Advanced Biology
Notes: Human Disorder

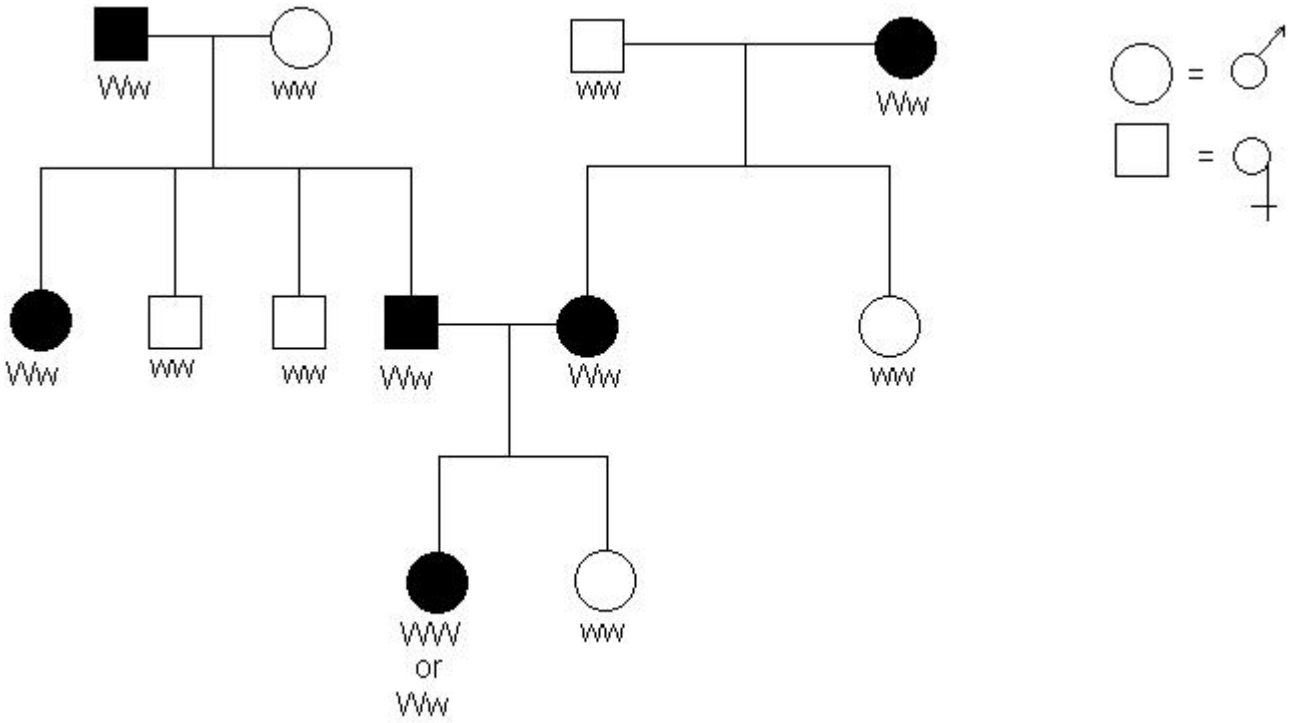
Pedigree analysis:

Our understanding of Mendelian inheritance in humans is based on the analysis of family pedigrees
or the results of mating that have already occurred.

***Pedigree*:** A family tree that diagrams the relationship among parents and children across generations
and that shows the inheritance pattern of a particular phenotypic character

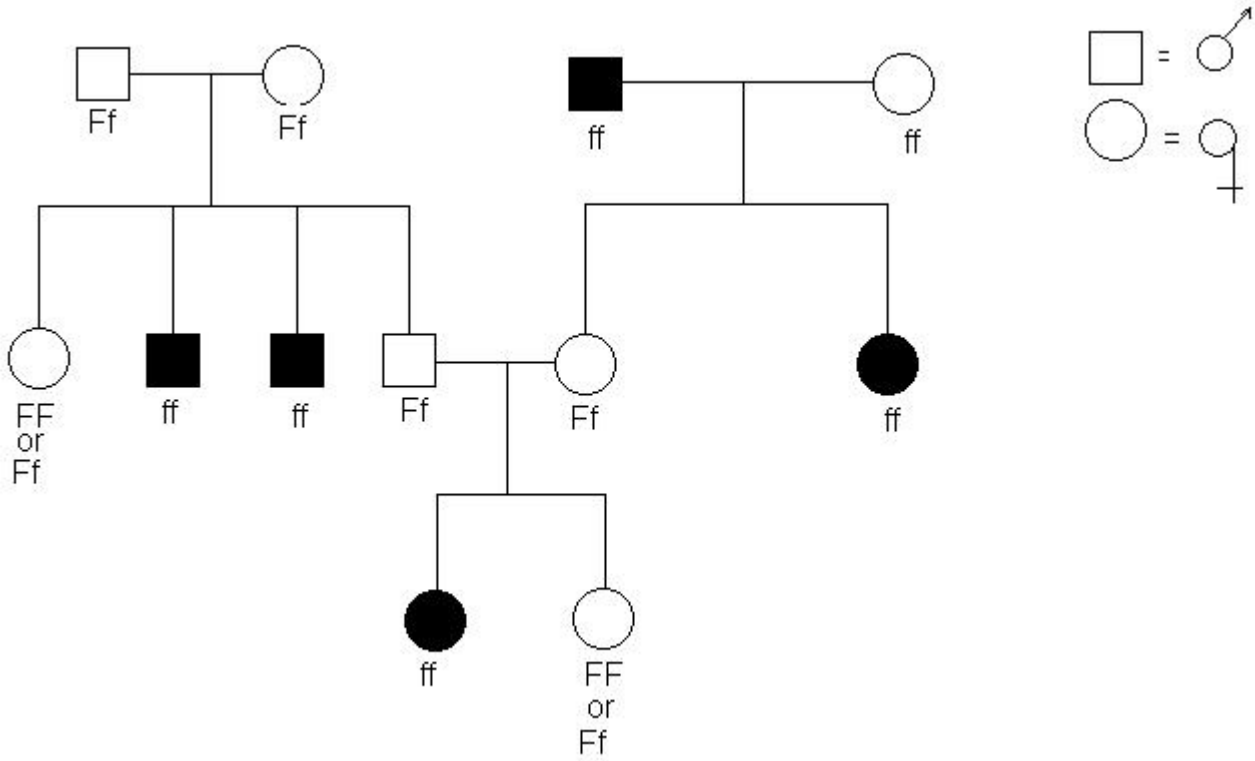
*Squares symbolize males and circles represent females.
*A horizontal below in birth order, from left to right
*Shaded symbols indicate individuals showing the trait being traced

***Dominate trait*:** Family members' genotypes can be deduced from a pedigree that races the
occurrence of widow's peak, the expression of a dominant allele.



*If a widow's peak results from a dominant allele, W, then all individuals that do not have a widow's peak
hairline must be homozygous recessive (ww) The genotypes of all recessive can be written on the pedigree
*If widow's peak results from a dominant allele, W, then individuals that have widow's peak hairline must be
either homozygous dominant (WW) or heterozygous (Ww)
*If only some of the second generation offspring have a widow's peak then the grandparents that show the
trait must be heterozygous (Ww). (Note: if the grandparents with widow's peak were homozygous
dominant then all their respective offspring should show the trait.)
*Second generation offspring with widow's peak must be heterozygous, because they are the result of
Ww X ww mating.
*The third generation sister with widow's peak may be either homozygous dominant (WW) or heterozygous
(Ww) because her parent are both heterozygous)

Recessive trait: The same family can be used to trace recessive trait such as attached ear lobes



*If attached earlobes is due to a recessive allele (f) then all individuals with attached

earlobes but be
homozygous recessive (ff)
*Since attached earlobes appears in second generation offspring g, the grandparents with free earlobes are
heterozygous (Ff) sine they must be capable of passing on a recessive allele (f)
*Since one of the third generation sisters attached earlobes (ff) her parents are heterozygous, they have free
earlobes (dominant trait) and yet must be able to contribute a recessive allele to their daughter. The other
sister shows the dominant trait, so her genotype is unknown; it is possible that she may be either
homozygous dominant or heterozygous.

Pedigree analysis can also be used to:

*Deduce whether a trait is determined by a recessive or dominated allele.

Using the example above:
The first born third generation daughter has attached earlobes.
Since both parents lack the trait, it must not be determined by a dominant allele.

*Predict the occurrence of a trait in future generations.
For example, if the second generations couple decide to have another child,
Q1 What is the probability the child will have a widows' peak? From a mating of Ww X Ww.
Probability of a child being WW = 1/4
Probability of a child being Ww = 2/4
Probability of a widow's Peak = 3/4
Q2 What is the probability the child will have attached earlobes? From a mating of Ff X Ff
Probability of a child being ff = 1/4
Q3 What is the probability the child will have a widow's peak an attached earlobes?
From a cross of WwFf X WwFf, use the rule of multiplication
3/4 (probability of widow's peak) X 1/4 (Probability of attached earlobes) = 3/16

Recessive inherited disorders

*Defective alleles code for either a malfunction protein or no protein at all
*Heterozygotes can be phenotypically normal, if one copy of the normal allele is all that is needed to produce sufficient quantities of the specific protein
*The phenotypes are expressed only in homozygous (aa) who inherit one recessive

allele from each parent

*Heterozygotes (Aa) can be phenotypically normal and act as carriers possible transmitting the recessive allele to their offspring

*Most people with recessive disorders are born to normal parents both of which are carriers

Cystic Fibrosis: the most common lethal genetic diseases in the US, strikes 1 in ever 2,500 Caucasians

*Four percent of the Caucasian population are carriers

*The dominant allele codes for a membrane protein that controls chloride traffic across the cell membrane. Chloride channels are defective or absent in individuals that are homozygous recessive of the cystic fibrosis allele

*Disease symptoms result form the accumulation of thickened mucus in the pancreas, intestinal tract and lungs, a condition that favors bacterial infections.

***Tay-Sachs*:** occurs in 1 out of 3,600 births. The incidence is about 100 times higher among

Ashkenzic Jews than among Sephardic Jews and non-Jews

*Brain cells of babies with this disease are unable to metabolize gangliosides (a type of lipid) because of crucial enzyme does not function properly

*As lipids accumulate in the brain, the infant begins to suffer seizures, blindness and degeneration of motor and mental performance The child usually dies after a few years.

Sickle-cell disease: the most common inherited disease among African Americas .

If affects 1 in ever 400 African Americans born in the US.

*The disease is caused by single amino acid substitution in hemoglobin

*The abnormal hemoglobin molecules tend to link together and crystallize, especially when blood oxygen content is lower than normal This causes red blood cells to form

from the normal disk-shape to a sickle-shape.

*The sickle cells clog tiny blood vessels, causing the pain and fever characteristic of a sickle-cell crisis

*About 1 in 10 African Americans hare heterozygous of the sickle-cell allele and are said to have the sickle-cell trait

*These carriers are usually healthy, although some suffer symptoms after an extended period of low blood oxygen levels

*Carriers can function normally because the tow alleles are codominant, the abnormal hemoglobin but also normal

*The high incidence of heterozygotes is related to the fact that in tropical Africa where malaria is endemic heterozygotes have enhanced resistance to malaria compared to

normal
homozygotes.

Dominantly inherited disorders

Lethal dominant alleles are much rare than lethal recessive, because they:
*are always expressed so their effects are not masked in heterozygotes
*Usually result from new genetic mutations that occur in gametes and later kill and developing embryo

Late-acting lethal dominants can escape elimination if the disorder does not appear until an advanced age after afflicted individuals may have transmitted the lethal gene to their children.

Huntington's' disease a degenerative disease of the nervous system, is caused by a late-acting lethal dominate allele. The phenotypic effects do not appear until 35 or 40
years of age. It is irreversible and lethal once the deterioration of the nervous system begins

*Molecule geneticists have recently located the gene for Huntington's near the tip
of chromosome #4
*Children of afflicted parent have a 50% chance of inheriting the lethal dominant allele.
A newly developed test can detect the Huntington's allele before disease symptoms appear.

Fetal testing:
Chronic villus sampling (CVS) is a newer technique during which a physician suctions off a small amount of fetal tissue from the chronic villi of the placenta.
*These rapidly dividing embryonic cells can be karotyped immediately, usually proving results in
24 hours major advantage over amniocentesis which can take several weeks.

Other techniques such as *ultrasound*and *fetoscopy* allow physicians to examine a fetus for major
abnormalities
*Ultrasound is a non-invasive procedure which uses sound waves to create an image of the fetus
*Fetoscopy involves inserting a thin fiber-optic scope into the uterus

Newborn screening
In most US hospitals simple tests are routinely performed at birth, to detect genetic disorders such as *phenylketonuria (PKU)*
*PKU is recessively inherited and occurs in about 1 in 15,000 births in the United

States

*Children with the disease cannot properly break down the amino acid phenyalanine

*Phenylalanine and its by-product (phnylpyruvic acid) can accumulate in the blood to toxic levels,

causing metal retardation.