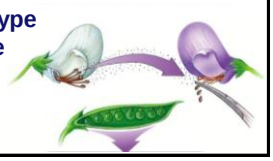
Beyond Mendel's Laws of Inheritance

Extending Mendelian genetics

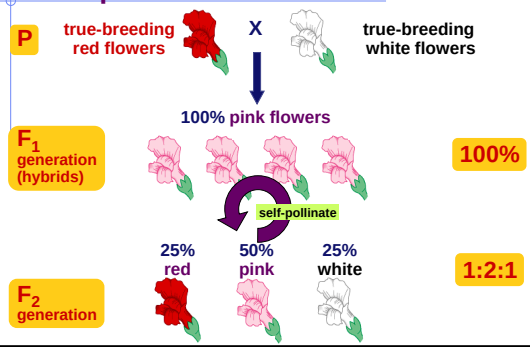
- Mendel worked with a simple system
  - peas are genetically simple
  - most traits are controlled by a single gene
  - each gene has only 2 alleles, 1 of which is completely dominant to the other
- The relationship between genotype & phenotype is rarely that simple



Incomplete dominance

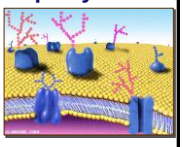
- Heterozygote shows an intermediate, blended phenotype
  - example:
    - RR = red flowers →RR
    - rr = white flowers →WW
    - Rr = pink flowers →RW
      - make 50% less color

Incomplete dominance



Co-dominance

- 2 alleles affect the phenotype equally & separately
  - not blended phenotype
  - human ABO blood groups
  - 3 alleles
    - I^A, I^B, *i*
    - I^A & I^B alleles are co-dominant
      - glycoprotein antigens on RBC
      - I^AI^B = both antigens are produced
    - *i* allele recessive to both



Genetics of Blood type

pheno-type	genotype	antigen on RBC	antibodies in blood	donation status
A		antigens on surface of RBC	antibodies	___
B		antigens on surface of RBC	antibodies	___
AB		antigens on surface of RBC	antibodies	
O		on surface of RBC	antibodies	

Pleiotropy

- Most genes are pleiotropic
  - one gene affects more than one phenotypic character
    - 1 gene affects more than 1 trait
    - dwarfism (achondroplasia)
    - gigantism (acromegaly)

Acromegaly: André the Giant

Inheritance pattern of Achondroplasia

Aa x aa

dominant inheritance

	a	a
A	Aa dwarf	Aa dwarf
a	aa	aa

50% dwarf:50% normal or 1:1

Aa x Aa

	A	a
A	AA lethal	Aa
a	Aa	aa

67% dwarf:33% normal or 2:1

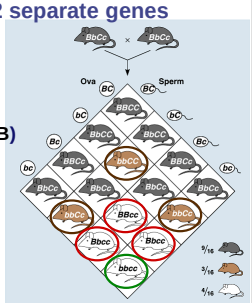
Epistasis

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

*B_C_*

*bbC_*

__cc



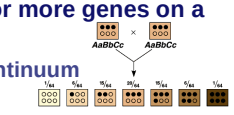
Epistasis in Labrador retrievers

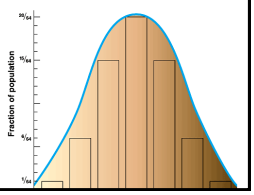
- 2 genes: (E,e) & (B,b)
  - pigment (E) or no pigment (e)
  - pigment concentration: black (B) to brown (b)

ee No dark pigment in fur		*E_* Dark pigment in fur	
Yellow Lab			
eebb	*eeB_*	*E_bb* Chocolate Lab	*E_B_* Black Lab
Yellow fur; brown nose, lips, eye rims	Yellow fur; black nose, lips, eye rims	Brown fur, nose, lips, eye rims	Black fur, nose, lips, eye rims
eebb	eeB–	E–bb	E–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
    - intelligence
    - behaviors





Skin color: Albinism

- However albinism can be inherited as a single gene trait
  - aa = albino

Johnny & Edgar Winter

albino Africans

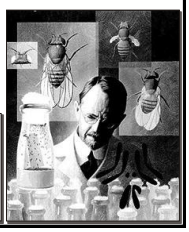
melanin = universal brown color

tyrosine —enzyme→ melanin → albinism

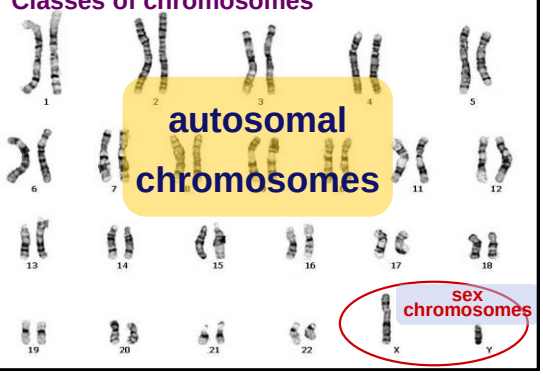
Sex linked traits

1910 | 1933

- Genes are on sex chromosomes
  - as opposed to autosomal chromosomes
  - first discovered by T.H. Morgan at Columbia U.
  - *Drosophila* breeding
    - good genetic subject
      - prolific
      - 2 week generations
      - 4 pairs of chromosomes
      - XX=female, XY=male



Classes of chromosomes



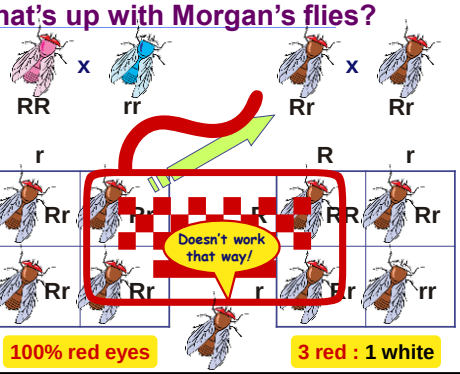
Discovery of sex linkage

P: true-breeding red-eye female × true-breeding white-eye male

F_1 generation (hybrids): 100% red eye offspring

F_2 generation: 100% red-eye female; 50% red-eye male, 50% white eye male

What's up with Morgan's flies?



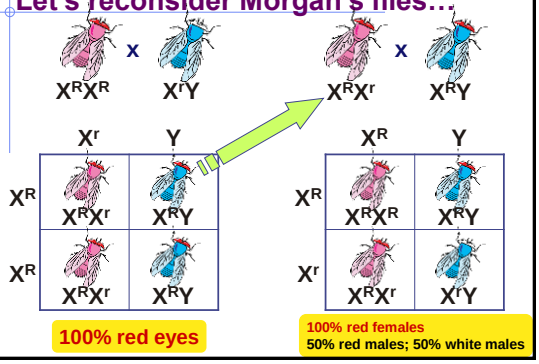
Genetics of Sex

- In humans & other mammals, there are 2 sex chromosomes: X & Y
  - 2 X chromosomes
    - develop as a female: XX
    - gene redundancy, like autosomal chromosomes
  - an X & Y chromosome
    - develop as a male: XY
    - no redundancy

	X	Y
X	XX	XY
X	XX	XY

50% female : 50% male

Let's reconsider Morgan's flies…



100% red eyes

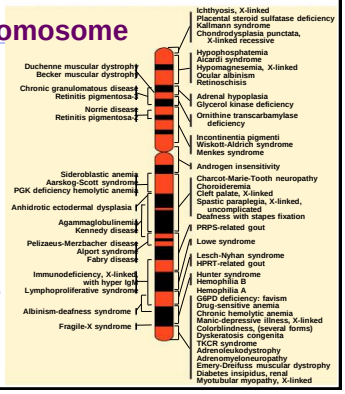
100% red females
50% red males; 50% white males

Genes on sex chromosomes

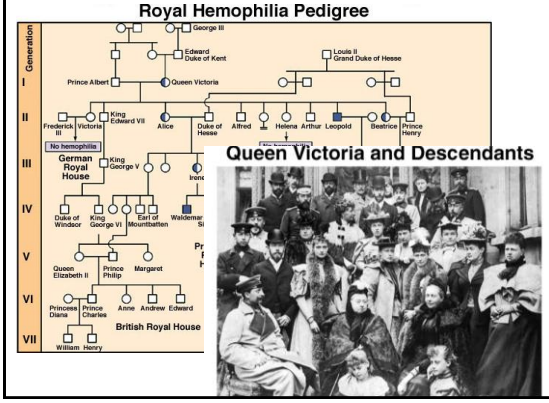
- Y chromosome
  - few genes other than SRY
    - sex-determining region
    - master regulator for maleness
    - turns on genes for production of male hormones
      - many effects = pleiotropy!
- X chromosome
  - other genes/traits beyond sex determination
    - mutations:
      - hemophilia
      - Duchenne muscular dystrophy
      - color-blindness

Human X chromosome

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

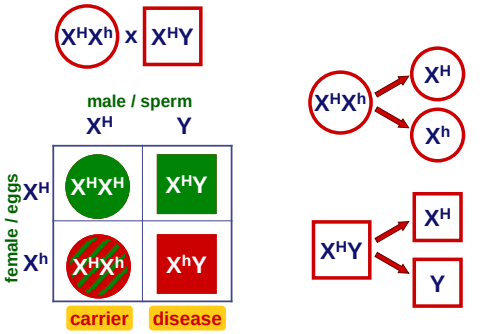


Royal Hemophilia Pedigree



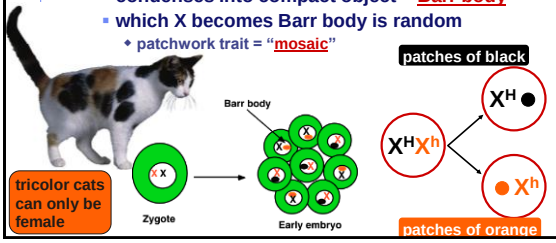
Hemophilia

sex-linked recessive



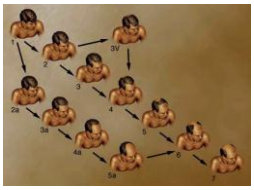
X-inactivation

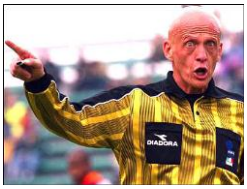
- Female mammals inherit 2 X chromosomes
  - one X becomes inactivated during embryonic development
    - condenses into compact object = Barr body
    - which X becomes Barr body is random
      - patchwork trait = "mosaic"



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





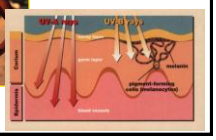
Environmental effects

- Phenotype is controlled by both environment & genes

Human skin color is influenced by both genetics & environmental conditions

(a)

Coat color in arctic fox influenced by heat sensitive alleles



Color of Hydrangea flowers is influenced by soil pH

Any Questions?