Geneticheck - Genetic Report

Gene

RAF1

Associated Diseases

Noonan Syndrome 5
Noonan Syndrome With Multiple Lentigines
Cardiomyopathy, Dilated, 1nn
Noonan Syndrome
Familial Isolated Dilated Cardiomyopathy
Leopard Syndrome 2

Phenotype

Dolichocephaly
An abnormality of skull shape characterized by a increased anterior-posterior diameter, i.e., an increased antero-posterior dimension of the skull. Cephalic index less than 76%. Alternatively, an apparently increased antero-posterior length of the head compared to width. Often due to premature closure of the sagittal suture.

Abnormality of the spleen
An abnormality of the spleen.

Subcutaneous nodule
Slightly elevated lesions on or in the skin with a diameter of over 5 mm.

Webbed neck
Pterygium colli is a congenital skin fold that runs along the sides of the neck down to the shoulders. It involves an ectopic fibrotic facial band superficial to the trapezius muscle. Excess hair-bearing skin is also present and extends down the cervical region well beyond the normal hairline.

Low-set, posteriorly rotated ears
Ears that are low-set (HP:0000369) and posteriorly rotated (HP:0000358).

Cryptorchidism
Testis in inguinal canal. That is, absence of one or both testes from the scrotum owing to failure of the testis or testes to descend through the inguinal canal to the scrotum.

Sprengel anomaly
A congenital skeletal deformity characterized by the elevation of one scapula (thus, one scapula is located superior to the other).

Severe sensorineural hearing impairment
A severe form of sensorineural hearing impairment.

Midface retrusion
Posterior positions and/or vertical shortening of the infraorbital and perialar regions, or increased concavity of the face and/or reduced nasolabial angle.

Abnormality of the genital system
An abnormality of the genital system.

Macrocephaly
Occipitofrontal (head) circumference greater than 97th centile compared to appropriate, age matched, sex-matched normal standards. Alternatively, a apparently increased size of the cranium.

Atrioventricular canal defect
A defect of the atrioventricular septum of the heart.

Bundle branch block
Block of conduction of electrical impulses along the Bundle of His or along one of its bundle branches.

Ptosis
The upper eyelid margin is positioned 3 mm or more lower than usual and covers the superior portion of the iris (objective); or, the upper lid margin obscures at least part of the pupil (subjective).

Prominent forehead
Forward prominence of the entire forehead, due to protrusion of the frontal bone.

Neurological speech impairment

Cystic hygroma
A cystic lymphatic lesion of the neck.

Epicanthus
A fold of skin starting above the medial aspect of the upper eyelid and arching downward to cover, pass in front of and lateral to the medial canthus.

Mitral valve prolapse
One or both of the leaflets (cusps) of the mitral valve bulges back into the left atrium upon contraction of the left ventricle.

High palate
Height of the palate more than 2 SD above the mean (objective) or palatal height at the level of the first permanent molar more than twice the height of the teeth (subjective).

Abnormal hair quantity
An abnormal amount of hair.

Downslanted palpebral fissures
The palpebral fissure inclination is more than two standard deviations below the mean.

Melanoma
The presence of a melanoma, a malignant cancer originating from pigment producing melanocytes. Melanoma can originate from the skin or the pigmented layers of the eye (the uvea).

Cubitus valgus

Abnormal positioning in which the elbows are turned out.

Autosomal dominant 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 heterozygotes. In the context of medical genetics, an autosomal dominant disorder is caused when a single copy of the mutant allele is present. Males and females are affected equally, and can both transmit the disorder with a risk of 50% for each child of inheriting the mutant allele.

Abnormal mitral valve morphology
Any structural anomaly of the mitral valve.

Abnormality of cardiovascular system morphology
Any structural anomaly of the heart and great vessels.

Thick vermilion border
Increased width of the skin of vermilion border region of upper lip.

Abnormality of the lymphatic system
An anomaly of the lymphatic system, a network of lymphatic vessels that carry a clear fluid called lymph unidirectionally towards either the right lymphatic duct or the thoracic duct, which in turn drain into the right and left subclavian veins respectively.

Hypogonadotropic hypogonadism
Hypogonadotropic hypogonadism is characterized by reduced function of the gonads (testes in males or ovaries in females) and results from the absence of the gonadal stimulating pituitary hormones: follicle stimulating hormone (FSH) and luteinizing hormone (LH).

Freckling
The presence of an increased number of freckles, small circular spots on the skin that are darker than the surrounding skin because of deposits of melanin.

Sensorineural hearing impairment
A type of hearing impairment in one or both ears related to an abnormal functionality of the cochlear nerve.

Curly hair

Spina bifida occulta
The closed form of spina bifida with incomplete closure of a vertebral body with intact overlying skin.

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.

Thickened nuchal skin fold
A thickening of the skin thickness in the posterior aspect of the fetal neck. A nuchal fold measurement is obtained in a transverse section of the fetal head at the level of the cavum septum pellucidum and thalami, angled posteriorly to include the cerebellum. The measurement is taken from the outer edge of the occiput

bone to the outer skin limit directly in the midline. A measurement 6 mm or more is considered significant between 18 and 24 weeks and a measurement of 5 mm or more is considered significant at 16 to 18 weeks (PMID:16100637).

Abnormality of the voice

Clinodactyly of the 5th finger
Clinodactyly refers to a bending or curvature of the fifth finger in the radial direction (i.e., towards the 4th finger).

Dysarthria
Dysarthric speech is a general description referring to a neurological speech disorder characterized by poor articulation. Depending on the involved neurological structures, dysarthria may be further classified as spastic, flaccid, ataxic, hyperkinetic and hypokinetic, or mixed.

Delayed skeletal maturation
A decreased rate of skeletal maturation. Delayed skeletal maturation can be diagnosed on the basis of an estimation of the bone age from radiographs of specific bones in the human body.

EMG abnormality
Abnormal results of investigations using electromyography (EMG).

Mandibular prognathia
Abnormal prominence of the chin related to increased length of the mandible.

Atrial septal defect
Atrial septal defect (ASD) is a congenital abnormality of the interatrial septum that enables blood flow between the left and right atria via the interatrial septum.

Thickened helices
Increased thickness of the helix of the ear.

Laryngomalacia
Laryngomalacia is a congenital abnormality of the laryngeal cartilage in which the cartilage is floppy and prolapses over the larynx during inspiration.

Mitral regurgitation
An abnormality of the mitral valve characterized by insufficiency or incompetence of the mitral valve resulting in retrograde leaking of blood through the mitral valve upon ventricular contraction.

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

Excessive wrinkled skin

Enlarged thorax

Depressed nasal bridge
Posterior positioning of the nasal root in relation to the overall facial profile for age.

Hepatomegaly
Abnormally increased size of the liver.

Melanocytic nevus
A oval and round, colored (usually medium-to dark brown, reddish brown, or flesh colored) lesion. Typically, a melanocytic nevus is less than 6 mm in diameter, but may be much smaller or larger.

Keratosis pilaris
An anomaly of the hair follicles of the skin that typically presents as small, rough, brown folliculocentric papules distributed over characteristic areas of the skin, particularly the outer-upper arms and thighs.

Abnormal sternum morphology
An anomaly of the sternum, also known as the breastbone.

Abnormality of the pulmonary artery
An abnormality of the pulmonary artery.

Muscle weakness
Reduced strength of muscles.

Joint hyperflexibility
Increased mobility and flexibility in the joint due to the tension in tissues such as ligaments and muscles.

Palmoplantar keratoderma
Abnormal thickening of the skin of the palms of the hands and the soles of the feet.

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

Neuroblastoma
Neuroblastoma is a solid tumor that originate in neural crest cells of the sympathetic nervous system. Most neuroblastomas originate in the abdomen, and most abdominal neuroblastomas originate in the adrenal gland. Neuroblastomas can also originate in the thorax, usually in the posterior mediastinum.

Abnormal dermatoglyphics
An abnormality of dermatoglyphs (fingerprints), which are present on fingers, palms, toes, and soles.

Proptosis
An eye that is protruding anterior to the plane of the face to a greater extent than is typical.

Abnormal bleeding
An abnormal susceptibility to bleeding, often referred to as a bleeding diathesis. A bleeding diathesis may be related to vascular, platelet and coagulation defects.

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.

Multiple lentigines
Presence of an unusually high number of lentigines (singular: lentigo), which are flat, tan to brown oval spots.

Pulmonary artery stenosis
An abnormal narrowing or constriction of the pulmonary artery, in the main pulmonary artery and/or in the left or right pulmonary artery branches.

Small nail
A nail that is diminished in length and width, i.e., underdeveloped nail.

Radioulnar synostosis
An abnormal osseous union (fusion) between the radius and the ulna.

Myopathy
A disorder of muscle unrelated to impairment of innervation or neuromuscular junction.

Micrognathia
Developmental hypoplasia of the mandible.

Ventricular arrhythmia

High forehead
An abnormally increased height of the forehead.

Brachydactyly
Digits that appear disproportionately short compared to the hand/foot. The word brachydactyly is used here to describe a series distinct patterns of shortened digits (brachydactyly types A-E). This is the sense used here.

Wide intermamillary distance
A larger than usual distance between the left and right nipple.

Myelodysplasia
Clonal hematopoietic stem cell disorders characterized by dysplasia (ineffective production) in one or more hematopoietic cell lineages, leading to anemia and cytopenia.

Polyhydramnios
The presence of excess amniotic fluid in the uterus during pregnancy.

Wide mouth
Distance between the oral commissures more than 2 SD above the mean. Alternatively, an apparently increased width of the oral aperture (subjective).

Triangular face
Facial contour, as viewed from the front, triangular in shape, with breadth at the temples and tapering to a narrow chin.

Short stature
A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).

Nevus
A nevus is a type of hamartoma that is a circumscribed stable malformation of the skin.

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

Pulmonic stenosis
A narrowing of the right ventricular outflow tract that can occur at the pulmonary valve (valvular stenosis) or just below the pulmonary valve (infundibular stenosis).

Scoliosis
The presence of an abnormal lateral curvature of the spine.

Coarse hair
Hair shafts are rough in texture.

Vascular dilatation
Abnormal outpouching or sac-like dilatation in the wall of an atery, vein or the heart.

Dry skin
Skin characterized by the lack of natural or normal moisture.

Abnormal platelet function
Any anomaly in the function of thrombocytes.

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.

Brachycephaly
An abnormality of skull shape characterized by a decreased anterior-posterior diameter. That is, a cephalic index greater than 81%. Alternatively, an apparently shortened anteroposterior dimension (length) of the head compared to width.

Hyperextensible skin
A condition in which the skin can be stretched beyond normal, and then returns to its initial position.

Hypertrophic cardiomyopathy
Hypertrophic cardiomyopathy (HCM) is defined by the presence of increased ventricular wall thickness or mass in the absence of loading conditions (hypertension, valve disease) sufficient to cause the observed abnormality.

Abnormality of neutrophils
A neutrophil abnormality.

Large for gestational age
The term large for gestational age applies to babies whose birth weight lies above the 90th percentile for that gestational age.

Lipoatrophy
Localized loss of fat tissue.

Aplasia/Hypoplasia of the abdominal wall musculature
Absence or underdevelopment of the abdominal musculature.

Thick lower lip vermilion
Increased thickness of the lower lip, leading to a prominent appearance of the lower lip. The height of the vermilion of the lower lip in the midline is more than 2 SD above the mean. Alternatively, an apparently increased height of the vermilion of the lower lip in the frontal view (subjective).

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.

Low posterior hairline
Hair on the neck extends more inferiorly than usual.

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.

Arrhythmia
Any cardiac rhythm other than the normal sinus rhythm. Such a rhythm may be either of sinus or ectopic origin and either regular or irregular. An arrhythmia may be due to a disturbance in impulse formation or conduction or both.

Abnormal pulmonary valve morphology
Any structural abnormality of the pulmonary valve.

Abnormality of the face
An abnormality of the face.

Lymphedema
Localized fluid retention and tissue swelling caused by a compromised lymphatic system.

Myocardial infarction
Necrosis of the myocardium caused by an obstruction of the blood supply to the heart and often associated with chest pain, shortness of breath, palpitations, and anxiety as well as characteristic EKG findings and

elevation of serum markers including creatine kinase-MB fraction and troponin.

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.

Fine hair
Hair that is fine or thin to the touch.

Wide nasal bridge
Increased breadth of the nasal bridge (and with it, the nasal root).

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

Sparse eyebrow
Decreased density/number of eyebrow hairs.

Short neck
Diminished length of the neck.

Hypospadias
Abnormal position of urethral meatus on the ventral penile shaft (underside) characterized by displacement of the urethral meatus from the tip of the glans penis to the ventral surface of the penis, scrotum, or perineum.

Decreased fertility

Hypertelorism
Interpupillary distance more than 2 SD above the mean (alternatively, the appearance of an increased interpupillary distance or widely spaced eyes).

Strabismus
A misalignment of the eyes so that the visual axes deviate from bifoveal fixation. The classification of strabismus may be based on a number of features including the relative position of the eyes, whether the deviation is latent or manifest, intermittent or constant, concomitant or otherwise and according to the age of onset and the relevance of any associated refractive error.

Abnormal endocardium morphology
An abnormality of the endocardium.

Scapular winging
Abnormal protrusion of the scapula away from the surface of the back.

Elevated circulating creatine kinase concentration
An elevation of the level of the enzyme creatine kinase (also known as creatine phosphokinase, CPK; EC 2.7.3.2) in the blood. CPK levels can be elevated in a number of clinical disorders such as myocardial infarction, rhabdomyolysis, and muscular dystrophy.

Cafe-au-lait spot
Cafe-au-lait spots are hyperpigmented lesions that can vary in color from light brown to dark brown with smooth borders and having a size of 1.5 cm or more in adults and 0.5 cm or more in children.

Aplasia of the semicircular canal
Absence of the semicircular canal.

Abnormality of coagulation
An abnormality of the process of blood coagulation. That is, altered ability or inability of the blood to clot.

Pectus carinatum
A deformity of the chest caused by overgrowth of the ribs and characterized by protrusion of the sternum.

Intellectual disability, mild
Mild intellectual disability is defined as an intelligence quotient (IQ) in the range of 50-69.

Pectus excavatum
A defect of the chest wall characterized by a depression of the sternum, giving the chest ("pectus") a caved-in ("excavatum") appearance.

Abnormal localization of kidney
An abnormal site of the kidney.