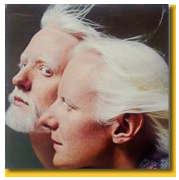
Chapter 10

Beyond Mendel's Laws of Inheritance

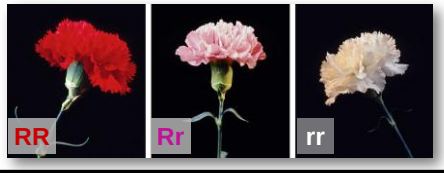


Extending Mendelian Genetics

- 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

- when one allele is ***partially*** dominant over the other
- hybrids have "in between" appearance
  - RR = red flowers
  - rr = white flowers
  - Rr = pink flowers
    - make 50% less color



Incomplete Dominance

4 O'clock flowers

Parent generation (P): RR (true-breeding red flowers) x R'R' (true-breeding white flowers)

100% pink flowers

1st generation (F_1 hybrids): RR' RR' RR' RR' — 100%

self-pollinate

2nd generation (F_2): 25% red, 50% pink, 25% white — 1:2:1

Incomplete Dominance (alt)

C^RC^W x C^RC^W

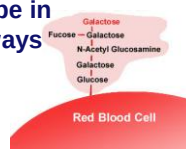
male / sperm: C^R, C^W

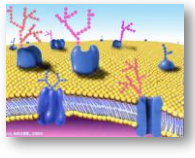
female / eggs: C^R, C^W

		% 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





Co-dominance example

- this time, both alleles are expressed, but they are NOT blended together
  - RR = red coat color
  - rr = white coat color
  - Rr = pink coat color???


Blood Types

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

Blood Type Compatibility

1901 | 1930

- 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


Karl Landsteiner (1868-1943)

Blood Type Compatibility

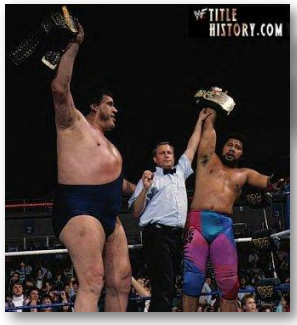
(a) Phenotype (blood group)	(b) Genotypes (see p.258)	(c) Antibodies present in blood serum	(d) Results from adding red blood cells from groups below to serum from groups at left			
			A	B	AB	O
A	$I^A I^A$ *or* $I^A i$	Anti-B				
B	$I^B I^B$ *or* $I^B i$	Anti-A				
AB	$I^A I^B$	—				
O	*ii*	Anti-A Anti-B				

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

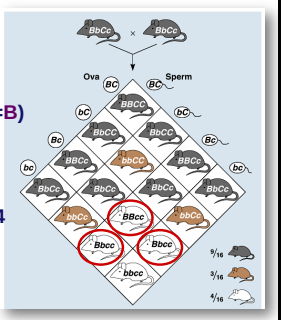


Pleiotropy

- 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

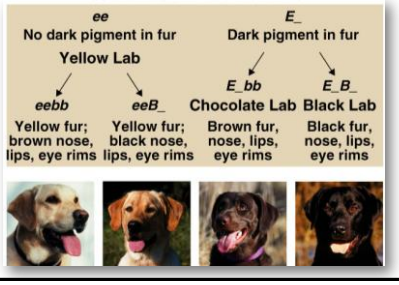
Epistasis

- 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 Labs

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



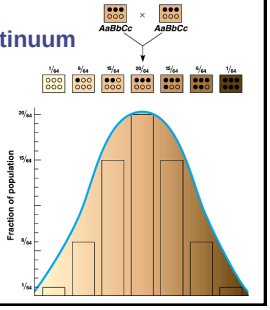
Epistasis in People

albino Africans

Johnny & Edgar Winter

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

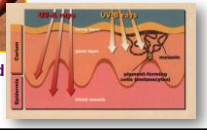


Nature vs. Nature

- Phenotype is controlled by both environment & genes

Coat color in arctic fox influenced by heat sensitive alleles

Color of Hydrangea flowers is influenced by soil pH



Human skin color is influenced by both genetics & environmental conditions

It all started with a fly…

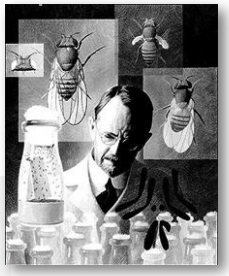
- Chromosome theory of inheritance
  - experimental evidence from improved microscopy & animal breeding led us to a better understanding of chromosomes & genes beyond Mendel
    - *Drosophila* studies

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

Thomas Hunt Morgan

1910 | 1933

- 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 found a mutant white-eyed male
  - traced the gene for eye color to a specific chromosome

Explanation of Sex Linkage

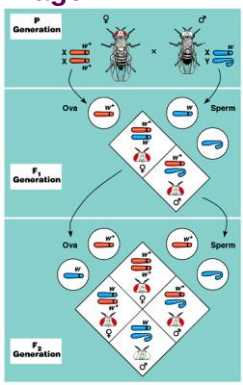
red eye female **X** white eye male

↓

all red eye offspring

↓

100% of females have red eyes **X** 50% of males have white eyes



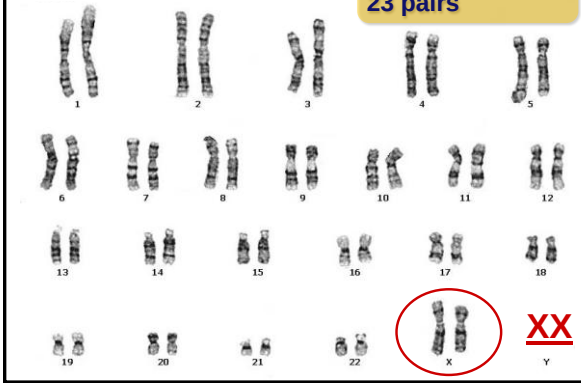
Sex-linked Traits

- 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

diploid (2n) = 2 copies

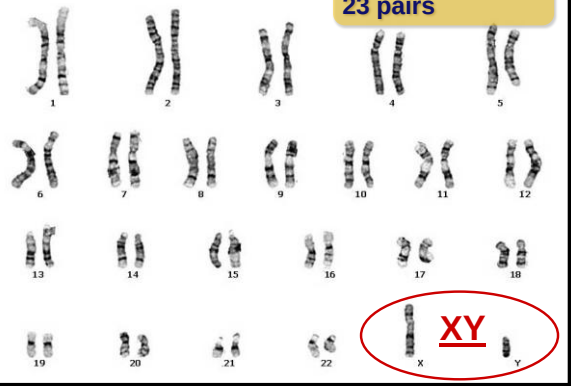
46 chromosomes
23 pairs



XX

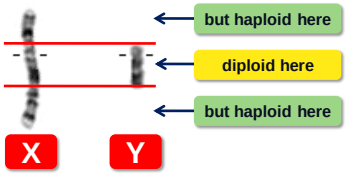
diploid (2n) = 2 copies

46 chromosomes
23 pairs



Sex Linked Traits

- because the Y chromosome is actually smaller than the X chromosome, men only have one copy of certain genes…
- so… if the X chromosome has a recessive allele, that has to be expressed because that is all that is there!

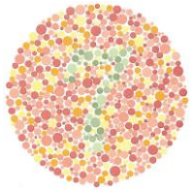


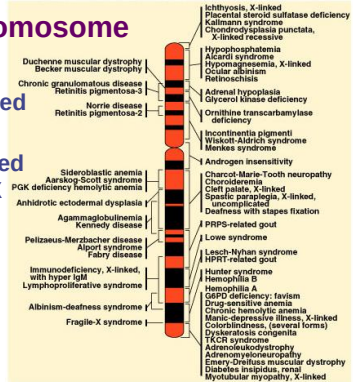
Genes on Sex Chromosomes

- Y chromosome
  - SRY: sex-determining region
    - master regulator for maleness
    - turns on genes for production of male hormones
      - pleiotropy!
- X chromosome
  - Contains a gene called DAX1, an anti-testes factor…SRY inhibits DAX1
  - 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

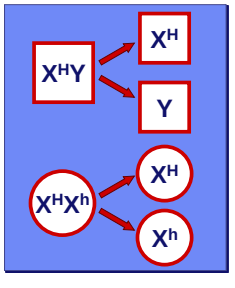


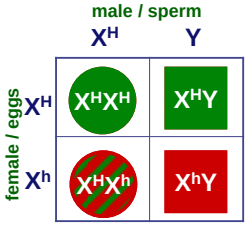


Sex-Linked Traits

X^HY x X^HX^h

2 'normal' parents, but mother is carrier for a sex-linked trait



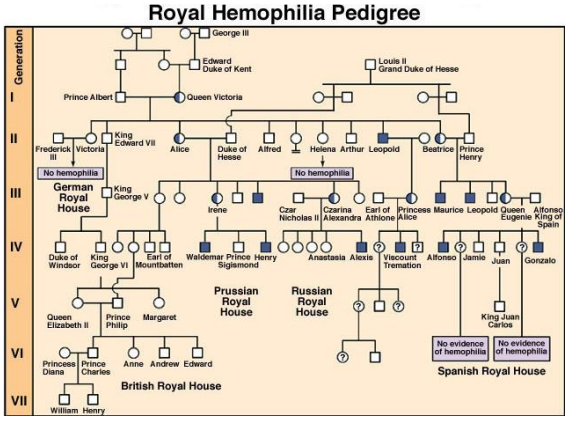


Sex-Linked Traits Hints

- 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

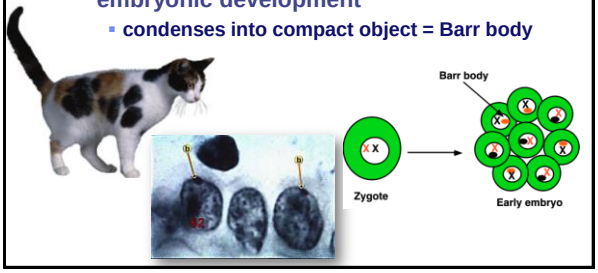
Queen Victoria and Descendants

Royal Hemophilia Pedigree



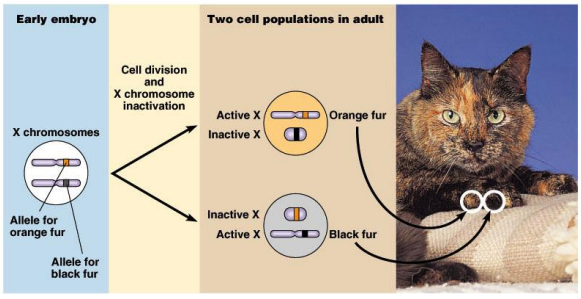
X Chromosome Inactivation

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



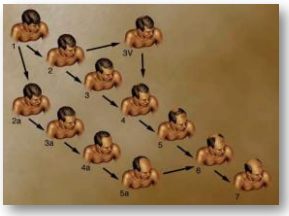
X-Inactivation & Tortoise Shell Cat

- 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

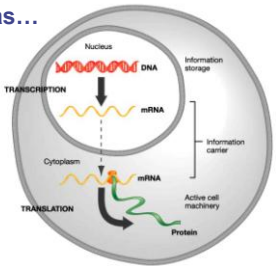


Mechanisms of Inheritance

- 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: Enzymes

= 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

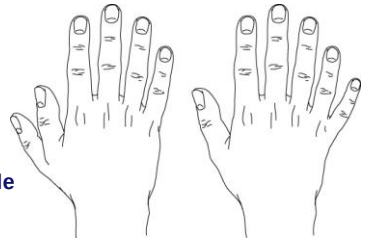
= 100% functional structure
- normal trait is exhibited

→ 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!

Is 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)

Hound Dog Taylor