Patterns of Inheritance

- Mendelian Genetics

Heredity

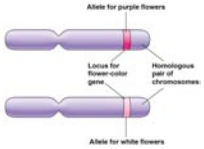
- Passing on a physical characteristic to future generations
  - Eye color, ear shape, diseases, feather color

Some things you probably already know about heredity

- Children resemble their parents.
- Children are *not* identical to their parents.

Genes

- Discrete hereditary units that determine physical traits
  - Segments of DNA coding for protein
- Genetics
  - The study of the transmission of inheritable traits

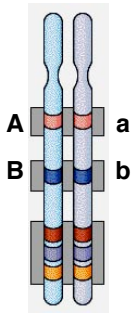


Some things you already know about genes

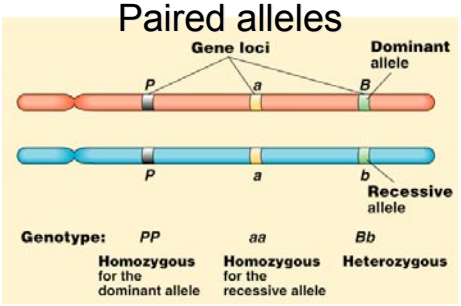
- **Genes are carried on chromosomes.**
- **Most eukaryotes are diploid. (have 2 copies of each chromosome).**
- **Genes are sequences of DNA that code for proteins (or at least for RNA).**
- **Mutations happen.**
- **There is variation in populations.**
- **Sex makes new combinations of variations.**

Terminology

- Genetic **locus**: site on a chromosome where a gene is located
- **Allele**: variation of same gene carried on homologous pairs of chromosomes



Paired alleles



- **Homozygous** (AA or aa): paired alleles on homologous chromosomes are the same
- **Heterozygous** (Aa): paired alleles are different

Relationship between alleles of the same gene

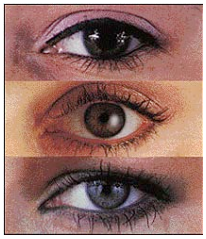
- **Dominant**: the allele that is expressed in a heterozygote (produces physical appearance)
- **Recessive**: the allele that is masked in a heterozygote

Genotype: genes carried on chromosomes

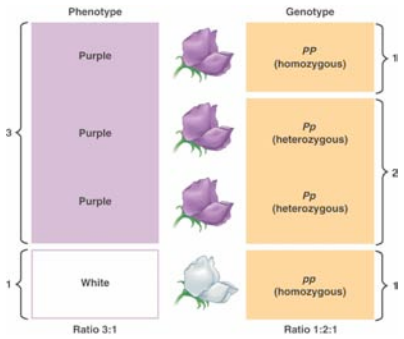
- **Genotype**: genetic make-up
  - Designated by letters
  - Dominant gene in upper case letters
  - Recessive gene in lower case letters

AA = homozygous dominant
Aa = heterozygous
aa = homozygous recessive

- **Phenotype**: physical manifestation of genotype
  - Brown eyes or blue eyes

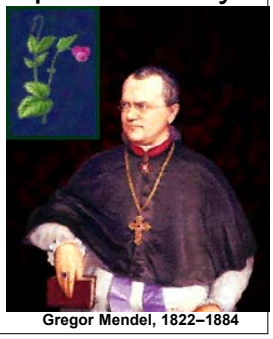


Phenotype vs. Genotype



Gregor Mendel was the first to study genetics experimentally

- Used pea plants as a model system
- Developed two major genetic principles
  - **Principle of Segregation**
  - **Principle of Independent Assortment**

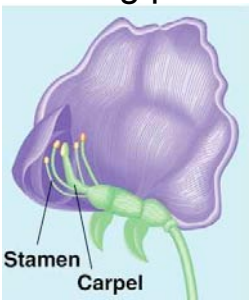


Gregor Mendel, 1822–1884

Peas can be mated by artificially transferring pollen

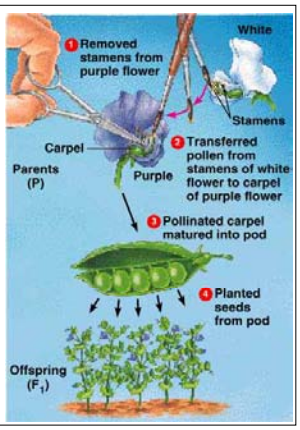
Hermaphroditic flowers

- Stamen: male parts
  - Pollen: carry male gametes
- Carpel: female parts
  - Ovary: contains female gametes



Artificial fertilization

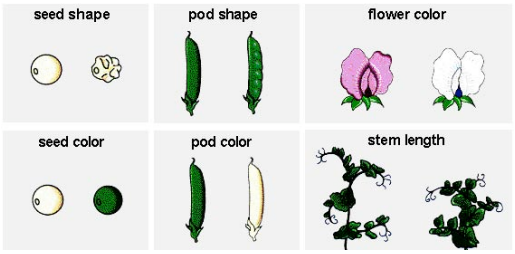
- Two plants that are mated are called a cross
- Resulting peas are seeds (embryos) that will mature into the next generation



Mendel used monohybrid crosses to study single traits

- Used pure breeding plants
  - Plant is homozygous for all genes
- Mated two individuals that differ by only one trait
  - E.g, purple flowers vs. white flowers

Various pea phenotypes

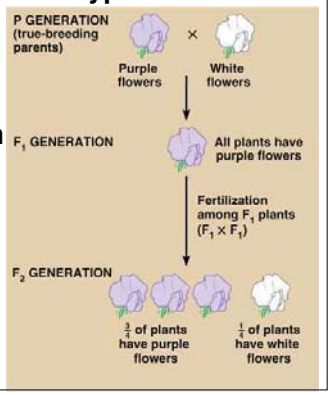


Phenotype: flower color

Parental generation

F_1: first generation offspring (first filial)

F_2: second generation Offspring (second filial)

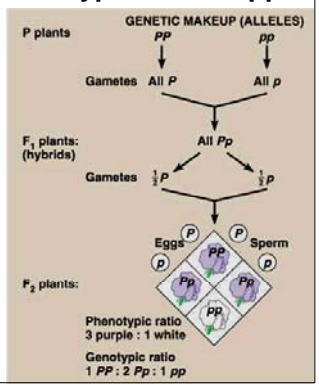


Genotype: PP and pp

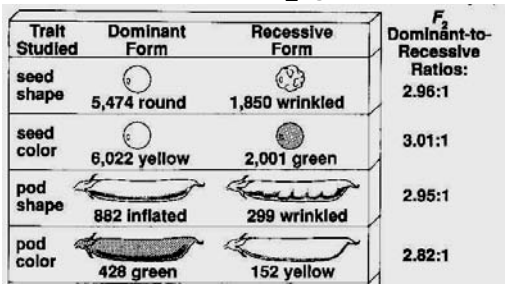
Parental cross: PP X pp

F_1: all heterozygous

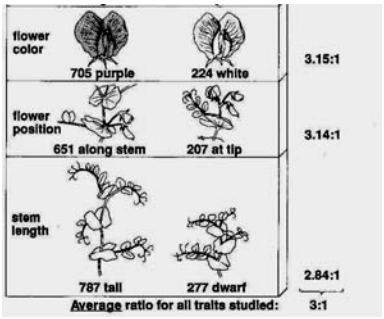
F2: genotypic ratio 1 PP **:** 2 Pp **:** 1 pp



Recessive phenotype reappeared in F_2 generation



Average phenotypic ratio for all traits studied: 3 to 1



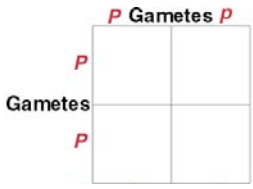
Offspring will have a phenotypic ratio of 3 to 1 only if paired alleles assort randomly

What happens to paired alleles during meiosis?

- **AA** genotype
  - Possible gametes made: only **A**
- **aa** genotype
  - Possible gametes made: only **a**
- **Aa** genotype
  - Possible gametes made: **A** or **a**
- So if both flowers are **Aa** genotype
  - 50% of sperm in pollen are **A**; 50% are **a**
  - 50% of ova in carpal are **A**; 50% are **a**

Fertilization is random

- Either **A** or **a** from one parent can be fertilized by **A** or **a** from other parent
- Can use a Punnett square to predict possible genotypes of offspring

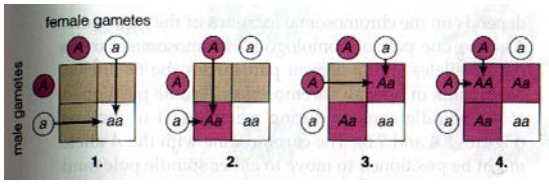


Punnett Square

- So if both parents are **Pp** genotype
  - 50% of sperm are **P**; 50% are **p**
  - 50% of ova are **P**; 50% are **p**

At any given locus, you have an equal chance of passing on mom's allele or dad's allele.

Punnett Square: Aa X Aa



Each allele has an equal chance of combining with either allele of other parent

Mendel's **Principle of Segregation**

- Pairs of genes separate during gamete formation
  - –Each gamete carries only one allele for each gene (haploid)
- Pairs of genes reform when gametes fuse during fertilization

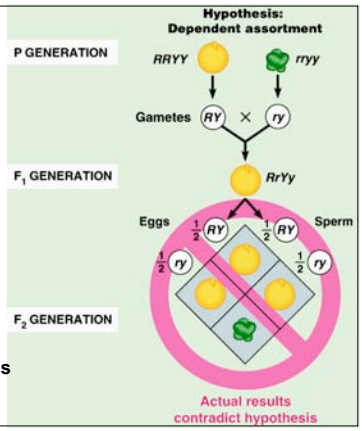
Are all the traits inherited from one parent passed on together to subsequent generations as a set?

Dihybrid cross: Tracking two characteristics at once

- Parental organisms differ in two characteristics
  - – For example,
    - Seed shape: round vs. wrinkled
    - *and*
    - Seed color: yellow vs. green

Hypothesis: **Dependent assortment**

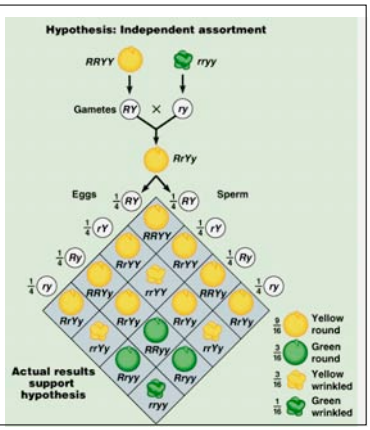
- Are traits of one parent always inherited together?
  - **NO!**
    - – **Reject hypothesis**



Actual results:

all four possible phenotypes appear in F_2 generation

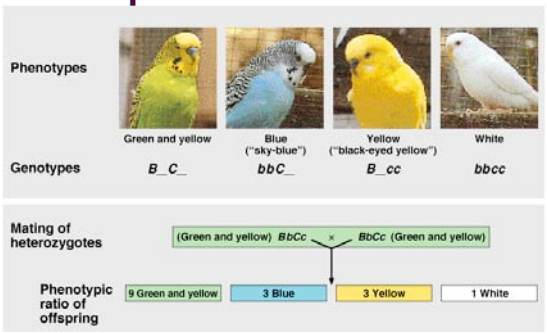
phenotypic ratio 9:3:3:1



Mendel's **Principle of Independent Assortment**

- Each different trait segregates independently during gamete formation
  - –Seed shape and seed color are inherited separately from each other

Independent Assortment

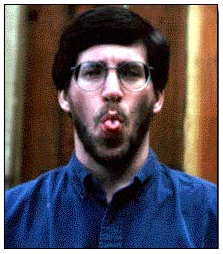


Understanding meiosis is key to understanding genetics

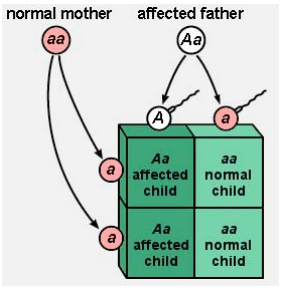
- Meiosis produces haploid gametes
- Paired alleles segregate (separate) during meiosis
- Knowing genotype of gamete allows prediction of phenotype and genotype of offspring

Simple dominance

- Heterozygote (**Aa**) has the same phenotype as homozygous dominant (**AA**)



Punnett square to predict inheritance of an autosomal dominant trait



How can you determine the genotype of an individual exhibiting the dominant phenotype?

Homozygous dominant or heterozygous?

- **Test cross**: Cross a dominant individual with a recessive individual to determine genotype of dominant parent
- Recessive allele will unmask a recessive allele carried by a heterozygous parent

Test Cross

If AA X aa

↓

All **Aa**
(All dominant phenotype)

If Aa X aa

↓

Half **Aa**
(dominant phenotype)
Half **aa**
(recessive phenotype)

Mendel's questions

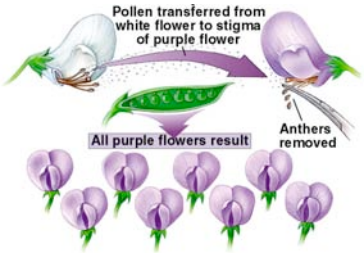
- **How can a trait "skip" a generation? (In other words, how can a trait be recessive?)**

How can an allele be recessive?

- Alleles at the same locus are expressed independently of each other.
- An allele doesn't know if its homolog is dominant or recessive.

How can an allele be recessive?

- Why does white show up only when it's homozygous?

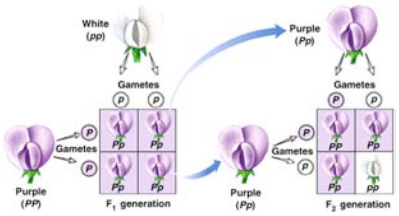


How can an allele be recessive?

- Why does white show up only when it's homozygous?
- Maybe white allele is a **loss-of-function** mutation: no pigment is created.
- Could code for non-functional protein, or not code for a protein at all.

How can an allele be recessive?

- If there's no functional pigment protein, flower will be white.

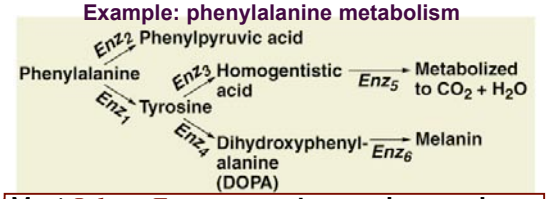


How can an allele be recessive?

- If there's no functional pigment allele, flower will be white.
- If there's a functional pigment allele, cells will keep making pigment protein until there's enough.
- **Dosage compensation**: it doesn't matter how many copies of an allele are present.

Remember *Inborn Errors of Metabolism*?

Example: phenylalanine metabolism



Most *Inborn Errors* are **autosomal recessive:**

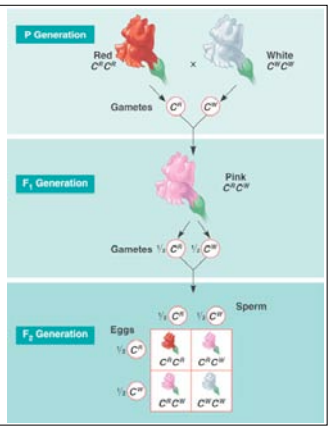
- As long as at least one allele codes correctly enough functional enzyme will be made.
- Only if both alleles code for nonfunctional enzyme will the pathway be interrupted.

Incomplete Dominance

AA aa Aa

- Alleles blend to produce intermediate phenotype in heterozygotes

Incomplete Dominance

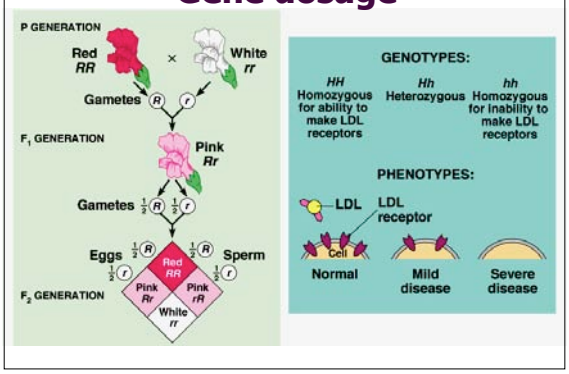


Most loci do not show complete dominance.

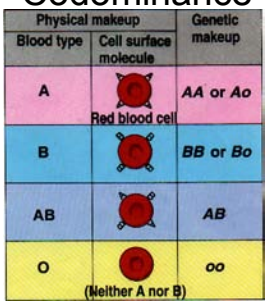
"Gene dosage"

Cells with two copies of the dominant allele make more gene product than do cells with only one copy.

"Gene dosage"



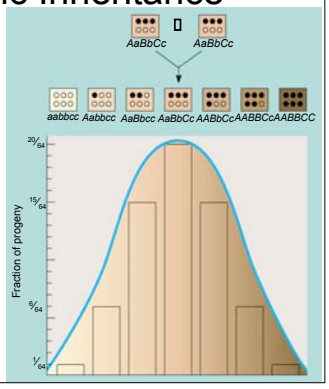
Codominance



Two alleles (A or B) are both dominant over a third allele (O), but not over each other

Polygenic Inheritance

Many phenotypes are the product of many genes interacting.



Inheritance of skin color in humans

Figure 14.12

Chromosome Theory of Inheritance

- Mendelian genes have specific loci on chromosomes
- Chromosomes undergo segregation and independent assortment

Molecular probe for a specific gene shows two distinct spots (one per chromatid) on each of two different chromosomes (homologous pair).

Chromosome Theory of Inheritance

- The chromosomal basis of Mendel's laws

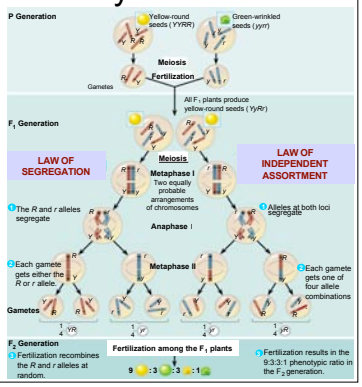


Figure 15.2

Chromosome Theory of Inheritance

- T.H. Morgan and the "Fly Room" ~ early 1900s
- Fruit-fly, *Drosophila melanogaster*
  - Generation time = 2 weeks; fecundity = >100 offspring
  - N = 4 pairs of large chromosomes
- Common allele in wild population: "wild type" (+).
- Spontaneous or experimentally induced variant: "mutant".
- Genes typically named for the mutant phenotype.

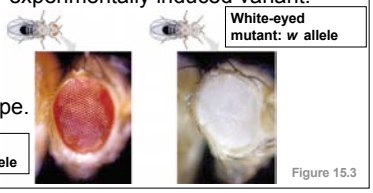
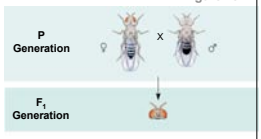


Figure 15.3

Segregation, yes — but not-so-independent assortment

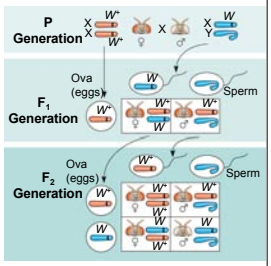
- Monohybrid cross of w^+w^+ x $w\,w$
  - 100% of F_1 red-eyed (w^+w)
  - Red-eyed allele must be dominant
    - So far so good
- Next, F_1 x F_1
  - F_2 red-eyed & white eyed (3:1)
    - As expected from Mendelian law of segregation
- *But*, **all** white-eyed progeny are **male**!?!
  - Inheritance of phenotype is dependent upon gender!
  - "sex-linked"

Figure 15.4



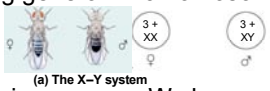
Sex-linked inheritance

- *Drosophila* has XY sex determination
  - XX are female
  - XY are male
- Thus, if eye-color gene is on the X chromosome, males are hemizygous (have only one version of that gene) and cannot ever be heterozygous
- The first solid evidence indicating that a specific gene is associated with a specific chromosome



Genetic sex determination

I. Male-determining gene on Y chromosome

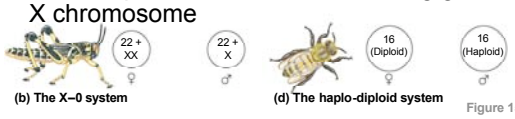


(a) The X–Y system

II. Female-determining gene on W chromosome

(c) The Z–W system

III. Dose-dependent female-determining gene on X chromosome

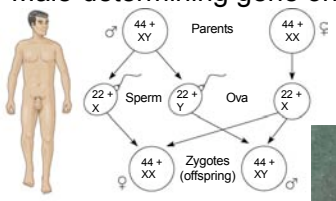


(b) The X–0 system (d) The haplo-diploid system

Figure 15.9

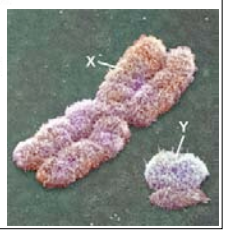
Genetic sex determination

I. Male-determining gene on Y



(a) The X-Y system in humans

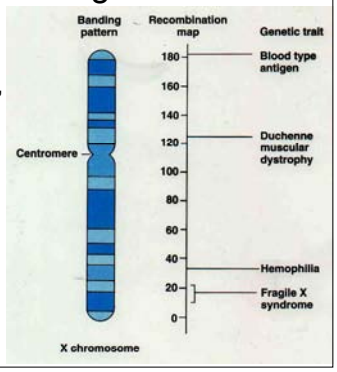
Figure 15.9



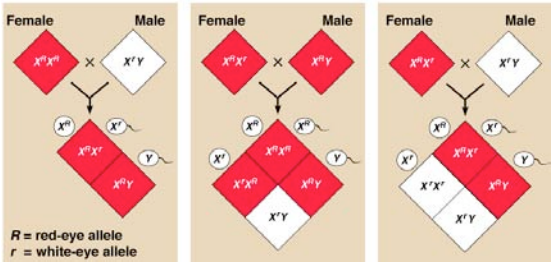
- **X chromosome: 153 Mbp, 900-1200 genes**
- **Y chromosome: 23 Mbp, 78 genes**

Sex-linked genes

- Genes carried on sex chromosomes, but not related to sex determination



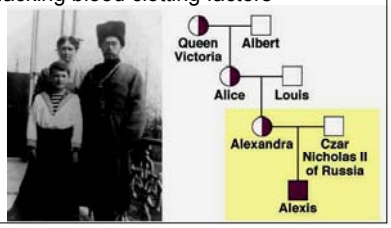
Inheritance of sex-linked genes



- X-linked traits are expressed in males with only 1 gene (X^rY)
- Females must be homozygous recessive for phenotype (X^rX^r)

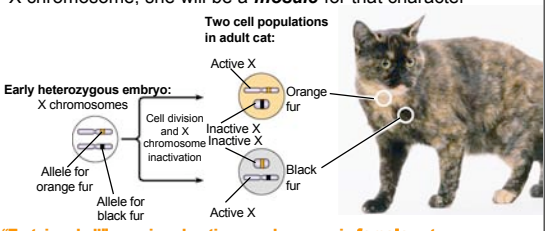
Recessive disorders on human X-linked genes

- Colorblindness: lacking receptors in retina that detect a particular color
- Duchenne Muscular Dystrophy (DMD): progressive muscle degeneration
- Hemophilia: lacking blood clotting factors



X inactivation in Female Mammals

- In mammalian females one of the two X chromosomes in each cell is randomly inactivated during embryonic development
  - So both males and females have only one functional **X** per cell
- If a female is heterozygous for a particular gene located on the X chromosome, she will be a ***mosaic*** for that character



Mendelian vs. chromosomal inheritance

- Independent assortment of chromosomes explains independent assortment of genes on separate chromosomes

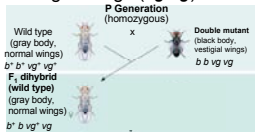
But …

- Each chromosomes has several hundred gene loci!
- So, how do you get independent assortment of genes occurring on the *same* chromosome?
- Sometimes you do, sometimes you don't!
  - "linked genes"

Linked genes

Morgan's Fly Room continues …

- **Dihybrid cross (b^+b^+ vg^+vg^+) x (bb $vgvg$)**
  - Gray body (b^+b^+) x black body (bb)
  - Normal wings (vg^+vg^+) x vestigial wings (vg vg)



  - **All F_1 gray body/normal wings (b^+b vg^+vg)**
    - As expected from Mendelian prediction

Figure 15.5

Linked genes

- Dihybrid cross (b^+b^+ vg^+vg^+) x (b b vg vg) ➔ **(b^+b vg^+vg)**
  ➔ all F_1 gray body/normal wings
- Now, perform **test cross of F_1**
  - **(b^+b vg^+vg) x (b b vg vg)**

– Mendelian prediction
independent assortment:
- **25%** gray body/normal wings (b^+b vg^+vg)
- **25%** gray body/vestigial wings (b^+b $vgvg$)
- **25%** black body/normal wings (bb vg^+vg)
- **25%** black body/vestigial wings (bb $vgvg$)

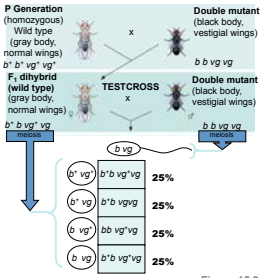


Figure 15.9

Linked genes

- Dihybrid cross (b^+b^+ vg^+vg^+) x (b b vg vg) ➔ **(b^+b vg^+vg)**
  ➔ all F_1 gray body/normal wings
- Now, perform **test cross of F_1**
  - **(b^+b vg^+vg) x (b b vg vg)**

– **dependent assortment** prediction:
- **50%** gray body/normal wings (b^+b vg^+vg)
- **50%** black body/vestigial wings (bb $vgvg$)

– **independent assortment** prediction:
- **25%** gray body/normal wings (b^+b vg^+vg)
- **25%** gray body/vestigial wings (b^+b vg vg)
- **25%** black body/normal wings (b b vg^+vg)
- **25%** black body/vestigial wings (b b vg vg)

– **Actual outcome (out of 2,300 progeny):**
- **42%** gray body/normal wings (b^+b vg^+vg)
- **9%** gray body/vestigial wings (b^+b vg vg)
- **8%** black body/normal wings (b b vg^+vg)
- **41%** black body/vestigial wings (b b vg vg)

– **Conclusions:**
- Parental phenotypes preferentially inherited
- *b* and *vg* genes are **linked** — *Usually* inherited as a unit

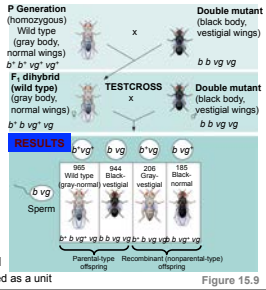
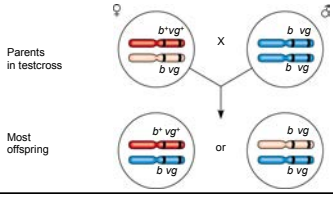


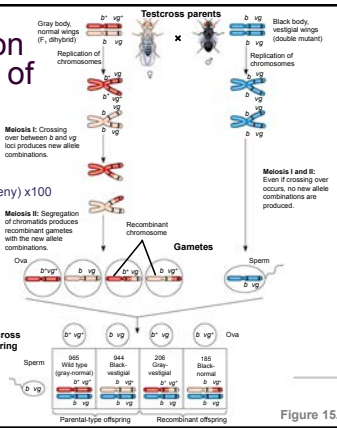
Figure 15.9

Linked genes

Morgan determined that
- Genes that are close together on the same chromosome are linked and do not assort independently
- Unlinked genes are either on separate chromosomes or are far apart on the same chromosome and assort independently
- **Crossing-over** can cause loci on the same chromosome to be segregated independently in meiosis
  – The closer the loci are to each other, the less likely a crossing-over event will occur between them — "tightly linked"
  – The farther apart, the more likely they will be inherited independently



Recombination & segregation of linked loci



- Recombination frequency
  = (# recombinations/total # progeny) x100

So for b & vg loci
(391/2300)100 = 17%
= 17 "linkage units" apart
on chromosome II

Figure 15.10

Linkage map of a chromosome

- The map of the relative position of loci on a chromosome based upon recombination frequencies between those loci
- Map units are expressed as ***centimorgans (cM)***
  - 1 centimorgan = 1% crossover frequency

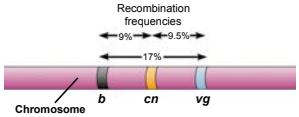
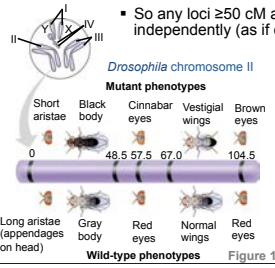


Figure 15.11

FOR EXAMPLE: On *Drosophila* chromosome II there occurs crossovers 9% of the time between the *b* locus and the *cn* locus during meiosis and gametogenesis; and there occur crossovers 9.5% of the time between the *cn* locus and the *vg* locus.
Hence *b* and *cn* are 9 cM apart; and *cn* and *vg* are 9.5 cM apart.
NOTE: The distance between *b* and *vg* is underestimated by crossover frequency. The farther apart two loci are, the more likely that a second crossover will negate the first one.

Linkage map of a chromosome

- In humans, 1 cM ≈ 1 million bp
  - But since crossing-over is not purely random, there is considerable intra-species and interspecies variation
- If linkage distance = 50 cM, then there is a 50:50 chance of a crossover.
  - So any loci ≥50 cM apart are segregated and inherited independently (as if on separate chromosomes)



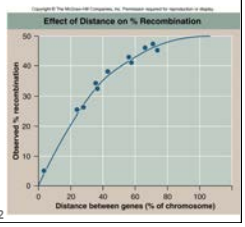


Figure 15.12

Some inheritance patterns seem to follow neither Mendelian nor chromosomal models

- Epistasis
- Pleiotropy
- Genomic imprinting
- Extra-nuclear genes
- Environmentally-restricted expression

Epistasis

- The expression or non-expression of the **epistatic gene** suppresses the expression of another gene
- E.g., …
  - For the mouse coat-color gene, black (B) is dominant over brown (b).
  - But if the pigment-production gene is homozygous recessive (cc), no pigment is produced and coat color is white, no matter what the genotype of the coat-color gene is!

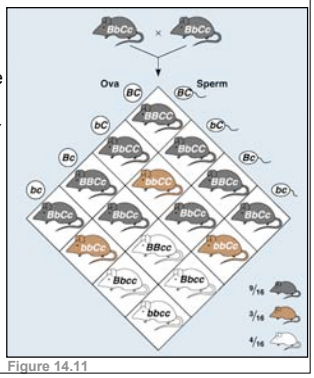
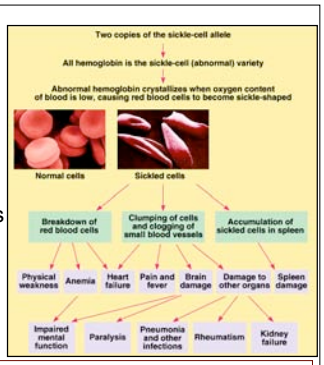


Figure 14.11

Pleiotropy

- A gene with **pleiotropic** expression affects multiple phenotypic characteristics.
- Some of these effects may epistatically modify other gene expression



Codominance: heterozygotes produce two kinds of hemoglobin
One in ten African-Americans carries the sickle-cell trait (heterozygous)
One in four-hundred has sickle-cell disease (homozygous)

Genomic imprinting

- The "silencing" of certain genes that are "stamped" with an imprint during gamete production
- The phenotypic effects of certain genes depend on which allele is inherited from the mother and which is inherited from the father

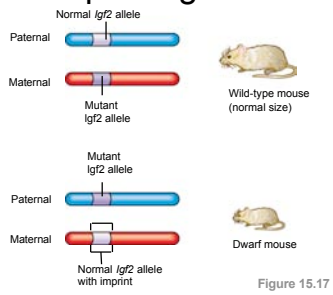


Figure 15.17

When a normal Igf2 allele is inherited from the father, heterozygous mice grow to normal size.
But when a mutant allele is inherited from the father, heterozygous mice have the dwarf phenotype.

Extra-nuclear genes

- Human mitochondrial DNA contains 37 genes
- Bryophyte chloroplast DNA contains 128 genes
- The inheritance of traits controlled by genes present in the chloroplasts or mitochondria usually depends solely on the maternal parent because the zygote's cytoplasm comes from the egg

Figure 15.18

- Yellow-blotch leaf phenotype inherited directly from maternal lineage
- Similarly, *mitochondrial myopathy* in humans inherited from mother

Environmentally-restricted expression

- Environmental determination of phenotype and gene expression

1. Temperature-dependent melanin production in bunnies
2. Soil-pH-dependent pigmentation in hydrangea flowers
3. Photoperiod-dependent coloration in arctic foxes