Class 19 10/6/17
human genetics

- Announcements
- Class administration
- Check iLearn for suggested problems
- **Monday 10/9 – Alternate Activity will be available on iLearn**
- **Wednesday 10/11 – Exam 2 (Classes 11 – 19)**
- **OFFICE HOURS**
  - **10/9 rescheduled to THU 10/12 2-4pm, HH668C**
  - **Extra office hours on TUE 10/10 4:30-6pm, HH525**
  - **10/16 rescheduled to THU 10/19 3-5pm, HH668C**
  - **Probably 10/23 will also be rescheduled…sigh…**

Biol 871 Colloquium in Microbiology, Cell & Molecular Biology

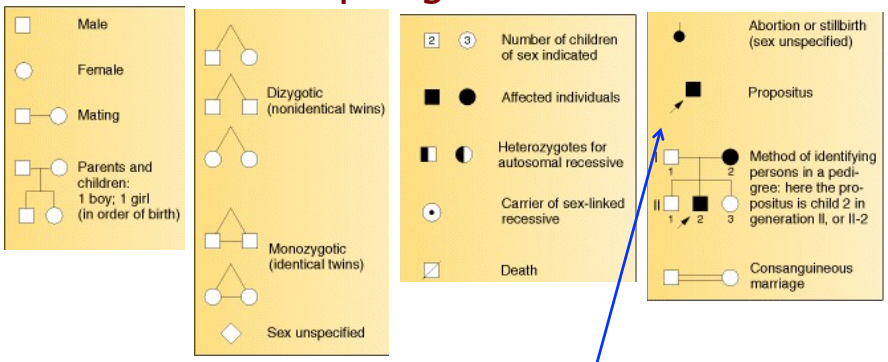
Thursday, 10/12/17
SCI 210, 2:10 pm

http://biology.sfsu.edu/content/MCMB

Steve Mack
CHORI
Understanding Human Diversity and Disease Through the Lens of Immunogenetics

http://www.chori.org/Principal_Investigators/Mack_Steve/mack_overview.html

Standard pedigree conventions



Or "proband"
Or "index case"

Figure 2-16

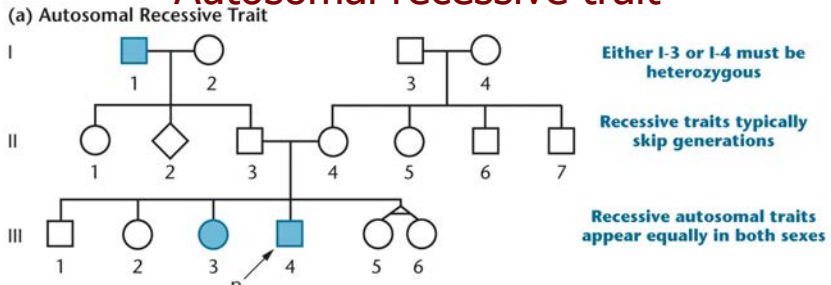
Standard pedigree symbols - 2

	Male	Female	Sex unknown
Pregnancy (P)	P LMP: 7/1/94	P 20 Weeks	V 16 Weeks
Spontaneous abortion (SAB), ectopic (ECT)	Male	Female	ECT
Affected SAB	Male	Female	16 Weeks
Termination of pregnancy (TOP)	Male	Female	12 Weeks
Affected TOP	Male	Female	12 Weeks

Standardized pedigree symbols and nomenclature for pregnancies and pregnancies not carried to term

http://what-when-how.com/genetics/genetic-family-history-pedigree-analysis-and-risk-assessment/

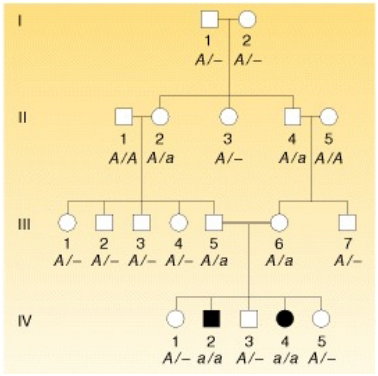
Autosomal recessive trait



- Autosomal recessive traits can skip generations (appear in progeny of unaffected persons) and affect both males and females equally.

Klug, 10th edition, Figure 3.13

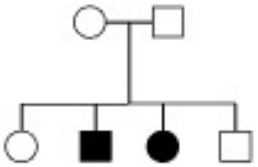
Autosomal recessive trait



- Autosomal recessive traits can skip generations (appear in progeny of unaffected persons) and affect both males and females equally.
- Rare recessive traits will often be expressed in consanguineous (blood relations) matings (first cousins)
- Example: The albino (*aa*) mutation inactivates the gene for tyrosinase enzyme, which normally converts tyrosine to melanin in the skin, hair and eyes.
  - Non-albino is *AA* or *Aa*

Figure 2-17

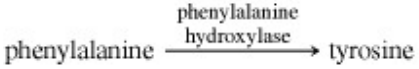
Autosomal recessive trait: PKU



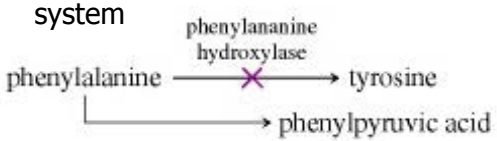
Newborn screening for PKU actually measures level of phenylalanine in infant's blood.

Equal/Nutrasweet/Aspartame is sugar substitute that contains **phenylalanine** and aspartic acid, 2 amino acids.

- PKU, Phenylketonuria
- Normally, the amino acid, phenylalanine is converted into tyrosine by phenylalanine hydroxylase



- If the enzyme has a mutation, then phenylalanine is converted to phenylpyruvic acid – which interferes with development of the nervous system



https://www.thinkgenetic.com/search-results;jsessionid=327D03E3A0963883DD5FA87EC9FE558B

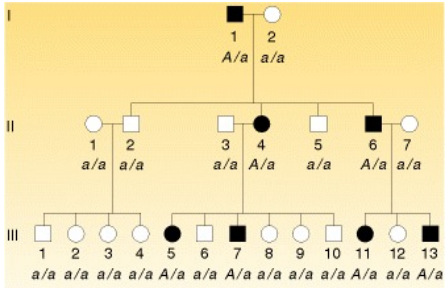
Figure from Ch 2, Human genetics

Autosomal dominant trait: pseudoachondroplasia

- The human pseudoachondroplasia phenotype, illustrated by a family of five sisters and two brothers
- The phenotype is determined by a dominant allele, D
- Most members of the human population can be represented as d/d

Figure 2-19

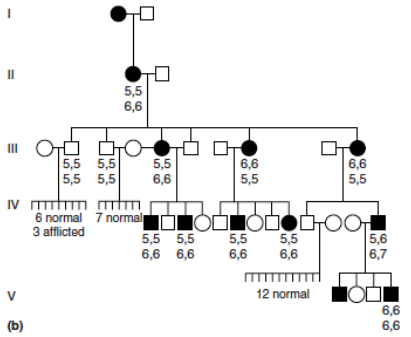
Autosomal dominant trait



- Autosomal dominant traits do not skip generations and affect both males and females.
- Some (but not all) children will be affected in every generation.
- Affected individuals are usually heterozygous since mutant allele is rare and usually have at least one affected parent
- Example: Hypotrichosis, hair loss begins in childhood for both males and females.

Figure 2-20

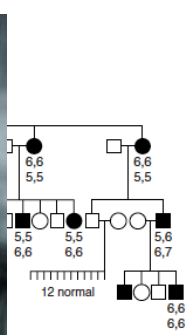
Autosomal dominant trait: Polydactyly



- Polydactyly phenotype involves extra fingers, toes, or both
- Allele P is dominant to p
- In the pedigree (b), the number of fingers is indicated on the upper line and the number of toes is indicated on the lower line

Figure 2-22

Autosomal dominant trait: Polydactyly



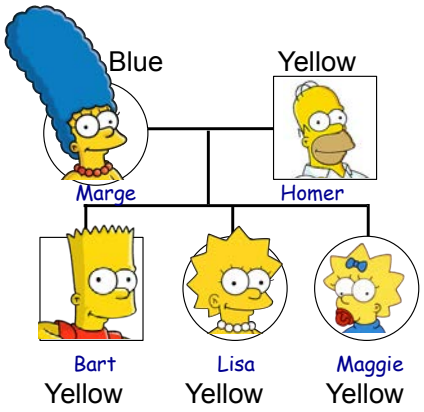
- Polydactyly p… …s, or both
- Allele P is do…
- In the pedigr… …cated on the upper line ar… …the lower line

Figure 2-22

Solving a pedigree problem

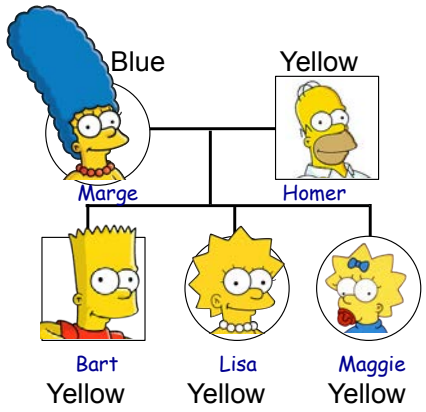
- Inspect the pedigree:
  - If trait is dominant, it will not skip generations nor will it be passed on to offspring unless parents have it.
  - If trait is recessive, it will skip generations (phenotype not observed) and it will exist in carriers (heterozygotes).
- Form a hypothesis, e.g. autosomal recessive.
- Deduce the genotypes.
- Check that genotypes are consistent with phenotypes.
- Revise hypothesis if necessary, e.g. autosomal dominant.

Clicker question: What is the mode of inheritance of hair color?



A. Yellow is dominant, Blue is recessive
B. Blue is dominant, Yellow is recessive
C. Not enough information to solve the problem

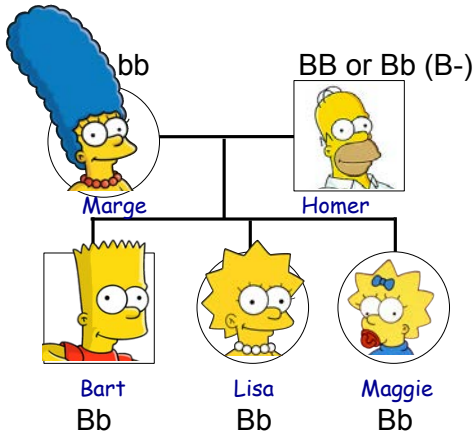
~~Clicker question~~: What is Homer's genotype?



For this problem, let b represent the blue allele and B represent the yellow allele.

A. BB
B. Bb
C. bb
D. B -
E. Not enough information to solve the problem

Clicker question: What is Homer's genotype?



Human X-linked traits

TABLE 4.3

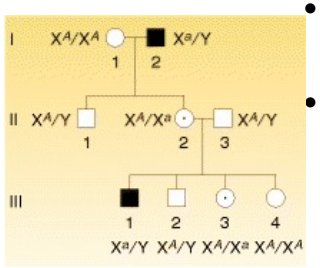
Human X-Linked Traits

Condition	Characteristics
Color blindness, deutan type	Insensitivity to green light
Color blindness, protan type	Insensitivity to red light
Fabry's disease	Deficiency of galactosidase A; heart and kidney defects, early death
G-6-PD deficiency	Deficiency of glucose-6-phosphate dehydrogenase; severe anemic reaction following intake of primaquines in drugs and certain foods, including fava beans
Hemophilia A	Classic form of clotting deficiency; deficiency of clotting factor VIII
Hemophilia B	Christmas disease; deficiency of clotting factor IX
Hunter syndrome	Mucopolysaccharide storage disease resulting from iduronate sulfatase enzyme deficiency; short stature, clawlike fingers, coarse facial features, slow mental deterioration, and deafness
Ichthyosis	Deficiency of steroid sulfatase enzyme; scaly dry skin, particularly on extremities
Lesch-Nyhan syndrome	Deficiency of hypoxanthine-guanine phosphoribosyltransferase enzyme (HPRT) leading to motor and mental retardation, self-mutilation, and early death
Muscular dystrophy	Progressive, life-shortening disorder characterized by muscle degeneration and weakness; (Duchenne type) sometimes associated with mental retardation; deficiency of the protein dystrophin

- Crisscross pattern of inheritance
  - Phenotype of homozygous mother observed in all sons

Klug et al., 10th edition, Table 4.3

X-linked recessive traits in humans



- X-linked recessive disorders are observed only in males (*affected homozygous females are rare*)
- Females are generally heterozygous carriers that do not develop the disorders (*allele is rare – normal female of unknown genotype is assumed to be homozygous dominant/wild type, unless evidence against this*)
- Males are hemizygous – show the phenotype
- Many traits controlled by X chromosome-linked traits
  - Red/green color blindness is classic example
  - Numerous significant genetic-based diseases, Duchenne muscular dystrophy

Figure 2-24

The Family of Queen Victoria in 1887

Tuxen, 1887; http://www.wga.hu/html_m/t/tuxen/family.html

Figure 2-25b

The inheritance of the X-linked recessive condition: hemophilia in the royal families of Europe

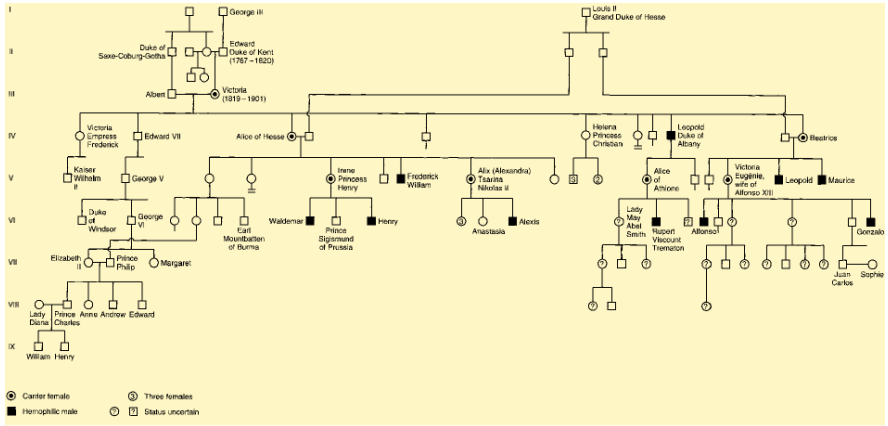


Figure 2-25a