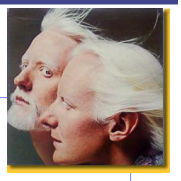


Chapter 14.

Beyond Mendel's Laws of Inheritance

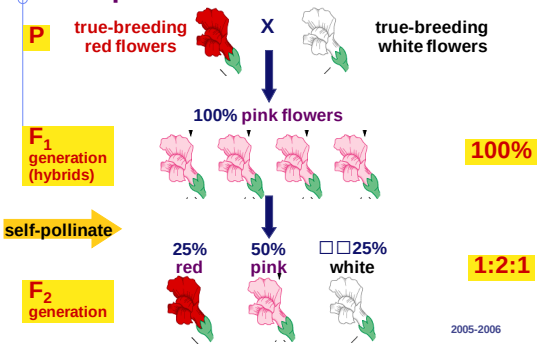
Extending Mendelian genetics

- Mendel worked with a simple system
  - peas are genetically simple
  - most traits are controlled by a single gene
  - each gene has only 2 alleles, 1 of which is completely dominant to the other
- The relationship between genotype & phenotype is rarely that simple

Incomplete dominance

- Heterozygotes show an intermediate phenotype
  - RR = red flowers
  - rr = white flowers
  - Rr = pink flowers
    - make 50% less color

Incomplete dominance



Incomplete dominance

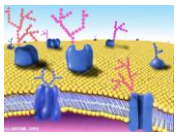
C^RC^W x C^RC^W

female / eggs \ male / sperm	C^R	C^W
C^R	C^RC^R	C^RC^W
C^W	C^RC^W	C^WC^W

	% genotype	% phenotype
C^RC^R	25%	25%
C^RC^W	50%	50%
C^RC^W		
C^WC^W	25%	25%
	1:2:1	1:2:1

Co-dominance

- 2 alleles affect the phenotype in separate, distinguishable ways
  - ABO blood groups
  - 3 alleles
    - I^A, I^B, i
    - both I^A & I^B are dominant to i allele
    - I^A & I^B alleles are co-dominant to each other
  - determines presences of oligosaccharides on the surface of red blood cells



Blood type

genotype	phenotype	phenotype	status
$I^A I^A$ $I^A i$	type A	type A oligosaccharides on surface of RBC	—
$I^B I^B$ $I^B i$	type B	type B oligosaccharides on surface of RBC	—
$I^A I^B$	type AB	both type A & type B oligosaccharides on surface of RBC	universal recipient
i i	type O	no oligosaccharides on surface of RBC	universal donor

1901 | 1930

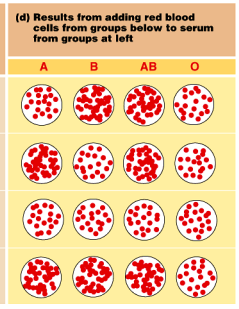
Blood compatibility

Karl Landsteiner (1868-1943)

- Matching compatible blood groups
  - critical for blood transfusions
- A person produces antibodies against oligosaccharides in foreign blood
  - wrong blood type
    - donor's blood has A or B oligosaccharide that is foreign to recipient
    - antibodies in recipient's blood bind to foreign molecules
    - cause donated blood cells to clump together
    - can kill the recipient

Blood donation

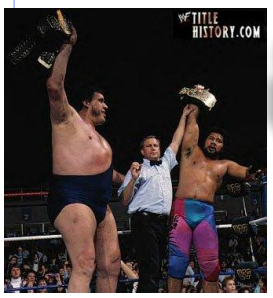
(a) Phenotype (blood group)	(b) Genotypes (see p.258)	(c) Antibodies present in blood serum	(d) Results from adding red blood cells from groups below to serum from groups at left			
			A	B	AB	O
A	$I^A I^A$ or $I^A i$	Anti-B				
B	$I^B I^B$ or $I^B i$	Anti-A				
AB	$I^A I^B$	—				
O	*ii*	Anti-A Anti-B				



Pleiotropy

- Most genes are pleiotropic
  - one gene affects more than one phenotypic character
    - wide-ranging effects due to a single gene:
    - dwarfism (achondroplasia)
    - gigantism (acromegaly)

Acromegaly: André the Giant

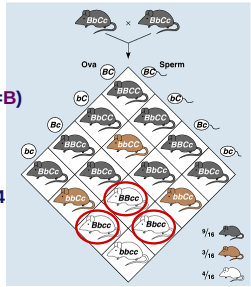


Pleiotropy

- It is not surprising that a gene can affect a number of organism's characteristics
  - consider the intricate molecular & cellular interactions responsible for an organism's development
    - cystic fibrosis
      - mucus build up in many organs
    - sickle cell anemia
      - sickling of blood cells

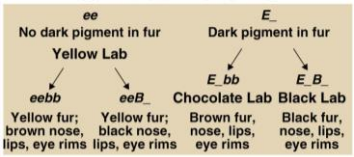
Epistasis

- One gene masks another
  - coat color in mice = 2 genes
    - pigment (C) or no pigment (c)
    - more pigment (black=B) or less (brown=b)
    - cc = albino, no matter B allele
    - 9:3:3:1 becomes 9:3:4



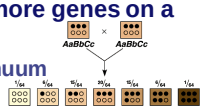
Epistasis in Labrador retrievers

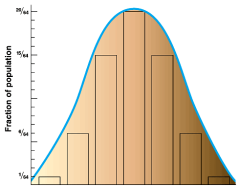
- 2 genes: E & B
  - pigment (E) or no pigment (e)
  - how dark pigment will be: black (B) to brown (b)



Polygenic inheritance

- Some phenotypes determined by additive effects of 2 or more genes on a single character
  - phenotypes on a continuum
  - human traits
    - skin color
    - height
    - weight
    - eye color
    - intelligence
    - behaviors





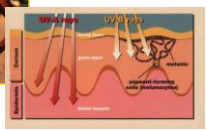
Nature vs. nurture

- Phenotype is controlled by both environment & genes

Human skin color is influenced by both genetics & environmental conditions

Coat color in arctic fox influenced by heat sensitive alleles

Color of Hydrangea flowers is influenced by soil pH



It all started with a fly…

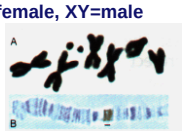
- Chromosome theory of inheritance
  - experimental evidence from improved microscopy & animal breeding led us to a better understanding of chromosomes & genes beyond Mendel
    - *Drosophila* studies

A. H. Sturtevant in the *Drosophila* stockroom at Columbia University

1910 | 1933

Thomas Hunt Morgan

- embryologist at Columbia University
  - 1st to associate a specific gene with a specific chromosome
  - *Drosophila* breeding
    - prolific
    - 2 week generations
    - 4 pairs of chromosomes
    - XX=female, XY=male



Morgan's first mutant…

- Wild type fly = red eyes
- Morgan discovered a mutant white-eyed male
  - traced the gene for eye color to a specific chromosome

Discovery of sex linkage

red eye female x white eye male

↓

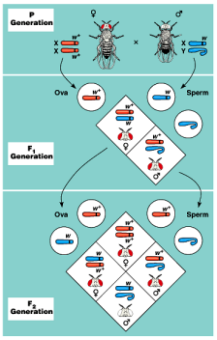
all red eye offspring

↓

75% red eye female x 25% white eye male

How is this possible?

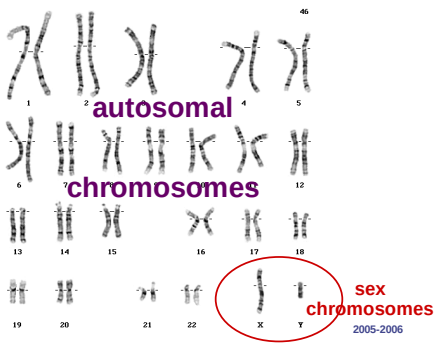
Sex-linked trait!



Sex-linked traits

- Although differences between women & men are many, the chromosomal basis of sex is rather simple
- In humans & other mammals, there are 2 sex chromosomes: X & Y
  - 2 X chromosomes develops as a female: XX
    - redundancy
  - an X & Y chromosome develops as a male: XY
    - no redundancy

Sex chromosomes

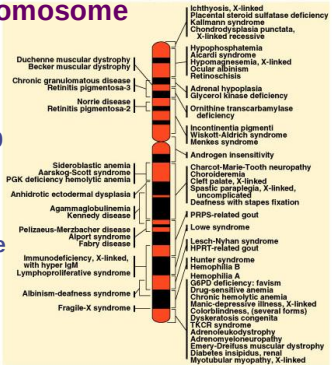


Genes on sex chromosomes

- Y chromosome
  - SRY: sex-determining region
    - master regulator for maleness
    - turns on genes for production of male hormones
      - pleiotropy!
- X chromosome
  - other traits beyond sex determination
    - hemophilia
    - Duchenne muscular dystrophy
    - color-blind

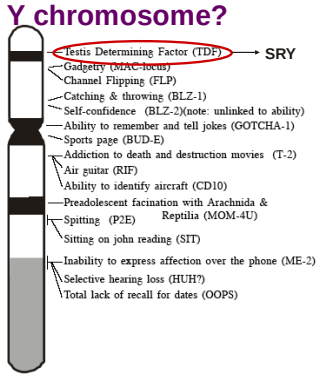
Human X chromosome

- Sex-linked
  - usually X-linked
  - more than 60 diseases traced to genes on X chromosome

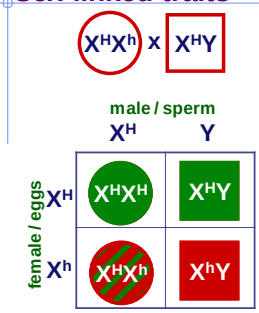


Map of Human Y chromosome?

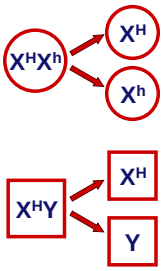
- < 30 genes on Y chromosome



Sex-linked traits



sex-linked recessive

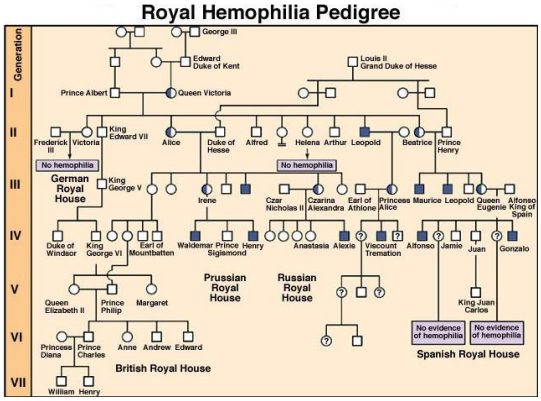


Sex-linked traits summary

- X-linked
  - follow the X chromosomes
  - males get their X from their mother
  - trait is never passed from father to son
- Y-linked
  - very few traits
  - only 26 genes
  - trait is only passed from father to son
  - females cannot inherit trait

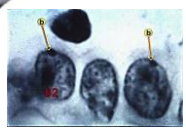
Queen Victoria and Descendants

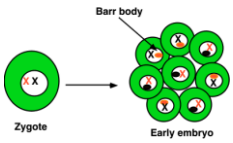
Royal Hemophilia Pedigree



X-inactivation

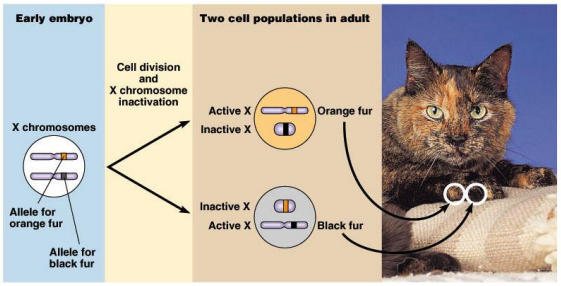
- Female mammals inherit two X chromosomes
  - one X becomes inactivated during embryonic development
    - condenses into compact object = Barr body





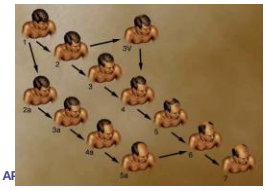
X-inactivation & tortoise shell cat

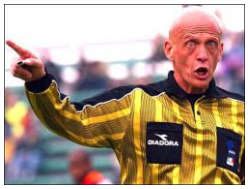
- 2 different cell lines in cat



Male pattern baldness

- Sex influenced trait
  - autosomal trait influenced by sex hormones
    - age effect as well: onset after 30 years old
  - dominant in males & recessive in females
    - B_ = bald in males; bb = bald in females



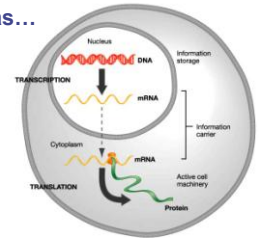


Mechanisms of inheritance

- What causes the differences in alleles of a trait?
  - yellow vs. green color
  - smooth vs. wrinkled seeds
  - dark vs. light skin
  - Tay sachs disease vs. no disease
  - Sickle cell anemia vs. no disease

Mechanisms of inheritance

- What causes dominance vs. recessive?
  - genes code for polypeptides
  - polypeptides are processed into proteins
  - proteins function as…
    - enzymes
    - structural proteins
    - hormones



How does dominance work: enzyme

= allele coding for functional enzyme

= allele coding for non-functional enzyme

= 50% functional enzyme
- sufficient enzyme present
- normal trait is exhibited
- NORMAL trait is DOMINANT

→ Aa carrier

= 100% non-functional enzyme
- normal trait is not exhibited

→ aa

= 100% functional enzyme
- normal trait is exhibited

→ AA

How does dominance work: structure

= allele coding for functional structural protein

= allele coding for non-functional structural protein

= 50% functional structure
- 50% proteins malformed
- normal trait is not exhibited
- MUTANT trait is DOMINANT

→ Aa

= 100% non-functional structure
- normal trait is not exhibited

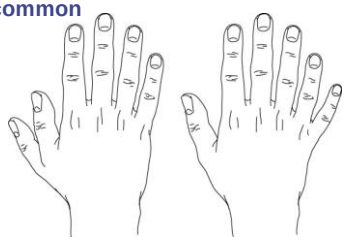
→ AA

= 100% functional structure
- normal trait is exhibited

→ aa

Prevalence of dominance

- Because an allele is dominant does not mean…
  - it is better
  - it is more common



Polydactyly: dominant allele

Polydactyly

individuals are born with extra fingers or toes

dominant to the recessive allele for 5 digits

recessive allele far more common than dominant

- → 399 individuals out of 400 have only 5 digits
- → most people are homozygous recessive (aa)

Any Questions??