

CADASIL FACT SHEET

CADASIL is caused by a Mutation in the Notch3 gene.

What genes are related to CADASIL? Mutations in the NOTCH3 gene cause CADASIL. The NOTCH3 gene makes a protein called the Notch3 receptor protein, which plays a role in the development, function and maintenance of vascular smooth muscle cells. Mutations in the NOTCH3 gene lead to an abnormal version of the Notch3 protein that builds up in vascular smooth muscle cells. Accumulation of the abnormal Notch3 protein is thought to cause the degeneration of these muscle cells, leading to the loss of function of blood vessels in the brain and heart.

What mutations are effected with CADASIL? Almost all CADASIL mutations alter the number of cysteine residues in the epidermal growth factor (EGF)-like repeats in the extra cellular domain of the protein. More than 70 mutations that cause CADASIL have been reported. Almost all of these mutations change a single amino acid (a building block of proteins) in the Notch3 receptor. Evidence suggests that these mutations play a role in the degeneration of vascular smooth muscle cells. Loss of the muscle cells leads to reduction of blood flow to the brain and heart.

What glossary definitions help with understanding CADASIL?

arteriopathy - (är-tir-ē-äp-ə-thē) A disease of the arteries.

arginine - is an amino acid that plays a role in cell division, healing of wounds, removing ammonia from the body, improving immunity to illness, and hormone secretion. Arginine is used by the body to make nitric oxide, a substance that relaxes blood vessels.

autosomal - (/i-öt-ə-ˈsō-məl/) Refers to any of the chromosomes other than the sex-determining chromosomes (i.e., the X and Y) or the genes on these chromosomes.

autosomal dominant - ((/i-öt-ə-ˈsō-məl/) A pattern of inheritance in which an affected individual has one copy of a mutant gene and one normal gene on a pair of autosomal chromosomes. (In contrast, autosomal recessive diseases require that the individual have two copies of the mutant gene.) Individuals with autosomal dominant diseases have a 50-50 chance of passing the mutant gene and therefore the disorder onto each of their children.

cerebral - (cé-ré-bral) Pertaining to the brain, the cerebrum or the intellect.

codon -three bases in a DNA or RNA sequence which specify a single amino acid.

dementia - (di-ˈmen-chə) Significant loss of intellectual abilities such as memory capacity, severe enough to interfere with social or occupational functioning. Criteria for the diagnosis of dementia include impairment of attention, orientation, memory, judgment, language, motor and spatial skills, and function.

familial - (fə-ˈmil-yəl) A condition that tends to occur more often in family members than expected by chance alone. A familial disease may be genetic.

gene - (ˈjēn)The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein.

Heterozygous - (het-er-o-zi-guis) Possessing two different forms of a particular gene, one inherited from each parent.

infarct - (ˈin-färkt-)A pathological process consisting of a sudden insufficient blood supply to an area, which results in necrosis of that area. An area of tissue death due to a local lack of oxygen.

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infarction (in-^lfärk-shən) The formation of an infarct, an area of tissue death due to a local lack of oxygen

leukoencephalopathy (/in-^lsef-ə-^läp-ə-thē/) Any of various diseases affecting the brain's white matter

mutation (myü-^ltā-shən) Any alteration in a gene from its natural state; may be disease causing or a benign, normal variant

myocardial infarction The term "myocardial infarction" focuses on the myocardium (the heart muscle) and the changes that occur in it due to the sudden deprivation of circulating blood. The main change is necrosis (death) of myocardial tissue.

new mutation An alteration in a gene that is present for the first time in one family member as a result of a mutation in a germ cell (egg or sperm) of one of the parents or in the fertilized egg itself

nucleotide (nukle-o-tid) One of the structural components, or building blocks, of DNA and RNA. A nucleotide consists of a base (one of four chemicals: adenine, thymine, guanine, and cytosine) plus a molecule of sugar and one of phosphoric acid.

prevalence (^lprev(-ə)-lən(t)s) The proportion of individuals in a population having a disease. Prevalence is a statistical concept referring to the number of cases of a disease that are present in a particular population at a given time.

protein (^lprōt-ē-ən) A large molecule composed of one or more chains of amino acids in a specific order determined by the base sequence of nucleotides in the DNA coding for the protein. Proteins are required for the structure, function, and regulation of the body's cells, tissues, and organs. Each protein has unique functions. Proteins are essential components

receptor (ri-^lsep-tər) A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell.

risk factors Something that may increase the chance of developing a disease. Some examples of risk factors for cancer include age, a family history of certain cancers, use of tobacco products, certain eating habits, obesity, lack of exercise, exposure to radiation or other cancer-causing agents, and certain genetic changes.

subcortical (-^lkōrt-i-kəl) Of, relating to, involving, or being nerve centers below the cerebral cortex.

Patient blood test report might look like this:

Heterozygous for a C to T base change at nucleotide 505 of the Notch 3 gene that changes a codon for arginine (CGC) to one for cysteine (TGC) at amino acid position 169. This patient's mutation would be a R159C- mutation.

The resources should not be used as a substitute for professional medical care or advice. Users seeking information about a personal genetic disease, syndrome, or condition should consult with a qualified healthcare professional.

This fact sheet was created by: CADASIL Together We Have Hope Non-Profit Organization (www.cadasilfoundation.org) 1-877-519-HOPE Billie Duncan-Smith (Director)
Resources from the Genetics Home Reference. <http://ghr.nlm.nih.gov/condition=cadasil>

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