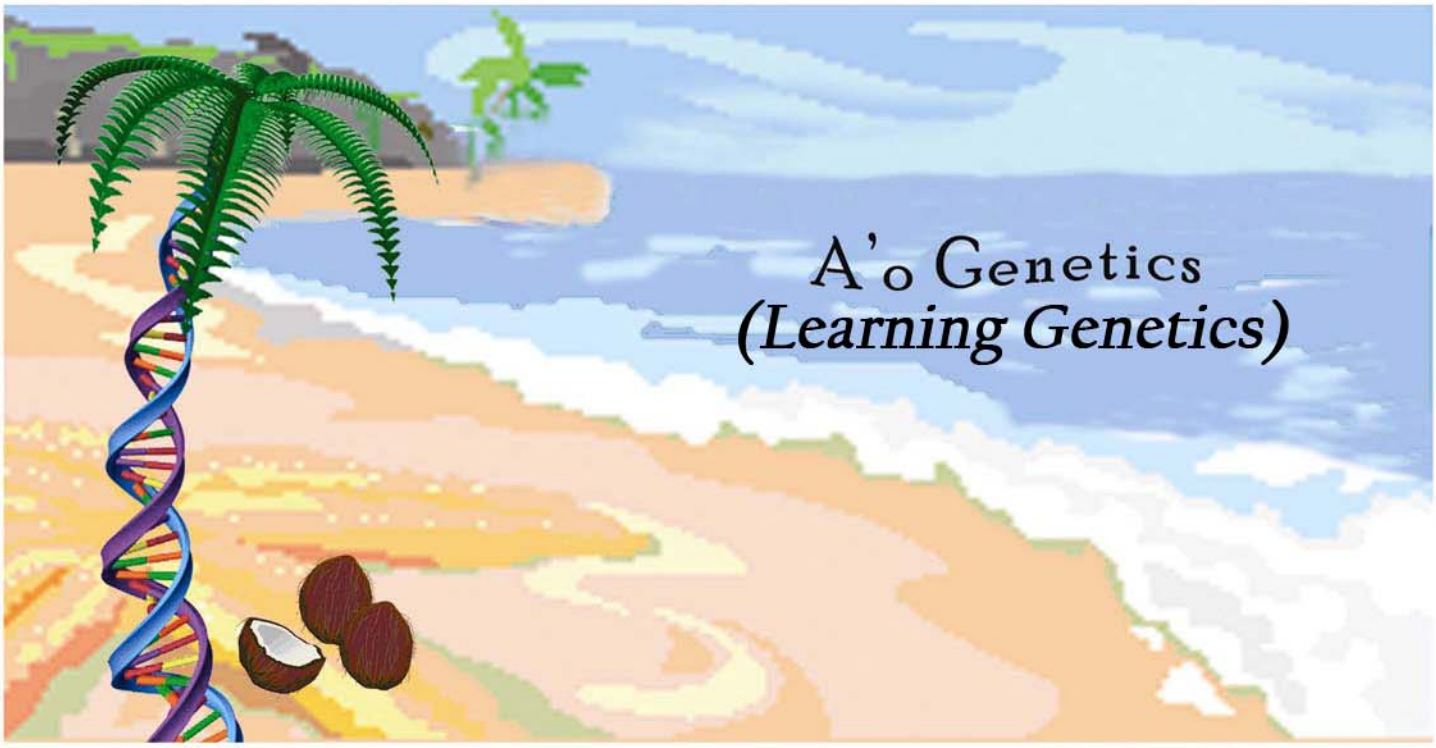
Genetics 101
A Review for Teachers



Hawai'i Department of Health
www.hawaiigenetics.org

Hawai'i Genetics Program

Introduction

*"The whole **art of teaching** is the art of awakening the natural curiosity of young minds for the purpose of satisfying it afterwards."*

- Anatole France (novelist 1844 - 1924)

*"**Humans** take great pride in identifying distinguishing traits from one generation to the next. We enjoy speculating on the resemblance of children to their parents and question which child has, for example, the father's eyebrows or the mother's chin. With such observations begins the study of **genetics** and the submicroscopic structures known as **genes**…There is probably some genetic component in almost all disease processes, but the extent of this component varies."*

-Jerry L. Northern & Marion P. Downs
(authors: Infants and Hearing)

*"Nearly **3000** genetic disorders have been identified. Of the…babies born in the United States each year, **2-3%** have a major genetic or congenital disease. The average person has **4-8** potentially harmful genes."*

-Jerry L. Northern & Marion P. Downs

*"**Identification of genes that are responsible for inherited disorders has become commonplace**, if not mundane; and genetic factors in common disorders are coming to light. The **promise of genetics in medicine is still largely unappreciated**, but this…is changing. Genetics used to be viewed as the discipline that studied rare disorders. Now genetics is recognized as an integral part of oncology... cardiology and neurology; **eventually it will leave no area untouched**."*

-Bruce R. Korf (geneticist)

Genetics affects each and every one of us. The odds that genetics will become a part of your students lives increases every day, making it vital that it be incorporated into classroom lessons and discussions.

"Genetics 101" has been designed to provide an overview of certain genetics terminology and concepts that will likely arise during Genetics units and lessons, as well as in each of our lives.

General Genetics

GENETICS

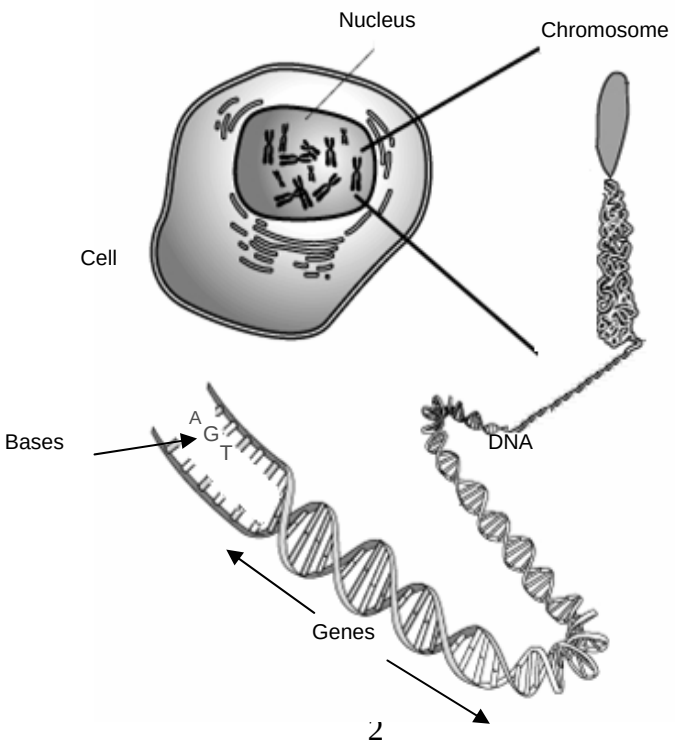
Genetics refers to the study of genes and chromosomes, and how traits and conditions are inherited and passed through families.

GENES & DNA

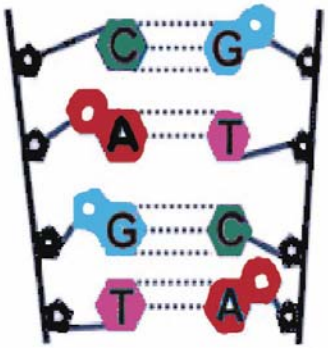
Genes are the instructions that tell the cells in our bodies how to grow and function. Genes are often thought of as an instruction manual or blueprint for how we develop and who we are. We all have two copies of almost all of the genes in our bodies, and each of our millions of cells contains one full set of all of our genes. We receive one copy of each gene from our mother, and one copy of gene from our father. Similarly, if a person has offspring, they pass one member of each gene pair onto each child.

Genes are made of a molecule called **deoxyribonucleic acid** (**DNA**). DNA is the basic unit of heredity. DNA is composed of four units (called bases): Adenine (A); Cytosine (C); Guanine (G); and Thymine (T). The four units that make up DNA are like the 26 letters of the English alphabet. The sequence, or specific order, of these bases spells out instructions for the body to make certain proteins or carry out certain functions (like how the 26 letters of the English alphabet are put together in specific orders to create words and sentences). The letters of DNA make up our genetic code.

The figure below shows the relationship between a cell, chromosome, DNA, gene, and bases. Chromosomes will be discussed later in this booklet.



DNA has a double helix structure, which is sometimes described as a twisted ladder. The "sides" of the DNA ladder are made of phosphate and sugar, and the "rungs" are made of base pairs. A always pairs with T, and C always pairs with G. Base pairs are also used as a unit of measure to indicate a length of DNA, or the size of a gene. For example, a gene or piece of DNA that is 10bp long consists of 10 base pairs, whereas a gene or piece of DNA that is 2Kb long consists of 2000 base pairs.



GENES & PROTEINS

The genetic code of DNA codes for the production of certain proteins. From DNA, a complementary molecule called ribonucleic acid (RNA) is made, and then proteins are made using the RNA. Thus, **RNA** is the intermediate molecule between DNA and protein; it translates the instructions of DNA into real proteins.

DNA → RNA → Protein

Proteins are the molecules in our body that make up the parts of our body, and that carry out different functions in our body. For example, our tissues and organs are all made up of proteins. In addition, enzymes, hormones and antibodies are all specific types of proteins. The smaller units of protein are called **amino acids**. There are over 100 different amino acids in nature, but our bodies use only 20 amino acids to make all of their proteins.

ALLELES, GENOTYPES & PHENOTYPES

As you know, we have two copies of each of our genes. **Alleles** refer to the different forms of a gene. For example, a difference in the sequence of bases between two copies of a gene would mean that these two copies are different alleles, or different forms of the gene. Different alleles of the same gene may code for different forms of a protein. Sometimes, however, different alleles will not affect the protein for which they code.

When a person is **heterozygous** for a certain gene, this means that their two alleles of this gene are different from each other. When a person is **homozygous** for a certain gene, this means that their two alleles of this gene are the same.

Genotype refers to all of the alleles of all of the genes that a person has. More broadly, the genotype of an individuals is their total genetic makeup. **Phenotype**, on the other hand, refers to the physical characteristics of an individual. These characteristics may be ones that are visible to the eye (such as hair color, eye color, and height), or they may be internal or biochemical (such as blood pressure and IQ). The phenotype of a person results from their genotype, often in combination with their environment.

The terms allele, heterozygous, homozygous, genotype and phenotype are explained in the following figure. Dominant and recessive will be reviewed later in this booklet. Please note that this illustration depicts a simplified example of eye color inheritance.

ALLELES OF THE EYE COLOR GENE:

B → allele for brown eyes (dominant to the b allele)
b → allele for blue eyes (recessive to the B allele)

POSSIBLE GENOTYPES:	lead to	CORRESPONDING PHENOTYPES:
Homozygous	BB ----------→	Brown  eyes
Heterozygous	Bb ----------→	Brown  eyes
Homozygous	bb ----------→	Blue  eyes

Alterations in Genes

MUTATIONS

A **mutation** is any change in the usual sequence of DNA. For example, suppose that part of a gene usually has the sequence GTAC. If the sequence in a copy of the gene was GTTC, this change from A to T would be considered a mutation. Some mutations cause diseases, others contribute to the healthy diversity between all people, and still other mutations do not cause any change and do not affect the person who has them. Whether or not a mutation has any effect depends upon whether it affects the form or function of the protein for which it codes.

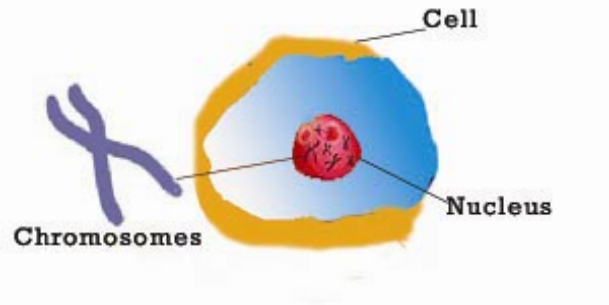
The causes of mutations are often unknown. Mutations in the genes of a person's germline (eggs and sperm), can be passed down to their offspring. On the other hand, some of the mutations we are born with likely occurred just by chance. Still other mutations may be caused by things such as the environment (sun, radiation, or chemicals) or aging.

POLYMORPHISMS

Polymorphisms refer to a change (mutation) in the DNA sequence that is present in at least one percent of the population. Polymorphisms are generally considered to be "normal" variations in the sequence of DNA, and are generally not considered harmful. One example of a polymorphism is variation in the genes for hair color. Slight changes in the DNA sequence codes for different colors of hair. Other polymorphisms do not cause any visible or significant change in the people who have them.

Information About Chromosomes

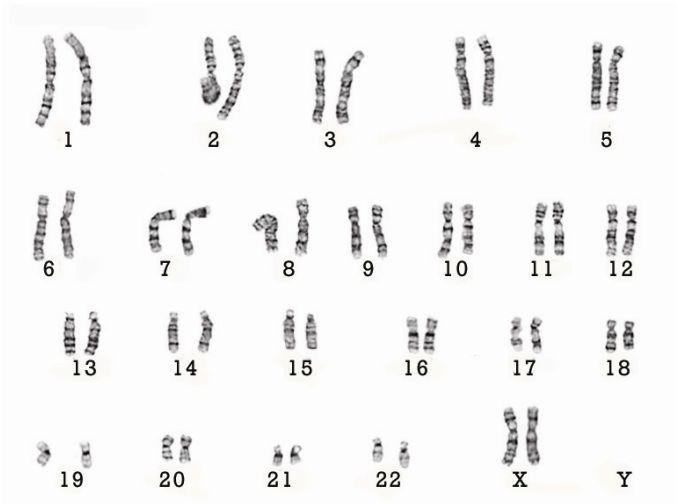
Chromosomes, tiny structures in the nuclei of our cells, are composed of DNA. Our genes are packaged into chromosomes and are located all along each of our chromosomes.



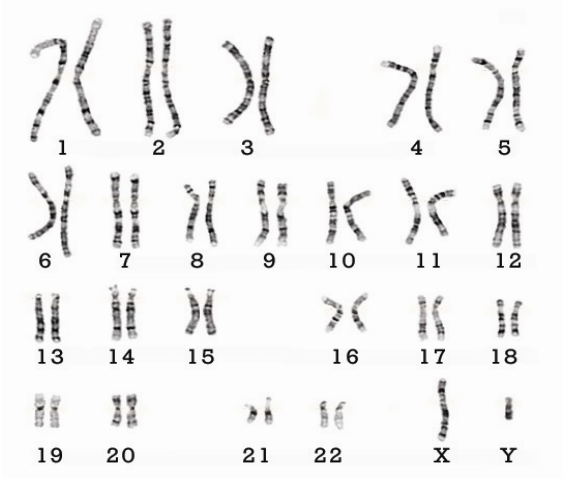
In humans, there are usually 46 chromosomes (23 pairs) in each cell. 44 of these chromosomes (22 pairs) are called **autosomes**, meaning that they are the same in males and females. The final two chromosomes are called the sex chromosomes. Females have two X chromosomes, while males have one X chromosome and one Y chromosome.

KARYOTYPES

When chromosomes are studied in a laboratory, they are isolated from a cell and treated with special stains. These stains cause specific, identifying bands to become visible on each chromosome. The chromosomes are put into order by pair, size and shape to make an organized picture called a **karyotype**. A karyotype allows **cytogeneticists** (scientists who study chromosomes) to see whether a person has any extra or missing genetic material, or any large rearrangements in their chromosomes. A karyotype does *not* allow for changes in individual genes to be seen.



Normal Female Karyotype: 46,XX



Normal Male Karyotype: 46,XY

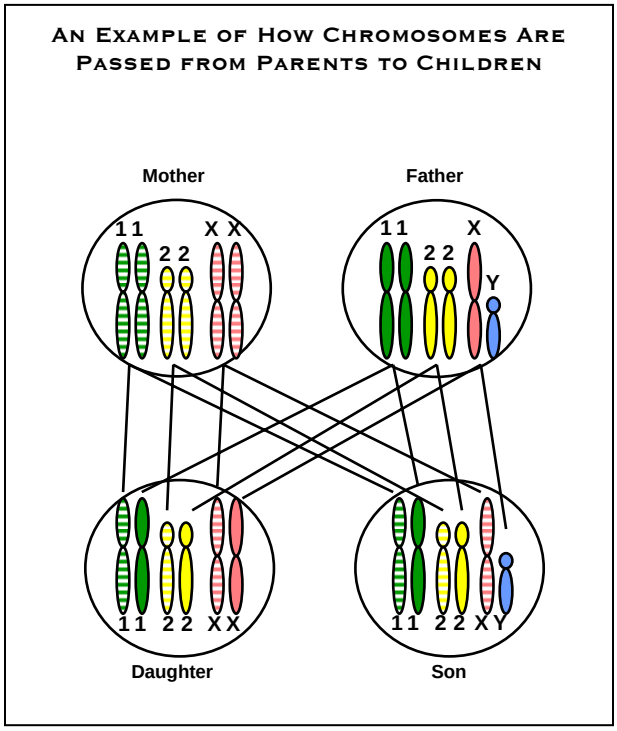
CHROMOSOME SEGREGATION

As with gene pairs, we receive one member of each chromosome pair from our mother and the other one from our father. Similarly, when we have offspring, we pass one member of each of our chromosome pairs to each child. When a male passes on an X chromosome, the child will be female, and when he passes on a Y chromosome, the child will be male.

The figure to the right shows the transmission of chromosomes (and therefore genes) from parents to children.

In this figure, three pairs of chromosomes are shown:
pair #1 (green);
pair #2 (yellow);
pair #3 - sex chromosomes (pink and blue).

*The father's chromosomes are shown in solid color, and the mother's are striped. Children randomly get one member of each chromosome pair from their mother (striped) and one member of each pair from their father (solid). Daughters get an **X** from their mother (striped) and an **X** from their father (solid). Sons get an **X** from their mother (striped) and a **Y** from their father (solid).*

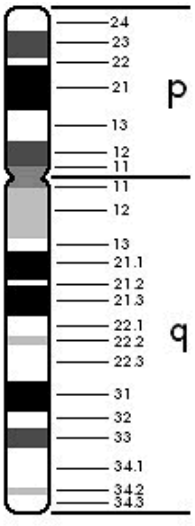


CHROMOSOME NOMENCLATURE

After viewing a karyotype, the chromosome makeup of an individual is written as 46,XX for a typical female and 46,XY for a typical male. The number refers to the total number of chromosomes in each cell, and the letters refer to the sex chromosomes. Additional notation is added when there is a difference from the usual chromosome complement.

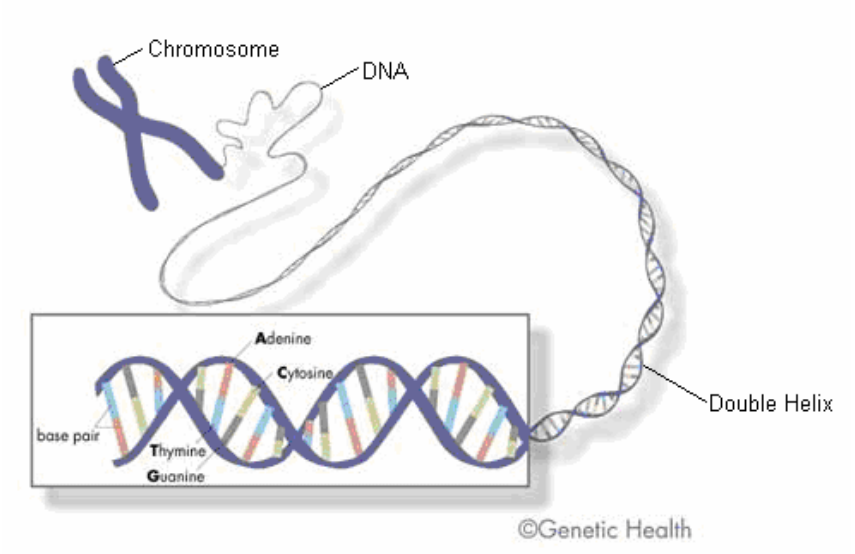
There is also a specific way in which a particular spot or region on a chromosome is written; this is used to refer to the particular location of a gene on a chromosome.

The figure on the right is called an ideogram; this simply means that it is a drawing of a chromosome with locations labeled. The shorter arm of the chromosomes is labeled p, and the longer arm is labeled q. Along each arm are numbers that indicate specific bands along the chromosome.



An example of a gene location on a chromosome is 17q21. This refers to a gene located on the long (q) arm of chromosome 17. The 21 following the q refers to the exact spot of the gene on that arm of the chromosome. 17q21 is the location of the BRCA1 gene. Certain mutations in this gene are associated with an increased risk of breast, ovarian and prostate cancers.

The Human Genome Project has worked towards the goal of mapping (finding the location of) and identifying all genes in the human genome. A **genetic map** is a map of the location of genes relative to each other on the chromosome. Genetic maps are also called linkage maps or ideograms.



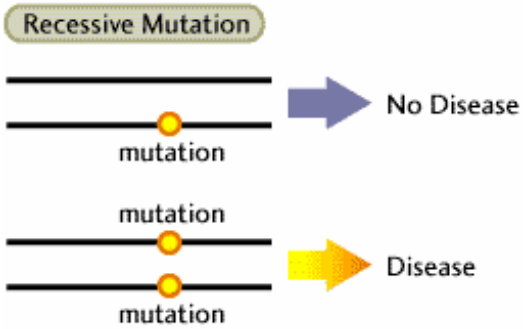
Inheritance Patterns

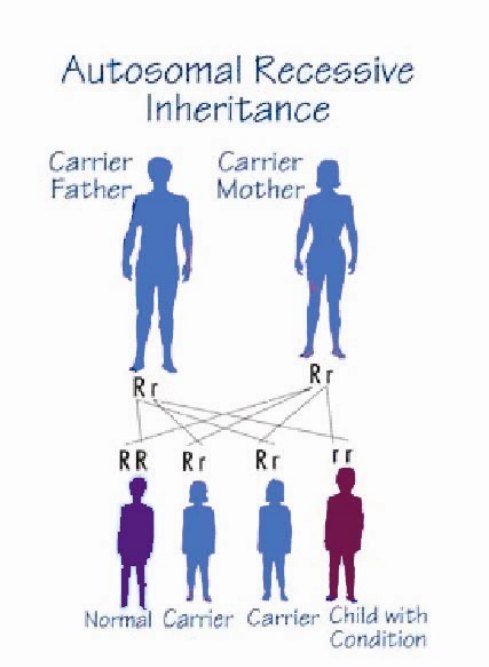
Inheritance patterns explain the ways in which traits or conditions are passed through families.

AUTOSOMAL RECESSIVE INHERITANCE

Autosomal means that the gene is located on an autosome (non-sex chromosome), so males and females are equally likely to be affected. **Recessive** means that both copies of the gene must be changed in order for a person to have the condition. In autosomal recessive inheritance, a person must inherit two copies of a changed gene in order to show the trait or have the condition. Phenylketonuria (PKU) is an example of a disorder inherited in an autosomal recessive manner.

The figure to the right shows that for conditions inherited in an autosomal recessive manner, both copies of the gene must be altered (mutated) and not working in order for a person to have the condition. If a person has a mutation in only one copy of the gene, they are a carrier and are not affected with the condition.





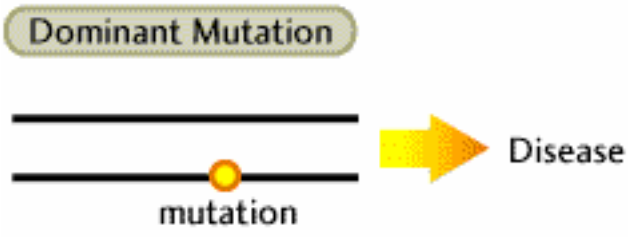
*The figure to the left shows that two parents who are carriers of an autosomal recessive condition have a **25% (1 in 4)** chance of having a child who inherits the condition.(i.e., 25% chance with each pregnancy).*

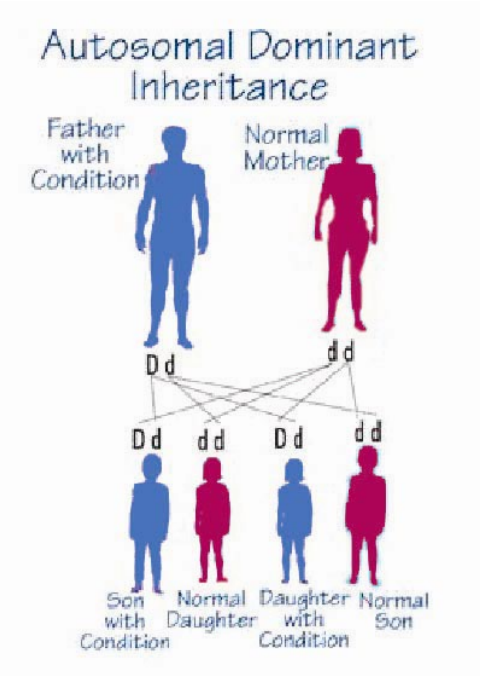
R = Working ("normal") gene
r = Non-working gene that causes a condition (i.e., no working copy present)

AUTOSOMAL DOMINANT INHERITANCE

Autosomal means that the gene is located on an autosome (non-sex chromosome), so males and females are equally likely to be affected. **Dominant** means that only one copy of the gene needs to be changed in order for a person to have the condition. In other words, although genes are always in pairs, a person needs to inherit only one copy of a gene mutation ("non-working" copy) in order to have an autosomal dominant condition. Huntington Disease is an example of a disorder inherited in an autosomal dominant manner.

The figure to the right shows that for conditions inherited in an autosomal dominant manner, only one copy of the gene needs to be altered (mutated) in order for a person to have the condition .





*The figure to the left shows that when an individual with an autosomal dominant condition has a child with an individual who does not have the condition, each of their children has a **50% (1 in 2**) chance of inheriting the condition.*

D = Non-working gene that causes a condition
d = Working ("normal") gene

Hawai'i Genetics Program

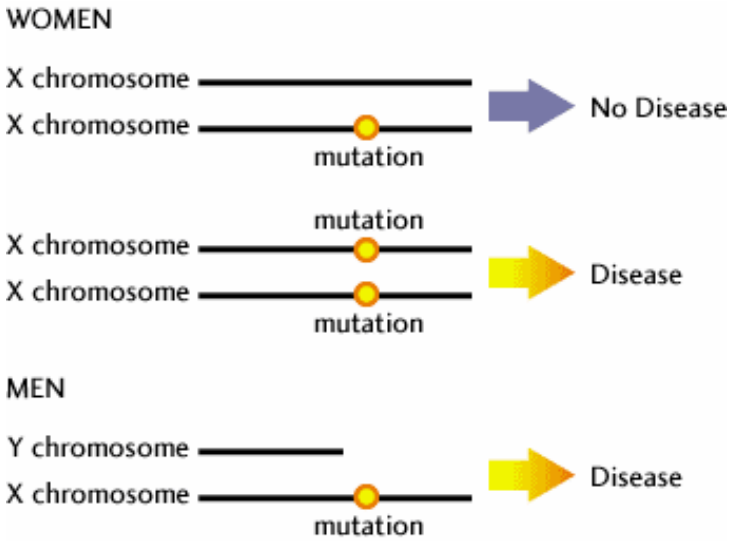
X-LINKED INHERITANCE

X-linked inheritance refers to conditions or traits for which the gene is located on the X chromosome. Remember, females have two X chromosomes while males have one.

The majority of X-linked conditions are **X-linked recessive**, meaning that one working (normal) copy of the gene would compensate for a non-working copy. It is much more common for males to have X-linked recessive conditions than females, since males do not have a second, working copy of their X chromosome to compensate for the non-working copy. In some cases, females can be affected with an X-linked recessive condition, but this is much less common.

X-linked dominant inheritance is rare. In this situation, only a single non-working copy of a gene on the X-chromosome is necessary for a person to be affected. An example of such a condition is Rett syndrome.

The figure to the right shows the mutations that would result in an X-linked recessive condition. If a female has a mutation in only one copy of the gene on her X chromosome, she will not have the condition. Males, on the other hand, will have the condition when the gene on their one X chromosome has a mutation, since they do not have a second copy to compensate.



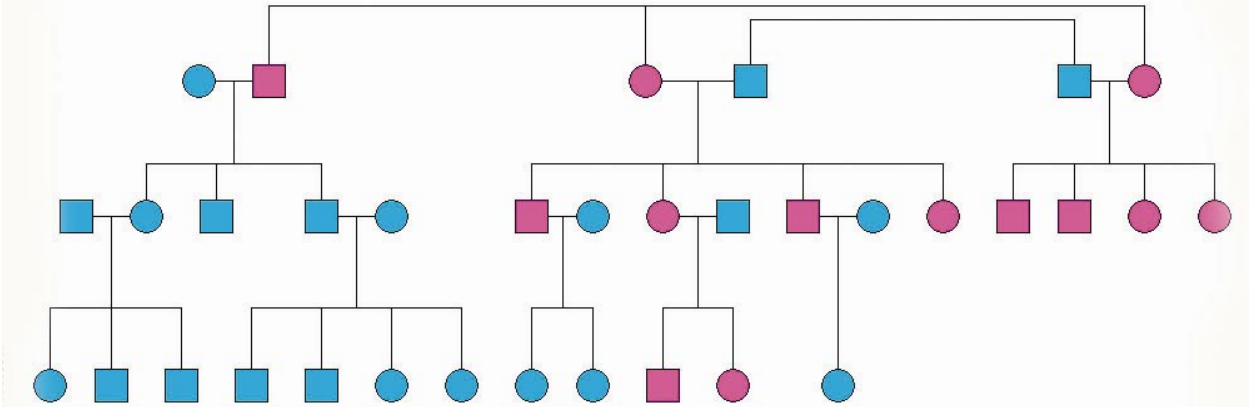
When a female is a carrier of an X-linked recessive condition (i.e., has a mutation in one copy of an X-linked gene), each of her offspring will have a 50% (1 in 2) chance of inheriting the working copy, and a 50% (1 in 2) chance of inheriting the non-working copy. Thus, daughters of a female carrier have a 50% chance of being a carrier and a 50% chance of being a non-carrier, and sons have a 50% chance of being affected and a 50% chance of not being affected.

When a male has an X-linked condition, all of his daughters will be carriers (since all female offspring receive an X from their father), and none of his sons will be affected (since he will pass on his Y chromosome to all of his sons).

MITOCHONDRIAL / MATERNAL INHERITANCE

The chromosomes in our body are contained in the nucleus. **Mitochondria** are structures located in the cytoplasm of the cell, outside the nucleus. They are organelles that provide much of the energy cells need for the work that they do. Mitochondria also contain genes that are separate from the ones in the nucleus. The **mitochondrial DNA** is arranged in one long circular string of genes rather than in chromosomes.

All of the mitochondria in a person's cells descend from the mitochondria present in the original egg from that person's conception. The sperm does not contribute any mitochondria to the fetus. Thus, a person's mitochondria are only inherited from his or her mother. This pattern of inheritance is called **mitochondrial** or **maternal inheritance**. An abnormality in one of the mitochondrial genes can therefore be passed by the mother in her egg cells. Since mitochondria can be inherited only from a mother's egg, mitochondrial genes show a very distinct pattern of inheritance: both males and females can be affected with a mitochondrial disease gene, but *only* females can transmit that mitochondrial disease gene to children.



Male with normal mitochondrial genes

Female with normal mitochondrial genes

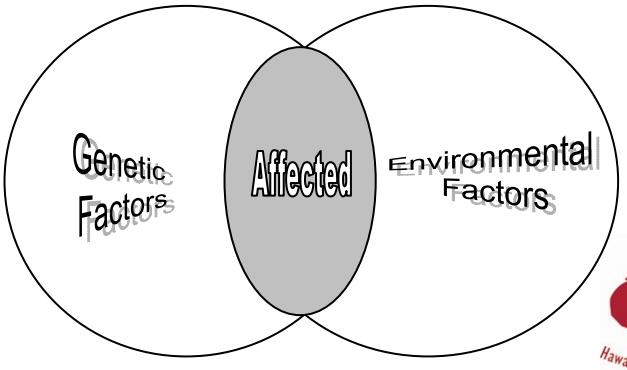
Male with mitochondrial disease gene

Female with mitochondrial disease gene

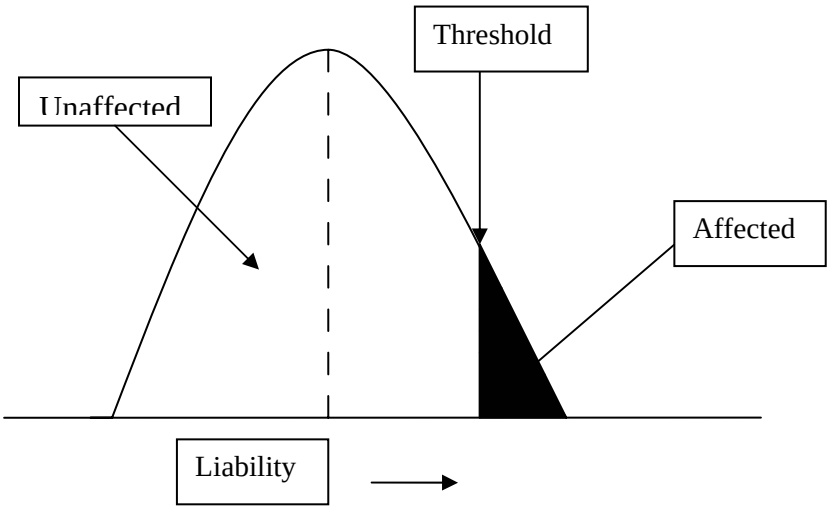
MULTIFACTORIAL INHERITANCE

Many conditions are caused by a combination of genes and other factors, such as the environment. These conditions are said to be "**multifactorial**". People who have such a condition are often born into families with no other affected people. However, parents of a child with the condition have a greater chance of having another child with the condition than couples who do not have a child with the condition.

Mutifactorial inheritance is actually the most common form of inheritance; most traits and characteristics are inherited in a multifactorial fashion.



Threshold Model of Disease



The figure above shows that a certain combination of genetic and environmental factors is needed in order for a person to be affected with a multifactorial condition. The genetic and environmental factors add together and, when they reach the threshold level, cause a person to be affected.

Genetic Testing & Screening

GENETIC TESTING

A **genetic test** involves looking at a person's DNA (genes) or chromosomes to see if certain mutations (changes) are present. Analysis of a small sample of blood (or other body tissue) allows scientists to look more closely at a person's genetic information. Genes can also be examined from other body tissues, such as cheek cells, or a tissue sample. There are two common types of genetic testing at the DNA level: **DNA Sequencing** and **Mutation Analysis**.

In "**DNA sequencing**" the DNA code of letters is read along an entire gene or gene segment. In this way, changes in the spelling of the gene's instructions can be observed. In some cases, a change may be found that is known to be associated with a condition or an increased risk for a condition. In other cases, no changes may be found. In still other cases, a change may be found, but the meaning of this change may be unknown at this time.

In "**mutation analysis**", testing is done to look at a specific region of a gene, rather than reading the code along an entire gene. Mutation testing is usually done if the mutation in a family is already known, or if there are certain mutations that are usually associated with a condition. Scientists are thus better able to know the gene location at which to focus their analysis.

What are Some Benefits of Genetic Testing?

If a mutation is detected, it may explain why a person has a condition. In some cases, knowing the particular mutation will allow doctors to predict how severe the condition might become and what other symptoms may be expected. This may allow the person's medical care to be adjusted accordingly. In cases when a person does not yet have any symptoms, results of predictive genetic testing can allow that person to prepare for the future. Knowing the mutation responsible can also predict the chances that the person's children may inherit the condition. **Prenatal testing** (testing a baby before it is born to see if it has the mutation) may also be possible.

What are Some Limitations of Genetic Testing?

Not all of the genes that are involved in conditions are known, so even if a condition runs in the family, it might not be possible to find the mutation involved.

Likewise, a **negative result** (no change is found) does not guarantee that a person will not get the condition. The person may have a different mutation that was not detectable by the test used, or the person may have a mutation in a different gene that also causes the same condition.

Genetic tests are different from other medical tests in that the results may provide information about other members of the family, and not just the person being tested. In addition, some people are concerned about keeping the results of their genetic testing private. Test results should not be seen by anyone who is not involved in the testing unless permission is obtained.

GENETIC SCREENING

Screening is the process of testing for disease in a person who does not show signs of having the disease (a non-symptomatic or asymptomatic person). Screening is often done at the population level, such as with Newborn Metabolic Screening. The goal of screening is to identify the disease in its early stages and thus allow for treatment and preparation. It is important to note that, with most screening, follow up testing is required to confirm a diagnosis.

Below are the possible results of screening.

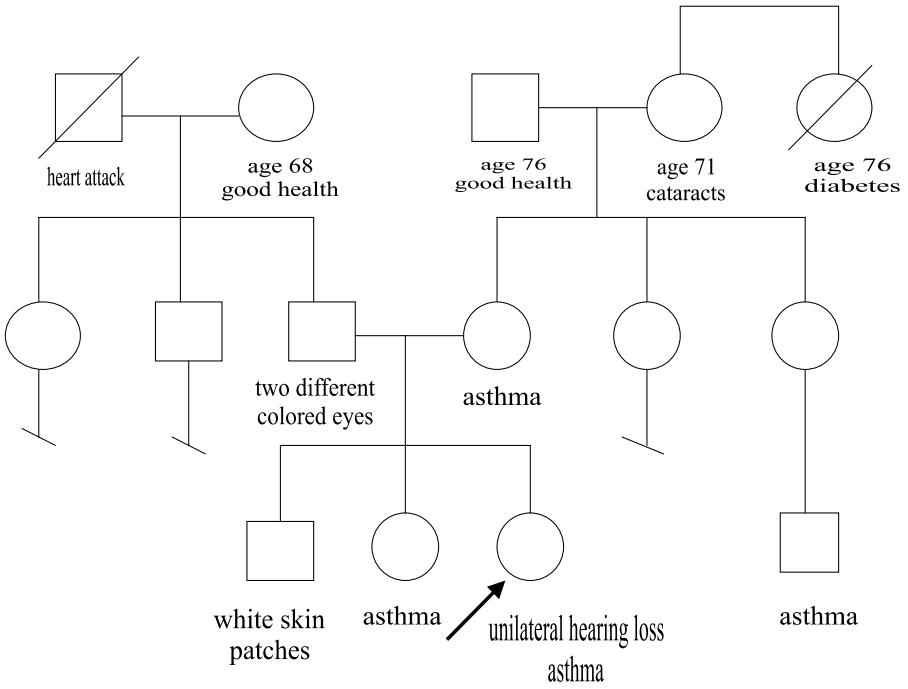
Possible Results	**True Positive**	**True Negative**	**False Positive**	**False Negative**
Person's health status	Person HAS the disease	Person does NOT have the disease	Person does NOT have the disease	Person HAS the disease
Test Result	Confirms that person HAS the disease	Confirms that person does NOT have the disease	Test results say that person HAS the disease	Test says that the person does NOT have the disease

GENETICS EVALUATION

A **geneticist** is a medical doctor with a specialty in genetics. A **genetic counselor** is a healthcare professional who provides information and support to individuals and families who have a genetic disorder, who might be at risk for developing an inherited condition, or who are concerned that they may have a child with an inherited disease. The geneticist and genetic counselor work together to obtain and analyze family medical histories, as well as to calculate and explain risks, options, and testing results. Other health professionals, such as genetics nurse specialists, can also be an important part of the genetics team.

A **pedigree** is a medical drawing of a family tree that includes all of a person's close relatives, the relationships between family members, and health information. A pedigree is used by health care professionals to analyze a family for conditions which certain family members may have or be at risk for. Pedigrees also show the relationships between individuals in a family. In a pedigree, males are indicated by squares, while females are indicated by circles. The lines between individuals indicate the different relationships (e.g., sibling, parent, husband, etc.).

Below is an example of a pedigree. In this family, the man with two different colored eyes, his son, and his daughter (the proband) are being evaluated in Genetics clinic for Waardenburg syndrome, an autosomal dominant condition.



We hope that you find this Genetics booklet helpful as you prepare to teach Genetics to your students!

Hawai'i Genetics Program

If you have questions or would like more information, please contact:

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