Exceptions to Simple Inheritance

Since Mendel's time, our knowledge of the mechanisms of genetic inheritance has grown immensely. For instance, it is now understood that inheriting one allele can, at times, increase the chance of inheriting another or can affect how and when a trait is expressed in an individual's phenotype. Likewise, there are degrees of dominance and recessiveness with some traits. The simple rules of Mendelian inheritance do not apply in these and other exceptions. They are said to have **non-Mendelian inheritance patterns**.

Polygenic Traits

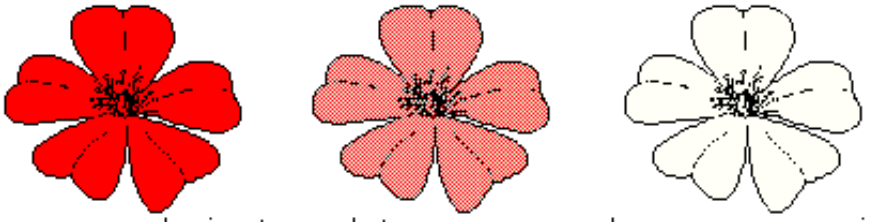
Polygenic traits: stature, body shape, hair and skin color

Some traits are determined by the combined effect of more than one pair of genes. These are referred to as polygenic, or continuous, traits. An example of this is human stature. The combined size of all of the body parts from head to foot determines the height of an individual. There is an additive effect. The sizes of all of these body parts are, in turn, determined by numerous genes. Human skin, hair, and eye color are also polygenic traits because they are influenced by more than one allele at different loci. The result is the perception of continuous gradation in the expression of these traits.

NOTE: whether an individual achieves his or her genetically programmed height is significantly affected by thyroid gland hormones and human growth hormones (HGH) produced in the pituitary gland . A deficiency in the amount of these hormones during childhood and puberty can result in stunted growth. Too much of them can cause excessive growth resulting in exceptional height. Differences in diet and other environmental factors during the crucial growth years can also be important in determining stature and other complex traits. Usually, about 10% of an individual's height is due to the environment.

Intermediate Expression

Apparent blending can occur in the phenotype when there is incomplete dominance resulting in an intermediate expression of a trait in heterozygous individuals. For instance, in primroses, snapdragons, and four-o'clocks, red or white flowers are homozygous while pink ones are heterozygous. The pink flowers result because the single "red" allele is unable to code for the production of enough red pigment to make the petals dark red.

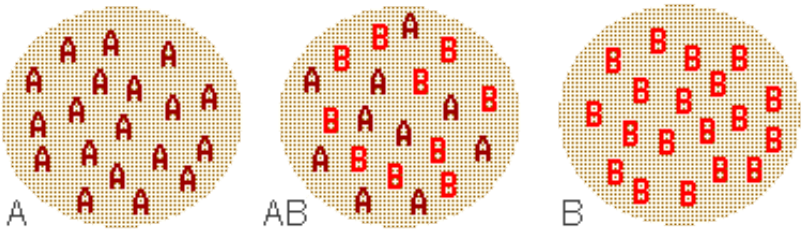


Another example of an intermediate expression may be the pitch of human male voices. The lowest and highest pitches apparently are found in men who are homozygous for this trait (AA and aa), while the intermediate range baritones are heterozygous (Aa). The child-killer disease known as Tay-Sachs is also characterized by incomplete dominance. Heterozygous individuals are genetically programmed to produce only 40-60% of the normal amount of an enzyme that prevents the disease.

Fortunately for Mendel, the pea plant traits that he studied were controlled by genes that do not exhibit an intermediate expression in the phenotype. Otherwise, he probably would not have discovered the basic rules of genetic inheritance.

Codominance

For some traits, two alleles can be codominant. That is to say, both are expressed in heterozygous individuals. An example of this is people who have an AB blood type for the ABO blood system. When they are tested, these individuals actually have the characteristics of both type A and type B blood. Their phenotype is not intermediate between the two.



Type AB blood testing as both A and B

Multiple-allele Series

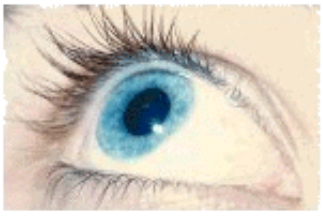
The ABO blood type system is also an example of a trait that is controlled by more than just a single pair of alleles. In other words, it is due to a multiple-allele series. In this case, there are three alleles (A, B, and O), but each individual only inherits two of them (one from each parent).

Some traits are controlled by far more alleles. For instance, the human HLA system, which is responsible for identifying and rejecting foreign tissue in our bodies, can have at least 30,000,000 different genotypes. It is the HLA system which causes the rejection of organ transplants. The more we learn about human genetics the more it becomes clear that multiple-allele series are very common. In fact, it now appears that they are more common than simple two allele ones.

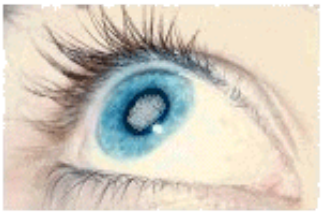
Modifying and Regulator Genes

There are two classes of genes that can have an effect on how other genes function. They are called modifying genes and regulator genes.

Modifying genes alter how certain other genes are expressed in the phenotype. For instance, there is a dominant cataract gene which will produce varying degrees of vision impairment depending on the presence of a specific allele for a companion modifying gene. However, cataracts also can be promoted by diabetes and common environmental factors such as excessive ultraviolet radiation, and alcoholism. Nearly half of all people in North America over 65 years of age eventually develop them.



normal



cataract

Regulator genes can either initiate or block the expression of other genes. They control the production of a variety of chemicals in plants and animals. For instance, the time of production of specific proteins that will be new structural parts of our bodies can be controlled by such regulator genes. Shortly after conception, regulator genes work as master switches orchestrating the timely development of our body parts. They are also responsible for changes that occur in our bodies as we grow older. In other words, they control the maturation and aging processes. Regulator genes that are involved in subdividing an embryo into what will become the major body parts of an individual are also referred to as **homeotic**, **homeobox**, or **Hox genes**. They are responsible for setting generalized cells on the path to become a head, torso, arms, legs, etc.

Gene Control--video clip from Teachers' Domain View in: *QuickTime* or *Windows Media Player* (length = 2 mins 58 secs)	Can We Slow Aging--video clip from Nova ScienceNow about a regulator gene that controls the aging process (length = 11 mins 30 secs)

Incomplete Penetrance

Some genes are incompletely penetrant. That is to say, their effect does not normally occur unless certain environmental factors are present. For example, you may inherit the genes that are responsible for type 2 diabetes but never get the disease unless you become greatly overweight, persistently stressed psychologically, or do not get enough sleep on a regular basis. Similarly, the genes that cause the chronic autoimmune disease, multiple sclerosis, may be triggered by the Epstein-Barr virus and possibly other specific environmental stresses. New research suggests that abundant exposure to the sun in childhood can provide some protection from developing MS. Subsequently, people who grow up in tropical and subtropical regions of the world have significantly lower rates of MS as adults.

Sex Related Genetic effects

There are three categories of genes that may have different effects depending on an individual's gender. These are referred to as:

1. sex-limited genes
2. sex-controlled genes
3. genome imprinting

Sex-limited genes are ones that are inherited by both men and women but are normally only expressed in the phenotype of one of them. The heavy male beard is an example. While women have facial hair it is most often very fine and comparatively sparse.

Human gender differences in facial hair

In contrast, **sex-controlled genes** are expressed in both sexes but differently. An example of this is gout, a disease that causes painfully inflamed joints. If the gene is present, men are nearly eight times more likely than women to have severe symptoms.

Some genes are known to have a different effect depending on the gender of the parent from whom they are inherited. This phenomenon is referred to as **genome imprinting** or genetic imprinting. Apparently, diabetes, psoriasis, and some rare genetically inherited diseases, such as a form of mental retardation known as Angelman syndrome, can follow this inheritance pattern. Recent research by Catherine Dulac of Harvard University points to genetic imprinting as being an important factor in causing male and female brains to develop somewhat differently. She suggests that this is due to the fact that some of the genes inherited from the opposite sex parent are likely to be turned off following conception.

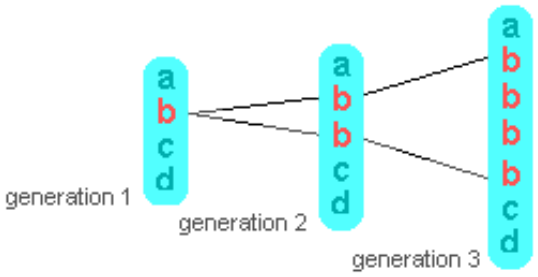
Pleiotropy

A single gene may be responsible for a variety of traits. This is called pleiotropy. The complex of symptoms that are collectively referred to as sickle-cell trait, or sickle-cell anemia, is an example. A single gene results in irregularly shaped red blood cells that painfully block blood vessels, cause poor overall physical development, as well as related heart, lung, kidney, and eye problems. Another pleiotropic trait is albinism. The gene for this trait not only results in a deficiency of skin, hair, and eye pigmentation but also causes defects in vision.

Stuttering Alleles

Lastly, it is now known that some genetically inherited diseases have more severe symptoms each succeeding generation due to segments of the defective genes being doubled in their transmission to children (as illustrated below). These are referred to as stuttering alleles or unstable alleles. Examples of this

phenomenon are Huntington's disease, fragile-X syndrome, and the myotonic form of muscular dystrophy.



Unstable allele doubling each generation

Mendel believed that all units of inheritance are passed on to offspring unchanged. Unstable alleles are an important exception to this rule.

Environmental Influences

The phenotype of an individual is not only the result of inheriting a particular set of parental genes. The specific environmental characteristics of the uterus in which a fertilized egg is implanted and the health of the mother can have major impacts on the phenotype of the future child. For instance, oxygen deprivation or inappropriate hormone levels can cause lifelong, devastating effects. Likewise, accidents, poor nutrition, and other environmental influences throughout life can alter an individual's phenotype for many traits.

Geneticists study identical or monozygotic twins to determine which traits are inherited and which ones were acquired following conception. Since monozygotic twins come from the same zygote, they are essentially identical in their genetic makeup. If there are any differences in their phenotypes, the environment is virtually always responsible. Such differences show up in basic capabilities such as handedness, which had been assumed to be entirely genetically determined. In rare instances, one monozygotic twin will be clearly right-handed while the other will be left-handed. This suggests that there may be both genetic and environmental influences in the development of this trait.

Summary

Researchers have identified more than 5,000 genetically inherited human diseases and abnormalities. As we learn more about the inheritance patterns for these traits, it is becoming clear that at least some of the twelve exceptions to the simple Mendelian rules of inheritance described here are, in fact, relatively common. It would not be surprising if other "exceptions" were discovered in the future. However, it is important to keep in mind that there are at least 18,000 human traits controlled by genes that follow the basic Mendelian rules of inheritance.

NEWS: Susan Lolle et al. reported in the March 2005 issue of Nature that they have discovered a plant species that can overwrite the genetic makeup inherited from parents. These cress plants seem to be able to revert back to the DNA sequences of their grandparents including genetic information that was lost in the

intervening generation. The researchers suggest that since the DNA sequences were not present in the parents that there may be a "template-directed process that makes use of an ancestral RNA-sequence cache." The implication is that this is a form of inheritance that does not follow the basic tenets of classical genetics. ("Genome-wide Non-Mendelian Inheritance of Extra-genomic Information in Arabidopsis", Nature, Vol. 434, No 7032, March 24, 2005)

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