Patterns of Inheritance

Some basic terminology

phenotype
= physical expression of a trait

genotype
= the actual genes that cause the trait (ie. produces the phenotype)

genome
= all the genes possessed by an organism

most organisms are **diploid**: have a pair of each kind of chromosome
= **homologous chromosomes**

and therefore a pair of each kind of gene

each pair of a gene = **allele**

alleles don't need to be identical

in diploid cells:
the **simplest genotype** is a single pair of alleles on homologous chromosomes

Mendel's Principles of Inheritance:

1. Inherited traits are transmitted by genes

   we now know that **genes** are located on **chromosomes** in the nucleus of cells (Mendel had no clue)

2. **Principle of Dominance**
   when 2 alternative forms of the same gene are present, often only 1 is expressed

3. **Principle of Segregation**
   when gametes form in meiosis the the two alleles segregate from each other and each gamete receives only 1 allele for each gene

4. **Principle of Independent Assortment**
   in most cases studied:
   when 2 or more traits are examined in single crosses

→ each trait is inherited without relation to other traits

The laws of inheritance use these principles developed by Mendel as a foundation

Modern Chromosomal Theory of Inheritance

1. Chromosomes contain the hereditary material
2. The Unit of heredity is the gene
3. diploid cells have homologous chromosomes
4. alleles are on homologous chromosomes
5. haploid cells (after meiosis) have 1 of each kind of chromosome
6. Independent Assortment of homologues
7. genes on the same chromosome travel as a unit (except for synapsis)
8. Occasional deletions, duplications, inversions or moves occur
9. these "errors" lead to genotypic variations
   → are a source of diversity and evolution

Sample Genetics Problems

Monohybrid Crosses

can study these laws of inheritance by looking at results of crosses (matings) on a single pair of alleles

in peas: the normal height of the plant is the result of interactions between two alleles:
T = tall
t = dwarf

can make **Punnet Square** to visualize all the probable combinations of alleles that might be produced in a cross

eg. if a Tall Parent is crossed with a dwarf parent:

	T	**T**
t	Tt	Tt
t	Tt	Tt

→ only 1 possible outcome

all "kids" will be tall

but will have a different genotype than either parent

the characteristics expressed by the genes can be characterized as ether **dominant** or **recessive**

parent #1: = **homozygous dominant** (genetically pure)
→ 2 dominant alleles
parent #2: = **homozygous recessive** (genetically pure)
→ 2 recessive alleles
offspring: = **heterozygous dominant**

what if we cross 2 Heterozygous dominant individuals:

	T	t
T	TT	Tt
t	Tt	tt

2 phenotypes
tall or dwarf

3 genotypes
TT or Tt = tall
tt = dwarf

can also calculate frequency or chance of each occurring

Variations on Heritability of Genetic Traits

there are many variations on these very basic principles of inheritance:

1. **Incomplete dominance**
2. **Polygenic Inheritance**
3. **Quantitative Traits**
4. **Multiple Alleles**
5. **Linked Genes**
6. **Sex Linkage**

1. Incomplete dominance

sometimes there is not a clear distinction between dominant and recessive traits

the offspring are phenotypically intermediate between dominant and recessive expression

eg. flower color in 4 o'clocks
red RR x white rr = Rr pink

2. Polygenic Inheritance

many, if not most, inherited traits are controlled by more than one gene

eg. flower color in sweet peas
two sets of genes are involved in producing a trait
in this case must have 1 dominant gene in each pair to get a purple flower
→ otherwise will have a white flower
neither dominant allele can express the purple phenotype by itself

3. Quantitative Traits (Continuous Variation)

In some polygenic traits, the phenotype is determined by the total number of dominant or recessive genes in all the alleles that interact

eg. height, weight, skin pigmentation, etc

ie, each gene makes a small contribution to the full trait

eg. hypothetical plant height

each dominant gene contributes 6" to final height:

tall: 32" → AABB

dwarf: 8" → aabb

} offspring 20" (2 dom, 2 recessive)

or could be 3 pairs of genes, etc

4. Multiple Alleles

so far we have only considered genes that occur in pairs

these genes may exhibit a dominant-recessive relationship or an intermediate one

at some gene loci:
more than 2 different alleles may occur

multiple alleles:
3 or more alternative conditions at a single locus producing different phenotypes

an individual may possess any two on the list

eg. Human Blood Groups (codominance)

due to a pair of alleles on homologous chromosomes

blood type depends on the presence or absence of 2 possible antigens on blood cells, A or B

A B AB O phenotypes

possible alleles: A, B, o
A and B are dominant, o is recessive

A & B blood has 2 possible genotypes

AB and o each only have 1

5. Linked Genes

during meiosis and gamete formation, in general the entire chromosome moves as a unit

when we talked about monogenetic traits we

assumed that each different trait we discussed were on a different pair of chromosomes

what if we're considering two different unrelated traits on the same chromosome

genes on the same chromosome cannot separate
→ they move as a unit during meiosis

such genes are said to be linked

but
linked genes don't always stay linked

meiosis at synapsis sometimes get crossing over
→ where homologous chromosomes exchange equal pieces

this could change the linkage pattern

crossing over is more likely to occur the further away from each other the genes are
→ can use the frequency of crossing over to map gene locations on a chromosome

= chromosome mapping

6. Sex Linkage

in the cells of most organisms the chromosomes are paired:
2 of each kind of chromosome

these are diploid cells

however in higher animals one pair of chromosomes are "sex chromosomes"; designated X & Y

females have 2 X chromosomes
males have an X and a Y chromosme

so in human females all chromosomes are paired

in human males 22 chromosomes are paired

the 2 sex chromosomes are each unpaired
→ any gene on the sex chromosome will be

expressed whether dominant or recessive

eg. Hemophilia

Effects of Environment

also the environment can exert a strong influence on phenotype
eg. some plants produce 2 different kinds of leaves
aerial leaves and water leaves

same genes, its strictly due to difference in immediate environment

generally, the more complex and organism is the greater influence the environment will have on its phenotype

Mutations

many, if not most diseases or physical abnormalities boil down to a chemical imbalance in the body

→of all patients in children hospitals 10-25% are being treated for genetic related problems

this chemical imbalance can be the result of a genetic defect:

eg. a specific protein or enzyme is completely missing or not made properly

eg. sickle cell anemia

hemoglobin is a protein in our RBC's that allows us to carry oxygen

without it we would die

hemoglobin is a protein composed of 286 amino acids

the protein code is contained in 858 base pairs of a DNA molecule

in sickel cell anemia the hemoglobin is misformed causing misshapen RBC's and decreased ability to carry oxygen

a single amino acid/codon is wrong:

should be: CTT → glutamic acid

instead: CAT → valine

There are over 20,000 known human genetic diseases

→ over 7000 are due to a single defective gene

mutations

= any change in genetic material that gives rise to an alternate genotype

There are 2 basic kinds of mutations that can occur:

A. Gene mutations (=point mutations)

→ could be a change in individual genes

B. Chromosomal Abnormalities

→ could be a change in chromosomes

A. Point Mutations

in general one **set of genes** codes for a single protein or polypeptide

any change in sequence of nucleotides may lead to change in sequence of amino acids in the protein

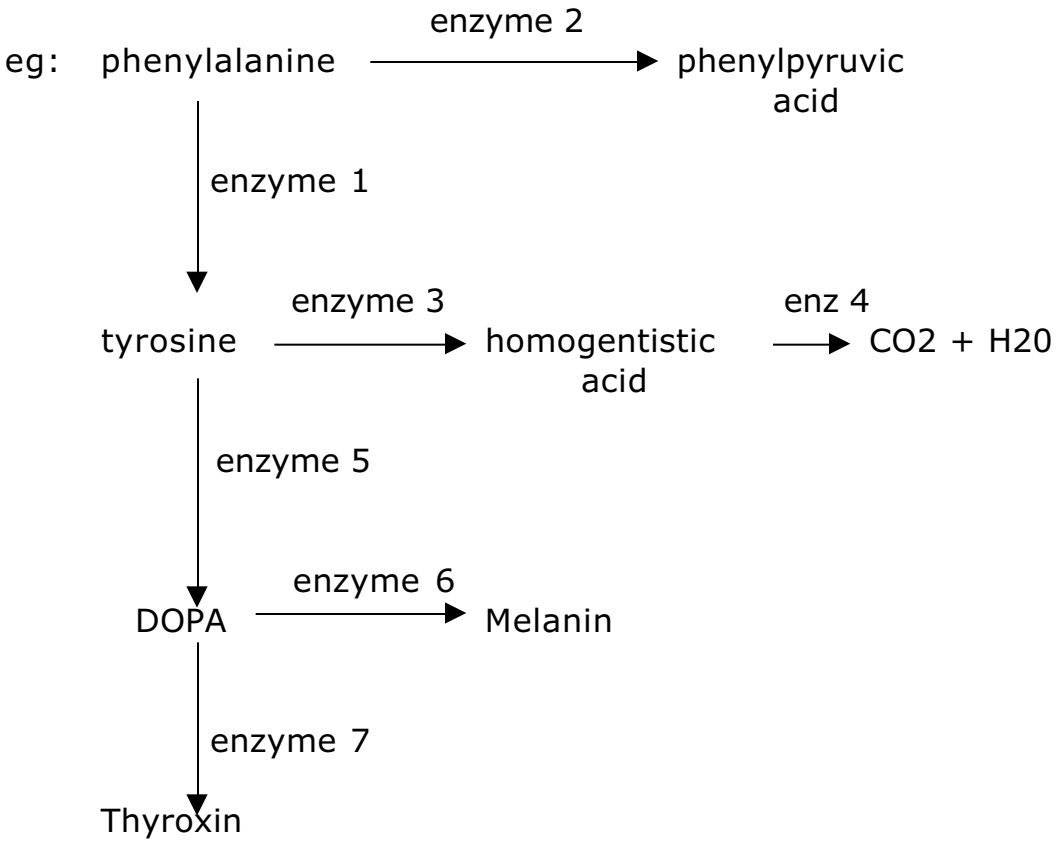
this change can alter the function of the protein
eg. protein carriers, hemoglobin structure, collagen, etc

most human diseases caused by gene mutations are known to be due to singe factors:

can be on **autosomal** chromosomes or on **sex** chromosomes
~74% autosomal dominant disease traits
~21% autosomal recessive disease traits
~5% sex linked traits

many are "metabolic variant" diseases
→ a particular enzyme or carrier protein is not produced or not properly produced

most reactions that occur in the body are grouped into interrelated metabolic pathways



Enzyme #1 defective
→ PKU disease
due to single recessive gene
no enzyme to break down phenylalanine
phenylalanine builds up in blood
very toxic

leads to severe mental retardation and brain damage 6 months after birth
phenylalanine is an essential AA needed in diet
if low phenylalanine diet is given early enough
→can reduce some of the impact

Enzyme #4 defective
→ alkaptoneuria
no significant effects
other than high levels of homogenistic acid in blood

Enzyme #6 defective
→ albinism
inability to produce pigment, melanin, in skin or eyes
very sensitive to light

Enzyme #7 defective
→ cretinism
cretinism is not always genetic

Other genetic diseases due to point mutations:

Autosomal Diseases (not on sex chromosomes)

1. **Maple Syrup Urine Disease**
   autosomal recessive
   mental and physical defects

2. **Methyl Mercaptan Disease**
   no mental or physical defects
   urine smells like asparagus
   dominant gene

3. **Porphyria variegata**
   failure of body to metabolize porphyrin
   causes brown patches of skin
   extremely sensitive to barbiturates
   leads to paralysis and death
   has been traced back through 8000 carriers to a couple who married in 1688, in South Africa
   →4 of their 8 children had it
   no good treatment

4. **Huntington's Chorea**
   autosomal dominant
   deterioration of CNS

symptoms don't appear until ~ 40 yrs old
after that only survive ~ 12 more years
→ carriers may have passed on trait before they know they are afflicted
no cure
25,000 in US have it
traced back to 17th century England
a woman had 3 sons who immigrated to US
their descendants were often burned as witches because of their behaviors as the disease progressed

5. Galactosemia

autosomal dominant? recessive?
inability to metabolize lactose in milk
1 in 100,000 individuals have the disease
adults can just avoid milk
afflicted infants: malnutrition, diarrhea, severe vomiting
can be treated by using lactose free milk
if not treated: eye, liver and brain damage → death

Sex Linked Diseases

all known are on X chromosome

most are recessive
→ women are "carriers", but don't have the disease

a few are dominant

1. Hemophilia

recessive gene (women are carriers)
blood doesn't clot → bleed to death from a small cut
traced to Queen Victoria
almost extinct today

2. Red-Green Color Blindness

recessive gene (women are carriers)
2/25 white males are red-green colorblind

3. Night Blindness

defective gene controls the production of rods in the retina of eye
rods give us our "night vision"
people lacking rods are completely blind in dim light
traced back 11 generations to a butcher in France

4. Lesch – Nynan Syndrome

high levels of uric acid in blood
results in brain damage
self mutilation
kidney damage

5. **Duchenne Muscular Dystrophy**
   10 different types of MS
   → only this one is sex linked

Y linked traits ??
contains genes responsible for "maleness"
ear hair??

B. Chromosomal Abnormalities

sometimes the problem is due to large pieces (many genes) or whole chromosomes duplicated, altered or missing

examples:
Change in the number of chromosomes (=Aneuploidy):

1. **duplication**
   having one or more extra copies of a chromosome

   trisomy → 3 of one kind of chromosome
   eg downs syndrome
2. **deletions**
   having one or more copies of a chromosome missing
   sometimes due to viral disease, chemicals or irradiation

   monosomy → only one of a pair of chromosomes present

3. **inversions**
   a portion of the chromosome (and its genes) occurs in reverse order

4. **translocations**
   a portion of a chromosome is cut and moved to a nonhomologous chromosome

can also be autosomal or sex linked
due to **mitotic** or **meiotic nondisjunction** during the formation of sex cells: eggs or sperm
→ a mistake in the process of cell division occurs
the chromosomes don't separate as they are

supposed to during anaphase

Autosomal Chromosomal Abnormalities

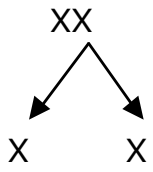
1. Down's Syndrome

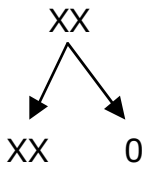
trisomy of chromosome #21
severe mental retardation
shortening and fattening of body
very happy individuals
more common in older mothers

Sex Linked Chromosomal Abnormalities

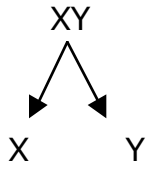
most known are due to meiotic nondisjunction during oogenesis usually during anaphase II

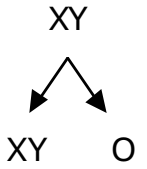
oogenesis: normal nondisjunction





spermatogenesis normal nondisjunction





Fertilization:

ovum	sperm	zygote
due to meiotic nondisjunction in women → egg cells		
xx	x	xxx =triplo X
xx	y	xxy =Kleinfelters
o	x	xo =Turners Syndrome
o	y	yo =inviable
due to meiotic nondisjunction in men → sperm cells		
x	o	
x	yy	xyy

1. **Triplo X**
   females
   predisposition to mental retardation
   no major abnormalities
   many are fertile

2. **Kleinfelter's Syndrome (XXY)**
   males
   1 in 800 males born
   → esp born to older women
   sterile, undeveloped testes
   sparse body hair
   enlarged breasts
   mentally retarded

3. **Turners Syndrome**
   females
   most secondary sex characteristics absent
   infertile
   some dwarfism
   1 in 3500 women born
   many will spontaneously abort

4. **Male meiotic nondisjunction XYY**
   higher incidence of antisocial behaviors
   hostility and violence
   but contrary to myth → no correlation with criminals

can also get **mitotic** nondisjunction in cells produced from fertilized egg

if it occurs early in development most cells will be abnormal

if later only some cells

can also produce Kleinfelters, etc

all of these occur more often in children of older mothers