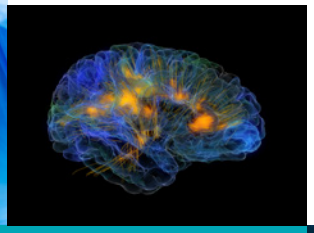

Genetics Primer

This material is provided by UCSF Weill Institute for Neurosciences as an educational resource for patients.

UCSF Weill Institute for Neurosciences

Memory and Aging Center

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The past few decades have yielded significant advances in genetics and genomics. The advances have been accompanied by growing appreciation of the impact of genetics and genomics in health and disease across the life spectrum. This section presents a broad overview of basic concepts of human genetics, with an emphasis on neurodegenerative disease.

What is genetics?

Genetics is the study of heritable biological variation. Genetics in the healthcare setting is the study of heritable variation in human health and disease.

What is genomics?

Genomics is the study of the constitution or make-up of entire genomes, which is all of the genetic material in a person or organism.

What is a gene?

A gene is a basic unit of inheritance. Genes are passed from parents to offspring. They contain information that tells the human body how to grow and develop. Genes are arranged, often one after another, on structures called chromosomes. Genes are made up of a chemical called DNA. Each person has a total of 20,000-25,000 genes in every cell of the body. A third of these genes are active in the brain. These genes control the development and function of the brain. Some genes make proteins, while other genes are responsible for turning genes on and off. Genes active in the brain are ultimately responsible for how the brain functions and can affect how we think, move, feel, and behave.

What is DNA?

DNA is the chemical that genes are made of. DNA stands for deoxyribonucleic acid. It contains the genetic instructions for all living things, including humans. It is represented as a long string of nucleotides, which are abbreviated as letters – A, C, T, and G where A stands for adenine, C stands for cytosine, T stands for thymine, and G stands for guanine. The string of letters is often referred to as a DNA “sequence” or “code.”

What is an allele?

An allele is one of two or more versions of a gene. A person inherits two alleles for each gene, one from each parent. If the two alleles are the same, the person is “homozygous” for that gene. If the two alleles are different, the person is “heterozygous” for that gene. The *APOE* gene has three alleles or versions, called e2, e3, and e4. Only the e4 allele is associated with an increased risk for Alzheimer’s disease. Each person has at most two separate alleles for the *APOE* gene, one from each parent, which means there are six different *APOE* genotypes in the population: e2/e2, e2/e3, e2/e4, e3/e3, e3/e4, and e4/e4. The most common genotype among people of European ancestry is e3/e3

What is a genotype?

A genotype is composed of two alleles (one from each parent) and defines the version of a gene associated with a particular trait.

What is a phenotype?

A phenotype is a person’s observable traits. In human health, these traits include height and eye color. In human illness, these traits include signs and symptoms of disease. A person’s phenotype is influenced in varying degrees by genotype.

What is genetic testing?

Genetic testing is a laboratory test used to look for variations or changes in a gene associated with disease. Genetic testing often involves analysis of a blood sample. However, sometimes other tissues can be tested. The results of genetic testing can be used

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to confirm or rule out a suspected genetic disease. In certain situations, results from genetic testing determine the likelihood of a person passing on a disease-causing variant or mutation to offspring. Genetic testing may also identify risk variants.

What is a disease-causing genetic variant?

A disease-causing genetic variant is a permanent change or variation in a gene that leads directly to a well-characterized set of signs and symptoms of disease. In the absence of such a variant, a person will not develop the disease. When a disease-causing genetic variant is in the germline or the sex cells (sperm or eggs), it can be passed on to offspring. A disease-causing genetic variant may also be referred to as a "genetic mutation." However, a mutation is simply a change in a DNA sequence. Some mutations play a role in disease development, some are protective against disease, and still others are neutral and have no impact on human health. Presently, genetic professionals emphasize the use of the term "disease-causing genetic variant" or "disease-causing mutation" rather than the imprecise term "genetic mutation."

What is a genetic risk variant?

A genetic risk variant is a permanent change or variation in a gene that increases a person's risk to develop disease. It does not cause disease directly. In the absence of such a variant, a person could still develop disease. In the presence of such a variant, a person is not guaranteed to develop disease. A genetic risk variant may also be referred to as a "susceptibility variant" or "susceptibility gene." The magnitude of disease risk conferred by any given genetic risk variant varies widely, depending on the variant and the disease in question. For example, a person with one copy of *APOE* e4, a known genetic risk variant for Alzheimer's disease, has an increased risk of 3:1 to 4:1 odds of developing Alzheimer's disease. However, not every person with one copy of *APOE* e4 will develop Alzheimer's disease. A person who has no copies of *APOE* e4 may still develop Alzheimer's disease during his/her lifetime. *APOE* e4 plays a role in common disease rather than in a rare single gene disorder (see below).

What is the difference between a single gene disorder and common disease?

Some human disease results from the direct effects of a variant in one gene. This is considered a single gene disorder. A single gene disorder is often conversationally referred to as "genetic disease." In general, single gene disorders are rare, affecting a small proportion of the population. This is distinct from common disease. Common disease results from the effects of variants in multiple genes, with each variant unable to cause disease directly, in concert with the effects of environmental factors, which vary in type, duration, and intensity through time. Common disease comprises most human illnesses, including heart disease, diabetes, and most cases of neurodegenerative disease. For example, Alzheimer's disease is usually a common disease; single gene forms of Alzheimer's disease are rare. In contrast, Huntington's disease only occurs as a single gene disorder.