

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

P true-breeding red flowers X true-breeding white flowers

↓

F₁ generation (hybrids) 100% pink flowers

↻ self-pollinate

F₂ generation 25% red, 50% pink, 25% white 1:2:1

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

phenotype	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

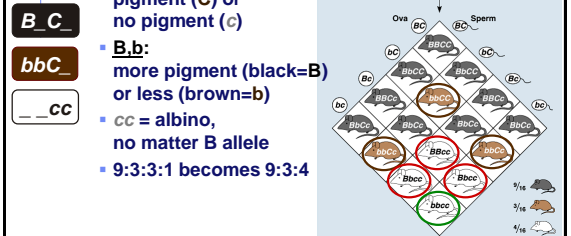
Aa x Aa (lethal)

	A	a
A	AA lethal	Aa
a	Aa	aa

67% dwarf:33% normal or 2:1

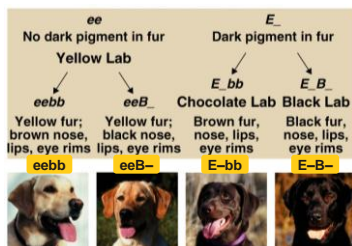
Epistasis

- 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



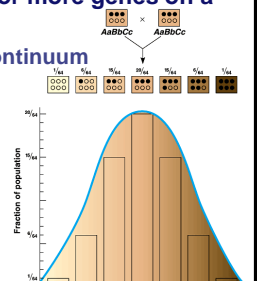
Epistasis in Labrador retrievers

- 2 genes: (E,e) & (B,b)
 - pigment (E) or no pigment (e)
 - pigment concentration: 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
 - intelligence
 - behaviors



Skin color: Albinism

Johnny & Edgar Winter

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

melanin = universal brown color

tyrosine $\xrightarrow{\text{enzyme}}$ melanin \rightarrow 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

autosomal chromosomes

sex chromosomes

Discovery of sex linkage

P generation: true-breeding red-eye female (RR) x true-breeding white-eye male (rr)

F₁ generation (hybrids): 100% red eye offspring (Rr)

F₂ generation: 100% red-eye female (RR) and 50% red-eye male (Rr) and 50% white eye male (rr)

What's up with Morgan's flies?

100% red eyes

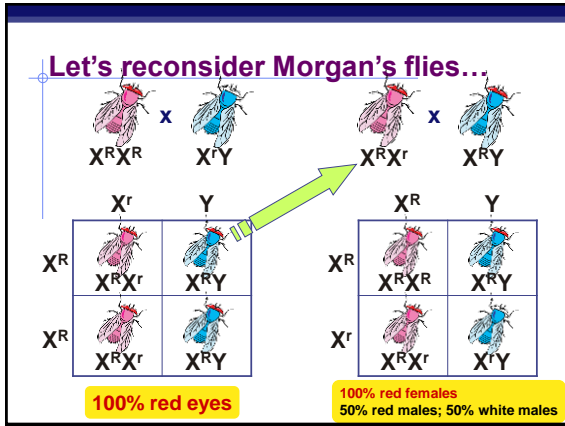
3 red : 1 white

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



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

Duchenne muscular dystrophy
Becker muscular dystrophy
Chronic granulomatous disease
Retinitis pigmentosa
Norrie disease
Retinitis pigmentosa

Sideroblastic anemia
Aarskog-Scott syndrome
PGK deficiency hemolytic anemia
Anhidrotic ectodermal dysplasia
Agammaglobulinemia
Kennedy disease
Pelizaeus-Merzbacher disease
Alport syndrome
Fabry disease
Immunodeficiency, X-linked with hyper IgM
Lymphoproliferative syndrome
Albinism-deafness syndrome
Fragile-X syndrome

Ichthyosis, X-linked
Phenylketonuria sulfatase deficiency
Kallmann syndrome
Chondrodysplasia punctata, X-linked recessive
Hypophosphatasia
Alcaldi syndrome
Hypomagnesemia, X-linked
Ocular albinism
Rottmochsis
Adrenal hypoplasia
Glycerol kinase deficiency
Omnitriase transcarbamylase deficiency
Incontinentia pigmenti
Wiskott-Aldrich syndrome
Menkes syndrome
Androgen insensitivity
Charcot-Marie-Tooth neuropathy
Chuvpaleremia
Cleft palate, Kitzkedo
Spastic paraplegia, X-linked, noncomplicated
Deafness with stapes fixation
PPDP-related gout
Lowis syndrome
Lesch-Nyhan syndrome
HPRT-related gout
Hunter syndrome
Hemophilia B
Hemophilia A
GSPD deficiency: favism
Ornithine transcarbamylase deficiency
Chronic hemolytic anemia
Melic-depressive illness, X-linked
Colorblindness, (several forms)
Dyskeratosis congenita
TSCR syndrome
Adrenoleukodystrophy
Adrenomyeloneuropathy
Eney-Ostrowski muscular dystrophy
Diabetes insipidus, renal
Mitochondrial myopathy, X-linked

Royal Hemophilia Pedigree

Queen Victoria and Descendants

British Royal House

Hemophilia

sex-linked recessive

male / sperm
 X^H Y

female / eggs
 X^H X^h

carrier **disease**

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**"

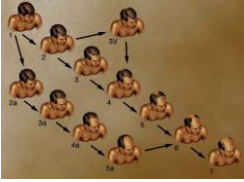
tricolor cats can only be female

patches of black

patches of orange

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



Color of Hydrangea flowers is influenced by soil pH



Coat color in arctic fox influenced by heat sensitive alleles



Any Questions?

