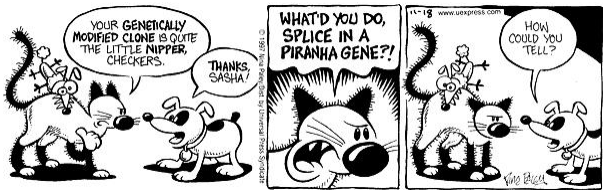
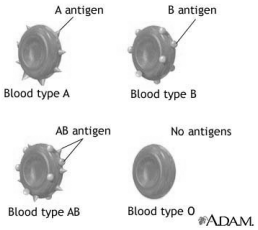
Psych 3102
Lecture 5
Extensions of Mendel
- continued



Multiple alleles

- where more than two alleles are present for the trait in the population

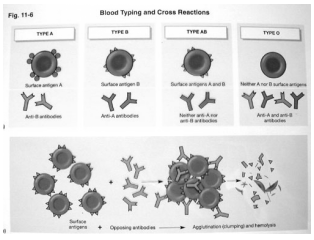
Example: ABO blood group system in humans



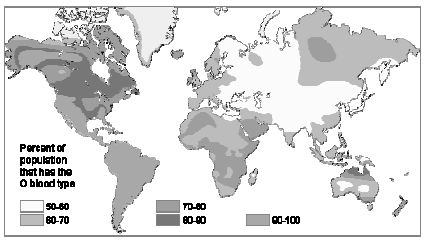
antigen

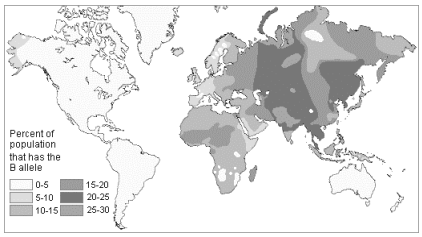
antibody

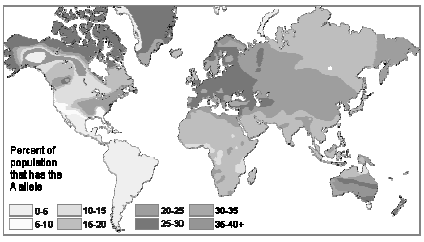
antigen A
+ antibody A → agglutination
(clumping of red cells)



Frequencies of blood group alleles vary across populations. Why?







I = blood group locus

A,B,O are alleles at that locus

The ABO Blood System

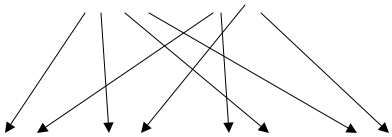
BLOOD TYPE	GENOTYPE	REACTION WITH ANTI-A SERUM	REACTION WITH ANTI-B SERUM	TYPE OF DONOR BLOOD ACCEPTED
A	I^AI^A or I^AI^O	Clumping of red blood cells	No clumping	A or O
B	I^BI^B or I^BI^O	No clumping	Clumping of red blood cells	B or O
AB	I^AI^B	Clumping of red blood cells	Clumping of red blood cells	A, B, AB, or O
O	I^OI^O	No clumping	No clumping	O

I^A and I^B are co-dominant

I^O is recessive to both I^A and I^B

Can a group A mother have a group O child with a group B father?

P I^AI^O x I^BI^O



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Phenotypes

Allelic interactions
- between alleles at one locus

- complete dominance
  - allele is expressed in the phenotype when present in heterozygous condition
  example:

- recessive
  - allele has be present in homozygous condition to show phenotypic expression
  example:

- codominance
  - both alleles at a locus are expressed in the phenotype
  example:

- incomplete dominance
  - heterozygote shows intermediate phenotype, full effects of 'dominant' allele are not shown
  examples: chickens
  horses
  humans

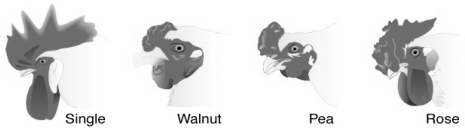
Gene interactions - nonallelic interactions

Phenotype is result of complex, integrated pattern of reactions under control of more than one gene and the environment.

1. Epistasis (true non-allelic interaction)

- expression of a single trait depends on interaction between 2 or more genes

examples: comb shape in chickens



behavioral example:

anorexia nervosa (AN)

allelic variants of MAOA 5HTT NET genes

Risk of AN

MAOA risk allele

5HTT alleles

NET risk allele

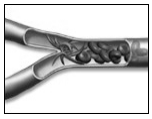
MAOA + 5HTT risk alleles

MAOA + NET risk alleles

2. Pleiotropy

- a single allele has multiple, correlated phenotypic effects

examples:



Maintained in the population by heterozygous advantage

- Sickle cell disease

heterozygote is not as severely affected, but retains resistance to malaria

allele frequency varies across world

pleiotropic effects:

point mutation: 6th amino acid in 146 amino acid chain glu → val causes red cells to be misshapen

- PKU

point mutation causes non-functional enzyme and inability to metabolize phenylalanine, subsequent brain damage

tyrosine normally produced from phenylalanine

tyrosine used to produce thyroxine epinephrin melanin

pleiotropic effects of PKU allele :

3. Penetrance

not everyone with a particular genotype shows the expected phenotype

dominant allele – penetrance = frequency with which it expresses itself in the phenotype, as percentage

100% penetrance = all individuals with the dominant allele show the expected phenotype

50% penetrance = 50% of individuals with the dominant allele display no effect of it in the phenotype (determined by other genes (epistasis) and environment)

Anything less than 100% = low (or incomplete) penetrance

Examples: fragile-X mutation -

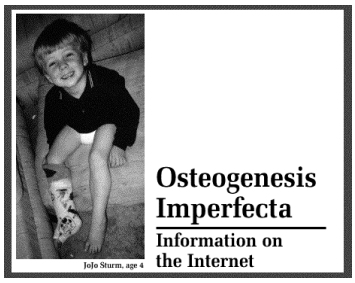
Huntington allele –

BRCA-1 - major risk factor allele for breast cancer, age-dependent

penetrance =	37% by age 40	w/out allele = 0.4%
	66% by age 55	3%
	85 % by age 80	8%

4. Expressivity

degree to which penetrant allele expresses itself in phenotype



Examples:

osteogenesis imperfecta

autosomal dominant

fragile-X syndrome

X-linked dominant, 50% penetrance

5. Internal environment

factors that can change expression of genes:

age

Huntington allele Duchenne muscular dystrophy male-pattern baldness

gender

sex-linked traits

sex-limited traits

Baldness sex-limited trait

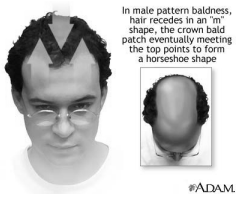
50% male population, small number of women

androgenic alopecia = male-pattern baldness, most common cause

2 major genes

androgen receptor on X (X-linked)	x 3.3 risk
transcription factor region on 20p	x 1.6 risk
both risk alleles (14% of men)	x 7 risk

epistasis



6. External environment genotype x environment interaction

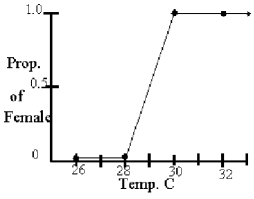
factors that can change gene expression:

temperature

coat color in Himalayan rabbits

sex-determination in crocodilians

environmental chemicals



phenocopies non-hereditary phenotypic modifications that mimic the effect of genes

German measles/hereditary deafness

thalidomide/phocomelia

Accutane/congenital deformities

effect of diet on PKU

effect of smoking/α-1-antitrypsin gene

effect of diet on coat color in mice

Possible mechanism for GxE : Epigenetics

- gene expression is altered
- phenotype is altered, genotype is unchanged

Example of an environmental factor changing gene expression : - coat color in agouti mice

pregnant female mice fed diet with supplements of vit B_{12}, folic acid, & choline had offspring with agouti coats

pregnant female mice fed diet without supplements had offspring with yellow coats + offspring had tendency to diabetes, heart disease, obesity

extra nutrients turned down expression of agouti gene, which has pleiotropic effects on appetite and metabolism as well as effecting coat color.