinate

Removed the stamens



Artificially fertilized the purple flowers with white pollen

All flowers are purple?

Mendel's Hypothesis

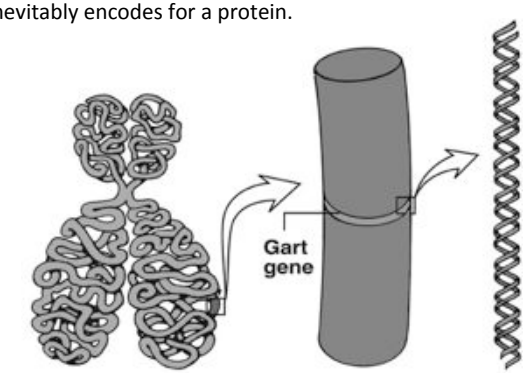
Four components contributed to Mendel's genetic hypothesis

1. *Alternative* versions of **genes** account for variations in inherited characteristics

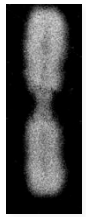
Genes are Instructions

Chromosomes = chromatin = (**DNA** + histones)

Gene: A distinct sequence of nucleotides within a chromosome that inevitably encodes for a protein.



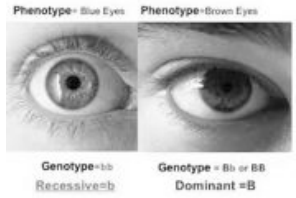
Genotype vs. Phenotype



• The 46 chromosomes (and the genes they carry) in each of your somatic cells constitute your **genotype**

• The *result* of the selective gene expression from your genotype constitutes your **phenotype**

• Specific elements in your phenotype, such as your hair color, eye color, skin tone, foot size... these are **phenotypic traits.**



Mendel's Hypothesis

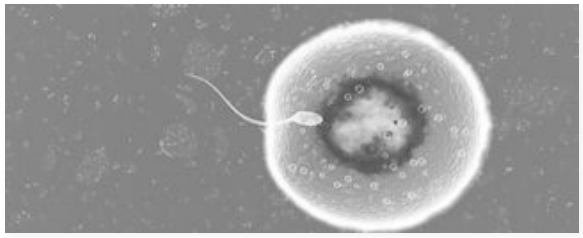
Four components contributed to Mendel's genetic hypothesis

1. *Alternative* versions of **genes** account for variations in inherited characteristics

2. For each **gene**, a human organism inherits two **alleles**, one from each parent

Humans are Diploid

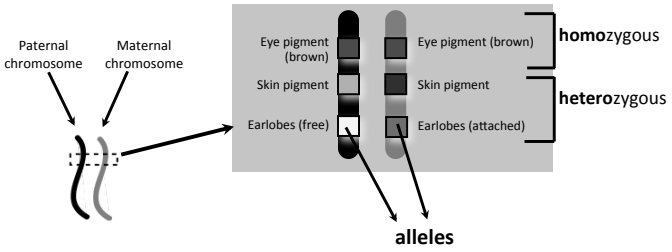
Through **fertilization** of an egg, there are two alleles for every gene in the **zygote**



Fertilization of egg by sperm

*Result is a **zygote***

Homologous Chromosomes



- The individual variants of any one gene are called **alleles**
- If two chromosomes contain the *same* allele, they are considered **homozygous.** If different = **heterozygous**

Mendel's Hypothesis

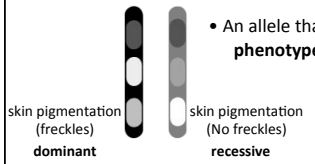
Four components contributed to Mendel's genetic hypothesis

1. *Alternative* versions of **genes** account for variations in inherited characteristics

2. For each **characteristic**, an organism inherits two **alleles**, one from each parent

3. If the two alleles at a **locus** are different, the **dominant** allele determines the organism's appearance; the **recessive** allele has no noticeable effect.

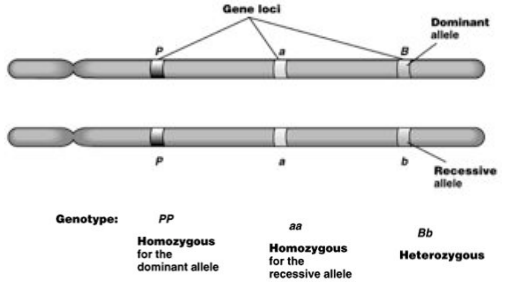
Interactions Between Alleles



- An allele that is **dominant** will be expressed in the **phenotype**, while the **recessive** allele will not

Phenotypic trait	Dominant	Recessive
Hairline	Widow's peak	Normal hairline
Ear lobes	Free	Attached
Skin Pigmentation	Freckles	No Freckles
Tongue rolling	Roll in "U" shape	Cannot roll tongue

Dominant vs. Recessive



- Dominant alleles are expressed as uppercase, recessive as lowercase
  - PP = **homozygous dominant**
  - aa = **homozygous recessive**
  - Bb = **heterozygous**

Mendel's Hypothesis

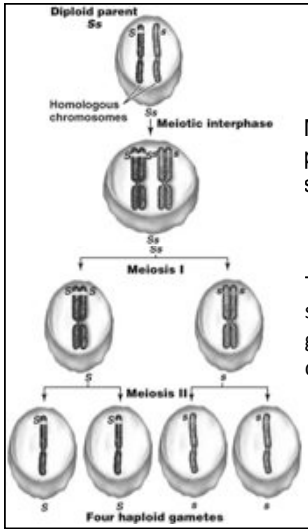
Four components contributed to Mendel's genetic hypothesis

1. *Alternative* versions of **genes** account for variations in inherited characteristics. These alternatives are called **alleles**.

2. For each **characteristic**, an organism inherits two alleles, one from each parent.

3. If the two alleles at a **locus** are different, the **dominant** allele determines the organism's appearance; the **recessive** allele has no noticeable effect.

4. **The law of segregation**: the two alleles are separated during gamete formation and must end up in <u>different</u> gametes. Therefore each gamete receives only one copy.



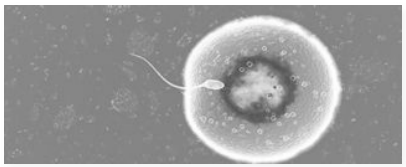
Mendel's first law- Law of segregation

Mendel verified this hypothesis by performing test crosses looking at a single trait.

The 2 alleles for a heritable character segregate from each other during gamete formation and end up in different gametes.

The Punnett symbolizes meiosis and conception

*Each letter represents a **gamete** (sperm or egg) carrying an allele for a gene.*



Fertilization of egg by sperm is random

Maternal alleles

	A	a
A	AA	Aa
a	Aa	aa

*The multiplication of two letters in the Punnet square represents **one possible conception**.*

Predicting Inheritance

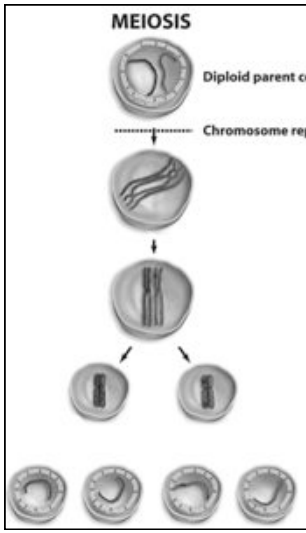
<u>Albinism</u>

`A = dominant allele (normal)`

`a = recessive allele (albino)`

`AA =` **`homozygous dominant`**
`Aa =` **`heterozygous`**
`aa =` **`homozygous recessive`**

? If father is **heterozygous** and mother is **homozygous recessive** (albino), what are the possible genotypes and phenotypes of their offspring?



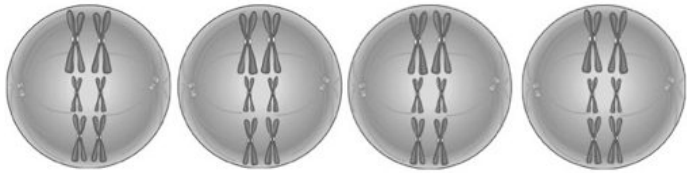
Mendel's second law- Law of independent assortment

1st law: Through meiosis, every allele is separated from its corresponding homologous allele

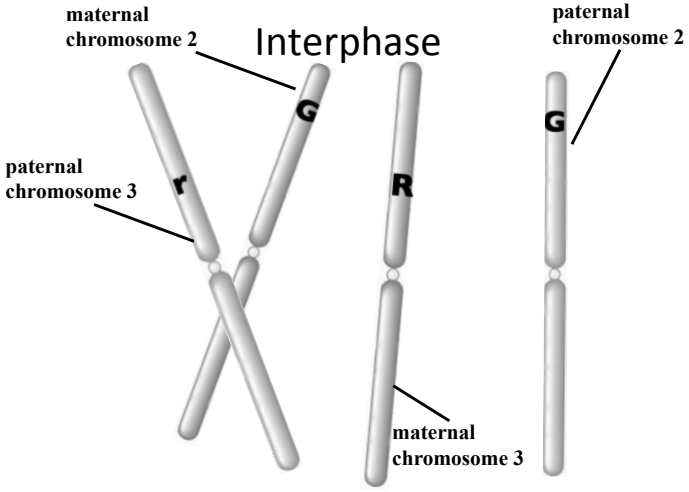
2nd law: Alleles of different genes assort independently of one another during gamete formation

Exception: linked traits

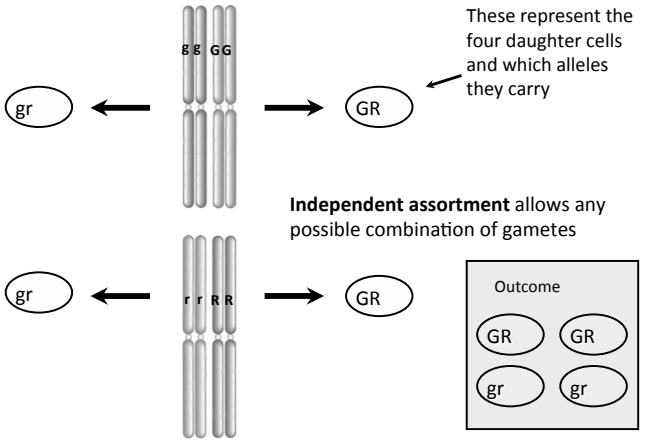
Independent Assortment



The **Punnett Square** is simulating all possible ways that chromosomes could line up and separate in **Meiosis I**

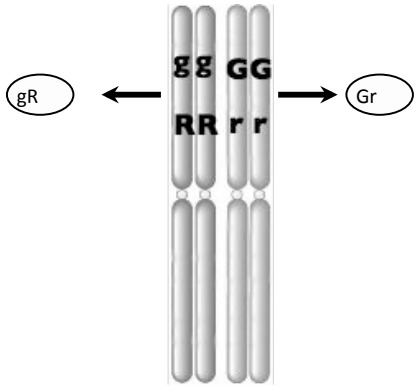


After Meiosis



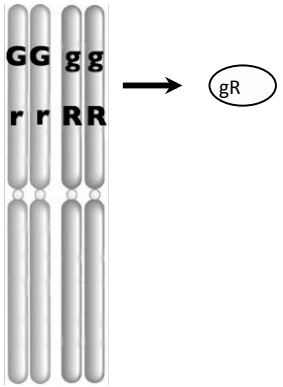
Linked Genes

What if the genes are on the same chromosome?



Linked Genes

What if the alleles are on the same chromosome?



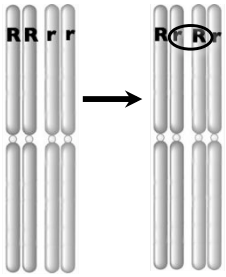
There is no chance the two dominant alleles for the "G" and "R" genes will segregate together.

Independent assortment no longer applies...

Linked Genes

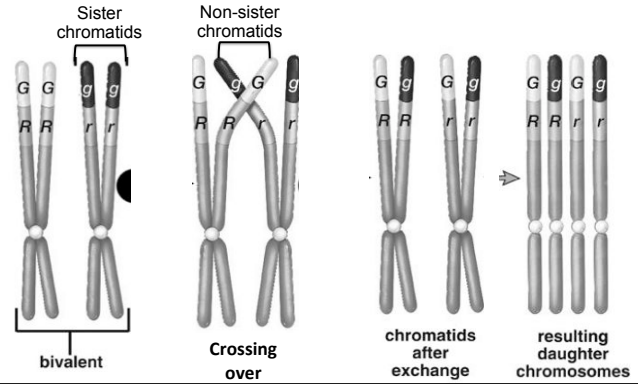
Does this mean that only alleles on separate chromosomes can **segregate** to different gametes?

What else happens at synapsis?

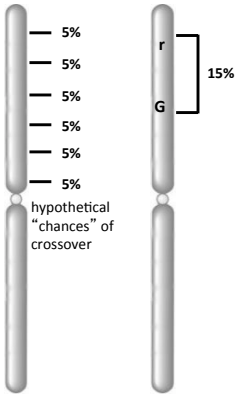


Recombination

Crossing-over creates **recombinant alleles** in a random fashion that is a function of the distance between the two alleles.



Recombination



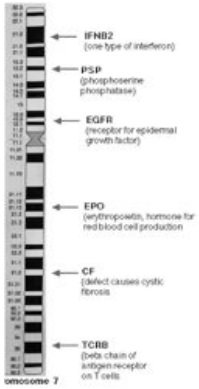
The further apart the alleles are, the greater the chance of a **recombination event** (crossing-over) *between the two alleles*

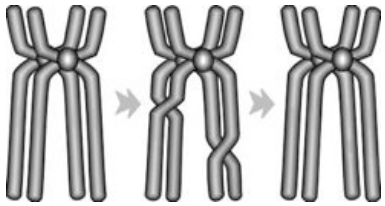
To unlink the alleles, crossing over must occur **between** them.

Recombination

Therefore, if two genes are together on the same chromosome, they are called **physically linked**, but if far enough apart, they can be **genetically unlinked**.

Recombination frequencies are greater for loci that are farther apart on the chromosome





Genes on the same chromosome are **linked**, but can be separated by crossing over in Meoisis

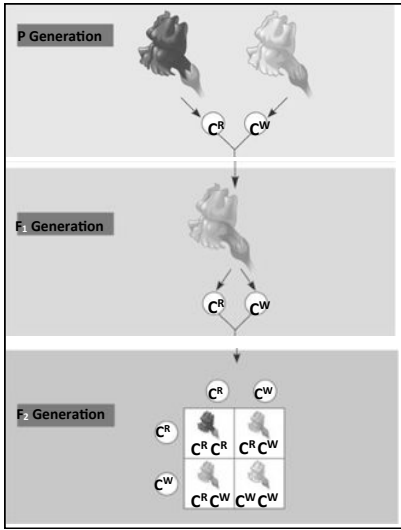
So, is crossing-over random?
...sorta

Human Traits and Mendel's Genetics

Some traits exhibit complete dominance

Trait	Dominant	Recessive
Dimples	Dimples	No Dimples
Rh factor	Rh (+)	Rh (-)
Fingers	Six Fingers	Five Fingers
Dwarfism	Dwarfism	Normal Growth

The most common characteristics are not necessarily the **dominant** ones.



Incomplete Dominance

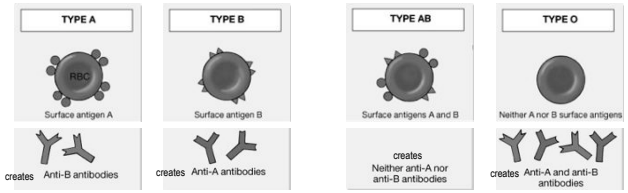
The red allele produces a certain "amount" of red pigment. More red alleles means more red pigment.

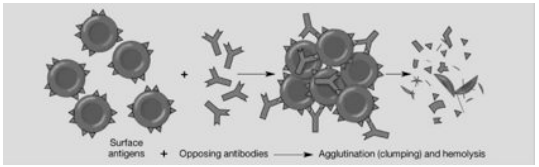
This is NOT blending of genes.

In incomplete dominance, the **heterozygote** has an *intermediate* phenotype

Codominance

- **Codominance** is when an individual is heterozygous for a given trait both alleles are expressed at equal levels, **creating a new, different phenotype**.





Dominance Varieties

1. Complete dominance

   Mendel's pea experiments

2. Incomplete Codominance

   Pink snapdragon flowers

3. Complete dominance

   Blood types

Polygenic Inheritance

Two or more genes work **additively** to affect a phenotype

Wide range of skin pigmentation, it is not determined by a single gene.

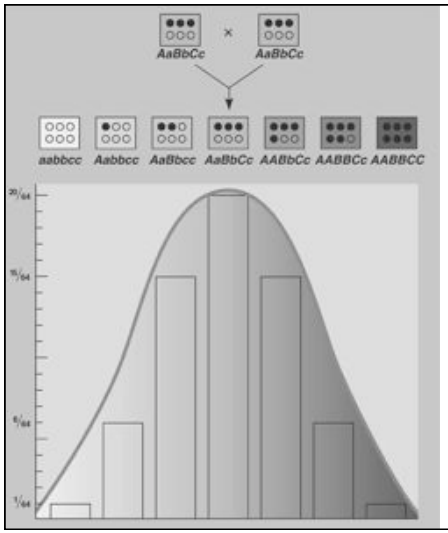
Example

Say that 3 genes (A, B and C) all contribute pigment to the skin.

These are **incompletely dominant to each other**.

Each incompletely dominant allele may contribute to phenotype as one "unit".

e.g. "**AaBbCc**" would contribute as much dark **gene product** as "**AABbcc**"



Polygenic Inheritance

- Dark pigment is incompletely dominant over light in all three alleles
- Two or more genes work **additively** to affect a phenotype

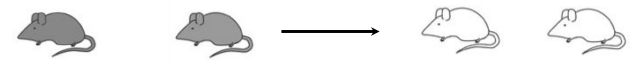
Epistasis

In **epistasis** one gene "controls" the expression of another.

Example

The pigment in coat color in a mouse is controlled by the "**B**" gene. Black (B) is dominant over brown (b)

Pigment *deposition in the hair* is controlled by the "**C**" gene



BB or Bb bb → cc BBcc Bbcc Bbcc

Depending on a different, **epistatic** gene, the mouse may be white (albino)

Environment and Phenotype

Environmental factors can also contribute to genetic expression

Nutrition affects height

Sunlight affects skin tone, tree shape

Coat color in Himalayan rabbits is dependent upon temperature

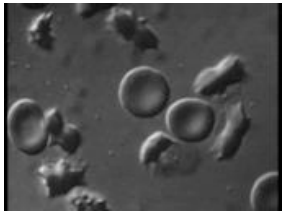
Environment and Phenotype

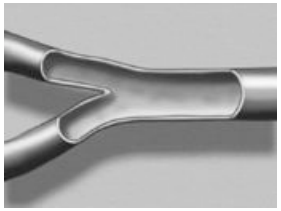
Coat color in Himalayan rabbits is dependent upon temperature

- The rabbit's back is shaved and an ice pack is applied until new fur begins to sprout.
- New coat fur is black (melanin pigmentation)
- The enzyme for melanin production is active at low temperatures

Sickle Cell Anemia

Cause: Mutation in Hemoglobin allele causes structural change in the protein





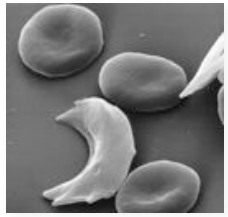
The red blood cells of sickle-cell anemia patient form irregular shapes, particularly when O_2 levels are low.

Heterozygotes generally have no symptoms unless exposed to low levels of O_2 for prolonged time

- **Incomplete dominance** at organismal level
- Considered **codominant** at the molecular level

Sickle Cell Anemia

Incidence: About 1 in 10 African-descent Americans are carriers of the allele. 1 in 400 have the disease.

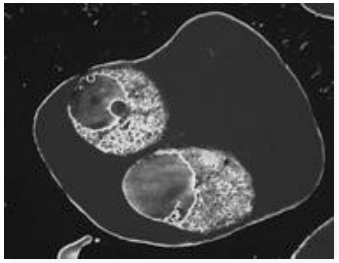


Sickle-Cell

Anopheles Mosquito

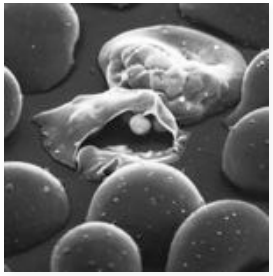
Sickle-Cell disease (even at **heterozygosity** levels) provides some resistance to **Malaria**

Malaria



Two developing malaria parasites, *Plasmodium falciparum*

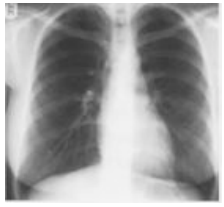
Plasmodium falciparum infecting red blood cells



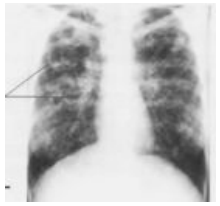
Human Disorders

Cystic Fibrosis

Caused by **recessive** allele



Normal X-ray



Cystic Fibrosis X-ray

Most common lethal genetic disease in the US of individuals of European descent.

Cause: Mutation in chloride channel causes fluid and mucus build-up, infection

Heterozygotes have no symptoms

Homozygotes traditionally die young,
but with modern therapies may live to 20s or 30s

Human Disorders

Cystic Fibrosis

Cause: Mutation in chloride channel causes fluid and mucus build-up and infection

1 in 2500 of European-descent caucasians carry the allele for CF

Typhoid Fever

Intestinal Typhoid ulcers

Chloride channel required for Typhoid infection

Universal Taboo

Mating of close relatives is nearly a universal taboo among cultures...

The chance of the **same recessive alleles** being passed on to one individual **increases** when close family members conceive.

Not All Genetic Disorders Are Recessive

A number of human disorders are due to dominant alleles

Despite being a **dominant allele**, the **Achondroplasia** (dwarfism) allele appears in less than 99.99% of the population (~1 in 25,000 worldwide)

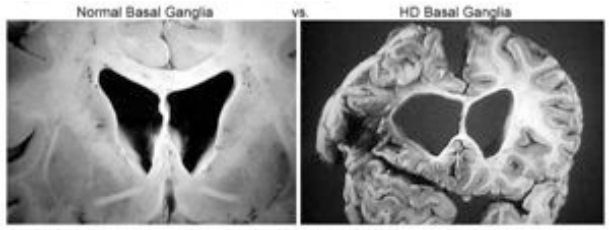
Dominant disorders cannot "hide" as well as recessive disorders. There are no hidden "carriers"... or are there?

Not All Genetic Disorders Are Recessive

A number of human disorders are due to dominant alleles

Huntington's Disease

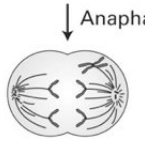
- Dominant allele. Leads to fatal disease. (odds of appearing at birth are ~1:10,000)



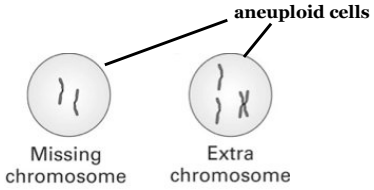
The basal ganglia of the human brain, showing the impact of HD on brain structure in this region. Note especially that the brain of a person with HD has bigger openings due to the death of nerve cells in that region.

- Has no obvious defect until the individual is 35-45 years old!
- Tests exist to determine if you are a carrier of the diseased allele... do you want to know?

Nondisjunction

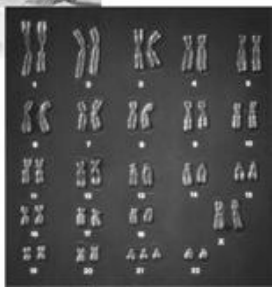


A loss (or gain) in a full chromosome, called **aneuploidy,** almost always results in death of the organism



Non-lethal aneuploidy

Down syndrome is caused by aneuploidy, specifically an extra copy of chromosome 21, "trisomy 21"



The frequency of **trisomy** increases with maternal age

Non-lethal aneuploidy

Table 12A

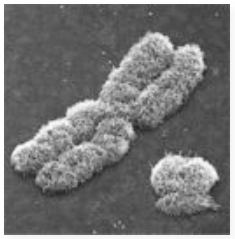
Syndromes from Abnormal Chromosome Numbers

Syndrome	Sex	Disorder	Chromosome Number	Frequency	
				Spontaneous Abortions	*Live Births*
Turner	F	XO	45	1/18	1/2,500
Klinefelter	M	XXY (or XXXY)	47 or 48	1/300	1/800
Poly-X	F	XXX (or XXXX)	47 or 48	0	1/1,500
Jacobs	M	XYY	47	?	1/1,000
Down	M or F	Trisomy 21	47	1/40	1/800

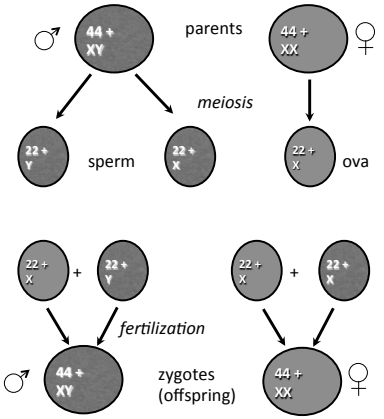
Due to the unique nature of the X chromosome (1 or 2 copies, depending on sex), there are several combinations of aneuploidy that are compatible with life

Sex-Linked Traits: The X and Y Chromosome

Male humans have only one X chromosome



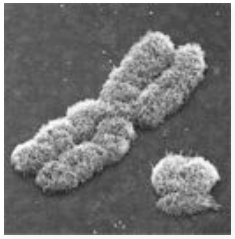
X and Y Chromosomes



The X Chromosome

Male humans have only one X chromosome, are **hemizygous**

There are a number of **recessive** alleles that may reside on the X chromosome



X and Y Chromosomes

- Color blindness
- Muscular dystrophy
- Hemophilia

Prokaryotes and Genetic variability

Prokaryotes lack nuclei, genetic material typically a single chromosome

How do they evolve?

Bacterial conjugation
-horizontal gene transfer
-recombination

Mutations

Plasmid DNA transfer

Horizontal gene transfer