

Chapter 15- The Chromosomal Basis of Inheritance

(Key Concepts are Underlined)

Relating Mendelism to Chromosomes

Mendelian inheritance has its physical basis in the behavior of chromosomes during sexual life cycles

Chromosome theory of inheritance- Mendelian genes have loci on chromosomes, which undergo segregation and independent assortment

Morgan traced a gene to a specific chromosome: *science as a process*

- Thomas Hunt Morgan of Columbia University first conferred the association of specific gene on a specific chromosome in the early 20th century, by deducing the gene for eye color in fruit flies was located on the X sex chromosome

Wild type- normal phenotypic character

Mutant phenotype

Sex-linked- genes located on a sex chromosome

Linked genes tend to be inherited together because they are located on the same chromosome

Linked genes- see “Key Concept” above; in breeding experiments, results deviate from what is expected according to Mendelian’s principle of independent assortment

Independent assortment of chromosomes and crossing over produce genetic recombinants

Genetic Recombination- production of offspring with new combinations of traits inherited from two parents

Parental types- offspring with phenotypes of one of the parents

Recombinants- offspring with different phenotypes than their parents (different combinations)

- crossing over accounts for the recombination of linked genes (somewhat mimicking independent assortment)

Geneticists can use recombination data to map a chromosome's genetic loci

Genetic Map- ordered list of genetic loci along a particular chromosome

Map Unit- sometimes used to express the relative distance between linked genes and is equivalent to 1%

recombination frequency

- the greater the distance between linked genes, the higher the probability of crossing over and therefore the higher the recombination frequency

- linkage is not observed in genetic crosses if the linked genes are too far apart on the chromosome (higher than 50% recombination frequency); e.g. flower and seed color in Mendel's experiments (both on chromosome 1)

Linkage map- a genetic map based on recombination frequencies; map units do not have absolute size, but they do portray the sequence of genes along a chromosome

Cytological map- chromosome map which locates genes with respect to chromosomal features, such as stained bands, and shows the actual distance between gene loci

Sex Chromosomes

The chromosomal basis of sex varies with the organism

- very little crossing over in sex chromosomes
- signs of sex begin to emerge when the embryo is about 2 months old- until then, gonads are generic
- SRY gene on the Y chromosome triggers the development of testes

Sex-linked genes have unique patterns of inheritance

- sex-linked trait usually refers to *X-linked*; if recessive, only homozygote females express the phenotype, whereas males express the trait if they receive the allele from their mother (i.e. *hemizygous*); e.g. color blindness

Sex-Linked Disorders in Humans:

Duchenne muscular dystrophy- progressive weakening of the muscles and loss of coordination due to the absence of a key muscle protein called dystrophin; rarely live past their early twenties; 1/3500 males born in US

Hemophilia- absence of a protein required for blood clotting; plagued the royal families of Europe

X-Inactivation in Female Mammals- one X chromosome becomes almost completely inactivated during embryonic development, thus both men and women have a single dose of the X chromosome

Barr body- a condensed inactive X which lies along the inside of the nuclear envelope of each cell of a female (reactivated in ovary cells to give rise to ova)

- X-inactivation occurs randomly and independently in each embryonic cell, which creates a mosaic of two types of cell (both active X's from mother and father)

- all descendants of same embryonic cells have the same inactive X chromosomes
- approximately half of her cells will express one allele, while others will express the alternate allele (e.g. calico cats, patchy sweat glands in female women)
- X chromosomes are inactivated by methylation (attachment of a methyl to cytosine); initiated by a product of a XIST gene (hypothesized)

Errors and Exceptions in Chromosomal Inheritance

Alterations of Chromosome number or structure cause some genetic disorders

Nondisjunction- homologous chromosomes fail to separate during meiosis I, or sister chromatids fail to separate during meiosis II; in both cases, gametes end up with either one too many of the same type of chromosome or missing one entirely; can also occur in mitosis

Aneuploidy- abnormal chromosome number

Trisomic- cell with $2n + 1$ chromosomes

Monosomic- cell with $2n - 1$ chromosomes

Polyploidy- more than two complete chromosome sets; usually caused by the fertilization of an egg produced by the nondisjunction of all its chromosomes

- polyploids are more nearly normal in appearance than aneuploids; having an extra set of chromosomes does not disrupt the genetic balance of the organism as much as ± 1 chromosome

Deletion- chromosomal fragment lost during cell division; caused by the nonreciprocal crossover during meiosis (lost)

Duplication- chromosomal fragment from one homologue joins to the other; caused by the nonreciprocal crossover during meiosis (gained)

Inversion- chromosomal fragment from one homologue joins to the other (but in reverse orientation)

Translocation- chromosomal fragment joins to a nonhomologous chromosome

Human Disorders Due to Chromosomal Alterations:

- most aneuploid embryos are naturally/spontaneously aborted, but some less deleterious aneuploids will survive and have a set symptoms referred to as a syndrome; can be diagnosed before birth via fetal testing

Down Syndrome- trisomic for chromosome 21; characteristic facial features, short stature, heart defects, susceptibility to respiratory infection, mental retardation, and most sexually underdeveloped and sterile; some live to middle age or beyond; 1/700 children born (increased incidence with maternal age)

Klinefelter Syndrome- XXY; have male sex organs, but the testes are abnormally small (sterile); breast enlargement and other feminine characteristics; 1/2000 live births

Turner Syndrome- X0, or monosomy X; phenotypically female, but sex organs do not mature and secondary sex characteristics fail to develop (sterile); 1/5000 births

- aneuploid conditions of the sex chromosomes appear to upset genetic balance less than those involving autosomes; may be due to the Y chromosome carrying relatively few genes and extra copies of X chromosomes become inactivated (i.e. Barr bodies)

Cri du chat (“cry of the cat”)- deletion in chromosome 5; mentally retarded, small head with unusual facial features, and a cry sounding like the

mewing of a distressed cat; usually die in infancy or early childhood

Chronic myelogenous leukemia (CML)- reciprocal translocation of a portion of chromosome 22 with chromosome 9; cancer affecting the cells giving rise to white blood cells

The Phenotypic effects of some genes depend on whether they were inherited from the mother or the father (imprinting)

- some inherited disorders depend on which parent passed along the alleles for those traits

Genomic imprinting- in mammals, the same alleles may have different effects on the offspring depending on whether they arrive in the zygote via the ovum or the sperm
- maternal and paternal imprints are apparently “erased” during gamete production and chromosomes are re-imprinted according to the sex of the individual they now reside; much evidence leads to chromosomes being methylated (i.e. attachment of methyl groups to nucleotides at specific loci), thus inactivated

Fragile X syndrome- an abnormal X sex chromosome; mentally retarded; more common when the chromosome is inherited from the mother; cannot be inactivated, or “silenced”; 1/1500 male and 1/2500 female children

Extranuclear genes exhibit a non-Mendelian pattern of inheritance

Extracellular genes- mitochondrial and plastid DNA
- variegated leaves of plants result from the genes in plastids, which are inherited from the maternal parent’s cytoplasm of the ovum

Mitochondrial myopathy- suffers weakness, intolerance of exercise, and muscle deterioration
- mitochondrial mutations inherited from a person's mother may contribute to diabetes, heart disease, Alzheimer's disease, and aging