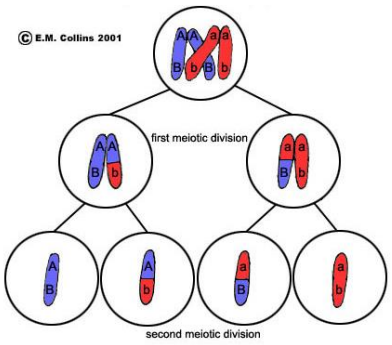
Chapter 15-Chromosomal Basis of Inheritance



CHROMOSOMAL THEORY OF INHERITANCE

Early 1900's cytology and genetics merge

~ parallels between chromosome behavior and Mendel's "factors"

- MENDEL's "hereditary factors" = genes on chromosomes
- Genes have specific loci (positions) on chromosomes
- SEGREGATION and INDEPENDENT ASSORTMENT of chromosomes during meiosis explains patterns of inheritance (ratios) seen by Mendel

GENE LINKAGE

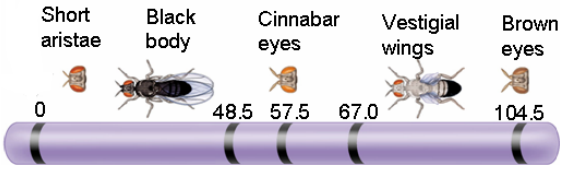
1st linked gene discovered by THOMAS HUNT MORGAN = white eyes in fruit flies

- Genes on same chromosomes don't sort independently
- More likely to be inherited together (unless separated by crossing over)

GENETIC MAP = ordered list of genetic loci along a particular chromosome

- Frequency of crossing over ~ related to the distance between genes
- Genes farther apart on a chromosome = more likely to be separated during crossing over
- Linked genes have recombination frequencies less than 50%
- Genes very far apart on same chromosome may appear to be "unlinked"

Max value 50%= genes on different chromosomes OR so far apart on same chromosome appear unlinked



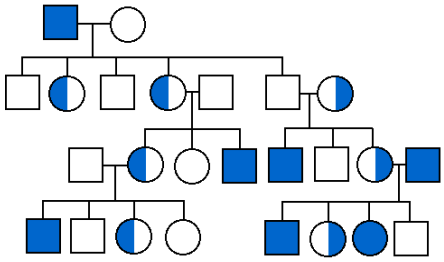
- Many fruit fly genes were mapped using recombination frequencies (**LINKAGE MAP**)
- 1% recombination frequency = 1 map unit (centimorgans)

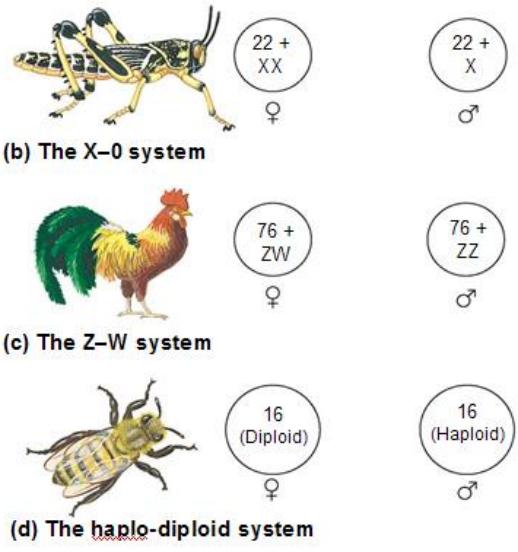
PEDIGREE

Show how trait is passed through generations in a family

Squares = males; circles = females;

Individuals with trait are colored in; carriers can be shown as half/half





DETERMINING SEX

- HUMANS/other MAMMALS USE XY SYSTEM:
  XX= female; XY = male:
- All humans start as females; SRY gene codes for "maleness"

- Some INSECTS (grasshoppers, cockroaches) use XO SYSTEM: XX = female; X0 = male

- BIRDS, some fish, some insects use ZW SYSTEM:
  ZW =female; ZZ = male

- BEES and ANTS use HAPLOID/DIPLOID SYSTEM:
  Diploid = females; Haploid (unfertilized eggs) = males

AUTOSOMAL RECESSIVE

- Parents are generally unaffected; Need two recessive alleles for trait to show
- two unaffected parents can have affected offspring
- Males and females both can be carriers for autosomal recessive traits
- Heterozygotes = normal but "carriers"
  Don't show trait but can pass allele on to offspring
- Can remain in population in heterozygote condition at high frequencies due to **HETEROZYGOTE ADVANTAGE**
  - Disorder is price paid for resistance to some other disease
  EX: Sickle cell heterozygotes resistant to malaria parasite
  Cystic fibrosis heterozygotes resistant to typhoid
  Changes in Vitamin D receptor protects against tuberculosis (may increase osteoporosis)

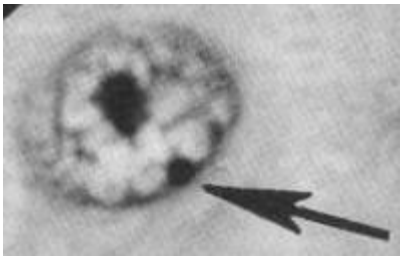
SEX LINKED GENES:

X LINKED: More common in males than females (Have only one X ~NO copilot)
- Only females can be carriers of X linked traits

Y LINKED: Only found in males; Fathers pass mutation on to sons
- EX: hairy pinna , SRY

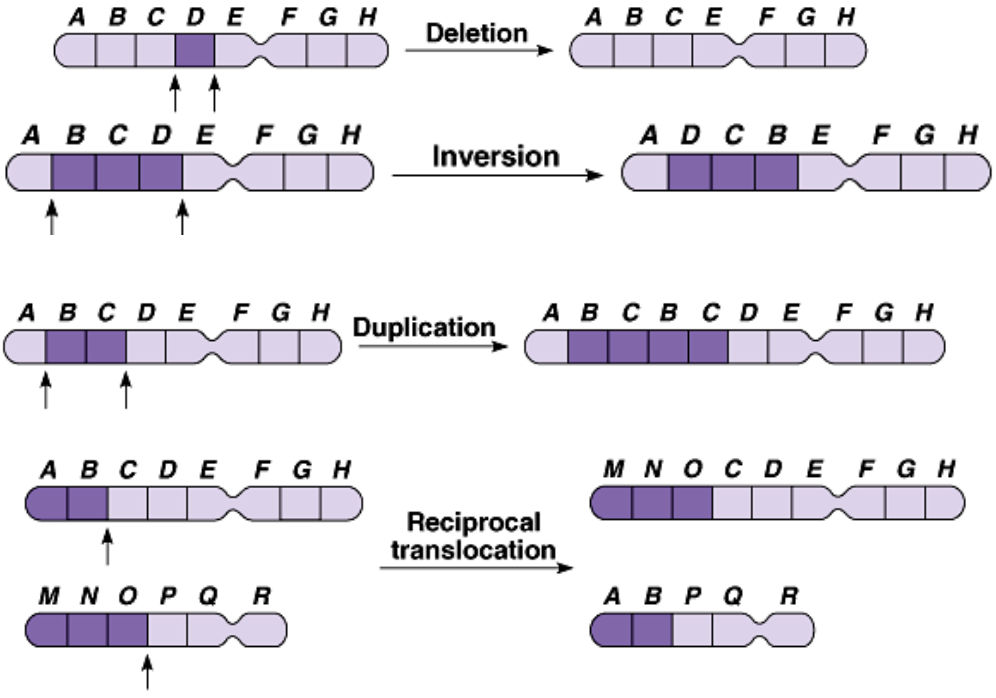
X-INACTIVATION in FEMALE MAMMALS

- One X chromosome in each cell is randomly inactivated by addition of methyl groups to DNA
- Becomes **BARR BODY**
- Seen attached to nuclear envelope
- Also seen in Klinefelter males
- Spot color allele in calico cats is X linked
  Female calico cats can have TWO COLORS OF SPOTS (have 2 X's)
  Males can have only ONE COLOR of spots (1 X)

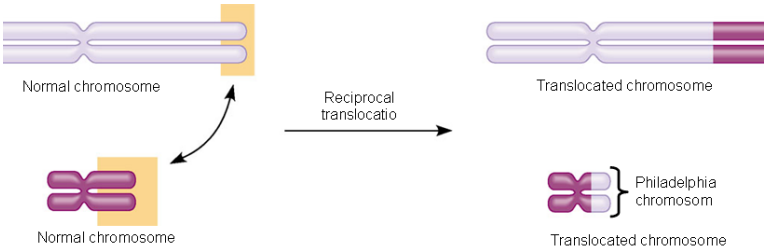


MUTATIONS

TYPES OF CHANGES IN CHROMOSOME STRUCTURE due to breakage of a chromosome



BALANCED TRANSLOCATION



Philadelphia chromosome
implicated in certain cancers
EX: *chronic myelogenous leukemia* (*CML*).
Equal exchange between #22 and #9

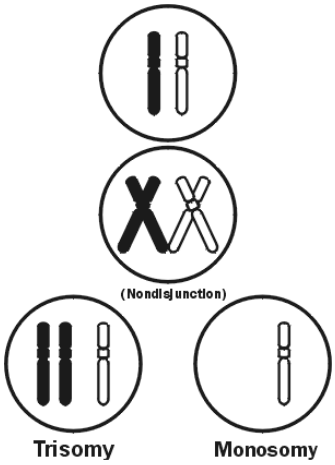
ANEUPLOIDY = Condition of having an abnormal number of certain chromosomes

Ex; 2n-1 (Turner syndrome) 2n+1 (Down syndrome)

Due to **NONDISJUNCTION**

= failure of homologous chromosomes to separate during meioisis

- may occur during Anaphase I or Anaphase II of meiosis
- results in gametes with missing or extra chromosomes (n-1 or n+1)
- Increased probability in women over 40 and under 16
- Oocytes start meiosis while in embryo; stay suspended in prophase I;
- each cell completes meiosis after it is released and fertilized
- Possible explanation: longer cell stays in prophase synapsis, more likely to fail to separate



POLYPLOIDY (3N, 4N)

= chromosome number that is more than two complete chromosome sets

Happens when all chromosomes pairs fail to separate OR when a cell copies its DNA then fails to divide

Lethal in humans/mammals

Increases size and hardiness in many plants

EX: strawberries, watermelon, tobacco, bananas, cotton, peanuts

EXTRANUCLEAR GENES

- exhibit a non-Mendelian pattern of inheritance
- Extranuclear genes are found in cytoplasmic organelles(plastids and mitochondria)
- Inherited from mother (egg cell)

EX: maternal plastid genes control variegation of leaves

In mammals, mitochondria come from mother (cytoplasm comes from egg)

EPIGENETIC INHERITANCE- inheritance of traits transmitted by mechanism other than DNA sequence

- non-genetic factors cause the organism's genes to behave (or "express themselves") differently
- *DNA methylation* may be one mechanism for genomic imprinting

- **GENOMIC IMPRINTING** = Process that induces changes in chromosomes inherited from males and females
- causes genes to be expressed differently depending upon whether they came from mom or dad

EX: Prader-Willi and Angelman's syndromes both caused by same #15 deletion

- imprints can be reversed in gamete-producing cells
- all the chromosomes are re-coded according to the sex of the individual in which they now reside.

GENETIC DISORDER	DUE TO	CHARACTERISTICS
PHENYLKETONURIA (PKU)	AUTOSOMAL RECESSIVE	Deletion in enzyme that breaks down amino acid phenylalanine; Build up of phenylalaine causes mental retardation Low protein diet can help prevent retardation
TAY-SACHS	AUTOSOMAL RECESSIVE	Lack functional enzyme in lysosome to breakdown lipids. Lipids accumulate in brain resulting in seizures, blindness, mental retardation, and early death
CYSTIC FIBROSIS	AUTOSOMAL RECESSIVE	Most common lethal genetic disease in the US More common in Caucasians Change in code for chloride ion channel protein affects glands that produce mucus, digestive enzymes, sweat Accumulation of thickened mucus in the pancreas, intestinal tract and lungs; Increase risk of bacterial infections Release of excessively salty sweat an indicator of disease.
HUNTINGTON'S DISEASE	AUTOSOMAL DOMINANT	Degenerative brain disease caused by extra CAG repeats on chromosome #4 ; more repeats = more severe symptoms Symptoms do not appear until 35 to 40 years of age (after childbearing age) Irreversible/lethal once deterioration of the nervous system begins; homozygous dominant = lethal before birth 50% chance of passing on to offspring
ACHONDROPLASIA "Dwarfism"	AUTOSOMAL DOMINANT	DD = LETHAL before birth; Heterozygote = shows trait Premature fusion of growth plates in long bones results in normal size torso/head and short arms/legs
SICKLE CELL DISEASE	AUTOSOMAL CODOMINANT	Substitution mutation (A → T) in hemoglobin gene Abnormal hemoglobin packs together to form rods creating crescent-shaped cells when oxygen is low (crisis) Pleiotropic effects: Breakdown of r.b.c →physical weakness, anemia, heart failure; clumping of cells in small blood vessels → heart failure, pain,fever, organ damage More common in African Americans; also found in Mediterranean/Middle East areas Heterozygote carriers: have *sickle-cell trait* •produce both normal/abnormal hemoglobin •show malaria resistance (HETEROZYGOTE ADVANTAGE)
HEMOPHILIA	X LINKED RECESSIVE	Mutation in blood clotting proteins
COLORBLINDNESS	X LINKED RECESSIVE	Inability to distinguish red/green most common
DUCHENNE MUSCULAR DYSTROPHY	X LINKED RECESSIVE	Deletion in muscle protein; Early death

DOWN SYNDROME Trisomy-21	NONDISJUNCTION	slanted eyes; protruding tongue mental retardation; Some have heart abnormalities Simian crease
KLINEFELTER SYNDROME (Most common XXY)	NONDISJUNCTION	*Can be XXY, XXXY, XXXXY, XXXXXY* Males with extra X chromosomes Feminized features/possible breast development Lack development of male characteristics at puberty Male sex organs with abnormally small testes; sterile; Usually of normal intelligence; may have learning disabilities; Treated with hormone replacement therapy
TURNER SYNDROME (XO)	NONDISJUNCTION	Females with only one X chromosome only known viable human monosomy webbed neck; broad chest; short stature At puberty, secondary sexual characteristics fail to develop; internal sex organs do not mature; sterile.
Xyy	NONDISJUNCTION	Normal male; usually taller than average; normal intelligence and fertility
XXX	NONDISJUNCTION	Usually fertile; can show a normal phenotype
Cri du chat	DELETION	Mental retardation, a small head with unusual facial features and a cry that sounds like a mewing cat.
Prader-Willi syndrome	IMPRINTING DELETION on fraternal chromosome	Deletion on #15 Mental retardation, obesity, short stature, and unusually small hands and feet; often die early from cardiovascular disease/diabetes;
Angelman's syndrome	IMPRINTING DELETION on maternal chromosome	Deletion on #15 Uncontrollable spontaneous laughter, jerky movements, and other motor and mental symptoms
Fragile X syndrome	May be due to maternal imprinting .	most common genetic cause of mental retardation abnormal X chromosome; tip hangs on by a thin DNA thread more likely to appear if the abnormal X chromosome is inherited from the mother rather than the father more common in males. unusual in that imprinting does not silence the abnormal allele somehow causes the syndrome