Geneticheck - Genetic Report

Gene

MMACHC

Associated Diseases

Methylmalonic Aciduria And Homocystinuria, Cblc Type
Methylmalonic Acidemia With Homocystinuria, Type Cblc

Phenotype

Pulmonary arterial hypertension
Pulmonary hypertension is defined mean pulmonary artery pressure of 25mmHg or more and pulmonary capillary wedge pressure of 15mmHg or less when measured by right heart catheterisation at rest and in a supine position.

Feeding difficulties
Impaired ability to eat related to problems gathering food and getting ready to suck, chew, or swallow it.

Hypoglycemia
A decreased concentration of glucose in the blood.

Infantile spasms
Infantile spasms represent a subset of "epileptic spasms". Infantile Spasms are epileptic spasms starting in the first year of life (infancy).

Jaundice
Yellow pigmentation of the skin due to bilirubin, which in turn is the result of increased bilirubin concentration in the bloodstream.

Severe demyelination of the white matter
A severe loss of myelin from nerve fibers in the central nervous system.

Glossitis
Inflammation of the tongue.

Long face
Facial height (length) is more than 2 standard deviations above the mean (objective); or, an apparent increase in the height (length) of the face (subjective).

Seizure
A seizure is an intermittent abnormality of nervous system physiology characterised by a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.

Renal insufficiency
A reduction in the level of performance of the kidneys in areas of function comprising the concentration of urine, removal of wastes, the maintenance of electrolyte balance, homeostasis of blood pressure, and calcium metabolism.

Reduced visual acuity

Ketonuria
High levels of ketone bodies (acetoacetic acid, beta-hydroxybutyric acid, and acetone) in the urine. Ketone bodies are insignificant in the blood and urine of normal individuals in the postprandial or overnight-fasted state.

Glomerulopathy
Inflammatory or noninflammatory diseases affecting the glomeruli of the nephron.

Cystathioninemia
An increased concentration of cystathionine in the blood.

Hypomethioninemia
A decreased concentration of methionine in the blood.

Pigmentary retinopathy
An abnormality of the retina characterized by pigment deposition. It is typically associated with migration and proliferation of macrophages or retinal pigment epithelial cells into the retina; melanin from these cells causes the pigmentary changes. Pigmentary retinopathy is a common final pathway of many retinal conditions and is often associated with visual loss.

Elevated circulating palmitoleylcarnitine concentration
An elevated level of propionylcarnitine in the circulation. Propionylcarnitine is present in high abundance in the urine of patients with Methylmalonyl-CoA mutase (MUT) deficiency.

Microcephaly
Head circumference below 2 standard deviations below the mean for age and gender.

Macular coloboma
A congenital defect of the macula distinct from coloboma associated with optic fissure closure defects. Macular coloboma is characterized by a sharply defined, rather large defect in the central area of the fundus that is oval or round, and coarsely pigmented.

Neurological speech impairment

Autosomal recessive inheritance
A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).

Leukoencephalopathy
This term describes abnormality of the white matter of the cerebrum resulting from damage to the myelin sheaths of nerve cells.

Failure to thrive

Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.

Abnormality of macular pigmentation
Abnormality of macular or foveal pigmentation.

High forehead
An abnormally increased height of the forehead.

Delirium
A state of sudden and severe confusion.

Decreased methionine synthase activity
A reduction in methionine synthase activity.

Metabolic acidosis
Metabolic acidosis (MA) is characterized by a fall in blood pH due to a reduction of serum bicarbonate concentration. This can occur as a result of either the accumulation of acids (high anion gap MA) or the loss of bicarbonate from the gastrointestinal tract or the kidney (hyperchloremic MA). By definition, MA is not due to a respirary cause.

Cerebral atrophy
Atrophy (wasting, decrease in size of cells or tissue) affecting the cerebrum.

Hematuria
The presence of blood in the urine. Hematuria may be gross hematuria (visible to the naked eye) or microscopic hematuria (detected by dipstick or microscopic examination of the urine).

Stomatitis
Stomatitis is an inflammation of the mucous membranes of any of the structures in the mouth.

Deep venous thrombosis
Formation of a blot clot in a deep vein. The clot often blocks blood flow, causing swelling and pain. The deep veins of the leg are most often affected.

Ataxia
Cerebellar ataxia refers to ataxia due to dysfunction of the cerebellum. This causes a variety of elementary neurological deficits including asynergy (lack of coordination between muscles, limbs and joints), dysmetria (lack of ability to judge distances that can lead to under- or overshoot in grasping movements), and dysdiadochokinesia (inability to perform rapid movements requiring antagonizing muscle groups to be switched on and off repeatedly).

Homocystinuria
An increased concentration of homocystine in the urine.

Psychosis
A condition characterized by changes of personality and thought patterns often accompanied by hallucinations and delusional beliefs.

Nystagmus

Rhythmic, involuntary oscillations of one or both eyes related to abnormality in fixation, conjugate gaze, or vestibular mechanisms.

Abnormality of brain morphology
A structural abnormality of the brain, which has as its parts the forebrain, midbrain, and hindbrain.

Abnormality of the nervous system
An abnormality of the nervous system.

Hydrocephalus
Hydrocephalus is an active distension of the ventricular system of the brain resulting from inadequate passage of CSF from its point of production within the cerebral ventricles to its point of absorption into the systemic circulation.

Hypotonia
Hypotonia is an abnormally low muscle tone (the amount of tension or resistance to movement in a muscle). Even when relaxed, muscles have a continuous and passive partial contraction which provides some resistance to passive stretching. Hypotonia thus manifests as diminished resistance to passive stretching. Hypotonia is not the same as muscle weakness, although the two conditions can co-exist.

Abnormality of extrapyramidal motor function
A neurological condition related to lesions of the basal ganglia leading to typical abnormalities including akinesia (inability to initiate changes in activity and perform volitional movements rapidly and easily), muscular rigidity (continuous contraction of muscles with constant resistance to passive movement), chorea (widespread arrhythmic movements of a forcible, rapid, jerky, and restless nature), athetosis (inability to sustain the muscles of the fingers, toes, or other group of muscles in a fixed position), and akathisia (inability to remain motionless).

Methylmalonic acidemia
Increased concentration of methylmalonic acid in the blood.

Dementia
A loss of global cognitive ability of sufficient amount to interfere with normal social or occupational function. Dementia represents a loss of previously present cognitive abilities, generally in adults, and can affect memory, thinking, language, judgment, and behavior.

Memory impairment
An impairment of memory as manifested by a reduced ability to remember things such as dates and names, and increased forgetfulness.

Neurodevelopmental delay

Confusion
Lack of clarity and coherence of thought, perception, understanding, or action.

Subdural hemorrhage
Hemorrhage occurring between the dura mater and the arachnoid mater.

Personality changes
An abnormal shift in patterns of thinking, acting, or feeling.

Generalized hypotonia
Generalized muscular hypotonia (abnormally low muscle tone).

Poor fine motor coordination
An abnormality of the ability (skills) to perform a precise movement of small muscles with the intent to perform a specific act. Fine motor skills are required to mediate movements of the wrists, hands, fingers, feet, and toes.

Low-set ears
Upper insertion of the ear to the scalp below an imaginary horizontal line drawn between the inner canthi of the eye and extending posteriorly to the ear.

Neutropenia
An abnormally low number of neutrophils in the peripheral blood.

Feeding difficulties in infancy
Impaired feeding performance of an infant as manifested by difficulties such as weak and ineffective sucking, brief bursts of sucking, and falling asleep during sucking. There may be difficulties with chewing or maintaining attention.

Cerebral cortical atrophy
Atrophy of the cortex of the cerebrum.

Dilated cardiomyopathy
Dilated cardiomyopathy (DCM) is defined by the presence of left ventricular dilatation and left ventricular systolic dysfunction in the absence of abnormal loading conditions (hypertension, valve disease) or coronary artery disease sufficient to cause global systolic impairment. Right ventricular dilation and dysfunction may be present but are not necessary for the diagnosis.

Hyperammonemia
An increased concentration of ammonia in the blood.

Lethargy
A state of disinterestedness, listlessness, and indifference, resulting in difficulty performing simple tasks or concentrating.

Global developmental delay
A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.

Thrombocytopenia
A reduction in the number of circulating thrombocytes.

Growth delay
A deficiency or slowing down of growth pre- and postnatally.

Intrauterine growth retardation
An abnormal restriction of fetal growth with fetal weight below the tenth percentile for gestational age.

Tremor
An unintentional, oscillating to-and-fro muscle movement about a joint axis.

Respiratory distress
Respiratory distress is objectively observable as the physical or emotional consequences from the experience of dyspnea. The physical presentation of respiratory distress is generally referred to as labored breathing, while the sensation of respiratory distress is called shortness of breath or dyspnea.

Hydrops fetalis
The abnormal accumulation of fluid in two or more fetal compartments, including ascites, pleural effusion, pericardial effusion, and skin edema.

Smooth philtrum
Flat skin surface, with no ridge formation in the central region of the upper lip between the nasal base and upper vermilion border.

Stroke
Sudden impairment of blood flow to a part of the brain due to occlusion or rupture of an artery to the brain.

Optic atrophy
Atrophy of the optic nerve. Optic atrophy results from the death of the retinal ganglion cell axons that comprise the optic nerve and manifesting as a pale optic nerve on fundoscopy.

Proteinuria
Increased levels of protein in the urine.

Decreased adenosylcobalamin
Decreased concentration of adenosylcobalamin. Adenosylcobalamin is one of the active forms of vitamin B12.

Visual impairment
Visual impairment (or vision impairment) is vision loss (of a person) to such a degree as to qualify as an additional support need through a significant limitation of visual capability resulting from either disease, trauma, or congenital or degenerative conditions that cannot be corrected by conventional means, such as refractive correction, medication, or surgery.

Abnormal facial shape
An abnormal morphology (form) of the face or its components.

Pulmonary embolism
An embolus (that is, an abnormal particle circulating in the blood) located in the pulmonary artery and thereby blocking blood circulation to the lung. Usually the embolus is a blood clot that has developed in an extremity (for instance, a deep venous thrombosis), detached, and traveled through the circulation before becoming trapped in the pulmonary artery.

Encephalopathy
Encephalopathy is a term that means brain disease, damage, or malfunction. In general, encephalopathy is

manifested by an altered mental state.

Megaloblastic anemia
Anemia characterized by the presence of erythroblasts that are larger than normal (megaloblasts).

Decreased methylcobalamin
Decreased concentration of methylcobalamin. Methylcobalamin is a form of vitamin B12.

Nephropathy
A nonspecific term referring to disease or damage of the kidneys.

Behavioral abnormality
An abnormality of mental functioning including various affective, behavioural, cognitive and perceptual abnormalities.

Periventricular white matter hyperintensities
Areas of brighter than expected signal on magnetic resonance imaging emanating from the cerebral white matter that surrounds the cerebral ventricles.

Mental deterioration
Loss of previously present mental abilities, generally in adults.

Developmental regression
Loss of developmental skills, as manifested by loss of developmental milestones.

Decreased methylmalonyl-CoA mutase activity
An abnormality of Krebs cycle metabolism that is characterized by a decreased rate of methylmalonyl-CoA mutase activity.

Thromboembolism
The formation of a blood clot inside a blood vessel that subsequently travels through the blood stream from the site where it formed to another location in the body, generally leading to vascular occlusion at the distant site.

Peripheral demyelination
A loss of myelin from the internode regions along myelinated nerve fibers of the peripheral nervous system.

Auditory hallucinations
The false perception of sound.

Cystathioninuria
An elevated urinary concentration of cystathionine.

Macrotia
Median longitudinal ear length greater than two standard deviations above the mean and median ear width greater than two standard deviations above the mean (objective); or, apparent increase in length and width of the pinna (subjective).

Retinal degeneration

A nonspecific term denoting degeneration of the retinal pigment epithelium and/or retinal photoreceptor cells.

Abnormal heart morphology
Any structural anomaly of the heart.

Hyperhomocystinemia
An increased concentration of homocystine in the blood.

Hypothermia
Reduced body temperature due to failed thermoregulation.

Atrophy of the spinal cord

Methylmalonic aciduria
Increased concentration of methylmalonic acid in the urine.

Dehydration

Hemolytic-uremic syndrome
A thrombotic microangiopathy with presence of non-immune, intravascular hemolytic anemia, thrombocytopenia and acute kidney injury. A vicious cycle of complement activation, endothelial cell damage, platelet activation, and thrombosis is the hallmark of the disease.

Intellectual disability
Subnormal intellectual functioning which originates during the developmental period. Intellectual disability, previously referred to as mental retardation, has been defined as an IQ score below 70.