Supplementary Table 6: List of putative RNA-binding proteins in the human genome that are implicated in disease.

Entry	Involvement in disease
P48740	3MC syndrome 1 (3MC1) [MIM:257920]: A disorder characterized by facial dysmorphism that includes hypertelorism, blepharophimosis, blepharoptosis and highly arched eyebrows, cleft lip and/or palate, craniosynostosis, learning disability and genital, limb and vesicorenal anomalies. The term 3MC syndrome includes Carnevale, Mingarelli, Malpuech, and Michels syndromes. {ECO:0000269|PubMed:21258343}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q13233	46,XY sex reversal 6 (SRXY6) [MIM:613762]: A disorder of sex development. Affected individuals have a 46,XY karyotype but present as phenotypically normal females. {ECO:0000269|PubMed:21129722}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y463	Abdominal obesity-metabolic syndrome 3 (AOMS3) [MIM:615812]: A form of abdominal obesity-metabolic syndrome, a disorder characterized by abdominal obesity, high triglycerides, low levels of high density lipoprotein cholesterol, high blood pressure, and elevated fasting glucose levels. AOMS3 is characterized by early-onset coronary artery disease, central obesity, hypertension, and diabetes. {ECO:0000269|PubMed:24827035}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P35858	Acid-labile subunit deficiency (ACLSD) [MIM:615961]: A disorder characterized by severely reduced serum IGF-I and IGFBP-3 concentrations and mild growth retardation. Pubertal delay in boys and insulin insensitivity are common findings. {ECO:0000269|PubMed:14762184, ECO:0000269|PubMed:16507628, ECO:0000269|PubMed:17726072, ECO:0000269|PubMed:18303074, ECO:0000269|PubMed:19129715, ECO:0000269|PubMed:20389102, ECO:0000269|PubMed:21396577}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q15427	Acrofacial dysostosis 1, Nager type (AFD1) [MIM:154400]: A form of acrofacial dysostosis, a group of disorders which are characterized by malformation of the craniofacial skeleton and the limbs. The major facial features of AFD1 include downslanted palpebral fissures, midface retrusion, and micrognathia, the latter of which often requires the placement of a tracheostomy in early childhood. Limb defects typically involve the anterior (radial) elements of the upper limbs and manifest as small or absent thumbs, triphalangeal thumbs, radial hyoplasia or aplasia, and radioulnar synostosis. Phocomelia of the upper limbs and, occasionally, lower-limb defects have also been reported. {ECO:0000269|PubMed:22541558}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P01871	Agammaglobulinemia 1, autosomal recessive (AGM1) [MIM:601495]: A primary immunodeficiency characterized by profoundly low or absent serum antibodies and low or absent circulating B cells due to an early block of B-cell development. Affected individuals develop severe infections in the first years of life. {ECO:0000269|PubMed:8890099}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P15814	Agammaglobulinemia 2, autosomal recessive (AGM2) [MIM:613500]: A primary immunodeficiency characterized by profoundly low or absent serum antibodies and low or absent circulating B cells due to an early block of B-cell development. Affected individuals develop severe infections in the first years of life. {ECO:0000269|PubMed:9419212}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q5TBB1	Aicardi-Goutieres syndrome 2 (AGS2) [MIM:610181]: A form of Aicardi-Goutieres syndrome, a genetically heterogeneous disease characterized by cerebral atrophy, leukoencephalopathy, intracranial calcifications, chronic cerebrospinal fluid (CSF) lymphocytosis, increased CSF alpha-interferon, and negative serologic investigations for common prenatal infection. Clinical features as thrombocytopenia, hepatosplenomegaly and elevated hepatic transaminases along with intermittent fever may erroneously suggest an infective process. Severe neurological dysfunctions manifest in infancy as progressive microcephaly, spasticity, dystonic posturing and profound psychomotor retardation. Death often occurs in early childhood. {ECO:0000269|PubMed:16845400, ECO:0000269|PubMed:17846997, ECO:0000269|PubMed:20131292}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8TDP1	Aicardi-Goutieres syndrome 3 (AGS3) [MIM:610329]: A form of Aicardi-Goutieres syndrome, a genetically heterogeneous disease characterized by cerebral atrophy, leukoencephalopathy, intracranial calcifications, chronic cerebrospinal fluid (CSF) lymphocytosis, increased CSF alpha-interferon, and negative serologic investigations for common prenatal infection. Clinical features as thrombocytopenia, hepatosplenomegaly and elevated hepatic transaminases along with intermittent fever may erroneously

	suggest an infective process. Severe neurological dysfunctions manifest in infancy as progressive microcephaly, spasticity, dystonic posturing and profound psychomotor retardation. Death often occurs in early childhood. {ECO:0000269|PubMed:16845400, ECO:0000269|PubMed:17846997, ECO:0000269|PubMed:20131292}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O75792	Aicardi-Goutieres syndrome 4 (AGS4) [MIM:610333]: A form of Aicardi-Goutieres syndrome, a genetically heterogeneous disease characterized by cerebral atrophy, leukoencephalopathy, intracranial calcifications, chronic cerebrospinal fluid (CSF) lymphocytosis, increased CSF alpha-interferon, and negative serologic investigations for common prenatal infection. Clinical features as thrombocytopenia, hepatosplenomegaly and elevated hepatic transaminases along with intermittent fever may erroneously suggest an infective process. Severe neurological dysfunctions manifest in infancy as progressive microcephaly, spasticity, dystonic posturing and profound psychomotor retardation. Death often occurs in early childhood. {ECO:0000269|PubMed:16845400, ECO:0000269|PubMed:17846997, ECO:0000269|PubMed:20131292}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q04721	Alagille syndrome 2 (ALGS2) [MIM:610205]: A form of Alagille syndrome, an autosomal dominant multisystem disorder. It is clinically defined by hepatic bile duct paucity and cholestasis in association with cardiac, skeletal, and ophthalmologic manifestations. There are characteristic facial features and less frequent clinical involvement of the renal and vascular systems. {ECO:0000269|PubMed:16773578}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Hajdu-Cheney syndrome (HJCYS) [MIM:102500]: A rare skeletal disorder characterized by the association of facial anomalies, acro-osteolysis, general osteoporosis, insufficient ossification of the skull, and periodontal disease (premature loss of permanent teeth). Other features include cleft palate, congenital heart defects, polycystic kidneys, orthopedic problems and anomalies of the genitalia, intestines and eyes. {ECO:0000269|PubMed:21378985, ECO:0000269|PubMed:21378989}. Note=The disease is caused by mutations affecting the gene represented in this entry. NOTCH2 mutations associated with Hajdu-Cheney syndrome cluster to the last coding exon of the gene. This suggests that the mutant mRNA products may escape nonsense-mediated decay and the resulting truncated NOTCH2 proteins act in a gain-of-function manner.
Q4G0J3	Alazami syndrome (ALAZS) [MIM:615071]: A syndromic form of primordial dwarfism, a condition characterized by severe growth restriction that has its onset in utero, and results in short stature and undersize. ALAZS patients manifest severe intellectual disability and distinct facial features including malar hypoplasia, deep-set eyes, broad nose, short philtrum, and macrostomia. Some patients have non-specific and inconsistent skeletal findings, for example, scoliosis and mild epiphyseal changes in the proximal phalanges, but no frank dysplasia. {ECO:0000269|PubMed:21937992, ECO:0000269|PubMed:22865833}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NW13	Alopecia, neurologic defects, and endocrinopathy syndrome (ANES) [MIM:612079]: Affected individuals have hair loss of variable severity, ranging from complete alopecia to near-normal scalp hair with absence of body hair. All have moderate to severe mental retardation, progressive motor deterioration and central hypogonadotropic hypogonadism with delayed or absent puberty and central adrenal insufficiency. Additional features included short stature, microcephaly, gynecomastia, pigmentary anomalies, hypodontia, kyphoscoliosis, ulnar deviation of the hands, and loss of subcutaneous fat. {ECO:0000269|PubMed:18439547}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y5K2	Amelogenesis imperfecta, hypomaturation type, 2A1 (AI2A1) [MIM:204700]: A defect of enamel formation. The disorder involves both primary and secondary dentitions. The teeth have a shiny agar jelly appearance and the enamel is softer than normal. Brown pigment is present in middle layers of enamel. {ECO:0000269|PubMed:15235027}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q3MJ13	Amelogenesis imperfecta, hypomaturation type, 2A3 (AI2A3) [MIM:613211]: A defect of enamel formation. The disorder involves both primary and secondary dentitions. The teeth have a shiny agar jelly appearance and the enamel is softer than normal. Brown pigment is present in middle layers of enamel. {ECO:0000269|PubMed:19853237}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P61626	Amyloidosis 8 (AMYL8) [MIM:105200]: A hereditary generalized amyloidosis due to deposition of apolipoprotein A1, fibrinogen and lysozyme amyloids. Viscera are particularly affected. There is no involvement of the nervous system. Clinical features include renal amyloidosis resulting in nephrotic syndrome, arterial hypertension, hepatosplenomegaly, cholestasis, petechial skin rash. {ECO:0000269|PubMed:8464497}. Note=The disease is caused by mutations affecting the gene

	represented in this entry.
Q13148	Amyotrophic lateral sclerosis 10 (ALS10) [MIM:612069]: A neurodegenerative disorder affecting upper motor neurons in the brain and lower motor neurons in the brain stem and spinal cord, resulting in fatal paralysis. Sensory abnormalities are absent. The pathologic hallmarks of the disease include pallor of the corticospinal tract due to loss of motor neurons, presence of ubiquitin-positive inclusions within surviving motor neurons, and deposition of pathologic aggregates. The etiology of amyotrophic lateral sclerosis is likely to be multifactorial, involving both genetic and environmental factors. The disease is inherited in 5-10% of the cases. {ECO:0000269|PubMed:18288693, ECO:0000269|PubMed:18309045, ECO:0000269|PubMed:18372902, ECO:0000269|PubMed:18396105, ECO:0000269|PubMed:18438952, ECO:0000269|PubMed:19224587, ECO:0000269|PubMed:19695877, ECO:0000269|PubMed:21220647, ECO:0000269|PubMed:21418058, ECO:0000269|PubMed:22456481}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P43243	Amyotrophic lateral sclerosis 21 (ALS21) [MIM:606070]: A neurodegenerative disorder affecting upper and lower motor neurons, resulting in muscle weakness and respiratory failure. Some patients may develop myopathic features or dementia. {ECO:0000269|PubMed:19344878, ECO:0000269|PubMed:24686783}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P00738	Anhaptoglobinemia (AHP) [MIM:614081]: A condition characterized by the absence of the serum glycoprotein haptoglobin. Serum levels of haptoglobin vary among normal persons: levels are low in the neonatal period and in the elderly, differ by population, and can be influenced by environmental factors, such as infection. Secondary hypohaptoglobinemia can occur as a consequence of hemolysis, during which haptoglobin binds to free hemoglobin. Congenital haptoglobin deficiency is a risk factor for anaphylactic non-hemolytic transfusion reactions. {ECO:0000269|PubMed:14999562}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q15746	Aortic aneurysm, familial thoracic 7 (AAT7) [MIM:613780]: A disease characterized by permanent dilation of the thoracic aorta usually due to degenerative changes in the aortic wall. It is primarily associated with a characteristic histologic appearance known as 'medial necrosis' or 'Erdheim cystic medial necrosis' in which there is degeneration and fragmentation of elastic fibers, loss of smooth muscle cells, and an accumulation of basophilic ground substance. {ECO:0000269|PubMed:21055718}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q13976	Aortic aneurysm, familial thoracic 8 (AAT8) [MIM:615436]: A disease characterized by permanent dilation of the thoracic aorta usually due to degenerative changes in the aortic wall. It is primarily associated with a characteristic histologic appearance known as 'medial necrosis' or 'Erdheim cystic medial necrosis' in which there is degeneration and fragmentation of elastic fibers, loss of smooth muscle cells, and an accumulation of basophilic ground substance. {ECO:0000269|PubMed:23910461}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P46531	Aortic valve disease 1 (AOVD1) [MIM:109730]: A common defect in the aortic valve in which two rather than three leaflets are present. It is often associated with aortic valve calcification, stenosis and insufficiency. In extreme cases, the blood flow may be so restricted that the left ventricle fails to grow, resulting in hypoplastic left heart syndrome. {ECO:0000269|PubMed:16025100}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Adams-Oliver syndrome 5 (AOS5) [MIM:616028]: A form of Adams-Oliver syndrome, a disorder characterized by the congenital absence of skin (aplasia cutis congenita) in combination with transverse limb defects. Aplasia cutis congenita can be located anywhere on the body, but in the vast majority of the cases, it is present on the posterior parietal region where it is often associated with an underlying defect of the parietal bones. Limb abnormalities are typically limb truncation defects affecting the distal phalanges or entire digits (true ectrodactyly). Only rarely, metatarsals/metacarpals or more proximal limb structures are also affected. Apart from transverse limb defects, syndactyly, most commonly of second and third toes, can also be observed. The clinical features are highly variable and can also include cardiovascular malformations, brain abnormalities and vascular defects such as cutis marmorata and dilated scalp veins. {ECO:0000269|PubMed:25132448}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q7Z2E3	Ataxia-oculomotor apraxia syndrome (AOA) [MIM:208920]: An autosomal recessive syndrome characterized by early-onset cerebellar ataxia, oculomotor apraxia, early areflexia and late peripheral neuropathy. {ECO:0000269|PubMed:11586299, ECO:0000269|PubMed:11586300, ECO:0000269|PubMed:12196655, ECO:0000269|PubMed:12629250, ECO:0000269|PubMed:14506070, ECO:0000269|PubMed:15699391, ECO:0000269|PubMed:15852392}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O75694	Atrial fibrillation, familial, 15 (ATFB15) [MIM:615770]: A familial form of atrial fibrillation, a common sustained cardiac rhythm disturbance. Atrial fibrillation is characterized by disorganized atrial electrical

	activity and ineffective atrial contraction promoting blood stasis in the atria and reduces ventricular filling. It can result in palpitations, syncope, thromboembolic stroke, and congestive heart failure. {ECO:0000269|PubMed:19070573}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P06730	Autism 19 (AUTS19) [MIM:615091]: A complex multifactorial, pervasive developmental disorder characterized by impairments in reciprocal social interaction and communication, restricted and stereotyped patterns of interests and activities, and the presence of developmental abnormalities by 3 years of age. Most individuals with autism also manifest moderate mental retardation. {ECO:0000269|PubMed:19556253}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry. A heterozygous single-nucleotide insertion has been found in families affected by autism. The variant results in increased promoter activity and is involved in disease pathogenesis through EIF4E deregulation (PubMed:19556253). {ECO:0000269|PubMed:19556253}.; Note=A chromosomal aberration involving EIF4E has been found in a patient with classic autism. Translocation t(45)(q23q31.3). The breakpoint on chromosome 4 is located 56 kb downstream of EIF4E (PubMed:19556253). {ECO:0000269|PubMed:19556253}.
P27635	Autism, X-linked 5 (AUTSX5) [MIM:300847]: A complex multifactorial, pervasive developmental disorder characterized by impairments in reciprocal social interaction and communication, restricted and stereotyped patterns of interests and activities, and the presence of developmental abnormalities by 3 years of age. Most individuals with autism also manifest moderate mental retardation. {ECO:0000269|PubMed:16940977, ECO:0000269|PubMed:21567917}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry. RPL10 is involved in autism only in rare cases. Two hypomorphic variants affecting the translation process have been found in families with autism spectrum disorders, suggesting that aberrant translation may play a role in disease mechanisms.
P53621	Autoimmune interstitial lung, joint, and kidney disease (AILJK) [MIM:616414]: An autoimmune disease characterized by inflammatory arthritis, interstitial lung disease, and immune complex-mediated renal disease. {ECO:0000269|PubMed:25894502}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q05655	Autoimmune lymphoproliferative syndrome 3 (ALPS3) [MIM:615559]: A primary immunodeficiency characterized by antibody deficiency, hypogammaglobulinemia, recurrent bacterial infections and an inability to mount an antibody response to antigen. The defect results from a failure of B-cell differentiation and impaired secretion of immunoglobulins; the numbers of circulating B-cells is usually in the normal range, but can be low. CVID9 patients have B-cell deficiency and severe autoimmunity. {ECO:0000269|PubMed:23319571}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q16625	Band-like calcification with simplified gyration and polymicrogyria (BLCPMG) [MIM:251290]: A neurologic disorder with characteristic clinical and neuroradiologic features that mimic intrauterine TORCH infection in the absence of evidence of infection. Affected individuals have congenital microcephaly, intracranial calcifications, and severe developmental delay. {ECO:0000269|PubMed:20727516}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q03518	Bare lymphocyte syndrome 1 (BLS1) [MIM:604571]: A HLA class I deficiency. Contrary to bare lymphocyte syndromes type 2 and type 3, which are characterized by early-onset severe combined immunodeficiency, class I antigen deficiencies are not accompanied by particular pathologic manifestations during the first years of life. Systemic infections have not been described. Chronic bacterial infections, often beginning in the first decade of life, are restricted to the respiratory tract. {ECO:0000269|PubMed:10074494}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8N9N2	Barrett esophagus (BE) [MIM:614266]: A condition characterized by a metaplastic change in which normal esophageal squamous epithelium is replaced by a columnar and intestinal-type epithelium. Patients with Barrett esophagus have an increased risk of esophageal adenocarcinoma. The main cause of Barrett esophagus is gastroesophageal reflux. The retrograde movement of acid and bile salts from the stomach into the esophagus causes prolonged injury to the esophageal epithelium and induces chronic esophagitis, which in turn is believed to trigger the pathologic changes. {ECO:0000269|PubMed:21791690}. Note=The gene represented in this entry may be involved in disease pathogenesis.
Q5VTD9	Bleeding disorder, platelet-type 17 (BDPLT17) [MIM:187900]: An autosomal dominant disorder characterized by increased bleeding tendency due to platelet dysfunction, and associated with macrothrombocytopenia and red cell anisopoikilocytosis. Platelets appear abnormal on light microscopy, while electron microscopy shows a heterogeneous decrease of alpha granules within platelets. Bone

	marrow biopsy shows increased numbers of abnormal megakaryocytes, suggesting a defect in megakaryopoiesis and platelet production. The severity of bleeding is variable with some affected individuals experiencing spontaneous bleeding while other exhibit only abnormal bleeding with surgery. {ECO:0000269|PubMed:23927492, ECO:0000269|PubMed:24325358}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P22612	Bleeding disorder, platelet-type 19 (BDPLT19) [MIM:616176]: A disorder characterized by increased bleeding tendency due to platelet dysfunction. Clinical features include epistaxis, hematomas, bleeding after tooth extraction, and menorrhagia. {ECO:0000269|PubMed:25061177}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P54132	Bloom syndrome (BLM) [MIM:210900]: An autosomal recessive disorder. It is characterized by proportionate pre- and postnatal growth deficiency, sun-sensitive telangiectatic hypo- and hyperpigmented skin, predisposition to malignancy, and chromosomal instability. {ECO:0000269|PubMed:10862105, ECO:0000269|PubMed:7585968, ECO:0000269|PubMed:9285778}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O76094	Bone marrow failure syndrome 1 (BMFS1) [MIM:614675]: An autosomal dominant disease characterized by aplastic anemia and myelodysplasia resulting from bone marrow failure. Aplastic anemia is a form of anemia in which the bone marrow fails to produce adequate numbers of peripheral blood elements. Myelodysplasia is a clonal hematopoietic stem cell disorder in which immature cells in the bone marrow become malformed and dysfunctional. {ECO:0000269|PubMed:22541560}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q92979	Bowen-Conradi syndrome (BWCNS) [MIM:211180]: A combination of malformations characterized in newborns by low birth weight, microcephaly, mild joint restriction, a prominent nose, micrognathia, fifth finger clinodactyly, and 'rocker-bottom' feet. The syndrome is transmitted as an autosomal recessive trait. The prognosis is poor, with all infants dying within the first few months of life. {ECO:0000269|PubMed:19463982}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P31749	Breast cancer (BC) [MIM:114480]: A common malignancy originating from breast epithelial tissue. Breast neoplasms can be distinguished by their histologic pattern. Invasive ductal carcinoma is by far the most common type. Breast cancer is etiologically and genetically heterogeneous. Important genetic factors have been indicated by familial occurrence and bilateral involvement. Mutations at more than one locus can be involved in different families or even in the same case. {ECO:0000269|PubMed:17611497}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.; Colorectal cancer (CRC) [MIM:114500]: A complex disease characterized by malignant lesions arising from the inner wall of the large intestine (the colon) and the rectum. Genetic alterations are often associated with progression from premalignant lesion (adenoma) to invasive adenocarcinoma. Risk factors for cancer of the colon and rectum include colon polyps, long-standing ulcerative colitis, and genetic family history. Note=The gene represented in this entry may be involved in disease pathogenesis.; Note=Genetic variations in AKT1 may play a role in susceptibility to ovarian cancer.; Proteus syndrome (PROTEUSS) [MIM:176920]: A highly variable, severe disorder of asymmetric and disproportionate overgrowth of body parts, connective tissue nevi, epidermal nevi, dysregulated adipose tissue, and vascular malformations. Many features of Proteus syndrome overlap with other overgrowth syndromes. {ECO:0000269|PubMed:21793738}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Cowden syndrome 6 (CWS6) [MIM:615109]: A form of Cowden syndrome, a hamartomatous polyposis syndrome with age-related penetrance. Cowden syndrome is characterized by hamartomatous lesions affecting derivatives of ectodermal, mesodermal and endodermal layers, macrocephaly, facial trichilemmomas (benign tumors of the hair follicle infundibulum), acral keratoses, papillomatous papules, and elevated risk for development of several types of malignancy, particularly breast carcinoma in women and thyroid carcinoma in both men and women. Colon cancer and renal cell carcinoma have also been reported. Hamartomas can be found in virtually every organ, but most commonly in the skin, gastrointestinal tract, breast and thyroid. Note=The disease is caused by mutations affecting the gene represented in this entry.
O75417	Breast cancer (BC) [MIM:114480]: A common malignancy originating from breast epithelial tissue. Breast neoplasms can be distinguished by their histologic pattern. Invasive ductal carcinoma is by far the most common type. Breast cancer is etiologically and genetically heterogeneous. Important genetic factors have been indicated by familial occurrence and bilateral involvement. Mutations at more than one locus can be involved in different families or even in the same case. {ECO:0000269|PubMed:20624954, ECO:0000269|PubMed:20700469, ECO:0000269|PubMed:25409685}. Note=The gene represented in this entry may be involved in disease pathogenesis.
Q9NQX1	Brittle cornea syndrome 2 (BCS2) [MIM:614170]: A disorder characterized by extreme corneal thinning resulting in corneal rupture after minor trauma, blue sclerae, keratoconus or keratoglobus, hyperelasticity

	of the skin, and hypermobile joints. {ECO:0000269|PubMed:21664999}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q59H18	Cardiac conduction disease with or without dilated cardiomyopathy (CCDD) [MIM:616117]: A cardiac disorder characterized by atrial tachyarrhythmia and conduction system disease. Some patients have dilated cardiomyopathy. {ECO:0000269|PubMed:24925317}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q02750	Cardiofaciocutaneous syndrome 3 (CFC3) [MIM:615279]: A form of cardiofaciocutaneous syndrome, a multiple congenital anomaly disorder characterized by a distinctive facial appearance, heart defects and mental retardation. Heart defects include pulmonic stenosis, atrial septal defects and hypertrophic cardiomyopathy. Some affected individuals present with ectodermal abnormalities such as sparse, friable hair, hyperkeratotic skin lesions and a generalized ichthyosis-like condition. Typical facial features are similar to Noonan syndrome. They include high forehead with bitemporal constriction, hypoplastic supraorbital ridges, downslanting palpebral fissures, a depressed nasal bridge, and posteriorly angulated ears with prominent helices. Distinctive features of CFC3 include macrostomia and horizontal shape of palpebral fissures. {ECO:0000269|PubMed:16439621, ECO:0000269|PubMed:18042262}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P36507	Cardiofaciocutaneous syndrome 4 (CFC4) [MIM:615280]: A form of cardiofaciocutaneous syndrome, a multiple congenital anomaly disorder characterized by a distinctive facial appearance, heart defects and mental retardation. Heart defects include pulmonic stenosis, atrial septal defects and hypertrophic cardiomyopathy. Some affected individuals present with ectodermal abnormalities such as sparse, friable hair, hyperkeratotic skin lesions and a generalized ichthyosis-like condition. Typical facial features are similar to Noonan syndrome. They include high forehead with bitemporal constriction, hypoplastic supraorbital ridges, downslanting palpebral fissures, a depressed nasal bridge, and posteriorly angulated ears with prominent helices. {ECO:0000269|PubMed:16439621, ECO:0000269|PubMed:18042262, ECO:0000269|PubMed:20358587}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O60706	Cardiomyopathy, dilated 1O (CMD1O) [MIM:608569]: A disorder characterized by ventricular dilation and impaired systolic function, resulting in congestive heart failure and arrhythmia. Patients are at risk of premature death. {ECO:0000269|PubMed:15034580}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Atrial fibrillation, familial, 12 (ATFB12) [MIM:614050]: A familial form of atrial fibrillation, a common sustained cardiac rhythm disturbance. Atrial fibrillation is characterized by disorganized atrial electrical activity and ineffective atrial contraction promoting blood stasis in the atria and reduces ventricular filling. It can result in palpitations, syncope, thromboembolic stroke, and congestive heart failure. {ECO:0000269|PubMed:17245405}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Hypertrichotic osteochondrodysplasia (HTOCD) [MIM:239850]: A rare disorder characterized by congenital hypertrichosis, neonatal macrosomia, a distinct osteochondrodysplasia, and cardiomegaly. The hypertrichosis leads to thick scalp hair, which extends onto the forehead, and a general increase in body hair. In addition, macrocephaly and coarse facial features, including a broad nasal bridge, epicanthal folds, a wide mouth, and full lips, can be suggestive of a storage disorder. About half of affected individuals are macrosomic and edematous at birth, whereas in childhood they usually have a muscular appearance with little subcutaneous fat. Thickened calvarium, narrow thorax, wide ribs, flattened or ovoid vertebral bodies, coxa valga, osteopenia, enlarged medullary canals, and metaphyseal widening of long bones have been reported. Cardiac manifestations such as patent ductus arteriosus, ventricular hypertrophy, pulmonary hypertension, and pericardial effusions are present in approximately 80% of cases. Motor development is usually delayed due to hypotonia. Most patients have a mild speech delay, and a small percentage have learning difficulties or intellectual disability. {ECO:0000269|PubMed:22608503, ECO:0000269|PubMed:22610116}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9H1R3	Cardiomyopathy, familial hypertrophic (CMH) [MIM:192600]: A hereditary heart disorder characterized by ventricular hypertrophy, which is usually asymmetric and often involves the interventricular septum. The symptoms include dyspnea, syncope, collapse, palpitations, and chest pain. They can be readily provoked by exercise. The disorder has inter- and intrafamilial variability ranging from benign to malignant forms with high risk of cardiac failure and sudden cardiac death. {ECO:0000269|PubMed:11733062}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8NHU6	Cataract 36 (CTRCT36) [MIM:613887]: An opacification of the crystalline lens of the eye becoming evident at birth. It frequently results in visual impairment or blindness. Opacities vary in morphology, are often confined to a portion of the lens, and may be static or progressive. In general, the more posteriorly located and dense an opacity, the greater the impact on visual function.

	{ECO:0000269|PubMed:21436445}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NSE4	Cataracts, growth hormone deficiency, sensory neuropathy, sensorineural hearing loss, and skeletal dysplasia (CAGSSS) [MIM:616007]: An autosomal recessive disorder characterized by cataracts, short-stature secondary to growth hormone deficiency, sensorineural hearing deficit, peripheral sensory neuropathy, skeletal dysplasia, scoliosis, and facial dysmorphism. {ECO:0000269|PubMed:25130867}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q562E7	Cerebellar ataxia, mental retardation, and dysequilibrium syndrome 2 (CAMRQ2) [MIM:610185]: A congenital cerebellar ataxia associated with cerebellar hypoplasia, mental retardation, and inability to walk bipedally, resulting in quadrupedal locomotion as a functional adaptation. Additional findings include generalized brain atrophy and mild hypoplasia of the corpus callosum. {ECO:0000269|PubMed:21885617}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9UM47	Cerebral arteriopathy with subcortical infarcts and leukoencephalopathy, autosomal dominant (CADASIL) [MIM:125310]: A cerebrovascular disease characterized by multiple subcortical infarcts, pseudobulbar palsy, dementia, and the presence of granular deposits in small cerebral arteries producing ischemic stroke. {ECO:0000269|PubMed:10227618, ECO:0000269|PubMed:10371548, ECO:0000269|PubMed:10802807, ECO:0000269|PubMed:10854111, ECO:0000269|PubMed:11058919, ECO:0000269|PubMed:11102981, ECO:0000269|PubMed:11559313, ECO:0000269|PubMed:11755616, ECO:0000269|PubMed:11810186, ECO:0000269|PubMed:12136071, ECO:0000269|PubMed:12146805, ECO:0000269|PubMed:12589106, ECO:0000269|PubMed:12810003, ECO:0000269|PubMed:15229130, ECO:0000269|PubMed:15300988, ECO:0000269|PubMed:15364702, ECO:0000269|PubMed:15378071, ECO:0000269|PubMed:15818833, ECO:0000269|PubMed:16009764, ECO:0000269|PubMed:24000151, ECO:0000269|PubMed:9388399}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Myofibromatosis, infantile 2 (IMF2) [MIM:615293]: A rare mesenchymal disorder characterized by the development of benign tumors in the skin, striated muscles, bones, and, more rarely, visceral organs. Subcutaneous or soft tissue nodules commonly involve the skin of the head, neck, and trunk. Skeletal and muscular lesions occur in about half of the patients. Lesions may be solitary or multicentric, and they may be present at birth or become apparent in early infancy or occasionally in adult life. Visceral lesions are associated with high morbidity and mortality. {ECO:0000269|PubMed:23731542}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q14678	Cerebral palsy, spastic quadriplegic 2 (CPSQ2) [MIM:612900]: A non-progressive disorder of movement and/or posture resulting from defects in the developing central nervous system. Affected individuals manifest congenital hypotonia evolving over the first year to spastic quadriplegia with accompanying transient nystagmus and varying degrees of mental retardation. Neuroimaging shows brain atrophy and ventriculomegaly. {ECO:0000269|PubMed:16301218}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P14678	Cerebrocostomandibular syndrome (CCMS) [MIM:117650]: A syndrome characterized by severe micrognathia, rib defects ranging from a few dorsal rib segments to complete absence of ossification, and mental retardation. {ECO:0000269|PubMed:25047197, ECO:0000269|PubMed:25504470}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P41250	Charcot-Marie-Tooth disease 2D (CMT2D) [MIM:601472]: A dominant axonal form of Charcot-Marie-Tooth disease, a disorder of the peripheral nervous system, characterized by progressive weakness and atrophy, initially of the peroneal muscles and later of the distal muscles of the arms. Charcot-Marie-Tooth disease is classified in two main groups on the basis of electrophysiologic properties and histopathology: primary peripheral demyelinating neuropathies (designated CMT1 when they are dominantly inherited) and primary peripheral axonal neuropathies (CMT2). Neuropathies of the CMT2 group are characterized by signs of axonal degeneration in the absence of obvious myelin alterations, normal or slightly reduced nerve conduction velocities, and progressive distal muscle weakness and atrophy. Nerve conduction velocities are normal or slightly reduced. {ECO:0000269|PubMed:12690580}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Neuronopathy, distal hereditary motor, 5A (HMN5A) [MIM:600794]: A disorder characterized by distal muscular atrophy mainly affecting the upper extremities, in contrast to other distal motor neuronopathies. These constitute a heterogeneous group of neuromuscular diseases caused by selective degeneration of motor neurons in the anterior horn of the spinal cord, without sensory deficit in the posterior horn. The overall clinical picture consists of a classical distal muscular atrophy syndrome in the legs without clinical sensory loss. The disease starts with weakness and wasting of distal muscles of the anterior tibial and peroneal compartments of the legs. Later on, weakness and atrophy may expand to the proximal muscles of the lower limbs and/or to the distal upper limbs. {ECO:0000269|PubMed:12690580, ECO:0000269|PubMed:24627108}. Note=The

	disease is caused by mutations affecting the gene represented in this entry.
P49588	Charcot-Marie-Tooth disease 2N (CMT2N) [MIM:613287]: An axonal form of Charcot-Marie-Tooth disease, a disorder of the peripheral nervous system, characterized by progressive weakness and atrophy, initially of the peroneal muscles and later of the distal muscles of the arms. Charcot-Marie-Tooth disease is classified in two main groups on the basis of electrophysiologic properties and histopathology: primary peripheral demyelinating neuropathies (designated CMT1 when they are dominantly inherited) and primary peripheral axonal neuropathies (CMT2). Neuropathies of the CMT2 group are characterized by signs of axonal degeneration in the absence of obvious myelin alterations, normal or slightly reduced nerve conduction velocities, and progressive distal muscle weakness and atrophy. Nerve conduction velocities are normal or slightly reduced. {ECO:0000269|PubMed:20045102, ECO:0000269|PubMed:22009580, ECO:0000269|PubMed:22206013}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Epileptic encephalopathy, early infantile, 29 (EIEE29) [MIM:616339]: A form of epileptic encephalopathy, a heterogeneous group of severe childhood onset epilepsies characterized by refractory seizures, neurodevelopmental impairment, and poor prognosis. Development is normal prior to seizure onset, after which cognitive and motor delays become apparent. EIEE29 patients manifest severe infantile epileptic encephalopathy, clubfoot, absent deep tendon reflexes, extrapyramidal symptoms, and persistently deficient myelination. {ECO:0000269|PubMed:25817015}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P54577	Charcot-Marie-Tooth disease, dominant, intermediate type, C (CMTDIC) [MIM:608323]: A form of Charcot-Marie-Tooth disease, a disorder of the peripheral nervous system, characterized by progressive weakness and atrophy, initially of the peroneal muscles and later of the distal muscles of the arms. The dominant intermediate type C is characterized by clinical and pathologic features intermediate between demyelinating and axonal peripheral neuropathies, and motor median nerve conduction velocities ranging from 25 to 45 m/sec. {ECO:0000269|PubMed:16429158}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9HAV0	Charcot-Marie-Tooth disease, dominant, intermediate type, F (CMTDIF) [MIM:615185]: A form of Charcot-Marie-Tooth disease, a disorder of the peripheral nervous system, characterized by progressive weakness and atrophy, initially of the peroneal muscles and later of the distal muscles of the arms. CMTDIF is characterized by onset around adolescence of slowly progressive distal muscle atrophy and weakness affecting the upper and lower limbs and resulting in steppage gait. There is distal sensory impairment with decreased reflexes. Nerve conduction velocities are variable, ranging from the demyelinating to the axonal range. {ECO:0000269|PubMed:23434117}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q15046	Charcot-Marie-Tooth disease, recessive, intermediate type, B (CMTRIB) [MIM:613641]: A form of Charcot-Marie-Tooth disease, a disorder of the peripheral nervous system, characterized by progressive weakness and atrophy, initially of the peroneal muscles and later of the distal muscles of the arms. Recessive intermediate forms of Charcot-Marie-Tooth disease are characterized by clinical and pathologic features intermediate between demyelinating and axonal peripheral neuropathies, and motor median nerve conduction velocities ranging from 25 to 45 m/sec. {ECO:0000269|PubMed:20920668}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Deafness, autosomal recessive, 89 (DFNB89) [MIM:613916]: A form of non-syndromic deafness characterized by bilateral, prelingual, moderate to severe hearing loss affecting all frequencies. {ECO:0000269|PubMed:23768514}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q99698	Chediak-Higashi syndrome (CHS) [MIM:214500]: A rare autosomal recessive disorder characterized by hypopigmentation, severe immunologic deficiency, a bleeding tendency, neurologic abnormalities, abnormal intracellular transport to and from the lysosome, and giant inclusion bodies in a variety of cell types. Most patients die at an early age unless they receive an allogeneic hematopoietic stem cell transplant (SCT). {ECO:0000269|PubMed:11857544, ECO:0000269|PubMed:24521565}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O95342	Cholestasis, progressive familial intrahepatic, 2 (PFIC2) [MIM:601847]: A disorder characterized by early onset of cholestasis that progresses to hepatic fibrosis, cirrhosis, and end-stage liver disease before adulthood. {ECO:0000269|PubMed:10579978, ECO:0000269|PubMed:11815775, ECO:0000269|PubMed:9806540}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Cholestasis, benign recurrent intrahepatic, 2 (BRIC2) [MIM:605479]: A disorder characterized by intermittent episodes of cholestasis without progression to liver failure. There is initial elevation of serum bile acids, followed by cholestatic jaundice which generally spontaneously resolves after periods of weeks to months. The cholestatic attacks vary in severity and duration. Patients are asymptomatic between episodes, both clinically and biochemically. {ECO:0000269|PubMed:15300568, ECO:0000269|PubMed:16039748}. Note=The disease is caused by

	mutations affecting the gene represented in this entry.
P21439	Cholestasis, progressive familial intrahepatic, 3 (PFIC3) [MIM:602347]: A disorder characterized by early onset of cholestasis that progresses to hepatic fibrosis, cirrhosis, and end-stage liver disease before adulthood. {ECO:0000269|PubMed:11313315, ECO:0000269|PubMed:12671900, ECO:0000269|PubMed:17726488, ECO:0000269|PubMed:21119540, ECO:0000269|PubMed:24045840, ECO:0000269|PubMed:24594635, ECO:0000269|PubMed:24806754, ECO:0000269|PubMed:9419367}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Cholestasis of pregnancy, intrahepatic 3 (ICP3) [MIM:614972]: A liver disorder of pregnancy. It presents during the second or, more commonly, the third trimester of pregnancy with intense pruritus which becomes more severe with advancing gestation and cholestasis. It causes fetal distress, spontaneous premature delivery and intrauterine death. Patients have spontaneous and progressive disappearance of cholestasis after delivery. Cholestasis results from abnormal biliary transport from the liver into the small intestine. {ECO:0000269|PubMed:10767346, ECO:0000269|PubMed:12746424, ECO:0000269|PubMed:15077010}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Gallbladder disease 1 (GBD1) [MIM:600803]: One of the major digestive diseases. Gallstones composed of cholesterol (cholelithiasis) are the common manifestations in western countries. Most people with gallstones, however, remain asymptomatic through their lifetimes. {ECO:0000269|PubMed:11313316, ECO:0000269|PubMed:12891548, ECO:0000269|PubMed:22331132, ECO:0000269|PubMed:23533021, ECO:0000269|PubMed:24723470, ECO:0000269|Ref.2}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NVR5	Ciliary dyskinesia, primary, 10 (CILD10) [MIM:612518]: A disorder characterized by abnormalities of motile cilia. Respiratory infections leading to chronic inflammation and bronchiectasis are recurrent, due to defects in the respiratory cilia; reduced fertility is often observed in male patients due to abnormalities of sperm tails. Half of the patients exhibit randomization of left-right body asymmetry and situs inversus, due to dysfunction of monocilia at the embryonic node. Primary ciliary dyskinesia associated with situs inversus is referred to as Kartagener syndrome. {ECO:0000269|PubMed:19052621, ECO:0000269|PubMed:25186273}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8IW40	Ciliary dyskinesia, primary, 17 (CILD17) [MIM:614679]: A disorder characterized by abnormalities of motile cilia. Respiratory infections leading to chronic inflammation and bronchiectasis are recurrent, due to defects in the respiratory cilia; reduced fertility is often observed in male patients due to abnormalities of sperm tails. Half of the patients exhibit randomization of left-right body asymmetry and situs inversus, due to dysfunction of monocilia at the embryonic node. Primary ciliary dyskinesia associated with situs inversus is referred to as Kartagener syndrome. {ECO:0000269|PubMed:22581229, ECO:0000269|PubMed:25186273}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q07617	Ciliary dyskinesia, primary, 28 (CILD28) [MIM:615505]: A disorder characterized by abnormalities of motile cilia. Respiratory infections leading to chronic inflammation and bronchiectasis are recurrent, due to defects in the respiratory cilia. Patients may exhibit randomization of left-right body asymmetry and situs inversus, due to dysfunction of monocilia at the embryonic node. Primary ciliary dyskinesia associated with situs inversus is referred to as Kartagener syndrome. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q13216	Cockayne syndrome A (CSA) [MIM:216400]: A rare disorder characterized by cutaneous sensitivity to sunlight, abnormal and slow growth, cachectic dwarfism, progeroid appearance, progressive pigmentary retinopathy and sensorineural deafness. There is delayed neural development and severe progressive neurologic degeneration resulting in mental retardation. Two clinical forms are recognized: in the classical form or Cockayne syndrome type 1, the symptoms are progressive and typically become apparent within the first few years or life; the less common Cockayne syndrome type 2 is characterized by more severe symptoms that manifest prenatally. Cockayne syndrome shows some overlap with certain forms of xeroderma pigmentosum. Unlike xeroderma pigmentosum, patients with Cockayne syndrome do not manifest increased freckling and other pigmentation abnormalities in the skin and have no significant increase in skin cancer. {ECO:0000269|PubMed:14661080, ECO:0000269|PubMed:15744458, ECO:0000269|PubMed:19894250}. Note=The disease is caused by mutations affecting the gene represented in this entry.; UV-sensitive syndrome 2 (UVSS2) [MIM:614621]: An autosomal recessive disorder characterized by cutaneous photosensitivity and mild freckling in the absence of neurological abnormalities or skin tumors. {ECO:0000269|PubMed:19329487}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O15111	Cocoon syndrome (COCOS) [MIM:613630]: A lethal syndrome characterized by multiple fetal malformations including defective face and seemingly absent limbs, which are bound to the trunk and

	encased under the skin. {ECO:0000269|PubMed:20961246}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8NI60	Coenzyme Q10 deficiency, primary, 4 (COQ10D4) [MIM:612016]: An autosomal recessive disorder characterized by childhood-onset of cerebellar ataxia and exercise intolerance. Patient manifest gait ataxia and cerebellar atrophy with slow progression. Additional features include brisk tendon reflexes and Hoffmann sign, variable psychomotor retardation and variable seizures. {ECO:0000269|PubMed:18319072, ECO:0000269|PubMed:18319074, ECO:0000269|PubMed:20580948, ECO:0000269|PubMed:22036850, ECO:0000269|PubMed:24048965, ECO:0000269|PubMed:24218524}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P51812	Coffin-Lowry syndrome (CLS) [MIM:303600]: A X-linked mental retardation associated with facial and digital dysmorphisms, progressive skeletal malformations, growth retardation, hearing deficit and paroxysmal movement disorders. {ECO:0000269|PubMed:10094187, ECO:0000269|PubMed:10528858, ECO:0000269|PubMed:14986828, ECO:0000269|PubMed:15214012, ECO:0000269|PubMed:8955270, ECO:0000269|PubMed:9837815}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Mental retardation, X-linked 19 (MRX19) [MIM:300844]: A non-syndromic form of mild to moderate mental retardation. Mental retardation is characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. In contrast to syndromic or specific X-linked mental retardation which also present with associated physical, neurological and/or psychiatric manifestations, intellectual deficiency is the only primary symptom of non-syndromic X-linked mental retardation. {ECO:0000269|PubMed:10319851, ECO:0000269|PubMed:17100996}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y467	Coloboma, ocular, autosomal recessive (COAR) [MIM:216820]: An ocular anomaly resulting from abnormal morphogenesis of the optic cup and stalk, and incomplete fusion of the fetal intra-ocular fissure during gestation. The clinical presentation is variable. Some individuals may present with minimal defects in the anterior iris leaf without other ocular defects. More complex malformations create a combination of iris, uveoretinal and/or optic nerve defects without or with microphthalmia or even anophthalmia. {ECO:0000269|PubMed:24412933}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q96RP9	Combined oxidative phosphorylation deficiency 1 (COXPD1) [MIM:609060]: A mitochondrial disease resulting in early rapidly progressive hepatoencephalopathy. {ECO:0000269|PubMed:15537906, ECO:0000269|PubMed:17160893}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y2Z2	Combined oxidative phosphorylation deficiency 10 (COXPD10) [MIM:614702]: An autosomal recessive disorder resulting in variable defects of mitochondrial oxidative respiration. Affected individuals present in infancy with hypertrophic cardiomyopathy and lactic acidosis. The severity is variable, but can be fatal in the most severe cases. {ECO:0000269|PubMed:22608499}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q5JPH6	Combined oxidative phosphorylation deficiency 12 (COXPD12) [MIM:614924]: An autosomal recessive, mitochondrial, neurologic disorder characterized by onset in infancy of hypotonia and delayed psychomotor development, or early developmental regression, associated with T2-weighted hyperintensities in the deep cerebral white matter, brainstem, and cerebellar white matter. Serum lactate is increased due to a defect in mitochondrial respiration. There are 2 main phenotypic groups: those with a milder disease course and some recovery of skills after age 2 years, and those with a severe disease course resulting in marked disability. {ECO:0000269|PubMed:22492562, ECO:0000269|PubMed:23008233}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8TCS8	Combined oxidative phosphorylation deficiency 13 (COXPD13) [MIM:614932]: A mitochondrial disorder characterized by early onset severe encephalomyopathy, dystonia, choreoathetosis, bucofacial dyskinesias and combined mitochondrial respiratory chain deficiency. Nerve conductions velocities are decreased. Levels of plasma and cerebrospinal fluid lactate are increased. {ECO:0000269|PubMed:23084291}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Deafness, autosomal recessive, 70 (DFNB70) [MIM:614934]: A form of non-syndromic deafness characterized by severe, bilateral hearing impairment with prelingual onset, resulting in inability to acquire normal speech. {ECO:0000269|PubMed:23084290}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O95363	Combined oxidative phosphorylation deficiency 14 (COXPD14) [MIM:614946]: A severe multisystemic autosomal recessive disorder characterized by neonatal onset of global developmental delay, refractory seizures, and lactic acidosis. Biochemical studies show deficiencies of multiple mitochondrial respiratory enzymes. {ECO:0000269|PubMed:22499341, ECO:0000269|PubMed:22833457}. Note=The disease is

	caused by mutations affecting the gene represented in this entry.
Q96DP5	Combined oxidative phosphorylation deficiency 15 (COXPD15) [MIM:614947]: An autosomal recessive, mitochondrial, neurologic disorder characterized by features of Leigh syndrome and combined oxidative phosphorylation deficiency. Clinical features include mild global developmental delay, white matter abnormalities, ataxia, incoordination, speech and reading difficulties, T2-weighted hyperintensities in the basal ganglia, corpus callosum, and brainstem. {ECO:0000269|PubMed:21907147}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Leigh syndrome (LS) [MIM:256000]: An early-onset progressive neurodegenerative disorder characterized by the presence of focal, bilateral lesions in one or more areas of the central nervous system including the brainstem, thalamus, basal ganglia, cerebellum and spinal cord. Clinical features depend on which areas of the central nervous system are involved and include subacute onset of psychomotor retardation, hypotonia, ataxia, weakness, vision loss, eye movement abnormalities, seizures, and dysphagia. {ECO:0000269|PubMed:22499348}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9H9J2	Combined oxidative phosphorylation deficiency 16 (COXPD16) [MIM:615395]: An autosomal recessive, mitochondrial disorder characterized by hypertrophic cardiomyopathy, liver steatosis, and decreased levels of mitochondrial complexes I and IV in heart and skeletal muscle. {ECO:0000269|PubMed:23315540}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y3D3	Combined oxidative phosphorylation deficiency 2 (COXPD2) [MIM:610498]: A mitochondrial disease resulting in fatal neonatal metabolic acidosis with agenesis of the corpus callosum. {ECO:0000269|PubMed:15505824}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q5ST30	Combined oxidative phosphorylation deficiency 20 (COXPD20) [MIM:615917]: A disorder due to mitochondrial respiratory chain complex defects. Clinical features are variable and include muscle weakness with hypotonia, central neurological disease with progressive external ophthalmoplegia, ptosis and ataxia, delayed psychomotor development, cardiomyopathy, abnormal liver function, facial dysmorphism, microcephaly and epilepsy. {ECO:0000269|PubMed:24827421, ECO:0000269|PubMed:25058219}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9BW92	Combined oxidative phosphorylation deficiency 21 (COXPD21) [MIM:615918]: A mitochondrial disorder characterized by a lethal encephalomyopathy. Shortly after birth, affected individuals manifest axial hypotonia, limb hypertonia, psychomotor delay, and increased serum lactate. Additional features include subsarcolemmal lipofuscin-positive deposits in muscle, cerebral spongiosis, and hepatic steatosis. {ECO:0000269|PubMed:24827421}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q969Y2	Combined oxidative phosphorylation deficiency 23 (COXPD23) [MIM:616198]: An autosomal recessive mitochondrial disorder characterized by hypertrophic cardiomyopathy and/or neurologic symptoms with onset in early childhood. Disease features include hypertrophic cardiomyopathy, hypotonia, delayed psychomotor development, lactic acidosis, impaired activities of respiratory complexes I and IV, and defective translation of mitochondrial proteins. Disease severity is variable, ranging from death in early infancy to survival into the second decade of life. {ECO:0000269|PubMed:25434004}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q96I59	Combined oxidative phosphorylation deficiency 24 (COXPD24) [MIM:616239]: An autosomal recessive mitochondrial disorder with wide phenotypic variability. Some patients have a milder form affecting only skeletal muscle, whereas others may have a more severe disorder, reminiscent of Alpers syndrome. Alpers syndrome is a progressive neurodegenerative disorder that presents in infancy or early childhood and is characterized by diffuse degeneration of cerebral gray matter. {ECO:0000269|PubMed:25385316, ECO:0000269|PubMed:25629079}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Note=NARS2 mutations may be the cause of deafness, autosomal recessive, 94 (DFNB94). DFNB94 is a form of non-syndromic sensorineural hearing loss. Sensorineural deafness results from damage to the neural receptors of the inner ear, the nerve pathways to the brain, or the area of the brain that receives sound information. {ECO:0000269|PubMed:25807530}.; Leigh syndrome (LS) [MIM:256000]: An early-onset progressive neurodegenerative disorder characterized by the presence of focal, bilateral lesions in one or more areas of the central nervous system including the brainstem, thalamus, basal ganglia, cerebellum and spinal cord. Clinical features depend on which areas of the central nervous system are involved and include subacute onset of psychomotor retardation, hypotonia, ataxia, weakness, vision loss, eye movement abnormalities, seizures, and dysphagia. {ECO:0000269|PubMed:25807530}. Note=The disease may be caused by mutations affecting the gene represented in this entry.

P43897	Combined oxidative phosphorylation deficiency 3 (COXPD3) [MIM:610505]: A mitochondrial disease resulting in severe metabolic acidosis with encephalomyopathy or with hypertrophic cardiomyopathy. Patients show a severe defect in mitochondrial translation leading to a failure to assemble adequate amounts of three of the oxidative phosphorylation complexes. {ECO:0000269|PubMed:17033963, ECO:0000269|PubMed:22499341}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P49411	Combined oxidative phosphorylation deficiency 4 (COXPD4) [MIM:610678]: A mitochondrial disease resulting in neonatal lactic acidosis, rapidly progressive encephalopathy, severely decreased mitochondrial protein synthesis, and combined deficiency of mtDNA-related mitochondrial respiratory chain complexes. {ECO:0000269|PubMed:17160893}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P82650	Combined oxidative phosphorylation deficiency 5 (COXPD5) [MIM:611719]: A mitochondrial disease resulting in severe metabolic acidosis, edema, hypertrophic cardiomyopathy, tubulopathy, and hypotonia. {ECO:0000269|PubMed:17873122}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9H3J6	Combined oxidative phosphorylation deficiency 7 (COXPD7) [MIM:613559]: A mitochondrial disease resulting in encephalomyopathy. Clinical manifestations include psychomotor delay and regression, ataxia, optic atrophy, nystagmus and muscle atrophy and weakness. {ECO:0000269|PubMed:20598281}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Spastic paraplegia 55, autosomal recessive (SPG55) [MIM:615035]: A form of spastic paraplegia, a neurodegenerative disorder characterized by a slow, gradual, progressive weakness and spasticity of the lower limbs. Rate of progression and the severity of symptoms are quite variable. Initial symptoms may include difficulty with balance, weakness and stiffness in the legs, muscle spasms, and dragging the toes when walking. Complicated forms are recognized by additional variable features including spastic quadriparesis, seizures, dementia, amyotrophy, extrapyramidal disturbance, cerebral or cerebellar atrophy, optic atrophy, and peripheral neuropathy, as well as by extra neurological manifestations. {ECO:0000269|PubMed:23188110}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q5JTZ9	Combined oxidative phosphorylation deficiency 8 (COXPD8) [MIM:614096]: A mitochondrial disease characterized by a lethal infantile hypertrophic cardiomyopathy, generalized muscle dysfunction and some neurologic involvement. The liver is not affected. {ECO:0000269|PubMed:21549344}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Leukoencephalopathy, progressive, with ovarian failure (LKENP) [MIM:615889]: An autosomal recessive neurodegenerative disorder characterized by childhood- to adulthood-onset of signs of neurologic deterioration consisting of ataxia, spasticity, and cognitive decline with features of frontal lobe dysfunction. Brain MRI shows leukoencephalopathy with striking involvement of deep white matter, and cerebellar atrophy. All female patients develop premature ovarian failure. {ECO:0000269|PubMed:24808023}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P09001	Combined oxidative phosphorylation deficiency 9 (COXPD9) [MIM:614582]: A mitochondrial disease characterized by failure to thrive, poor feeding, hypertrophic cardiomyopathy, hepatomegaly, and psychomotor retardation. Death in infancy has been observed in some cases. {ECO:0000269|PubMed:21786366}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P06681	Complement component 2 deficiency (C2D) [MIM:217000]: A rare defect of the complement classical pathway associated with the development of autoimmune disorders, mainly systemic lupus erythematosus. Skin and joint manifestations are common and renal disease is relatively rare. Patients with complement component 2 deficiency are also reported to have recurrent invasive infections. {ECO:0000269|PubMed:8621452, ECO:0000269|PubMed:9670930}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P09871	Complement component C1s deficiency (C1SD) [MIM:613783]: A rare defect resulting in C1 deficiency and impaired activation of the complement classical pathway. C1 deficiency generally leads to severe immune complex disease with features of systemic lupus erythematosus and glomerulonephritis. {ECO:0000269|PubMed:11390518}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P00746	Complement factor D deficiency (CFDD) [MIM:613912]: An immunologic disorder characterized by increased susceptibility to bacterial infections, particularly Neisseria infections, due to a defect in the alternative complement pathway. {ECO:0000269|PubMed:16527897}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8TC44	Cone-rod dystrophy 20 (CORD20) [MIM:615973]: A form of cone-rod dystrophy, an inherited retinal dystrophy characterized by retinal pigment deposits visible on fundus examination, predominantly in the

	macular region, and initial loss of cone photoreceptors followed by rod degeneration. This leads to decreased visual acuity and sensitivity in the central visual field, followed by loss of peripheral vision. Severe loss of vision occurs earlier than in retinitis pigmentosa. {ECO:0000269|PubMed:24945461, ECO:0000269|PubMed:25018096, ECO:0000269|PubMed:25044745}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P28288	Congenital bile acid synthesis defect 5 (CBAS5) [MIM:616278]: An autosomal recessive disorder characterized by hepatosplenomegaly, hepatic fibrosis, progressive liver failure, and accumulation of peroxisomal C27-bile acid intermediates in plasma. {ECO:0000269|PubMed:25168382}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P07585	Corneal dystrophy, congenital stromal (CSCD) [MIM:610048]: A corneal dystrophy characterized by congenital corneal opacification consisting of a large number of flakes and spots throughout all layers of the stroma. It results in progressive, painless visual loss. Corneal erosions and photophobia are absent. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q92626	Corneal opacification with other ocular anomalies (COPOA) [MIM:269400]: An ocular disease characterized by sclerocornea associated with other ocular anomalies, such as cataract, microcornea, microphthalmia, and anterior segment dysgenesis. Sclerocornea is a primary anomaly in which scleralization of a peripheral part of the cornea, or the entire corneal tissue, occurs. In the peripheral type of sclerocornea, the affected area is vascularized with regular arcades of superficial scleral vessels. In total sclerocornea, the entire cornea is opaque and vascularized. {ECO:0000269|PubMed:21907015}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O60229	Coronary heart disease 5 (CHDS5) [MIM:608901]: A multifactorial disease characterized by an imbalance between myocardial functional requirements and the capacity of the coronary vessels to supply sufficient blood flow. Decreased capacity of the coronary vessels is often associated with thickening and loss of elasticity of the coronary arteries. {ECO:0000269|PubMed:17357071}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
Q9HBG6	Cranioectodermal dysplasia 1 (CED1) [MIM:218330]: A disorder characterized by craniofacial, skeletal and ectodermal abnormalities. Clinical features include dolichocephaly (with or without sagittal suture synostosis), scaphocephaly, short stature, limb shortening, short ribs, narrow chest, brachydactyly, renal failure and hepatic fibrosis, small and abnormally shaped teeth, sparse hair, skin laxity and abnormal nails. {ECO:0000269|PubMed:20493458}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8WXD0	Cryptorchidism (CRYPTO) [MIM:219050]: One of the most frequent congenital abnormalities in humans, involving 2-5% of male births. Cryptorchidism is associated with increased risk of infertility and testicular cancer. {ECO:0000269|PubMed:12217959}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P13569	Cystic fibrosis (CF) [MIM:219700]: A common generalized disorder of the exocrine glands which impairs clearance of secretions in a variety of organs. It is characterized by the triad of chronic bronchopulmonary disease (with recurrent respiratory infections), pancreatic insufficiency (which leads to malabsorption and growth retardation) and elevated sweat electrolytes. It is the most common genetic disease in Caucasians, with a prevalence of about 1 in 2'000 live births. Inheritance is autosomal recessive. {ECO:0000269|PubMed:10094564, ECO:0000269|PubMed:1284466, ECO:0000269|PubMed:1284468, ECO:0000269|PubMed:1284529, ECO:0000269|PubMed:1284530, ECO:0000269|PubMed:1695717, ECO:0000269|PubMed:1710600, ECO:0000269|PubMed:2236053, ECO:0000269|PubMed:7504969, ECO:0000269|PubMed:7505694, ECO:0000269|PubMed:7513296, ECO:0000269|PubMed:7517264, ECO:0000269|PubMed:7520022, ECO:0000269|PubMed:7522211, ECO:0000269|PubMed:7524909, ECO:0000269|PubMed:7524913, ECO:0000269|PubMed:7525450, ECO:0000269|PubMed:7537150, ECO:0000269|PubMed:7541273, ECO:0000269|PubMed:7541510, ECO:0000269|PubMed:7543567, ECO:0000269|PubMed:7544319, ECO:0000269|PubMed:7581407, ECO:0000269|PubMed:7680525, ECO:0000269|PubMed:7683628, ECO:0000269|PubMed:7683954, ECO:0000269|PubMed:8081395, ECO:0000269|PubMed:8522333, ECO:0000269|PubMed:8723693, ECO:0000269|PubMed:8723695, ECO:0000269|PubMed:8800923, ECO:0000269|PubMed:8829633, ECO:0000269|PubMed:8956039, ECO:0000269|PubMed:9101301, ECO:0000269|PubMed:9222768, ECO:0000269|PubMed:9375855, ECO:0000269|PubMed:9401006, ECO:0000269|PubMed:9443874, ECO:0000269|PubMed:9452048, ECO:0000269|PubMed:9452054, ECO:0000269|PubMed:9452073, ECO:0000269|PubMed:9482579, ECO:0000269|PubMed:9521595, ECO:0000269|PubMed:9554753, ECO:0000269|PubMed:9736778, ECO:0000269|PubMed:9921909}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Congenital bilateral absence of the vas deferens (CBAVD) [MIM:277180]: Important cause of sterility in men and could represent an incomplete form of cystic fibrosis, as the majority of men suffering from cystic fibrosis lack the vas deferens. {ECO:0000269|PubMed:10651488, ECO:0000269|PubMed:7529962, ECO:0000269|PubMed:7539342,

	ECO:0000269|PubMed:9067761, ECO:0000269|Ref.77}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9H5Y7	Deafness and myopia (DFNMYP) [MIM:221200]: An autosomal recessive disorder characterized by prelingual sensorineural hearing loss associated with high myopia. {ECO:0000269|PubMed:23543054, ECO:0000269|PubMed:23946138}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8NEV4	Deafness, autosomal recessive, 30 (DFNB30) [MIM:607101]: A form of non-syndromic deafness characterized by bilateral progressive hearing loss, which first affects the high frequencies. Hearing loss begins in the second decade, and by age 50 is severe in high and middle frequencies and moderate at low frequencies. {ECO:0000269|PubMed:12032315}. Note=The disease is caused by mutations affecting the gene represented in this entry.
B1AK53	Deafness, autosomal recessive, 36, with or without vestibular involvement (DFNB36) [MIM:609006]: A form of non-syndromic sensorineural hearing loss. Sensorineural deafness results from damage to the neural receptors of the inner ear, the nerve pathways to the brain, or the area of the brain that receives sound information. DFNB36 is characterized by prelingual, profound hearing loss, and vestibular areflexia in some patients. {ECO:0000269|PubMed:15286153, ECO:0000269|PubMed:15930085}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P14210	Deafness, autosomal recessive, 39 (DFNB39) [MIM:608265]: A form of profound prelingual sensorineural hearing loss. Sensorineural deafness results from damage to the neural receptors of the inner ear, the nerve pathways to the brain, or the area of the brain that receives sound information. {ECO:0000269|PubMed:19576567}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8N4S9	Deafness, autosomal recessive, 49 (DFNB49) [MIM:610153]: A form of non-syndromic sensorineural hearing loss. Sensorineural deafness results from damage to the neural receptors of the inner ear, the nerve pathways to the brain, or the area of the brain that receives sound information. {ECO:0000269|PubMed:17186462}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P57727	Deafness, autosomal recessive, 8 (DFNB8) [MIM:601072]: A form of non-syndromic sensorineural hearing loss. Sensorineural deafness results from damage to the neural receptors of the inner ear, the nerve pathways to the brain, or the area of the brain that receives sound information. {ECO:0000269|PubMed:11424922, ECO:0000269|PubMed:11462234, ECO:0000269|PubMed:11907649, ECO:0000269|PubMed:12393794, ECO:0000269|PubMed:16021470}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9BYX4	Diabetes mellitus, insulin-dependent, 19 (IDDM19) [MIM:610155]: A multifactorial disorder of glucose homeostasis that is characterized by susceptibility to ketoacidosis in the absence of insulin therapy. Clinical features are polydipsia, polyphagia and polyuria which result from hyperglycemia-induced osmotic diuresis and secondary thirst. These derangements result in long-term complications that affect the eyes, kidneys, nerves, and blood vessels. {ECO:0000269|PubMed:16699517}. Note=Disease susceptibility may be associated with variations affecting the gene represented in this entry.; Note=IFIH1 is the CADM-140 autoantigen, involved in clinically amyopathic dermatomyositis (CADM). This is a chronic inflammatory disorder that shows typical skin manifestations of dermatomyositis but has no or little evidence of clinical myositis. Anti-CADM-140 antibodies appear to be specific to dermatomyositis, especially CADM. Patients with anti-CADM-140 antibodies frequently develop life-threatening acute progressive interstitial lung disease (ILD).; Aicardi-Goutieres syndrome 7 (AGS7) [MIM:615846]: A form of Aicardi-Goutieres syndrome, a genetically heterogeneous disease characterized by cerebral atrophy, leukoencephalopathy, intracranial calcifications, chronic cerebrospinal fluid (CSF) lymphocytosis, increased CSF alpha-interferon, and negative serologic investigations for common prenatal infection. Clinical features as thrombocytopenia, hepatosplenomegaly and elevated hepatic transaminases along with intermittent fever may erroneously suggest an infective process. Severe neurological dysfunctions manifest in infancy as progressive microcephaly, spasticity, dystonic posturing and profound psychomotor retardation. Death often occurs in early childhood. {ECO:0000269|PubMed:24686847, ECO:0000269|PubMed:24995871}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Singleton-Merten syndrome 1 (SGMRT1) [MIM:182250]: An autosomal dominant disorder with variable expression. Core features are marked aortic calcification, dental anomalies, osteopenia, acro-osteolysis, and to a lesser extend glaucoma, psoriasis, muscle weakness, and joint laxity. Dental anomalies include delayed eruption and immature root formation of anterior permanent teeth, early loss of permanent teeth due to short roots, acute root resorption, high caries, and aggressive alveolar bone loss. Additional clinical manifestations include particular facial characteristics and abnormal joint and muscle ligaments.

	{ECO:0000269|PubMed:25620204}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P39019	Diamond-Blackfan anemia 1 (DBA1) [MIM:105650]: A form of Diamond-Blackfan anemia, a congenital non-regenerative hypoplastic anemia that usually presents early in infancy. Diamond-Blackfan anemia is characterized by a moderate to severe macrocytic anemia, erythroblastopenia, and an increased risk of developing leukemia. 30 to 40% of Diamond-Blackfan anemia patients present with short stature and congenital anomalies, the most frequent being craniofacial (Pierre-Robin syndrome and cleft palate), thumb and urogenital anomalies. {ECO:0000269|PubMed:10590074, ECO:0000269|PubMed:11112378, ECO:0000269|PubMed:12586610, ECO:0000269|PubMed:12750732, ECO:0000269|PubMed:15384984, ECO:0000269|PubMed:9988267, ECO:0000269|Ref.21}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P61254	Diamond-Blackfan anemia 11 (DBA11) [MIM:614900]: A form of Diamond-Blackfan anemia, a congenital non-regenerative hypoplastic anemia that usually presents early in infancy. Diamond-Blackfan anemia is characterized by a moderate to severe macrocytic anemia, erythroblastopenia, and an increased risk of malignancy. 30 to 40% of Diamond-Blackfan anemia patients present with short stature and congenital anomalies, the most frequent being craniofacial (Pierre-Robin syndrome and cleft palate), thumb and urogenital anomalies. {ECO:0000269|PubMed:22431104}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P61313	Diamond-Blackfan anemia 12 (DBA12) [MIM:615550]: A form of Diamond-Blackfan anemia, a congenital non-regenerative hypoplastic anemia that usually presents early in infancy. Diamond-Blackfan anemia is characterized by a moderate to severe macrocytic anemia, erythroblastopenia, and an increased risk of malignancy. 30 to 40% of Diamond-Blackfan anemia patients present with short stature and congenital anomalies, the most frequent being craniofacial (Pierre-Robin syndrome and cleft palate), thumb and urogenital anomalies. {ECO:0000269|PubMed:23812780}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P62273	Diamond-Blackfan anemia 13 (DBA13) [MIM:615909]: A form of Diamond-Blackfan anemia, a congenital non-regenerative hypoplastic anemia that usually presents early in infancy. Diamond-Blackfan anemia is characterized by a moderate to severe macrocytic anemia, erythroblastopenia, and an increased risk of malignancy. 30 to 40% of Diamond-Blackfan anemia patients present with short stature and congenital anomalies, the most frequent being craniofacial (Pierre-Robin syndrome and cleft palate), thumb and urogenital anomalies. {ECO:0000269|PubMed:24829207}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P46777	Diamond-Blackfan anemia 6 (DBA6) [MIM:612561]: A form of Diamond-Blackfan anemia, a congenital non-regenerative hypoplastic anemia that usually presents early in infancy. Diamond-Blackfan anemia is characterized by a moderate to severe macrocytic anemia, erythroblastopenia, and an increased risk of malignancy. 30 to 40% of Diamond-Blackfan anemia patients present with short stature and congenital anomalies, the most frequent being craniofacial (Pierre-Robin syndrome and cleft palate), thumb and urogenital anomalies. {ECO:0000269|PubMed:19061985, ECO:0000269|PubMed:19191325}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P62913	Diamond-Blackfan anemia 7 (DBA7) [MIM:612562]: A form of Diamond-Blackfan anemia, a congenital non-regenerative hypoplastic anemia that usually presents early in infancy. Diamond-Blackfan anemia is characterized by a moderate to severe macrocytic anemia, erythroblastopenia, and an increased risk of malignancy. 30 to 40% of Diamond-Blackfan anemia patients present with short stature and congenital anomalies, the most frequent being craniofacial (Pierre-Robin syndrome and cleft palate), thumb and urogenital anomalies. {ECO:0000269|PubMed:19061985, ECO:0000269|PubMed:19191325}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P46783	Diamond-Blackfan anemia 9 (DBA9) [MIM:613308]: A form of Diamond-Blackfan anemia, a congenital non-regenerative hypoplastic anemia that usually presents early in infancy. Diamond-Blackfan anemia is characterized by a moderate to severe macrocytic anemia, erythroblastopenia, and an increased risk of malignancy. 30 to 40% of Diamond-Blackfan anemia patients present with short stature and congenital anomalies, the most frequent being craniofacial (Pierre-Robin syndrome and cleft palate), thumb and urogenital anomalies. {ECO:0000269|PubMed:20116044}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q15020	Disseminated superficial actinic porokeratosis 1 (DSAP1) [MIM:175900]: Autosomal dominant disorder, characterized by multiple superficial keratotic lesions surrounded by a slightly raised keratotic border, developing during the third or fourth decade of life on sun-exposed areas of skin. {ECO:0000269|PubMed:15840095}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9UJQ4	Duane-radial ray syndrome (DRRS) [MIM:607323]: Disorder characterized by the association of forearm malformations with Duane retraction syndrome. {ECO:0000269|PubMed:12393809,

	ECO:0000269|PubMed:12395297, ECO:0000269|PubMed:16402211}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Oculootoradial syndrome (OORS) [MIM:147750]: Autosomal dominant condition characterized by upper limbs anomalies (radial ray defects, carpal bones fusion), extraocular motor disturbances, congenital bilateral non-progressive mixed hearing loss. Other less consistent malformations include heart involvement, mild thrombocytopenia and leukocytosis (before age 50), shoulder girdle hypoplasia, imperforate anus, kidney malrotation or rectovaginal fistula. The IVIC syndrome is an allelic disorder of Duane-radial ray syndrome (DRRS) with a similar phenotype. {ECO:0000269|PubMed:17256792}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q92887	Dubin-Johnson syndrome (DJS) [MIM:237500]: Autosomal recessive disorder characterized by conjugated hyperbilirubinemia, an increase in the urinary excretion of coproporphyrin isomer I, deposition of melanin-like pigment in hepatocytes, and prolonged retention of sulfobromophthalein, but otherwise normal liver function. {ECO:0000269|PubMed:10053008, ECO:0000269|PubMed:10464142, ECO:0000269|PubMed:11266082, ECO:0000269|PubMed:11477083, ECO:0000269|PubMed:25336012, ECO:0000269|PubMed:9425227}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P55265	Dyschromatosis symmetrica hereditaria (DSH) [MIM:127400]: An autosomal dominant pigmentary genodermatosis characterized by a mixture of hyperpigmented and hypopigmented macules distributed on the face and the dorsal parts of the hands and feet, that appear in infancy or early childhood. {ECO:0000269|PubMed:12916015, ECO:0000269|PubMed:15146470, ECO:0000269|PubMed:15659327}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Aicardi-Goutieres syndrome 6 (AGS6) [MIM:615010]: A form of Aicardi-Goutieres syndrome, a genetically heterogeneous disease characterized by cerebral atrophy, leukoencephalopathy, intracranial calcifications, chronic cerebrospinal fluid (CSF) lymphocytosis, increased CSF alpha-interferon, and negative serologic investigations for common prenatal infection. Clinical features as thrombocytopenia, hepatosplenomegaly and elevated hepatic transaminases along with intermittent fever may erroneously suggest an infective process. Severe neurological dysfunctions manifest in infancy as progressive microcephaly, spasticity, dystonic posturing and profound psychomotor retardation. Death often occurs in early childhood. {ECO:0000269|PubMed:23001123}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NPE3	Dyskeratosis congenita, autosomal recessive, 1 (DKCB1) [MIM:224230]: A rare multisystem disorder caused by defective telomere maintenance. It is characterized by progressive bone marrow failure, and the clinical triad of reticulated skin hyperpigmentation, nail dystrophy, and mucosal leukoplakia. Common but variable features include premature graying, aplastic anemia, low platelets, osteoporosis, pulmonary fibrosis, and liver fibrosis among others. Early mortality is often associated with bone marrow failure, infections, fatal pulmonary complications, or malignancy. {ECO:0000269|PubMed:17507419}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NX24	Dyskeratosis congenita, autosomal recessive, 2 (DKCB2) [MIM:613987]: A rare multisystem disorder caused by defective telomere maintenance. It is characterized by progressive bone marrow failure, and the clinical triad of reticulated skin hyperpigmentation, nail dystrophy, and mucosal leukoplakia. Common but variable features include premature graying, aplastic anemia, low platelets, osteoporosis, pulmonary fibrosis, and liver fibrosis among others. Early mortality is often associated with bone marrow failure, infections, fatal pulmonary complications, or malignancy. {ECO:0000269|PubMed:18523010}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9BUR4	Dyskeratosis congenita, autosomal recessive, 3 (DKCB3) [MIM:613988]: A rare multisystem disorder caused by defective telomere maintenance. It is characterized by progressive bone marrow failure, and the clinical triad of reticulated skin hyperpigmentation, nail dystrophy, and mucosal leukoplakia. Common but variable features include premature graying, aplastic anemia, low platelets, osteoporosis, pulmonary fibrosis, and liver fibrosis among others. Early mortality is often associated with bone marrow failure, infections, fatal pulmonary complications, or malignancy. {ECO:0000269|PubMed:21205863}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O95453	Dyskeratosis congenita, autosomal recessive, 6 (DKCB6) [MIM:616353]: A form of dyskeratosis congenita, a rare multisystem disorder caused by defective telomere maintenance. It is characterized by progressive bone marrow failure, and the clinical triad of reticulated skin hyperpigmentation, nail dystrophy, and mucosal leukoplakia. Common but variable features include premature graying, aplastic anemia, low platelets, osteoporosis, pulmonary fibrosis, and liver fibrosis among others. Early mortality is often associated with bone marrow failure, infections, fatal pulmonary complications, or malignancy. {ECO:0000269|PubMed:25893599}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Pulmonary fibrosis, and/or bone marrow failure, telomere-related, 4 (PFBMFT4) [MIM:616371]: A disease associated with shortened telomeres. Pulmonary fibrosis is the

	most common manifestation. Other manifestations include aplastic anemia due to bone marrow failure, hepatic fibrosis, and increased cancer risk, particularly myelodysplastic syndrome and acute myeloid leukemia. Phenotype, age at onset, and severity are determined by telomere length. {ECO:0000269|PubMed:25848748}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O60832	Dyskeratosis congenita, X-linked (DKCX) [MIM:305000]: A rare, progressive bone marrow failure syndrome characterized by the triad of reticulated skin hyperpigmentation, nail dystrophy, and mucosal leukoplakia. Early mortality is often associated with bone marrow failure, infections, fatal pulmonary complications, or malignancy. {ECO:0000269|PubMed:10364516, ECO:0000269|PubMed:15304085, ECO:0000269|PubMed:17417794, ECO:0000269|PubMed:18802941, ECO:0000269|PubMed:19734544, ECO:0000269|PubMed:19879169, ECO:0000269|PubMed:9590285}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Hoyeraal-Hreidarsson syndrome (HHS) [MIM:305000]: A clinically severe variant of dyskeratosis congenita that is characterized by multisystem involvement, early onset in utero, and often results in death in childhood. Affected individuals show intrauterine growth retardation, microcephaly, cerebellar hypoplasia, delayed development, and bone marrow failure resulting in immunodeficiency. {ECO:0000269|PubMed:10583221, ECO:0000269|PubMed:12437656, ECO:0000269|PubMed:19734544, ECO:0000269|PubMed:24914498}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O75569	Dystonia 16 (DYT16) [MIM:612067]: An early-onset dystonia-parkinsonism disorder. Dystonia is defined by the presence of sustained involuntary muscle contraction, often leading to abnormal postures. DYT16 patients have progressive, generalized dystonia with axial muscle involvement, oro-mandibular (sardonic smile) and laryngeal dystonia and, in some cases, parkinsonian features. {ECO:0000269|PubMed:18243799, ECO:0000269|PubMed:18420150}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NR56	Dystrophia myotonica 1 (DM1) [MIM:160900]: A muscular disorder characterized by myotonia, muscle wasting in the distal extremities, cataract, hypogonadism, defective endocrine functions, male baldness and cardiac arrhythmias. {ECO:0000269|PubMed:11929853}. Note=The protein represented in this entry may be involved in disease pathogenesis. In muscle cells from patients, MBNL1 is sequestered by DMPK RNAs containing pathogenic CUG triplet repeat expansions. MBNL1 binding is proportional to repeat length consistent with the direct correlation between the length of repeat expansion and disease severity.
Q09013	Dystrophia myotonica 1 (DM1) [MIM:160900]: A muscular disorder characterized by myotonia, muscle wasting in the distal extremities, cataract, hypogonadism, defective endocrine functions, male baldness and cardiac arrhythmias. {ECO:0000269|PubMed:1302022, ECO:0000269|PubMed:1310900, ECO:0000269|PubMed:1546326, ECO:0000269|PubMed:19514047}. Note=The disease is caused by mutations affecting the gene represented in this entry. The causative mutation is a CTG expansion in the 3'-UTR of the DMPK gene. A length exceeding 50 CTG repeats is pathogenic, while normal individuals have 5 to 37 repeats. Intermediate alleles with 35-49 triplets are not disease-causing but show instability in intergenerational transmissions. Disease severity varies with the number of repeats: mildly affected persons have 50 to 150 repeats, patients with classic DM have 100 to 1,000 repeats, and those with congenital onset can have more than 2,000 repeats. {ECO:0000269|PubMed:1310900, ECO:0000269|PubMed:19514047}.
P62633	Dystrophia myotonica 2 (DM2) [MIM:602668]: A multisystem disease characterized by the association of proximal muscle weakness with myotonia, cardiac manifestations and cataract. Additional features can include hyperhidrosis, testicular atrophy, insulin resistance and diabetes and central nervous system anomalies in rare cases. Note=The disease is caused by mutations affecting the gene represented in this entry. The causative mutation is a CCTG expansion (mean approximately 5000 repeats) located in intron 1 of the CNBP gene.
P25963	Ectodermal dysplasia, anhidrotic, with T-cell immunodeficiency autosomal dominant (ADEDAID) [MIM:612132]: A form of ectoderma dysplasia, a heterogeneous group of disorders due to abnormal development of two or more ectodermal structures. This form of ectodermal dysplasia is associated with decreased production of pro-inflammatory cytokines and certain interferons, rendering patients susceptible to infection. {ECO:0000269|PubMed:14523047, ECO:0000269|PubMed:18412279}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9UPZ9	Endocrine-cerebroosteodysplasia (ECO) [MIM:612651]: Previously unidentified neonatal lethal recessive disorder with multiple anomalies involving the endocrine, cerebral, and skeletal systems. {ECO:0000269|PubMed:19185282}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P20585	Endometrial cancer (ENDMC) [MIM:608089]: A malignancy of endometrium, the mucous lining of the uterus. Most endometrial cancers are adenocarcinomas, cancers that begin in cells that make and release

	mucus and other fluids. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
P98073	Enterokinase deficiency (ENTKD) [MIM:226200]: Life-threatening intestinal malabsorption disorder characterized by diarrhea and failure to thrive. {ECO:0000269|PubMed:11719902}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q15149	Epidermolysis bullosa simplex with pyloric atresia (EBS-PA) [MIM:612138]: Autosomal recessive genodermatosis characterized by severe skin blistering at birth and congenital pyloric atresia. Death usually occurs in infancy. This disorder is allelic to MD-EBS. {ECO:0000269|PubMed:14675180, ECO:0000269|PubMed:20665883}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Epidermolysis bullosa simplex, with muscular dystrophy (MD-EBS) [MIM:226670]: A form of epidermolysis bullosa characterized by the association of blister formation at the level of the hemidesmosome with late-onset muscular dystrophy. {ECO:0000269|PubMed:11159198, ECO:0000269|PubMed:8894687}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Epidermolysis bullosa simplex, Ogna type (O-EBS) [MIM:131950]: A form of intraepidermal epidermolysis bullosa characterized by generalized skin bruising, skin fragility with non-scarring blistering and small hemorrhagic blisters on hands. At the ultrastructural level, it is differentiated from classical cases of K-EBS, WC-EBS and DM-EBS, by the occurrence of blisters originating in basal cells above hemidesmosomes, and abnormal hemidesmosome intracellular attachment plates. {ECO:0000269|PubMed:11851880}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Limb-girdle muscular dystrophy 2Q (LGMD2Q) [MIM:613723]: A form of limb-girdle muscular dystrophy characterized by early childhood onset of proximal muscle weakness. Limb-girdle muscular dystrophies are characterized by proximal weakness, weakness of the hip and shoulder girdles and prominent asymmetrical quadriceps femoris and biceps brachii atrophy. {ECO:0000269|PubMed:21109228}. Note=The disease is caused by mutations affecting the gene represented in this entry. A 9 bp deletion containing the initiation codon in exon 1f of PLEC have been found in limb-girdle muscular dystrophy patients. The mutation results in deficient expression of isoform 9 and disorganization of the myofibers, without any effect on the skin.
P57059	Epileptic encephalopathy, early infantile, 30 (EIEE30) [MIM:616341]: A form of epileptic encephalopathy, a heterogeneous group of severe childhood onset epilepsies characterized by refractory seizures, neurodevelopmental impairment, and poor prognosis. Development is normal prior to seizure onset, after which cognitive and motor delays become apparent. {ECO:0000269|PubMed:25839329}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Note=Defects in SIK1 may be associated with some cancers, such as breast cancers. Loss of SIK1 correlates with poor patient outcome in breast cancers (PubMed:19622832). {ECO:0000269|PubMed:19622832}.
Q05639	Epileptic encephalopathy, early infantile, 33 (EIEE33) [MIM:616409]: A form of epileptic encephalopathy, a heterogeneous group of severe childhood onset epilepsies characterized by refractory seizures, neurodevelopmental impairment, and poor prognosis. Development is normal prior to seizure onset, after which cognitive and motor delays become apparent. {ECO:0000269|PubMed:23033978, ECO:0000269|PubMed:23647072}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Mental retardation, autosomal dominant 38 (MRD38) [MIM:616393]: A form of mental retardation, a disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. MRD38 common features are severe intellectual disability, autistic behavior, absent speech, neonatal hypotonia, epilepsy and progressive microcephaly. {ECO:0000269|PubMed:24697219}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O75762	Episodic pain syndrome, familial, 1 (FEPS1) [MIM:615040]: An autosomal dominant neurologic disorder characterized by onset in infancy of episodic debilitating upper body pain triggered by fasting, cold, and physical stress. The period of intense pain is accompanied by breathing difficulties, tachycardia, sweating, generalized pallor, peribuccal cyanosis, and stiffness of the abdominal wall. Affected individuals do not manifest altered pain sensitivity outside the episodes. {ECO:0000269|PubMed:20547126}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y252	Esophageal cancer (ESCR) [MIM:133239]: A malignancy of the esophagus. The most common types are esophageal squamous cell carcinoma and adenocarcinoma. Cancer of the esophagus remains a devastating disease because it is usually not detected until it has progressed to an advanced incurable stage. {ECO:0000269|PubMed:12154016}. Note=The disease may be caused by mutations affecting the gene represented in this entry.
P00734	Factor II deficiency (FA2D) [MIM:613679]: A very rare blood coagulation disorder characterized by mucocutaneous bleeding symptoms. The severity of the bleeding manifestations correlates with blood factor II levels. {ECO:0000269|PubMed:1349838, ECO:0000269|PubMed:1354985, ECO:0000269|PubMed:1421398, ECO:0000269|PubMed:14962227, ECO:0000269|PubMed:2719946,

	ECO:0000269|PubMed:3242619, ECO:0000269|PubMed:3567158, ECO:0000269|PubMed:3771562, ECO:0000269|PubMed:3801671, ECO:0000269|PubMed:6405779, ECO:0000269|PubMed:7792730, ECO:0000269|PubMed:7865694}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Ischemic stroke (ISCHSTR) [MIM:601367]: A stroke is an acute neurologic event leading to death of neural tissue of the brain and resulting in loss of motor, sensory and/or cognitive function. Ischemic strokes, resulting from vascular occlusion, is considered to be a highly complex disease consisting of a group of heterogeneous disorders with multiple genetic and environmental risk factors. {ECO:0000269|PubMed:15534175}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.; Thrombophilia due to thrombin defect (THPH1) [MIM:188050]: A multifactorial disorder of hemostasis characterized by abnormal platelet aggregation in response to various agents and recurrent thrombi formation. Note=The disease is caused by mutations affecting the gene represented in this entry. A common genetic variation in the 3-prime untranslated region of the prothrombin gene is associated with elevated plasma prothrombin levels and an increased risk of venous thrombosis.; Pregnancy loss, recurrent, 2 (RPRGL2) [MIM:614390]: A common complication of pregnancy, resulting in spontaneous abortion before the fetus has reached viability. The term includes all miscarriages from the time of conception until 24 weeks of gestation. Recurrent pregnancy loss is defined as 3 or more consecutive spontaneous abortions. {ECO:0000269|PubMed:11506076}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
P08709	Factor VII deficiency (FA7D) [MIM:227500]: A hemorrhagic disease with variable presentation. The clinical picture can be very severe, with the early occurrence of intracerebral hemorrhages or repeated hemarthroses, or, in contrast, moderate with cutaneous-mucosal hemorrhages (epistaxis, menorrhagia) or hemorrhages provoked by a surgical intervention. Finally, numerous subjects are completely asymptomatic despite very low factor VII levels. {ECO:0000269|PubMed:10862079, ECO:0000269|PubMed:11091194, ECO:0000269|PubMed:11129332, ECO:0000269|PubMed:12472587, ECO:0000269|PubMed:14717781, ECO:0000269|PubMed:1634227, ECO:0000269|PubMed:18976247, ECO:0000269|PubMed:19432927, ECO:0000269|PubMed:19751712, ECO:0000269|PubMed:2070047, ECO:0000269|PubMed:21206266, ECO:0000269|PubMed:21372693, ECO:0000269|PubMed:7974346, ECO:0000269|PubMed:7981691, ECO:0000269|PubMed:8043443, ECO:0000269|PubMed:8204879, ECO:0000269|PubMed:8364544, ECO:0000269|PubMed:8652821, ECO:0000269|PubMed:8844208, ECO:0000269|PubMed:8883260, ECO:0000269|PubMed:8940045, ECO:0000269|PubMed:9414278, ECO:0000269|PubMed:9452082, ECO:0000269|PubMed:9576180}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P00742	Factor X deficiency (FA10D) [MIM:227600]: A hemorrhagic disease with variable presentation. Affected individuals can manifest prolonged nasal and mucosal hemorrhage, menorrhagia, hematuria, and occasionally hemarthrosis. Some patients do not have clinical bleeding diathesis. {ECO:0000269|PubMed:10468877, ECO:0000269|PubMed:10746568, ECO:0000269|PubMed:11248282, ECO:0000269|PubMed:11728527, ECO:0000269|PubMed:12574802, ECO:0000269|PubMed:12945883, ECO:0000269|PubMed:15075089, ECO:0000269|PubMed:15650540, ECO:0000269|PubMed:17393015, ECO:0000269|PubMed:19135706, ECO:0000269|PubMed:1973167, ECO:0000269|PubMed:1985698, ECO:0000269|PubMed:25313940, ECO:0000269|PubMed:2790181, ECO:0000269|PubMed:7669671, ECO:0000269|PubMed:7860069, ECO:0000269|PubMed:8529633, ECO:0000269|PubMed:8845463, ECO:0000269|PubMed:8910490}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P03951	Factor XI deficiency (FA11D) [MIM:612416]: A hemorrhagic disease characterized by reduced levels and activity of factor XI resulting in moderate bleeding symptoms, usually occurring after trauma or surgery. Patients usually do not present spontaneous bleeding but women can present with menorrhagia. Hemorrhages are usually moderate. {ECO:0000269|PubMed:10027710, ECO:0000269|PubMed:10606881, ECO:0000269|PubMed:11895778, ECO:0000269|PubMed:15026311, ECO:0000269|PubMed:15180874, ECO:0000269|PubMed:1547342, ECO:0000269|PubMed:15953011, ECO:0000269|PubMed:16607084, ECO:0000269|PubMed:18005151, ECO:0000269|PubMed:21457405, ECO:0000269|PubMed:21668437, ECO:0000269|PubMed:21999818, ECO:0000269|PubMed:22016685, ECO:0000269|PubMed:22159456, ECO:0000269|PubMed:22322133, ECO:0000269|PubMed:2813350, ECO:0000269|PubMed:7669672, ECO:0000269|PubMed:7888672, ECO:0000269|PubMed:9401068, ECO:0000269|PubMed:9787168}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P00748	Factor XII deficiency (FA12D) [MIM:234000]: An asymptomatic anomaly of in vitro blood coagulation. Its diagnosis is based on finding a low plasma activity of the factor in coagulating assays. It is usually only accidentally discovered through pre-operative blood tests. Factor XII deficiency is divided into two categories, a cross-reacting material (CRM)-negative group (negative F12 antigen detection) and a CRM-

	positive group (positive F12 antigen detection). {ECO:0000269|PubMed:10361128, ECO:0000269|PubMed:11776307, ECO:0000269|PubMed:15205584, ECO:0000269|PubMed:15617741, ECO:0000269|PubMed:2510163, ECO:0000269|PubMed:2882793, ECO:0000269|PubMed:8049433, ECO:0000269|PubMed:8528215, ECO:0000269|PubMed:9354665}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Hereditary angioedema 3 (HAE3) [MIM:610618]: An hereditary angioedema occurring only in women. Hereditary angioedema is an autosomal dominant disorder characterized by episodic local swelling involving subcutaneous or submucous tissue of the upper respiratory and gastrointestinal tracts, face, extremities, and genitalia. Hereditary angioedema type 3 differs from types 1 and 2 in that both concentration and function of C1 esterase inhibitor are normal. Hereditary angioedema type 3 is precipitated or worsened by high estrogen levels (e.g., during pregnancy or treatment with oral contraceptives). {ECO:0000269|PubMed:16638441, ECO:0000269|PubMed:17186468}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NPI8	Fanconi anemia complementation group F (FANCF) [MIM:603467]: A disorder affecting all bone marrow elements and resulting in anemia, leukopenia and thrombopenia. It is associated with cardiac, renal and limb malformations, dermal pigmentary changes, and a predisposition to the development of malignancies. At the cellular level it is associated with hypersensitivity to DNA-damaging agents, chromosomal instability (increased chromosome breakage) and defective DNA repair. {ECO:0000269|PubMed:10615118}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8IYD8	Fanconi anemia complementation group M (FANCM) [MIM:614087]: A disorder affecting all bone marrow elements and resulting in anemia, leukopenia and thrombopenia. It is associated with cardiac, renal and limb malformations, dermal pigmentary changes, and a predisposition to the development of malignancies. At the cellular level it is associated with hypersensitivity to DNA-damaging agents, chromosomal instability (increased chromosome breakage) and defective DNA repair. {ECO:0000269|PubMed:16116422}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q7Z4S6	Fibrosis of extraocular muscles, congenital, 1 (CFEOM1) [MIM:135700]: A congenital ocular motility disorder marked by restrictive ophthalmoplegia affecting extraocular muscles innervated by the oculomotor and/or trochlear nerves. It is clinically characterized by anchoring of the eyes in downward gaze, ptosis, and backward tilt of the head. Patients affected by congenital fibrosis of extraocular muscles type 1 show an absence of the superior division of the oculomotor nerve (cranial nerve III) and corresponding oculomotor subnuclei. {ECO:0000269|PubMed:14595441, ECO:0000269|PubMed:16157808}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q06787	Fragile X syndrome (FRAX) [MIM:300624]: Common genetic disease (has a prevalence of one in every 2000 children) which is characterized by moderate to severe mental retardation, macroorchidism (enlargement of the testicles), large ears, prominent jaw, and high-pitched, jocular speech. The defect in most fragile X syndrome patients results from an amplification of a CGG repeat region which is directly in front of the coding region. {ECO:0000269|PubMed:7688265, ECO:0000269|PubMed:8401578, ECO:0000269|PubMed:8490650}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Fragile X tremor/ataxia syndrome (FXTAS) [MIM:300623]: In FXTAS, the expanded repeats range in size from 55 to 200 repeats and are referred to as 'premutations'. Full repeat expansions with greater than 200 repeats results in fragile X mental retardation syndrome [MIM:300624]. Carriers of the premutation typically do not show the full fragile X syndrome phenotype, but comprise a subgroup that may have some physical features of fragile X syndrome or mild cognitive and emotional problems. {ECO:0000269|PubMed:11445641}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Premature ovarian failure 1 (POF1) [MIM:311360]: An ovarian disorder defined as the cessation of ovarian function under the age of 40 years. It is characterized by oligomenorrhea or amenorrhea, in the presence of elevated levels of serum gonadotropins and low estradiol. {ECO:0000269|PubMed:9719368}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q96LT7	Frontotemporal dementia and/or amyotrophic lateral sclerosis 1 (FTDALS1) [MIM:105550]: An autosomal dominant neurodegenerative disorder characterized by adult onset of frontotemporal dementia and/or amyotrophic lateral sclerosis in an affected individual. There is high intrafamilial variation. Frontotemporal dementia is characterized by frontal and temporal lobe atrophy associated with neuronal loss, gliosis, and dementia. Patients exhibit progressive changes in social, behavioral, and/or language function. Amyotrophic lateral sclerosis is characterized by the death of motor neurons in the brain, brainstem, and spinal cord, resulting in fatal paralysis. {ECO:0000269|PubMed:21944778, ECO:0000269|PubMed:21944779, ECO:0000269|PubMed:22936364}. Note=The disease is caused by

	mutations affecting the gene represented in this entry. In the first intron of the gene, the expansion of a GGGGCC hexanucleotide that can vary from 10 to thousands of repeats, represents the most common genetic cause of both familial and sporadic FTDALS. The hexanucleotide repeat expansion (HRE) is structurally polymorphic and during transcription, is responsible for the formation of RNA and DNA G-quadruplexes resulting in the production of aborted transcripts at the expense of functional transcripts. The accumulation of those aborted transcripts may cause nucleolar stress and indirectly cell death (PubMed:24598541). {ECO:0000269|PubMed:24598541}.
Q5TAQ9	Giant axonal neuropathy 2, autosomal dominant (GAN2) [MIM:610100]: An autosomal dominant peripheral axonal neuropathy characterized by onset of distal sensory impairment with lower extremity muscle weakness and atrophy after the second decade. Clinical features include foot deformities apparent in childhood, and cardiomyopathy in severely affected individuals. Sural nerve biopsy shows giant axonal swelling with neurofilament accumulation. {ECO:0000269|PubMed:24500646}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q96PX8	Gilles de la Tourette syndrome (GTS) [MIM:137580]: Neurologic disorder manifested particularly by motor and vocal tics and associated with behavioral abnormalities. {ECO:0000269|PubMed:16224024}. Note=The disease may be caused by mutations affecting the gene represented in this entry.; Trichotillomania (TTM) [MIM:613229]: A neuropsychiatric disorder characterized by chronic, repetitive, or compulsive hair pulling resulting in noticeable hair loss. Affected individuals may develop physical complications and often have overlapping psychological disorders, such as Gilles de la Tourette syndrome or obsessive-compulsive disorder. {ECO:0000269|PubMed:16224024}. Note=The disease may be caused by mutations affecting the gene represented in this entry.
Q8WXI3	Glaucoma 1, open angle, F (GLC1F) [MIM:603383]: A form of primary open angle glaucoma (POAG). POAG is characterized by a specific pattern of optic nerve and visual field defects. The angle of the anterior chamber of the eye is open, and usually the intraocular pressure is increased. However, glaucoma can occur at any intraocular pressure. The disease is generally asymptomatic until the late stages, by which time significant and irreversible optic nerve damage has already taken place. {ECO:0000269|PubMed:22156576}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8NI36	Glaucoma 1, open angle, G (GLC1G) [MIM:609887]: A form of primary open angle glaucoma (POAG). POAG is characterized by a specific pattern of optic nerve and visual field defects. The angle of the anterior chamber of the eye is open, and usually the intraocular pressure is increased. However, glaucoma can occur at any intraocular pressure. The disease is generally asymptomatic until the late stages, by which time significant and irreversible optic nerve damage has already taken place. {ECO:0000269|PubMed:15677485}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P15735	Glycogen storage disease 9C (GSD9C) [MIM:613027]: A metabolic disorder manifesting in infancy with hepatomegaly, growth retardation, hypotonia, liver dysfunction, and elevated plasma aminotransferases and lipids. These symptoms improve with age in most cases; however, some patients may develop hepatic fibrosis or cirrhosis. {ECO:0000269|PubMed:12930917, ECO:0000269|PubMed:8896567, ECO:0000269|PubMed:9245685}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9C0B1	Growth retardation developmental delay coarse facies early death (GDFD) [MIM:612938]: A severe polymalformation syndrome characterized by postnatal growth retardation, microcephaly, severe psychomotor delay, functional brain deficits and characteristic facial dysmorphism. In some patients, structural brain malformations, cardiac defects, genital anomalies, and cleft palate are observed. Early death occurs by the age of 3 years. {ECO:0000269|PubMed:19559399}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P05156	Hemolytic uremic syndrome atypical 3 (AHUS3) [MIM:612923]: An atypical form of hemolytic uremic syndrome. It is a complex genetic disease characterized by microangiopathic hemolytic anemia, thrombocytopenia, renal failure and absence of episodes of enterocolitis and diarrhea. In contrast to typical hemolytic uremic syndrome, atypical forms have a poorer prognosis, with higher death rates and frequent progression to end-stage renal disease. {ECO:0000269|PubMed:15173250, ECO:0000269|PubMed:16621965, ECO:0000269|PubMed:17106690, ECO:0000269|PubMed:20513133}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry. Other genes may play a role in modifying the phenotype.; Complement factor I deficiency (CFI deficiency) [MIM:610984]: Autosomal recessive condition associated with a propensity to pyogenic infections. {ECO:0000269|PubMed:12562389, ECO:0000269|PubMed:17018561, ECO:0000269|PubMed:8613545}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Macular degeneration, age-related, 13 (ARMD13) [MIM:615439]: A form of age-related macular degeneration, a multifactorial eye disease and the most common cause of irreversible

	vision loss in the developed world. In most patients, the disease is manifest as ophthalmoscopically visible yellowish accumulations of protein and lipid that lie beneath the retinal pigment epithelium and within an elastin-containing structure known as Bruch membrane. {ECO:0000269|PubMed:23685748}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
P00751	Hemolytic uremic syndrome atypical 4 (AHUS4) [MIM:612924]: An atypical form of hemolytic uremic syndrome. It is a complex genetic disease characterized by microangiopathic hemolytic anemia, thrombocytopenia, renal failure and absence of episodes of enterocolitis and diarrhea. In contrast to typical hemolytic uremic syndrome, atypical forms have a poorer prognosis, with higher death rates and frequent progression to end-stage renal disease. {ECO:0000269|PubMed:17182750, ECO:0000269|PubMed:20513133}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry. Susceptibility to the development of atypical hemolytic uremic syndrome can be conferred by mutations in various components of or regulatory factors in the complement cascade system. Other genes may play a role in modifying the phenotype.; Complement factor B deficiency (CFBD) [MIM:615561]: An immunologic disorder characterized by increased susceptibility to bacterial infections, particularly Neisseria infections, due to a defect in the alternative complement pathway. {ECO:0000269|PubMed:24152280}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P00740	Hemophilia B (HEMB) [MIM:306900]: An X-linked blood coagulation disorder characterized by a permanent tendency to hemorrhage, due to factor IX deficiency. It is phenotypically similar to hemophilia A, but patients present with fewer symptoms. Many patients are asymptomatic until the hemostatic system is stressed by surgery or trauma. {ECO:0000269|PubMed:10094553, ECO:0000269|PubMed:10698280, ECO:0000269|PubMed:11122099, ECO:0000269|PubMed:12588353, ECO:0000269|PubMed:12604421, ECO:0000269|PubMed:1346975, ECO:0000269|PubMed:1615485, ECO:0000269|PubMed:1902289, ECO:0000269|PubMed:1958666, ECO:0000269|PubMed:2162822, ECO:0000269|PubMed:2339358, ECO:0000269|PubMed:2372509, ECO:0000269|PubMed:2472424, ECO:0000269|PubMed:25470321, ECO:0000269|PubMed:2592373, ECO:0000269|PubMed:2713493, ECO:0000269|PubMed:2714791, ECO:0000269|PubMed:2738071, ECO:0000269|PubMed:2753873, ECO:0000269|PubMed:2773937, ECO:0000269|PubMed:2775660, ECO:0000269|PubMed:3009023, ECO:0000269|PubMed:3243764, ECO:0000269|PubMed:3401602, ECO:0000269|PubMed:3790720, ECO:0000269|PubMed:6603618, ECO:0000269|PubMed:7981722, ECO:0000269|PubMed:8076946, ECO:0000269|PubMed:8199596, ECO:0000269|PubMed:8257988, ECO:0000269|PubMed:8295821, ECO:0000269|PubMed:8680410, ECO:0000269|PubMed:9222764, ECO:0000269|PubMed:9452115, ECO:0000269|PubMed:9590153, ECO:0000269|PubMed:9600455}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Note=Mutations in position 43 (Oxford-3, San Dimas) and 46 (Cambridge) prevents cleavage of the propeptide, mutation in position 93 (Alabama) probably fails to bind to cell membranes, mutation in position 191 (Chapel-Hill) or in position 226 (Nagoya OR Hilo) prevent cleavage of the activation peptide.; Thrombophilia, X-linked, due to factor IX defect (THPH8) [MIM:300807]: A hemostatic disorder characterized by a tendency to thrombosis. {ECO:0000269|PubMed:19846852}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P43246	Hereditary non-polyposis colorectal cancer 1 (HNPCC1) [MIM:120435]: An autosomal dominant disease associated with marked increase in cancer susceptibility. It is characterized by a familial predisposition to early-onset colorectal carcinoma (CRC) and extra-colonic tumors of the gastrointestinal, urological and female reproductive tracts. HNPCC is reported to be the most common form of inherited colorectal cancer in the Western world. Clinically, HNPCC is often divided into two subgroups. Type I is characterized by hereditary predisposition to colorectal cancer, a young age of onset, and carcinoma observed in the proximal colon. Type II is characterized by increased risk for cancers in certain tissues such as the uterus, ovary, breast, stomach, small intestine, skin, and larynx in addition to the colon. Diagnosis of classical HNPCC is based on the Amsterdam criteria: 3 or more relatives affected by colorectal cancer, one a first degree relative of the other two; 2 or more generation affected; 1 or more colorectal cancers presenting before 50 years of age; exclusion of hereditary polyposis syndromes. The term 'suspected HNPCC' or 'incomplete HNPCC' can be used to describe families who do not or only partially fulfill the Amsterdam criteria, but in whom a genetic basis for colon cancer is strongly suspected. {ECO:0000269|PubMed:10375096, ECO:0000269|PubMed:10386556, ECO:0000269|PubMed:10528862, ECO:0000269|PubMed:10573010, ECO:0000269|PubMed:10612836, ECO:0000269|PubMed:10777691, ECO:0000269|PubMed:10829038, ECO:0000269|PubMed:11726306, ECO:0000269|PubMed:11870161, ECO:0000269|PubMed:11920458, ECO:0000269|PubMed:12112654, ECO:0000269|PubMed:12124176, ECO:0000269|PubMed:12132870, ECO:0000269|PubMed:12200596, ECO:0000269|PubMed:12362047, ECO:0000269|PubMed:12373605, ECO:0000269|PubMed:12655564, ECO:0000269|PubMed:12655568, ECO:0000269|PubMed:12658575, ECO:0000269|PubMed:14635101, ECO:0000269|PubMed:15046096, ECO:0000269|PubMed:15300854, ECO:0000269|PubMed:15342696,

	ECO:0000269|PubMed:15365995, ECO:0000269|PubMed:15613555, ECO:0000269|PubMed:15870828, ECO:0000269|PubMed:15896463, ECO:0000269|PubMed:15991316, ECO:0000269|PubMed:15996210, ECO:0000269|PubMed:16451135, ECO:0000269|PubMed:17101317, ECO:0000269|PubMed:17128465, ECO:0000269|PubMed:18561205, ECO:0000269|PubMed:18625694, ECO:0000269|PubMed:22371642, ECO:0000269|PubMed:7874129, ECO:0000269|PubMed:8261515, ECO:0000269|PubMed:8700523, ECO:0000269|PubMed:8872463, ECO:0000269|PubMed:9048925, ECO:0000269|PubMed:9240418, ECO:0000269|PubMed:9298827, ECO:0000269|PubMed:9311737, ECO:0000269|PubMed:9419403, ECO:0000269|PubMed:9559627, ECO:0000269|PubMed:9718327}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Muir-Torre syndrome (MRTES) [MIM:158320]: Rare autosomal dominant disorder characterized by sebaceous neoplasms and visceral malignancy. {ECO:0000269|PubMed:7713503}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Endometrial cancer (ENDMC) [MIM:608089]: A malignancy of endometrium, the mucous lining of the uterus. Most endometrial cancers are adenocarcinomas, cancers that begin in cells that make and release mucus and other fluids. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
P52701	Hereditary non-polyposis colorectal cancer 5 (HNPCC5) [MIM:614350]: An autosomal dominant disease associated with marked increase in cancer susceptibility. It is characterized by a familial predisposition to early-onset colorectal carcinoma (CRC) and extra-colonic tumors of the gastrointestinal, urological and female reproductive tracts. HNPCC is reported to be the most common form of inherited colorectal cancer in the Western world. Clinically, HNPCC is often divided into two subgroups. Type I is characterized by hereditary predisposition to colorectal cancer, a young age of onset, and carcinoma observed in the proximal colon. Type II is characterized by increased risk for cancers in certain tissues such as the uterus, ovary, breast, stomach, small intestine, skin, and larynx in addition to the colon. Diagnosis of classical HNPCC is based on the Amsterdam criteria: 3 or more relatives affected by colorectal cancer, one a first degree relative of the other two; 2 or more generation affected; 1 or more colorectal cancers presenting before 50 years of age; exclusion of hereditary polyposis syndromes. The term 'suspected HNPCC' or 'incomplete HNPCC' can be used to describe families who do not or only partially fulfill the Amsterdam criteria, but in whom a genetic basis for colon cancer is strongly suspected. {ECO:0000269|PubMed:10480359, ECO:0000269|PubMed:10521294, ECO:0000269|PubMed:11586295, ECO:0000269|PubMed:12658575, ECO:0000269|PubMed:14974087, ECO:0000269|PubMed:15365995, ECO:0000269|PubMed:9354786}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Endometrial cancer (ENDMC) [MIM:608089]: A malignancy of endometrium, the mucous lining of the uterus. Most endometrial cancers are adenocarcinomas, cancers that begin in cells that make and release mucus and other fluids. {ECO:0000269|PubMed:11153917, ECO:0000269|PubMed:14961575}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.; Mismatch repair cancer syndrome (MMRCS) [MIM:276300]: An autosomal recessive, rare, childhood cancer predisposition syndrome encompassing a broad tumor spectrum. This includes hematological malignancies, central nervous system tumors, Lynch syndrome-associated malignancies such as colorectal tumors as well as multiple intestinal polyps, embryonic tumors and rhabdomyosarcoma. Multiple cafe-au-lait macules, a feature reminiscent of neurofibromatosis type 1, are often found as first manifestation of the underlying cancer. Areas of skin hypopigmentation have also been reported in MMRCS patients. {ECO:0000269|PubMed:17557300}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O15455	Herpes simplex encephalitis 2 (HSE2) [MIM:613002]: A rare complication of human herpesvirus 1 (HHV-1) infection, occurring in only a small minority of HHV-1 infected individuals. HSE is characterized by hemorrhagic necrosis of parts of the temporal and frontal lobes. Onset is over several days and involves fever, headache, seizures, stupor, and often coma, frequently with a fatal outcome. {ECO:0000269|PubMed:17872438}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry. TLR3 mutations predispose otherwise healthy individuals to isolated herpes simplex encephalitis through a mechanism that involves impaired IFNs production and reduced immune defense against viral infection in the central nervous system.
O60481	Heterotaxy, visceral, 1, X-linked (HTX1) [MIM:306955]: A form of visceral heterotaxy, a complex disorder due to disruption of the normal left-right asymmetry of the thoracoabdominal organs. Visceral heterotaxy or situs ambiguus results in randomization of the placement of visceral organs, including the heart, lungs, liver, spleen, and stomach. The organs are oriented randomly with respect to the left-right axis and with respect to one another. It can been associated with variety of congenital defects including cardiac malformations. {ECO:0000269|PubMed:14681828, ECO:0000269|PubMed:17295247, ECO:0000269|PubMed:24123890, ECO:0000269|PubMed:9354794}. Note=The disease is caused by mutations affecting the gene represented in this entry.; VACTERL association X-linked with or without hydrocephalus (VACTERLX) [MIM:314390]: A syndrome characterized by a non-random association of

	congenital defects. Affected individuals manifest vertebral anomalies (V), anal atresia (A), cardiac malformations (C), tracheoesophageal fistula (TE), renal anomalies (R) such as urethral atresia with hydronephrosis, and limb anomalies (L) such as hexadactyly, humeral hypoplasia, radial aplasia, and proximally placed thumb. Some patients may have hydrocephalus. Some cases of VACTERL-H are associated with increased chromosome breakage and rearrangement. {ECO:0000269|PubMed:20452998, ECO:0000269|PubMed:24123890}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Congenital heart defects, multiple types, 1, X-linked (CHTD1) [MIM:306955]: A disorder characterized by congenital developmental abnormalities involving structures of the heart. Common defects include transposition of the great arteries, aortic stenosis, atrial septal defect, ventricular septal defect, pulmonic stenosis, and patent ductus arteriosus. The etiology of CHTD is complex, with contributions from environmental exposure, chromosomal abnormalities, and gene defects. Some patients with CHTD also have cardiac arrhythmias, which may be due to the anatomic defect itself or to surgical interventions. {ECO:0000269|PubMed:14681828, ECO:0000269|PubMed:24123890}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O95477	High density lipoprotein deficiency 1 (HDLD1) [MIM:205400]: Recessive disorder characterized by absence of high density lipoprotein (HDL) cholesterol from plasma, accumulation of cholesteryl esters, premature coronary artery disease (CAD), hepatosplenomegaly, recurrent peripheral neuropathy and progressive muscle wasting and weakness. {ECO:0000269|PubMed:10431236, ECO:0000269|PubMed:10431237, ECO:0000269|PubMed:10706591, ECO:0000269|PubMed:10938021, ECO:0000269|PubMed:11086027, ECO:0000269|PubMed:11257260, ECO:0000269|PubMed:11476961, ECO:0000269|PubMed:11476965, ECO:0000269|PubMed:11785958, ECO:0000269|PubMed:12111371, ECO:0000269|PubMed:12111381, ECO:0000269|PubMed:12407001, ECO:0000269|PubMed:14576201, ECO:0000269|PubMed:15019541, ECO:0000269|PubMed:15158913, ECO:0000269|PubMed:15262183, ECO:0000269|PubMed:15297675, ECO:0000269|PubMed:15520867}. Note=The disease is caused by mutations affecting the gene represented in this entry.; High density lipoprotein deficiency 2 (HDLD2) [MIM:604091]: Inherited as autosomal dominant trait. It is characterized by moderately low HDL cholesterol, predilection toward premature coronary artery disease (CAD) and a reduction in cellular cholesterol efflux. {ECO:0000269|PubMed:10431236, ECO:0000269|PubMed:10533863, ECO:0000269|PubMed:10938021, ECO:0000269|PubMed:11086027, ECO:0000269|PubMed:12009425, ECO:0000269|PubMed:12204794, ECO:0000269|PubMed:15722566}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O95409	Holoprosencephaly 5 (HPE5) [MIM:609637]: A structural anomaly of the brain, in which the developing forebrain fails to correctly separate into right and left hemispheres. Holoprosencephaly is genetically heterogeneous and associated with several distinct facies and phenotypic variability. {ECO:0000269|PubMed:11285244, ECO:0000269|PubMed:15221788, ECO:0000269|PubMed:19177455}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NP81	Hyperuricemia, pulmonary hypertension, renal failure, and alkalosis syndrome (HUPRAS) [MIM:613845]: A multisystem disorder characterized by onset in infancy of progressive renal failure leading to electrolyte imbalances, metabolic alkalosis, pulmonary hypertension, hypotonia, and delayed development. Affected individuals are born prematurely. {ECO:0000269|PubMed:21255763}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NZU0	Hypogonadotropic hypogonadism 21 with or without anosmia (HH21) [MIM:615271]: A disorder characterized by absent or incomplete sexual maturation by the age of 18 years, in conjunction with low levels of circulating gonadotropins and testosterone and no other abnormalities of the hypothalamic-pituitary axis. In some cases, it is associated with non-reproductive phenotypes, such as anosmia, cleft palate, and sensorineural hearing loss. Anosmia or hyposmia is related to the absence or hypoplasia of the olfactory bulbs and tracts. Hypogonadism is due to deficiency in gonadotropin-releasing hormone and probably results from a failure of embryonic migration of gonadotropin-releasing hormone-synthesizing neurons. In the presence of anosmia, idiopathic hypogonadotropic hypogonadism is referred to as Kallmann syndrome, whereas in the presence of a normal sense of smell, it has been termed normosmic idiopathic hypogonadotropic hypogonadism (nIHH). {ECO:0000269|PubMed:23643382}. Note=The disease is caused by mutations affecting distinct genetic loci, including the gene represented in this entry. Some patients carrying mutations in FLRT3 also have a mutation in another HH-associated gene including FGFR1, HS6ST1 and FGF17 (PubMed:23643382). {ECO:0000269|PubMed:23643382}.
P14868	Hypomyelination with brainstem and spinal cord involvement and leg spasticity (HBSL) [MIM:615281]: An autosomal recessive leukoencephalopathy characterized by onset in the first year of life of severe spasticity, mainly affecting the lower limbs and resulting in an inability to achieve independent ambulation. Affected individuals show delayed motor development and nystagmus; some may have mild mental retardation. Brain MRI shows hypomyelination and white matter lesions in the cerebrum,

	brainstem, cerebellum, and spinal cord. {ECO:0000269|PubMed:23643384}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P62304	Hypotrichosis 11 (HYPT11) [MIM:615059]: A form of hypotrichosis, a condition characterized by the presence of less than the normal amount of hair and abnormal hair follicles and shafts, which are thin and atrophic. The extent of scalp and body hair involvement can be very variable, within as well as between families. HYPT11 is characterized by scanty or absent eyebrows and a highly variable degree of alopecia since birth, ranging from slight thinning of scalp and axillary hair to complete loss of scalp and body hair. Pubic hair remains mainly unaffected. {ECO:0000269|PubMed:23246290}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y5Y6	Ichthyosis, congenital, autosomal recessive 11 (ARCI11) [MIM:602400]: A form of autosomal recessive congenital ichthyosis, a disorder of keratinization with abnormal differentiation and desquamation of the epidermis, resulting in abnormal skin scaling over the whole body. The main skin phenotypes are lamellar ichthyosis (LI) and non-bullous congenital ichthyosiform erythroderma (NCIE), although phenotypic overlap within the same patient or among patients from the same family can occur. Lamellar ichthyosis is a condition often associated with an embedment in a collodion-like membrane at birth; skin scales later develop, covering the entire body surface. Non-bullous congenital ichthyosiform erythroderma characterized by fine whitish scaling on an erythrodermal background; larger brownish scales are present on the buttocks, neck and legs. {ECO:0000269|PubMed:17273967, ECO:0000269|PubMed:18843291}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q86UK0	Ichthyosis, congenital, autosomal recessive 4A (ARCI4A) [MIM:601277]: A form of autosomal recessive congenital ichthyosis, a disorder of keratinization with abnormal differentiation and desquamation of the epidermis, resulting in abnormal skin scaling over the whole body. The main skin phenotypes are lamellar ichthyosis (LI) and non-bullous congenital ichthyosiform erythroderma (NCIE), although phenotypic overlap within the same patient or among patients from the same family can occur. Lamellar ichthyosis is a condition often associated with an embedment in a collodion-like membrane at birth; skin scales later develop, covering the entire body surface. Non-bullous congenital ichthyosiform erythroderma characterized by fine whitish scaling on an erythrodermal background; larger brownish scales are present on the buttocks, neck and legs. {ECO:0000269|PubMed:12915478, ECO:0000269|PubMed:17508018, ECO:0000269|PubMed:18284401, ECO:0000269|PubMed:19262603, ECO:0000269|PubMed:22257947}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Ichthyosis, congenital, autosomal recessive 4B (ARCI4B) [MIM:242500]: A rare, very severe form of congenital ichthyosis, in which the neonate is born with a thick covering of armor-like scales. The skin dries out to form hard diamond-shaped plaques separated by fissures, resembling 'armor plating'. The normal facial features are severely affected, with distortion of the lips (eclabion), eyelids (ectropion), ears, and nostrils. Affected babies are often born prematurely and rarely survive the perinatal period. Babies who survive into infancy and beyond develop skin changes resembling severe non-bullous congenital ichthyosiform erythroderma. {ECO:0000269|PubMed:15756637, ECO:0000269|PubMed:16675967, ECO:0000269|PubMed:16902423}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O14920	Immunodeficiency 15 (IMD15) [MIM:615592]: An autosomal recessive primary immunodeficiency disorder characterized by onset in infancy of life-threatening bacterial, fungal, and viral infections and failure to thrive. Laboratory studies show hypo- or agammaglobulinemia with relatively normal numbers of B and T-cells, and impaired differentiation and activation of immune cells. {ECO:0000269|PubMed:24369075}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q02556	Immunodeficiency 32A (IMD32A) [MIM:614893]: An immunologic disorder characterized by abnormal peripheral blood myeloid phenotype with a marked loss of CD11C-positive/CD1C dendritic cells, resulting in selective susceptibility to mycobacterial infections. {ECO:0000269|PubMed:21524210}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Immunodeficiency 32B (IMD32B) [MIM:614894]: A life-threatening pediatric disease characterized by monocyte and dendritic cell deficiency, myeloproliferation, and susceptibility to severe opportunistic infections, including disseminated BCG infection and oral candidiasis. {ECO:0000269|PubMed:21524210}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P05161	Immunodeficiency 38, with basal ganglia calcification (IMD38) [MIM:616126]: A primary immunodeficiency predisposing individuals to severe clinical disease upon infection with weakly virulent mycobacteria, including Mycobacterium bovis Bacille Calmette-Guerin (BCG) vaccines. Patients are also susceptible to Salmonella and Mycobacterium tubercolosis infections. Affected individuals have intracranial calcification. {ECO:0000269|PubMed:22859821}. Note=The disease is caused by mutations affecting the gene represented in this entry.

Q92985	Immunodeficiency 39 (IMD39) [MIM:616345]: A primary immunodeficiency causing severe, life-threatening acute respiratory distress upon infection with H1N1 influenza A. {ECO:0000269|PubMed:25814066}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P31146	Immunodeficiency 8 (IMD8) [MIM:615401]: A disease of the immune system leading to recurrent infections, and characterized by CD4+ T-cells lymphopenia. Patients can develop B-cell lymphoproliferation associated with Epstein-Barr virus infection. {ECO:0000269|PubMed:19097825, ECO:0000269|PubMed:23522482}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9GZX7	Immunodeficiency with hyper-IgM 2 (HIGM2) [MIM:605258]: A rare immunodeficiency syndrome characterized by normal or elevated serum IgM levels with absence of IgG, IgA, and IgE. It results in a profound susceptibility to bacterial infections. {ECO:0000269|PubMed:11007475}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O43167	Immunodeficiency-centromeric instability-facial anomalies syndrome 2 (ICF2) [MIM:614069]: A rare disorder characterized by a variable immunodeficiency resulting in recurrent infections, facial anomalies, and branching of chromosomes 1, 9, and 16. Other variable symptoms include growth retardation, failure to thrive, and psychomotor retardation. Laboratory studies show limited hypomethylation of DNA in a small fraction of the genome in some, but not all, patients. {ECO:0000269|PubMed:21596365}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P50851	Immunodeficiency, common variable, 8, with autoimmunity (CVID8) [MIM:614700]: An autosomal recessive immunologic disorder associated with defective B-cell differentiation and decreased or absent antibody production. Affected individuals have early-childhood onset of recurrent infections, particularly respiratory infections, and also develop variable autoimmune disorders, including idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, and inflammatory bowel disease. {ECO:0000269|PubMed:22608502}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P01834	Immunoglobulin kappa light chain deficiency (IGKCD) [MIM:614102]: A disease characterized by the complete absence of immunoglobulin kappa chains. {ECO:0000269|PubMed:3931219}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P22626	Inclusion body myopathy with early-onset Paget disease with or without frontotemporal dementia 2 (IBMPFD2) [MIM:615422]: An autosomal dominant disease characterized by disabling muscle weakness clinically resembling to limb girdle muscular dystrophy, osteolytic bone lesions consistent with Paget disease, and premature frontotemporal dementia. Clinical features show incomplete penetrance. {ECO:0000269|PubMed:23455423}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P09651	Inclusion body myopathy with early-onset Paget disease with or without frontotemporal dementia 3 (IBMPFD3) [MIM:615424]: An autosomal dominant disease characterized by disabling muscle weakness clinically resembling to limb girdle muscular dystrophy, osteolytic bone lesions consistent with Paget disease, and premature frontotemporal dementia. Clinical features show incomplete penetrance. {ECO:0000269|PubMed:23455423}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Amyotrophic lateral sclerosis 20 (ALS20) [MIM:615426]: A neurodegenerative disorder affecting upper motor neurons in the brain and lower motor neurons in the brain stem and spinal cord, resulting in fatal paralysis. Sensory abnormalities are absent. The pathologic hallmarks of the disease include pallor of the corticospinal tract due to loss of motor neurons, presence of ubiquitin-positive inclusions within surviving motor neurons, and deposition of pathologic aggregates. The etiology of amyotrophic lateral sclerosis is likely to be multifactorial, involving both genetic and environmental factors. The disease is inherited in 5-10% of the cases. {ECO:0000269|PubMed:23455423}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q99798	Infantile cerebellar-retinal degeneration (ICRD) [MIM:614559]: A severe autosomal recessive neurodegenerative disorder characterized by onset between ages 2 and 6 months of truncal hypotonia, athetosis, seizures, and ophthalmologic abnormalities, particularly optic atrophy and retinal degeneration. Affected individuals show profound psychomotor retardation, with only some achieving rolling, sitting, or recognition of family. Brain MRI shows progressive cerebral and cerebellar degeneration. {ECO:0000269|PubMed:22405087, ECO:0000269|PubMed:25351951}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Optic atrophy 8 (OPA8) [MIM:616289]: A condition that features progressive visual loss in association with optic atrophy. Atrophy of the optic disk indicates a deficiency in the number of nerve fibers which arise in the retina and converge to form the optic disk, optic nerve, optic chiasm and optic tracts. {ECO:0000269|PubMed:25351951}. Note=The disease is caused by mutations affecting the gene represented in this entry.

Q9P2J5	Infantile liver failure syndrome 1 (ILFS1) [MIM:615438]: A life-threatening disorder of hepatic function that manifests with acute liver failure in the first few months of life. Clinical features include anemia, renal tubulopathy, developmental delay, seizures, failure to thrive, and liver steatosis and fibrosis. {ECO:0000269|PubMed:22607940}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P56192	Infantile liver failure syndrome 2 (ILFS2) [MIM:615486]: A life-threatening disorder of hepatic function that manifests with liver failure in the first months of life. Clinical features include failure to thrive, hypotonia, intermittent lactic acidosis, aminoaciduria, hypothyroidism, interstitial lung disease, anemia, liver canalicular cholestasis, steatosis, and iron deposition. {ECO:0000269|PubMed:24103465}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Charcot-Marie-Tooth disease 2U (CMT2U) [MIM:616280]: An axonal form of Charcot-Marie-Tooth disease, a disorder of the peripheral nervous system, characterized by progressive weakness and atrophy, initially of the peroneal muscles and later of the distal muscles of the arms. Charcot-Marie-Tooth disease is classified in two main groups on the basis of electrophysiologic properties and histopathology: primary peripheral demyelinating neuropathies (designated CMT1 when they are dominantly inherited) and primary peripheral axonal neuropathies (CMT2). Neuropathies of the CMT2 group are characterized by signs of axonal degeneration in the absence of obvious myelin alterations, normal or slightly reduced nerve conduction velocities, and progressive distal muscle weakness and atrophy. CMT2U is a slowly progressive, autosomal dominant form characterized by late-adult onset. {ECO:0000269|PubMed:23729695, ECO:0000269|PubMed:24354524}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q676U5	Inflammatory bowel disease 10 (IBD10) [MIM:611081]: A chronic, relapsing inflammation of the gastrointestinal tract with a complex etiology. It is subdivided into Crohn disease and ulcerative colitis phenotypes. Crohn disease may affect any part of the gastrointestinal tract from the mouth to the anus, but most frequently it involves the terminal ileum and colon. Bowel inflammation is transmural and discontinuous; it may contain granulomas or be associated with intestinal or perianal fistulas. In contrast, in ulcerative colitis, the inflammation is continuous and limited to rectal and colonic mucosal layers; fistulas and granulomas are not observed. Both diseases include extraintestinal inflammation of the skin, eyes, or joints. {ECO:0000269|PubMed:17200669, ECO:0000269|PubMed:17435756}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
P08183	Inflammatory bowel disease 13 (IBD13) [MIM:612244]: A chronic, relapsing inflammation of the gastrointestinal tract with a complex etiology. It is subdivided into Crohn disease and ulcerative colitis phenotypes. Crohn disease may affect any part of the gastrointestinal tract from the mouth to the anus, but most frequently it involves the terminal ileum and colon. Bowel inflammation is transmural and discontinuous; it may contain granulomas or be associated with intestinal or perianal fistulas. In contrast, in ulcerative colitis, the inflammation is continuous and limited to rectal and colonic mucosal layers; fistulas and granulomas are not observed. Both diseases include extraintestinal inflammation of the skin, eyes, or joints. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
Q13568	Inflammatory bowel disease 14 (IBD14) [MIM:612245]: A chronic, relapsing inflammation of the gastrointestinal tract with a complex etiology. It is subdivided into Crohn disease and ulcerative colitis phenotypes. Crohn disease may affect any part of the gastrointestinal tract from the mouth to the anus, but most frequently it involves the terminal ileum and colon. Bowel inflammation is transmural and discontinuous; it may contain granulomas or be associated with intestinal or perianal fistulas. In contrast, in ulcerative colitis, the inflammation is continuous and limited to rectal and colonic mucosal layers; fistulas and granulomas are not observed. Both diseases include extraintestinal inflammation of the skin, eyes, or joints. {ECO:0000269|PubMed:17881657}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.; Systemic lupus erythematosus 10 (SLEB10) [MIM:612251]: A chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys and serosal membranes. It is of unknown etiology, but is thought to represent a failure of the regulatory mechanisms of the autoimmune system. The disease is marked by a wide range of system dysfunctions, an elevated erythrocyte sedimentation rate, and the formation of LE cells in the blood or bone marrow. {ECO:0000269|PubMed:15657875}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.; Rheumatoid arthritis (RA) [MIM:180300]: An inflammatory disease with autoimmune features and a complex genetic component. It primarily affects the joints and is characterized by inflammatory changes in the synovial membranes and articular structures, widespread fibrinoid degeneration of the collagen fibers in mesenchymal tissues, and by atrophy and rarefaction of bony structures. {ECO:0000269|PubMed:17599733}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.

Q8IU80	Iron-refractory iron deficiency anemia (IRIDA) [MIM:206200]: Key features include congenital hypochromic microcytic anemia, very low mean corpuscular erythrocyte volume, low transferrin saturation, abnormal iron absorption characterized by no hematologic improvement following treatment with oral iron, and abnormal iron utilization characterized by a sluggish, incomplete response to parenteral iron. {ECO:0000269|PubMed:18408718, ECO:0000269|PubMed:18603562, ECO:0000269|PubMed:19357398, ECO:0000269|PubMed:19592582, ECO:0000269|PubMed:19708871, ECO:0000269|PubMed:19747362, ECO:0000269|PubMed:20232450, ECO:0000269|PubMed:20704562, ECO:0000269|PubMed:21618415, ECO:0000269|PubMed:22581667, ECO:0000269|PubMed:25156943, ECO:0000269|PubMed:25588876}. Note=The disease is caused by mutations affecting the gene represented in this entry. Mutations leading to abrogation of TMPRSS6 activity are associated with IRIDA due to elevated levels of hepcidin, a negative regulator of plasma iron pool (PubMed:20232450). {ECO:0000269|PubMed:20232450}.
P24723	Ischemic stroke (ISCHSTR) [MIM:601367]: A stroke is an acute neurologic event leading to death of neural tissue of the brain and resulting in loss of motor, sensory and/or cognitive function. Ischemic strokes, resulting from vascular occlusion, is considered to be a highly complex disease consisting of a group of heterogeneous disorders with multiple genetic and environmental risk factors. {ECO:0000269|PubMed:17206144}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
Q8N157	Joubert syndrome 3 (JBTS3) [MIM:608629]: A disorder presenting with cerebellar ataxia, oculomotor apraxia, hypotonia, neonatal breathing abnormalities and psychomotor delay. Neuroradiologically, it is characterized by cerebellar vermian hypoplasia/aplasia, thickened and reoriented superior cerebellar peduncles, and an abnormally large interpeduncular fossa, giving the appearance of a molar tooth on transaxial slices (molar tooth sign). Additional variable features include retinal dystrophy and renal disease. Joubert syndrome type 3 shows minimal extra central nervous system involvement and appears not to be associated with renal dysfunction. {ECO:0000269|PubMed:15322546, ECO:0000269|PubMed:15467982, ECO:0000269|PubMed:16453322, ECO:0000269|PubMed:22425360, ECO:0000269|PubMed:23532844}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O15550	Kabuki syndrome 2 (KABUK2) [MIM:300867]: A congenital mental retardation syndrome with additional features, including postnatal dwarfism, a peculiar facies characterized by long palpebral fissures with eversion of the lateral third of the lower eyelids, a broad and depressed nasal tip, large prominent earlobes, a cleft or high-arched palate, scoliosis, short fifth finger, persistence of fingerpads, radiographic abnormalities of the vertebrae, hands, and hip joints, and recurrent otitis media in infancy. {ECO:0000269|PubMed:22197486}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9H9B1	Kleefstra syndrome (KLESTS) [MIM:610253]: A syndrome characterized by severe mental retardation, hypotonia, brachy(micro)cephaly, and facial dysmorphisms. Additionally, congenital heart defects, urogenital defects, epilepsy and behavioral problems are frequently observed. {ECO:0000269|PubMed:16826528, ECO:0000269|PubMed:19264732}. Note=The disease is caused by mutations affecting the gene represented in this entry (PubMed:16826528). The syndrome can be either caused by intragenic EHMT1 mutations leading to haploinsufficiency of the EHMT1 gene or by a submicroscopic 9q34.3 deletion. Although it is not known if and to what extent other genes in the 9q34.3 region contribute to the syndrome observed in deletion cases, EHMT1 seems to be the major determinant of the core disease phenotype (PubMed:19264732). {ECO:0000269|PubMed:16826528, ECO:0000269|PubMed:19264732}.
Q8N302	Klippel-Trenaunay syndrome (KTS) [MIM:149000]: Congenital disease characterized by malformations of capillary (98% of KTS patients), venous (72%) and lymphatic (11%) vessels, and bony and soft tissue hypertrophy that leads to large cutaneous hemangiomata with hypertrophy of the related bones and soft tissues. {ECO:0000269|PubMed:14961121}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O75054	Lacrimal duct defect (LCDD) [MIM:149700]: A condition resulting in the imbalance between tear production and tear drainage. Infants typically manifest persistent epiphora and/or recurrent infections of the lacrimal pathway, such as conjunctivitis. LCDD is caused by failure of the nasolacrimal duct to open into the inferior meatus. {ECO:0000269|PubMed:24372406}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q86YT6	Left ventricular non-compaction 7 (LVNC7) [MIM:615092]: A disease due to an arrest of myocardial morphogenesis. It is characterized by a hypertrophic left ventricle with deep trabeculations and with poor systolic function, with or without associated left ventricular dilation. In some cases, it is associated with other congenital heart anomalies. {ECO:0000269|PubMed:23314057}. Note=The disease is caused by mutations affecting the gene represented in this entry.

Q9HAZ2	Left ventricular non-compaction 8 (LVNC8) [MIM:615373]: A disease due to an arrest of myocardial morphogenesis. It is characterized by a hypertrophic left ventricle with deep trabeculations and with poor systolic function, with or without associated left ventricular dilation. In some cases, it is associated with other congenital heart anomalies. {ECO:0000269|PubMed:23768516}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Cardiomyopathy, dilated 1LL (CMD1LL) [MIM:615373]: A disorder characterized by ventricular dilation and impaired systolic function, resulting in congestive heart failure and arrhythmia. Patients are at risk of premature death. {ECO:0000269|PubMed:23768516}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Note=A chromosomal aberration involving PRDM16 is found in myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). Reciprocal translocation t(1;3)(p36;q21). Isoform 4 is specifically expressed in adult T-cell leukemia.
P42704	Leigh syndrome French-Canadian type (LSFC) [MIM:220111]: Severe neurological disorder characterized by bilaterally symmetrical necrotic lesions in subcortical brain regions that is commonly associated with systemic cytochrome c oxidase (COX) deficiency. In the Saguenay-Lac Saint Jean region of Quebec province in Canada, a biochemically distinct form of Leigh syndrome with COX deficiency has been described. Patients have been observed to have a developmental delay, hypotonia, mild facial dysmorphism, chronic well-compensated metabolic acidosis, and high mortality due to episodes of severe acidosis and coma. Enzyme activity was close to normal in kidney and heart, 50% of normal in fibroblasts and skeletal muscle, and nearly absent in brain and liver. LSFC patients show reduced (<30%) levels of LRPPRC in both fibroblast and liver mitochondria and a specifically reduced translation of COX subunits MT-CO1/COXI and MT-CO3 (COXIII). {ECO:0000269|PubMed:12529507}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q53GS7	Lethal congenital contracture syndrome 1 (LCCS1) [MIM:253310]: A form of lethal congenital contracture syndrome, an autosomal recessive disorder characterized by degeneration of anterior horn neurons, extreme skeletal muscle atrophy, and congenital non-progressive joint contractures (arthrogryposis). The contractures can involve the upper or lower limbs and/or the vertebral column, leading to various degrees of flexion or extension limitations evident at birth. LCCS1 patients manifest early fetal hydrops and akinesia, micrognathia, pulmonary hypoplasia, pterygia, and multiple joint contractures. It leads to prenatal death. {ECO:0000269|PubMed:18204449}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Lethal arthrogryposis with anterior horn cell disease (LAAHD) [MIM:611890]: A disorder characterized by fetal akinesia, arthrogryposis and motor neuron loss. The fetus often survives delivery, but dies early as a result of respiratory failure. Neuropathological findings resemble those of lethal congenital contracture syndrome type 1, but are less severe. {ECO:0000269|PubMed:18204449}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q09428	Leucine-induced hypoglycemia (LIH) [MIM:240800]: Rare cause of hypoglycemia and is described as a condition in which symptomatic hypoglycemia is provoked by high protein feedings. Hypoglycemia is also elicited by administration of oral or intravenous infusions of a single amino acid, leucine. {ECO:0000269|PubMed:15356046}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Familial hyperinsulinemic hypoglycemia 1 (HHF1) [MIM:256450]: Most common cause of persistent hypoglycemia in infancy. Unless early and aggressive intervention is undertaken, brain damage from recurrent episodes of hypoglycemia may occur. {ECO:0000269|PubMed:10202168, ECO:0000269|PubMed:10334322, ECO:0000269|PubMed:12364426, ECO:0000269|PubMed:12941782, ECO:0000269|PubMed:15562009, ECO:0000269|PubMed:15579781, ECO:0000269|PubMed:15807877, ECO:0000269|PubMed:16357843, ECO:0000269|PubMed:16429405, ECO:0000269|PubMed:24814349, ECO:0000269|PubMed:25720052, ECO:0000269|PubMed:8751851, ECO:0000269|PubMed:8923011, ECO:0000269|PubMed:9618169, ECO:0000269|PubMed:9769320}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Diabetes mellitus, permanent neonatal (PNDM) [MIM:606176]: A rare form of diabetes distinct from childhood-onset autoimmune diabetes mellitus type 1. It is characterized by insulin-requiring hyperglycemia that is diagnosed within the first months of life. Permanent neonatal diabetes requires lifelong therapy. {ECO:0000269|PubMed:16613899, ECO:0000269|PubMed:16885549, ECO:0000269|PubMed:17213273, ECO:0000269|PubMed:17668386}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Transient neonatal diabetes mellitus 2 (TNDM2) [MIM:610374]: Neonatal diabetes is a form of diabetes mellitus defined by the onset of mild-to-severe hyperglycemia within the first months of life. Transient neonatal diabetes remits early, with a possible relapse during adolescence. {ECO:0000269|PubMed:16885549}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P49770	Leukodystrophy with vanishing white matter (VWM) [MIM:603896]: A leukodystrophy that occurs mainly in children. Neurological signs include progressive cerebellar ataxia, spasticity, inconstant optic

	atrophy and relatively preserved mental abilities. The disease is chronic-progressive with, in most individuals, additional episodes of rapid deterioration following febrile infections or minor head trauma. While childhood onset is the most common form of the disorder, some severe forms are apparent at birth. A severe, early-onset form seen among the Cree and Chippewayan populations of Quebec and Manitoba is called Cree leukoencephalopathy. Milder forms may not become evident until adolescence or adulthood. Some females with milder forms of the disease who survive to adolescence exhibit ovarian dysfunction. This variant of the disorder is called ovarioleukodystrophy. {ECO:0000269|PubMed:11704758, ECO:0000269|PubMed:12707859, ECO:0000269|PubMed:15776425, ECO:0000269|PubMed:21484434, ECO:0000269|PubMed:22285377, ECO:0000269|PubMed:22729508}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9UI10	Leukodystrophy with vanishing white matter (VWM) [MIM:603896]: A leukodystrophy that occurs mainly in children. Neurological signs include progressive cerebellar ataxia, spasticity, inconstant optic atrophy and relatively preserved mental abilities. The disease is chronic-progressive with, in most individuals, additional episodes of rapid deterioration following febrile infections or minor head trauma. While childhood onset is the most common form of the disorder, some severe forms are apparent at birth. A severe, early-onset form seen among the Cree and Chippewayan populations of Quebec and Manitoba is called Cree leukoencephalopathy. Milder forms may not become evident until adolescence or adulthood. Some females with milder forms of the disease who survive to adolescence exhibit ovarian dysfunction. This variant of the disorder is called ovarioleukodystrophy. {ECO:0000269|PubMed:11835386, ECO:0000269|PubMed:12707859, ECO:0000269|PubMed:15776425}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q14232	Leukodystrophy with vanishing white matter (VWM) [MIM:603896]: A leukodystrophy that occurs mainly in children. Neurological signs include progressive cerebellar ataxia, spasticity, inconstant optic atrophy and relatively preserved mental abilities. The disease is chronic-progressive with, in most individuals, additional episodes of rapid deterioration following febrile infections or minor head trauma. While childhood onset is the most common form of the disorder, some severe forms are apparent at birth. A severe, early-onset form seen among the Cree and Chippewayan populations of Quebec and Manitoba is called Cree leukoencephalopathy. Milder forms may not become evident until adolescence or adulthood. Some females with milder forms of the disease who survive to adolescence exhibit ovarian dysfunction. This variant of the disorder is called ovarioleukodystrophy. {ECO:0000269|PubMed:11835386, ECO:0000269|PubMed:15776425}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q12904	Leukodystrophy, hypomyelinating, 3 (HLD3) [MIM:260600]: A severe autosomal recessive hypomyelinating leukodystrophy characterized by early infantile onset of global developmental delay, lack of development, lack of speech acquisition, and peripheral spasticity associated with decreased myelination in the central nervous system. {ECO:0000269|PubMed:21092922}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O14802	Leukodystrophy, hypomyelinating, 7, with or without oligodontia and/or hypogonadotropic hypogonadism (HLD7) [MIM:607694]: An autosomal recessive neurodegenerative disorder characterized by childhood onset of progressive motor decline manifest as spasticity, ataxia, tremor, and cerebellar signs, as well as mild cognitive regression. Other features may include hypodontia or oligodontia and hypogonadotropic hypogonadism. There is considerable inter- and intrafamilial variability. {ECO:0000269|PubMed:21855841, ECO:0000269|PubMed:22036171, ECO:0000269|PubMed:23355746, ECO:0000269|PubMed:23694757}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NW08	Leukodystrophy, hypomyelinating, 8, with or without oligodontia and/or hypogonadotropic hypogonadism (HLD8) [MIM:614381]: An autosomal recessive neurodegenerative disorder characterized by early childhood onset of cerebellar ataxia and mild intellectual disabilities associated with diffuse hypomyelination apparent on brain MRI. Variable features include oligodontia and/or hypogonadotropic hypogonadism. {ECO:0000269|PubMed:22036171, ECO:0000269|PubMed:22036172, ECO:0000269|PubMed:23355746}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P54136	Leukodystrophy, hypomyelinating, 9 (HLD9) [MIM:616140]: An autosomal recessive neurodegenerative disorder characterized by delayed psychomotor development, severe spasticity, nystagmus, and ataxia associated with diffuse hypomyelination apparent on brain MRI. {ECO:0000269|PubMed:24777941}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q6PI48	Leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL) [MIM:611105]: Autosomal recessive disease and is defined on the basis of a highly characteristic

	constellation of abnormalities observed by magnetic resonance imaging and spectroscopy. Affected individuals develop slowly progressive cerebellar ataxia, spasticity, and dorsal column dysfunction, sometimes with a mild cognitive deficit or decline. {ECO:0000269|PubMed:17384640}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O96017	Li-Fraumeni syndrome 2 (LFS2) [MIM:609265]: A highly penetrant familial cancer syndrome that in its classic form is defined by the existence of a proband affected by a sarcoma before 45 years with a first degree relative affected by any tumor before 45 years and another first degree relative with any tumor before 45 years or a sarcoma at any age. Other clinical definitions for LFS have been proposed (PubMed:8118819 and PubMed:8718514) and called Li-Fraumeni like syndrome (LFL). In these families affected relatives develop a diverse set of malignancies at unusually early ages. Four types of cancers account for 80% of tumors occurring in TP53 germline mutation carriers: breast cancers, soft tissue and bone sarcomas, brain tumors (astrocytomas) and adrenocortical carcinomas. Less frequent tumors include choroid plexus carcinoma or papilloma before the age of 15, rhabdomyosarcoma before the age of 5, leukemia, Wilms tumor, malignant phyllodes tumor, colorectal and gastric cancers. {ECO:0000269|PubMed:11719428}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Prostate cancer (PC) [MIM:176807]: A malignancy originating in tissues of the prostate. Most prostate cancers are adenocarcinomas that develop in the acini of the prostatic ducts. Other rare histopathologic types of prostate cancer that occur in approximately 5% of patients include small cell carcinoma, mucinous carcinoma, prostatic ductal carcinoma, transitional cell carcinoma, squamous cell carcinoma, basal cell carcinoma, adenoid cystic carcinoma (basaloid), signet-ring cell carcinoma and neuroendocrine carcinoma. {ECO:0000269|PubMed:12533788}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.; Osteogenic sarcoma (OSRC) [MIM:259500]: A sarcoma originating in bone-forming cells, affecting the ends of long bones. Note=The gene represented in this entry may be involved in disease pathogenesis.; Breast cancer (BC) [MIM:114480]: A common malignancy originating from breast epithelial tissue. Breast neoplasms can be distinguished by their histologic pattern. Invasive ductal carcinoma is by far the most common type. Breast cancer is etiologically and genetically heterogeneous. Important genetic factors have been indicated by familial occurrence and bilateral involvement. Mutations at more than one locus can be involved in different families or even in the same case. {ECO:0000269|PubMed:12094328, ECO:0000269|PubMed:21618645, ECO:0000269|PubMed:25619829}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry. {ECO:0000269|PubMed:12094328}.
O14979	Limb-girdle muscular dystrophy 1G (LGMD1G) [MIM:609115]: An autosomal dominant degenerative myopathy characterized by slowly progressive wasting and weakness of the proximal muscles of arms and legs around the pelvic or shoulder girdles, elevated creatine kinase levels and dystrophic features on muscle biopsy. LGMD1G is characterized by a mild late-onset and is associated with progressive fingers and toes flexion limitation. Affected individuals may also develop cataracts before age 50. {ECO:0000269|PubMed:24647604}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P43034	Lissencephaly 1 (LIS1) [MIM:607432]: A classical lissencephaly. It is characterized by agyria or pachygyria and disorganization of the clear neuronal lamination of normal six-layered cortex. The cortex is abnormally thick and poorly organized with 4 primitive layers. Associated with enlarged and dysmorphic ventricles and often hypoplasia of the corpus callosum. {ECO:0000269|PubMed:11502906, ECO:0000269|PubMed:15007136, ECO:0000269|PubMed:9063735}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Subcortical band heterotopia (SBH) [MIM:607432]: SBH is a mild brain malformation of the lissencephaly spectrum. It is characterized by bilateral and symmetric plates or bands of gray matter found in the central white matter between the cortex and cerebral ventricles, cerebral convolutions usually appearing normal. {ECO:0000269|PubMed:10441340, ECO:0000269|PubMed:14581661}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Miller-Dieker lissencephaly syndrome (MDLS) [MIM:247200]: A contiguous gene deletion syndrome of chromosome 17p13.3, characterized by classical lissencephaly and distinct facial features. Additional congenital malformations can be part of the condition. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9BVA0	Lissencephaly 6, with microcephaly (LIS6) [MIM:616212]: A form of lissencephaly, a disorder of cortical development characterized by agyria or pachygyria and disorganization of the clear neuronal lamination of normal six-layered cortex. LIS6 features include hypoplasia of the corpus callosum, severe microcephaly and developmental delay. {ECO:0000269|PubMed:25521378, ECO:0000269|PubMed:25521379}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q00535	Lissencephaly 7, with cerebellar hypoplasia (LIS7) [MIM:616342]: A form of lissencephaly, a disorder of

	cortical development characterized by agyria or pachygyria and disorganization of the clear neuronal lamination of normal six-layered cortex. LIS7 patients manifest lack of psychomotor development, facial dysmorphism, arthrogryposis, and early-onset intractable seizures resulting in death in infancy. {ECO:0000269|PubMed:25560765}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O75648	Liver failure, infantile, transient (LFIT) [MIM:613070]: A transient disorder of hepatic function characterized by elevated liver enzymes, jaundice, vomiting, coagulopathy, hyperbilirubinemia, increased serum lactate. Patients who survive the initial acute episode can recover, show normal development and have no recurrence. {ECO:0000269|PubMed:19732863}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q01484	Long QT syndrome 4 (LQT4) [MIM:600919]: A heart disorder characterized by a prolonged QT interval on the ECG and polymorphic ventricular arrhythmias. They cause syncope and sudden death in response to exercise or emotional stress, and can present with a sentinel event of sudden cardiac death in infancy. Long QT syndrome type 4 shows many atypical features compared to classical long QT syndromes, including pronounced sinus bradycardia, polyphasic T waves and atrial fibrillation. Cardiac repolarization defects may be not as severe as in classical LQT syndromes and prolonged QT interval on EKG is not a consistent feature. {ECO:0000269|PubMed:12571597, ECO:0000269|PubMed:15178757}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O00206	Macular degeneration, age-related, 10 (ARMD10) [MIM:611488]: A form of age-related macular degeneration, a multifactorial eye disease and the most common cause of irreversible vision loss in the developed world. In most patients, the disease is manifest as ophthalmoscopically visible yellowish accumulations of protein and lipid that lie beneath the retinal pigment epithelium and within an elastin-containing structure known as Bruch membrane. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
Q15029	Mandibulofacial dysostosis with microcephaly (MFDM) [MIM:610536]: A rare syndrome characterized by progressive microcephaly, midface and malar hypoplasia, micrognathia, microtia, dysplastic ears, preauricular skin tags, significant developmental delay, and speech delay. Many patients have major sequelae, including choanal atresia that results in respiratory difficulties, conductive hearing loss, and cleft palate. {ECO:0000269|PubMed:22305528}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O00187	MASP2 deficiency (MASPD) [MIM:613791]: A disorder that results in autoimmune manifestations, recurrent severe infections, and chronic inflammatory disease. {ECO:0000269|PubMed:12904520, ECO:0000269|PubMed:17252003}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NUX5	Melanoma, cutaneous malignant 10 (CMM10) [MIM:615848]: A malignant neoplasm of melanocytes, arising de novo or from a pre-existing benign nevus, which occurs most often in the skin but also may involve other sites. {ECO:0000269|PubMed:24686846, ECO:0000269|PubMed:24686849}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
P11802	Melanoma, cutaneous malignant 3 (CMM3) [MIM:609048]: A malignant neoplasm of melanocytes, arising de novo or from a pre-existing benign nevus, which occurs most often in the skin but also may involve other sites. {ECO:0000269|PubMed:7652577, ECO:0000269|PubMed:8528263, ECO:0000269|PubMed:9311594, ECO:0000269|PubMed:9425228}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
O14936	Mental retardation and microcephaly with pontine and cerebellar hypoplasia (MICPCH) [MIM:300749]: A disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. Affected individuals can manifest a severe phenotype consisting of severe intellectual deficit, congenital or postnatal microcephaly, disproportionate brainstem and cerebellar hypoplasia. A milder phenotype consists of mental retardation alone or associated with nystagmus. {ECO:0000269|PubMed:19165920, ECO:0000269|PubMed:19377476}. Note=The disease is caused by mutations affecting the gene represented in this entry.; FG syndrome 4 (FGS4) [MIM:300422]: FG syndrome (FGS) is an X-linked disorder characterized by mental retardation, relative macrocephaly, hypotonia and constipation. {ECO:0000269|PubMed:19200522}. Note=The disease is caused by mutations affecting the gene represented in this entry.
A7XYQ1	Mental retardation, anterior maxillary protrusion, and strabismus (MRAMS) [MIM:613671]: A syndrome characterized by severe mental retardation, strabismus and dysmorphic features such as anterior maxillary protrusion with vertical maxillary excess, open bite and prominent crowded teeth. Some patients may lack dysmorphic features and manifest temporal lobe epilepsy and psychosis. Esotropia and amblyopia are present in some individuals. {ECO:0000269|PubMed:21035105}. Note=The disease is caused by mutations affecting the gene represented in this entry.

Q13627	Mental retardation, autosomal dominant 7 (MRD7) [MIM:614104]: A disease characterized by primary microcephaly, severe mental retardation without speech, anxious autistic behavior, and dysmorphic features, including bitemporal narrowing, deep-set eyes, large simple ears, and a pointed nasal tip. Mental retardation is characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. {ECO:0000269|PubMed:21294719}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P56730	Mental retardation, autosomal recessive 1 (MRT1) [MIM:249500]: A disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. Non-syndromic mental retardation patients do not manifest other clinical signs. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q96EY9	Mental retardation, autosomal recessive 36 (MRT36) [MIM:615286]: A disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. MRT36 is often associated with esotropia and failure to thrive. Other more variable features included microcephaly, hypotonia, and mild brain abnormalities on MRI, such as dilated ventricles or delayed myelination. {ECO:0000269|PubMed:23620220}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O75914	Mental retardation, X-linked 30 (MRX30) [MIM:300558]: A disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. Intellectual deficiency is the only primary symptom of non-syndromic X-linked mental retardation, while syndromic mental retardation presents with associated physical, neurological and/or psychiatric manifestations. {ECO:0000269|PubMed:10946356, ECO:0000269|PubMed:12884430, ECO:0000269|PubMed:9731525}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9UET6	Mental retardation, X-linked 44 (MRX44) [MIM:309549]: A disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. Intellectual deficiency is the only primary symptom of non-syndromic X-linked mental retardation, while syndromic mental retardation presents with associated physical, neurological and/or psychiatric manifestations. {ECO:0000269|PubMed:15162322}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P51508	Mental retardation, X-linked 45 (MRX45) [MIM:300498]: A disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. Intellectual deficiency is the only primary symptom of non-syndromic X-linked mental retardation, while syndromic mental retardation presents with associated physical, neurological and/or psychiatric manifestations. {ECO:0000269|PubMed:15121780}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Note=A chromosomal aberration involving ZNF81 is found in a severe mental retardation patient. Translocation t(X;9)(p11.23;q34.3).
Q9BZI7	Mental retardation, X-linked, syndromic, 14 (MRXS14) [MIM:300676]: A disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. MRXS14 patients manifest mental retardation associated with other variable signs such as autistic features, slender build, poor musculature, long, thin face, high-arched palate, high nasal bridge, and pectus deformities. {ECO:0000269|PubMed:17704778}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P41229	Mental retardation, X-linked, syndromic, Claes-Jensen type (MRXSCJ) [MIM:300534]: A disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. MRXSCJ patients manifest mental retardation associated with variable features such as slowly progressive spastic paraplegia, seizures, facial dysmorphism. {ECO:0000269|PubMed:15586325, ECO:0000269|PubMed:16538222, ECO:0000269|PubMed:16541399}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9UPP1	Mental retardation, X-linked, syndromic, Siderius type (MRXSSD) [MIM:300263]: A syndrome characterized by mild to borderline mental retardation with or without cleft lip/cleft palate. {ECO:0000269|PubMed:16199551, ECO:0000269|PubMed:17661819}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y462	Mental retardation, X-linked, ZNF711-related (MRXZ) [MIM:300803]: A disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. {ECO:0000269|PubMed:19377476}.

	Note=The disease is caused by mutations affecting the gene represented in this entry.
Q00534	Microcephaly 12, primary, autosomal recessive (MCPH12) [MIM:616080]: A form of microcephaly, a disease defined as a head circumference more than 3 standard deviations below the age-related mean. Brain weight is markedly reduced and the cerebral cortex is disproportionately small. {ECO:0000269|PubMed:23918663}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O43379	Microcephaly 2, primary, autosomal recessive, with or without cortical malformations (MCPH2) [MIM:604317]: A disease characterized by microcephaly, moderate to severe mental retardation, and various type of cortical malformations in most patients. Microcephaly is defined as a head circumference more than 3 standard deviations below the age-related mean. Cortical malformations include pachygyria with cortical thickening, microgyria, lissencephaly, hypoplasia of the corpus callosum, schizencephaly. All affected individuals have delayed psychomotor development. Some patients have seizures. {ECO:0000269|PubMed:20729831, ECO:0000269|PubMed:20890278, ECO:0000269|PubMed:20890279, ECO:0000269|PubMed:21496009}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O00444	Microcephaly and chorioretinopathy, autosomal recessive, 2 (MCCRP2) [MIM:616171]: A severe disorder characterized by microcephaly, delayed psychomotor development, growth retardation with dwarfism, and ocular abnormalities. {ECO:0000269|PubMed:25344692}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P47897	Microcephaly, progressive, with seizures and cerebral and cerebellar atrophy (MSCCA) [MIM:615760]: A severe, autosomal recessive, neurodevelopmental and neurodegenerative disorder characterized by progressive microcephaly, severe seizures in infancy, atrophy of the cerebral cortex and cerebellar vermis, and mild atrophy of the cerebellar hemispheres, resulting in profoundly delayed development and hypotonia. {ECO:0000269|PubMed:24656866}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8TBZ6	Microcephaly, short stature, and impaired glucose metabolism (MSSGM) [MIM:616033]: A disease characterized by microcephaly, mental retardation, short stature, and disturbed glucose metabolism. Additional clinical features include delayed puberty, hypoglycemia-related seizures, hyperinsulinemic hypoglycemia, and early-onset diabetes. {ECO:0000269|PubMed:24204302, ECO:0000269|PubMed:25053765}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P0CW18	Microphthalmia, isolated, 6 (MCOP6) [MIM:613517]: A developmental ocular disorder characterized by small malformed eyes. Clinical features are extreme hyperopia due to short axial length with essentially normal anterior segment, steep corneal curvatures, shallow anterior chamber, thick lenses, and thickened scleral wall. Palpebral fissures appear narrow because of relatively deep-set eyes, visual acuity is mildly to moderately reduced, and anisometropic or strabismic amblyopia is common. The fundus of the eye shows crowded optical disks, tortuous vessels, and an abnormal foveal avascular zone. {ECO:0000269|PubMed:21397065, ECO:0000269|PubMed:21532570, ECO:0000269|PubMed:21850159}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NP58	Microphthalmia, isolated, with coloboma, 7 (MCOPCB7) [MIM:614497]: A disorder of eye formation, ranging from small size of a single eye to complete bilateral absence of ocular tissues. Ocular abnormalities like opacities of the cornea and lens, scaring of the retina and choroid, and other abnormalities may also be present. Ocular colobomas are a set of malformations resulting from abnormal morphogenesis of the optic cup and stalk, and the fusion of the fetal fissure (optic fissure). {ECO:0000269|PubMed:22226084}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Dyschromatosis universalis hereditaria 3 (DUH3) [MIM:615402]: An autosomal dominant pigmentary genodermatosis characterized by a mixture of hyperpigmented and hypopigmented macules distributed randomly over the body, that appear in infancy or early childhood. The trunk and extremities are the dominant sites of abnormal pigmentation. Facial lesions can be seen in 50% of affected individuals, but involvement of palms and soles is unusual. Abnormalities of hair and nails have also been reported. Dyschromatosis universalis hereditaria may be associated with abnormalities of dermal connective tissue, nerve tissue, or other systemic complications. {ECO:0000269|PubMed:23519333, ECO:0000269|PubMed:24224009, ECO:0000269|PubMed:24498303}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Note=ABCB6 mutations are involved in familial pseudohyperkalemia, a dominantly inherited condition characterized by increased serum potassium levels, measured in whole-blood specimens stored at or below room temperature. This condition is not accompanied by clinical symptoms or biological signs except for borderline abnormalities of red cell shape (PubMed:23180570).

	{ECO:0000269|PubMed:23180570}.
Q6W2J9	Microphthalmia, syndromic, 2 (MCOPS2) [MIM:300166]: A very rare multiple congenital anomaly syndrome characterized by eye anomalies (congenital cataract, microphthalmia, or secondary glaucoma), facial abnormalities (long narrow face, high nasal bridge, pointed nose with cartilages separated at the tip, cleft palate, or submucous cleft palate), cardiac anomalies (atrial septal defect, ventricular septal defect, or floppy mitral valve) and dental abnormalities (canine radiculomegaly, delayed dentition, oligodontia, persistent primary teeth, or variable root length). Microphthalmia is a disorder of eye formation, ranging from small size of a single eye to complete bilateral absence of ocular tissues (anophthalmia). In many cases, microphthalmia/anophthalmia occurs in association with syndromes that include non-ocular abnormalities. {ECO:0000269|PubMed:15004558}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P01857	Multiple myeloma (MM) [MIM:254500]: A malignant tumor of plasma cells usually arising in the bone marrow and characterized by diffuse involvement of the skeletal system, hyperglobulinemia, Bence-Jones proteinuria and anemia. Complications of multiple myeloma are bone pain, hypercalcemia, renal failure and spinal cord compression. The aberrant antibodies that are produced lead to impaired humoral immunity and patients have a high prevalence of infection. Amyloidosis may develop in some patients. Multiple myeloma is part of a spectrum of diseases ranging from monoclonal gammopathy of unknown significance (MGUS) to plasma cell leukemia. {ECO:0000269|PubMed:11972529, ECO:0000269|PubMed:8943038}. Note=The disease is caused by mutations affecting the gene represented in this entry. A chromosomal aberration involving IGHG1 is found in multiple myeloma. Translocation t(11;14)(q13;q32) with the IgH locus. Translocation t(11;14)(q13;q32) with CCND1; translocation t(4;14)(p16.3;q32.3) with FGFR3; translocation t(6;14)(p25;q32) with IRF4.
Q15306	Multiple myeloma (MM) [MIM:254500]: A malignant tumor of plasma cells usually arising in the bone marrow and characterized by diffuse involvement of the skeletal system, hyperglobulinemia, Bence-Jones proteinuria and anemia. Complications of multiple myeloma are bone pain, hypercalcemia, renal failure and spinal cord compression. The aberrant antibodies that are produced lead to impaired humoral immunity and patients have a high prevalence of infection. Amyloidosis may develop in some patients. Multiple myeloma is part of a spectrum of diseases ranging from monoclonal gammopathy of unknown significance (MGUS) to plasma cell leukemia. {ECO:0000269|PubMed:9326949}. Note=The gene represented in this entry may be involved in disease pathogenesis. A chromosomal aberration involving IRF4 has been found in multiple myeloma. Translocation t(6;14)(p25;q32) with the IgH locus.
Q9Y606	Myopathy with lactic acidosis and sideroblastic anemia 1 (MLASA1) [MIM:600462]: A rare oxidative phosphorylation disorder specific to skeletal muscle and bone marrow. Affected individuals manifest progressive muscle weakness, exercise intolerance, lactic acidosis, sideroblastic anemia and delayed growth. {ECO:0000269|PubMed:15108122, ECO:0000269|PubMed:16959974, ECO:0000269|PubMed:19731322}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y2Z4	Myopathy with lactic acidosis and sideroblastic anemia 2 (MLASA2) [MIM:613561]: A rare oxidative phosphorylation disorder specific to skeletal muscle and bone marrow. Affected individuals manifest sideroblastic anemia, progressive lethargy, muscle weakness, and exercise intolerance associated with persistent lactic acidemia. {ECO:0000269|PubMed:20598274, ECO:0000269|PubMed:22504945}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q15772	Myopathy, centronuclear, 5 (CNM5) [MIM:615959]: A form of centronuclear myopathy, a congenital muscle disorder characterized by progressive muscular weakness and wasting involving mainly limb girdle, trunk, and neck muscles. It may also affect distal muscles. Weakness may be present during childhood or adolescence or may not become evident until the third decade of life. Ptosis is a frequent clinical feature. The most prominent histopathologic features include high frequency of centrally located nuclei in muscle fibers not secondary to regeneration, radial arrangement of sarcoplasmic strands around the central nuclei, and predominance and hypotrophy of type 1 fibers. CNM5 features include severe neonatal hypotonia with respiratory insufficiency, difficulty feeding, and delayed motor development. Some patients die in infancy, and some develop dilated cardiomyopathy. {ECO:0000269|PubMed:25087613}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q2M1K9	Nephronophthisis 14 (NPHP14) [MIM:614844]: An autosomal recessive disorder manifesting as infantile-onset kidney disease, cerebellar vermis hypoplasia, and situs inversus. Nephronophthisis is a progressive tubulo-interstitial kidney disorder histologically characterized by modifications of the tubules with thickening of the basement membrane, interstitial fibrosis and, in the advanced stages, medullary cysts. {ECO:0000269|PubMed:22863007}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Joubert syndrome 19 (JBTS19) [MIM:614844]: A form of Joubert syndrome, a

	disorder presenting with cerebellar ataxia, oculomotor apraxia, hypotonia, neonatal breathing abnormalities and psychomotor delay. Neuroradiologically, it is characterized by cerebellar vermian hypoplasia/aplasia, thickened and reoriented superior cerebellar peduncles, and an abnormally large interpeduncular fossa, giving the appearance of a molar tooth on transaxial slices (molar tooth sign). JBTS19 patients have polycystic kidney disease, Leber congenital amaurosis, cerebellar vermis hypoplasia, and breathing abnormality. {ECO:0000269|PubMed:22863007}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q68DC2	Nephronophthisis 16 (NPHP16) [MIM:615382]: A form of nephronophthisis, a chronic tubulo-interstitial nephritis that progresses to end-stage renal failure. Some patients have cystic kidneys of normal size and no extrarenal manifestations, whereas others have enlarged renal size and severe extrarenal defects, including hypertrophic obstructive cardiomyopathy, aortic stenosis, pulmonary stenosis, patent ductus arteriosus, situs inversus, and periportal liver fibrosis. {ECO:0000269|PubMed:23793029}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y283	Nephronophthisis 2 (NPHP2) [MIM:602088]: An autosomal recessive disorder resulting in end-stage renal disease. It is characterized by early onset and rapid progression. Phenotypic manifestations include enlarged kidneys, chronic tubulo-interstitial nephritis, anemia, hyperkalemic metabolic acidosis. Some patients also display situs inversus. Pathologically, it differs from later-onset nephronophthisis by the absence of medullary cysts and thickened tubular basement membranes, and by the presence of cortical microcysts. {ECO:0000269|PubMed:12872123}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q86SG6	Nephronophthisis 9 (NPHP9) [MIM:613824]: An autosomal recessive disorder resulting in end-stage renal disease. It is a progressive tubulo-interstitial kidney disorder histologically characterized by modifications of the tubules with thickening of the basement membrane, interstitial fibrosis and, in the advanced stages, medullary cysts. {ECO:0000269|PubMed:18199800}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Renal-hepatic-pancreatic dysplasia 2 (RHPD2) [MIM:615415]: A form of renal-hepatic-pancreatic dysplasia, a disease characterized by cystic malformations of the kidneys, liver, and pancreas. The pathological findings consist of multicystic dysplastic kidneys, dilated and dysgenetic bile ducts, a dysplastic pancreas with dilated ducts, cysts, fibrosis and inflammatory infiltrates. {ECO:0000269|PubMed:23418306}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q96D53	Nephrotic syndrome 9 (NPHS9) [MIM:615573]: A form of nephrotic syndrome, a renal disease clinically characterized by progressive renal failure, severe proteinuria, hypoalbuminemia, hyperlipidemia and edema. Kidney biopsies show focal segmental glomerulosclerosis. {ECO:0000269|PubMed:24270420}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q14160	Neural tube defects (NTD) [MIM:182940]: Congenital malformations of the central nervous system and adjacent structures related to defective neural tube closure during the first trimester of pregnancy. Failure of neural tube closure can occur at any level of the embryonic axis. Common NTD forms include anencephaly, myelomeningocele and spina bifida, which result from the failure of fusion in the cranial and spinal region of the neural tube. NTDs have a multifactorial etiology encompassing both genetic and environmental components. {ECO:0000269|PubMed:22095531}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O60733	Neurodegeneration with brain iron accumulation 2B (NBIA2B) [MIM:610217]: A neurodegenerative disorder associated with iron accumulation in the brain, primarily in the basal ganglia. It is characterized by progressive extrapyramidal dysfunction leading to rigidity, dystonia, dysarthria and sensorimotor impairment. {ECO:0000269|PubMed:16783378}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Neurodegeneration with brain iron accumulation 2A (NBIA2A) [MIM:256600]: A neurodegenerative disease characterized by pathologic axonal swelling and spheroid bodies in the central nervous system. Onset is within the first 2 years of life with death by age 10 years. {ECO:0000269|PubMed:16783378, ECO:0000269|PubMed:17033970, ECO:0000269|PubMed:23749988}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Parkinson disease 14 (PARK14) [MIM:612953]: An adult-onset progressive neurodegenerative disorder characterized by parkinsonism, dystonia, severe cognitive decline, cerebral and cerebellar atrophy and absent iron in the basal ganglia on magnetic resonance imaging. {ECO:0000269|PubMed:18570303}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y3E5	Neurologic, endocrine, and pancreatic disease, multisystem, infantile-onset (IMNEPD) [MIM:616263]: A progressive multisystem disease characterized by a variety of neurologic, endocrine, and, in some patients, pancreatic features. Variable clinical symptoms include global developmental delay, hypotonia, hearing loss, ataxia, hyporeflexia, facial dysmorphism, hypothyroidism, and pancreatic insufficiency. {ECO:0000269|PubMed:25558065, ECO:0000269|PubMed:25574476}. Note=The disease is caused by

	mutations affecting the gene represented in this entry.
P49773	Neuromyotonia and axonal neuropathy, autosomal recessive (NMAN) [MIM:137200]: An autosomal recessive neurologic disorder characterized by onset in the first or second decade of a peripheral axonal neuropathy predominantly affecting motor more than sensory nerves. The axonal neuropathy is reminiscent of Charcot-Marie-Tooth disease type 2 and distal hereditary motor neuropathy. Individuals with NMAN also have delayed muscle relaxation and action myotonia associated with neuromyotonic discharges on needle EMG resulting from hyperexcitability of the peripheral nerves. {ECO:0000269|PubMed:22961002}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O95163	Neuropathy, hereditary sensory and autonomic, 3 (HSAN3) [MIM:223900]: A form of hereditary sensory and autonomic neuropathy, a genetically and clinically heterogeneous group of disorders characterized by degeneration of dorsal root and autonomic ganglion cells, and by sensory and/or autonomic abnormalities. HSAN3 patients manifest a variety of symptoms such as alacrima, decreased taste, decreased sensitivity to pain and temperature, vasomotor instability, hypoactive or absent deep tendon reflexes, vomiting crises, and gastrointestinal dysfunction. {ECO:0000269|PubMed:11179008, ECO:0000269|PubMed:11179021}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q99684	Neutropenia, severe congenital 2, autosomal dominant (SCN2) [MIM:613107]: A disorder of hematopoiesis characterized by maturation arrest of granulopoiesis at the level of promyelocytes with peripheral blood absolute neutrophil counts below 0.5 x 10(9)/l and early onset of severe bacterial infections. {ECO:0000269|PubMed:12778173}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Dominant nonimmune chronic idiopathic neutropenia of adults (NI-CINA) [MIM:607847]: Relatively mild form of neutropenia diagnosed in adults, but predisposing to leukemia in a subset of patients. {ECO:0000269|PubMed:12778173}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9GZU5	Night blindness, congenital stationary, 1A (CSNB1A) [MIM:310500]: A non-progressive retinal disorder characterized by impaired night vision. Congenital stationary night blindness type 1A is characterized by impaired scotopic vision, myopia, hyperopia, nystagmus and reduced visual acuity. {ECO:0000269|PubMed:11062471, ECO:0000269|PubMed:11062472}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q15835	Night blindness, congenital stationary, Oguchi type 2 (CSNBO2) [MIM:613411]: A non-progressive retinal disorder characterized by impaired night vision, often associated with nystagmus and myopia. Congenital stationary night blindness Oguchi type is associated with fundus discoloration and abnormally slow dark adaptation. {ECO:0000269|PubMed:17070587, ECO:0000269|PubMed:9020843}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P04049	Noonan syndrome 5 (NS5) [MIM:611553]: A form of Noonan syndrome, a disease characterized by short stature, facial dysmorphic features such as hypertelorism, a downward eyeslant and low-set posteriorly rotated ears, and a high incidence of congenital heart defects and hypertrophic cardiomyopathy. Other features can include a short neck with webbing or redundancy of skin, deafness, motor delay, variable intellectual deficits, multiple skeletal defects, cryptorchidism, and bleeding diathesis. Individuals with Noonan syndrome are at risk of juvenile myelomonocytic leukemia, a myeloproliferative disorder characterized by excessive production of myelomonocytic cells. {ECO:0000269|PubMed:17603482, ECO:0000269|PubMed:17603483, ECO:0000269|PubMed:20683980}. Note=The disease is caused by mutations affecting the gene represented in this entry.; LEOPARD syndrome 2 (LPRD2) [MIM:611554]: A disorder characterized by lentigines, electrocardiographic conduction abnormalities, ocular hypertelorism, pulmonic stenosis, abnormalities of genitalia, retardation of growth, and sensorineural deafness. {ECO:0000269|PubMed:17603483}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Cardiomyopathy, dilated 1NN (CMD1NN) [MIM:615916]: A disorder characterized by ventricular dilation and impaired systolic function, resulting in congestive heart failure and arrhythmia. Patients are at risk of premature death. {ECO:0000269|PubMed:24777450}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q969X6	North American Indian childhood cirrhosis (NAIC) [MIM:604901]: Severe autosomal recessive intrahepatic cholestasis, originally described in Ojibway-Cree children from northwestern Quebec. NAIC typically presents with transient neonatal jaundice, in a child who is otherwise healthy, and progresses to biliary cirrhosis and portal hypertension. Biochemical and histopathological features suggest involvement of the bile ducts rather than of the bile canaliculi. They include elevated gamma glutamyltransferase and alkaline phosphatase levels, and, typically, marked fibrosis around bile ducts. Clinically, NAIC is distinct from other nonsyndromic familial cholestases because of its marked cholangiopathic features and severe degree of fibrosis on liver histology. {ECO:0000269|PubMed:12417987}. Note=The disease is caused by

	mutations affecting the gene represented in this entry.
P20749	Note=A chromosomal aberration involving BCL3 may be a cause of B-cell chronic lymphocytic leukemia (B-CLL). Translocation t(14;19)(q32;q13.1) with immunoglobulin gene regions.
Q6RI45	Note=A chromosomal aberration involving BRWD3 can be found in patients with B-cell chronic lymphocytic leukemia (B-CLL). Translocation t(X;11)(q21;q23) with ARHGAP20 does not result in fusion transcripts but disrupts both genes.; Mental retardation, X-linked 93 (MRX93) [MIM:300659]: A disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. Intellectual deficiency is the only primary symptom of non-syndromic X-linked mental retardation, while syndromic mental retardation presents with associated physical, neurological and/or psychiatric manifestations. MRX93 is associated with macrocephaly. {ECO:0000269|PubMed:17668385}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9ULH7	Note=A chromosomal aberration involving C11orf95 is found in 3 chondroid lipomas. Translocation t(11;16)(q13;p13) with C11orf95 produces a C11orf95-MKL2 fusion protein (PubMed:20607705). {ECO:0000269|PubMed:20607705}.
Q04206	Note=A chromosomal aberration involving C11orf95 is found in more than two-thirds of supratentorial ependymomas. Translocation with C11orf95 produces a C11orf95-RELA fusion protein. C11orf95-RELA translocations are potent oncogenes that probably transform neural stem cells by driving an aberrant NF-kappa-B transcription program (PubMed:24553141). {ECO:0000269|PubMed:24553141}.
P49589	Note=A chromosomal aberration involving CARS is associated with inflammatory myofibroblastic tumors (IMTs). Translocation t(2;11)(p23;p15) with ALK.
Q99459	Note=A chromosomal aberration involving CDC5L is found in multicystic renal dysplasia. Translocation t(6;19)(p21;q13.1) with USF2.
P26196	Note=A chromosomal aberration involving DDX6 may be a cause of hematopoietic tumors such as B-cell lymphomas. Translocation t(11;14)(q23;q32).
P55199	Note=A chromosomal aberration involving ELL is found in acute leukemias. Translocation t(11;19)(q23;p13.1) with KMT2A/MLL1. The result is a rogue activator protein.
Q03112	Note=A chromosomal aberration involving EVI1 is a cause of chronic myelogenous leukemia (CML). Translocation t(3;21)(q26;q22) with RUNX1/AML1.
Q6UN15	Note=A chromosomal aberration involving FIP1L1 is found in some cases of hypereosinophilic syndrome. Interstitial chromosomal deletion del(4)(q12q12) causes the fusion of FIP1L1 and PDGFRA (FIP1L1-PDGFRA). {ECO:0000269|PubMed:12660384, ECO:0000269|PubMed:12808148}.
P35637	Note=A chromosomal aberration involving FUS is found in a patient with malignant myxoid liposarcoma. Translocation t(12;16)(q13;p11) with DDIT3.; Note=A chromosomal aberration involving FUS is a cause of acute myeloid leukemia (AML). Translocation t(16;21)(p11;q22) with ERG.; Angiomatoid fibrous histiocytoma (AFH) [MIM:612160]: A distinct variant of malignant fibrous histiocytoma that typically occurs in children and adolescents and is manifest by nodular subcutaneous growth. Characteristic microscopic features include lobulated sheets of histiocyte-like cells intimately associated with areas of hemorrhage and cystic pseudovascular spaces, as well as a striking cuffing of inflammatory cells, mimicking a lymph node metastasis. Note=The disease may be caused by mutations affecting the gene represented in this entry. A chromosomal aberration involving FUS is found in a patient with angiomatoid fibrous histiocytoma. Translocation t(12;16)(q13;p11.2) with ATF1 generates a chimeric FUS/ATF1 protein.; Amyotrophic lateral sclerosis 6 (ALS6) [MIM:608030]: A neurodegenerative disorder affecting upper motor neurons in the brain and lower motor neurons in the brain stem and spinal cord, resulting in fatal paralysis. Sensory abnormalities are absent. The pathologic hallmarks of the disease include pallor of the corticospinal tract due to loss of motor neurons, presence of ubiquitin-positive inclusions within surviving motor neurons, and deposition of pathologic aggregates. The etiology of amyotrophic lateral sclerosis is likely to be multifactorial, involving both genetic and environmental factors. The disease is inherited in 5-10% of the cases. {ECO:0000269|PubMed:19251627, ECO:0000269|PubMed:19251628, ECO:0000269|PubMed:19861302, ECO:0000269|PubMed:20124201}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Tremor, hereditary essential 4 (ETM4) [MIM:614782]: A common movement disorder mainly characterized by postural tremor of the arms. Head, legs, trunk, voice, jaw, and facial muscles also may be involved. The condition can be aggravated by emotions, hunger, fatigue and temperature extremes, and may cause a functional disability or even incapacitation. Inheritance is autosomal dominant. {ECO:0000269|PubMed:22863194}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P01876	Note=A chromosomal aberration involving IGHA1 is found in multiple myeloma (MM) cell lines. Translocation t(1;14)(q21;q32) that forms a FCRL4-IGHA1 fusion protein.
Q9Y4C4	Note=A chromosomal aberration involving MFHAS1 may be a cause of B-cell lymphoma. Translocation

	t(8;14)(p23.1;q21) with a cryptic exon named '14q21 element'. The resulting fusion protein named 'chimeric MASL1' is tumorigenic in nude mice. {ECO:0000269|PubMed:14691450}.
Q969V6	Note=A chromosomal aberration involving MKL1 may be a cause of acute megakaryoblastic leukemia. Translocation t(1;22)(p13;q13) with RBM15. Although both reciprocal fusion transcripts are detected in acute megakaryoblastic leukemia (AMKL, FAB-M7), the RBM15-MKL1 chimeric protein has all the putative functional domains encoded by each gene and is the candidate oncogene.
Q00653	Note=A chromosomal aberration involving NFKB2 is found in a case of B-cell non Hodgkin lymphoma (B-NHL). Translocation t(10;14)(q24;q32) with IGHA1. The resulting oncogene is also called Lyt-10C alpha variant.; Note=A chromosomal aberration involving NFKB2 is found in a cutaneous T-cell leukemia (C-TCL) cell line. This rearrangement produces the p80HT gene which codes for a truncated 80 kDa protein (p80HT).; Note=In B-cell leukemia (B-CLL) cell line, LB40 and EB308, can be found after heterogeneous chromosomal aberrations, such as internal deletions.; Immunodeficiency, common variable, 10 (CVID10) [MIM:615577]: A primary immunodeficiency characterized by childhood-onset of recurrent infections, hypogammaglobulinemia, and decreased numbers of memory and marginal zone B-cells. Some patients may develop autoimmune features and have circulating autoantibodies. An unusual feature is central adrenal insufficiency. {ECO:0000269|PubMed:24140114}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q15233	Note=A chromosomal aberration involving NONO may be a cause of papillary renal cell carcinoma (PRCC). Translocation t(X;X)(p11.2;q13.1) with TFE3.
Q9H1B4	Note=A chromosomal aberration involving NXF5 has been observed in one patient with a syndromic form of mental retardation and short stature. Pericentric inversion inv(X)(p21.1;q22) that interrupts NXF5.
Q5VST9	Note=A chromosomal aberration involving OBSCN has been found in Wilms tumor. Translocation t(1;7)(q42;p15) with PTHB1.
Q9HBE1	Note=A chromosomal aberration involving PATZ1 is associated with small round cell sarcoma. Translocation t(1;22)(p36.1;q12) with EWSR1.
Q92733	Note=A chromosomal aberration involving PRCC is found in patients with papillary renal cell carcinoma. Translocation t(X;1)(p11.2;q21.2) with TFE3.
P51817	Note=A chromosomal aberration involving PRKX is a cause of sex reversal disorder. Translocation t(X;Y)(p22;p11) with PRKY. Chromosomal translocations proximal to PRKY account for about 30% of the cases of sex reversal disorder in XX males and XY females.
O43930	Note=A chromosomal aberration involving PRKY is a cause of sex reversal disorder. Translocation t(X;Y)(p22;p11) with PRKX. Chromosomal translocations proximal to PRKY account for about 30% of the cases of sex reversal disorder in XX males and XY females.
Q96T37	Note=A chromosomal aberration involving RBM15 may be a cause of acute megakaryoblastic leukemia. Translocation t(1;22)(p13;q13) with MKL1. Although both reciprocal fusion transcripts are detected in acute megakaryoblastic leukemia (AMKL, FAB-M7), the RBM15-MKL1 chimeric protein has all the putative functional domains encoded by each gene and is the candidate oncogene.
P23246	Note=A chromosomal aberration involving SFPQ may be a cause of papillary renal cell carcinoma (PRCC). Translocation t(X;1)(p11.2;p34) with TFE3.
A2RRD8	Note=A chromosomal aberration involving ZNF320 is found in a form of glioblastoma. Translocation t(10;19)(q26;q13.3) with BRWD2/WDR11.
P51814	Note=A chromosomal aberration involving ZNF41 has been found in a patient with severe mental retardation. Translocation t(X;7)(p11.3;q11.21).
Q96K83	Note=A chromosomal aberration involving ZNF521 is found in acute lymphoblastic leukemia. Translocation t(9;18)(p13;q11.2) with PAX5. The translocation generates the PAX5-ZNF521 oncogene consisting of the N-terminus part of PAX5 and the C-terminus part of ZNF521.
O14746	Note=Activation of telomerase has been implicated in cell immortalization and cancer cell pathogenesis.; Aplastic anemia (AA) [MIM:609135]: A form of anemia in which the bone marrow fails to produce adequate numbers of peripheral blood elements. It is characterized by peripheral pancytopenia and marrow hypoplasia. {ECO:0000269|PubMed:15885610, ECO:0000269|PubMed:16627250, ECO:0000269|PubMed:16990594, ECO:0000269|PubMed:19760749}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.; Note=Genetic variations in TERT are associated with coronary artery disease (CAD).; Dyskeratosis congenita, autosomal dominant, 2 (DKCA2) [MIM:613989]: A rare multisystem disorder caused by defective telomere maintenance. It is characterized by progressive bone marrow failure, and the clinical triad of reticulated skin hyperpigmentation, nail dystrophy, and mucosal leukoplakia. Common but variable features include premature graying, aplastic anemia, low platelets, osteoporosis, pulmonary fibrosis, and liver fibrosis among others. Early mortality is often associated with bone marrow failure, infections, fatal pulmonary

	complications, or malignancy. {ECO:0000269|PubMed:15885610, ECO:0000269|PubMed:16247010}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Pulmonary fibrosis, and/or bone marrow failure, telomere-related, 1 (PFBMFT1) [MIM:614742]: A disease associated with shortened telomeres. Pulmonary fibrosis is the most common manifestation. Other manifestations include aplastic anemia due to bone marrow failure, hepatic fibrosis, and increased cancer risk, particularly myelodysplastic syndrome and acute myeloid leukemia. Phenotype, age at onset, and severity are determined by telomere length. {ECO:0000269|PubMed:15814878, ECO:0000269|PubMed:17460043, ECO:0000269|PubMed:21436073, ECO:0000269|PubMed:21483807, ECO:0000269|PubMed:22512499}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Dyskeratosis congenita, autosomal recessive, 4 (DKCB4) [MIM:613989]: A severe form of dyskeratosis congenita, a rare multisystem disorder caused by defective telomere maintenance. It is characterized by progressive bone marrow failure, and the clinical triad of reticulated skin hyperpigmentation, nail dystrophy, and mucosal leukoplakia. Common but variable features include premature graying, aplastic anemia, low platelets, osteoporosis, pulmonary fibrosis, and liver fibrosis among others. Early mortality is often associated with bone marrow failure, infections, fatal pulmonary complications, or malignancy. {ECO:0000269|PubMed:16332973, ECO:0000269|PubMed:17785587, ECO:0000269|PubMed:18042801}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Pulmonary fibrosis, idiopathic (IPF) [MIM:178500]: A lung disease characterized by shortness of breath, radiographically evident diffuse pulmonary infiltrates, and varying degrees of inflammation and fibrosis on biopsy. In some cases, the disorder can be rapidly progressive and characterized by sequential acute lung injury with subsequent scarring and end-stage lung disease. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.; Melanoma, cutaneous malignant 9 (CMM9) [MIM:615134]: A malignant neoplasm of melanocytes, arising de novo or from a pre-existing benign nevus, which occurs most often in the skin but also may involve other sites. {ECO:0000269|PubMed:23348503}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
P36896	Note=ACVRIB is abundantly expressed in systemic sclerosis patient fibroblasts and production of collagen is also induced by activin-A/INHBA. This suggests that the activin/ACRV1B signaling mechanism is involved in systemic sclerosis.
Q9Y243	Note=AKT3 is a key modulator of several tumors like melanoma, glioma and ovarian cancer. Active AKT3 increases progressively during melanoma tumor progression with highest levels present in advanced-stage metastatic melanomas. Promotes melanoma tumorigenesis by decreasing apoptosis. Plays a key role in the genesis of ovarian cancers through modulation of G2/M phase transition. With AKT2, plays a pivotal role in the biology of glioblastoma.; Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome 2 (MPPH2) [MIM:615937]: A syndrome characterized by megalencephaly, hydrocephalus, and polymicrogyria; polydactyly may also be seen. There is considerable phenotypic similarity between this disorder and the megalencephaly-capillary malformation syndrome. {ECO:0000269|PubMed:22500628, ECO:0000269|PubMed:22729223, ECO:0000269|PubMed:22729224}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P41182	Note=Chromosomal aberrations involving BCL6 are a cause of B-cell non-Hodgkin lymphomas (B-cell NHL), including diffuse large B-cell lymphoma and follicular lymphoma. Approximately 40% of diffuse large B-cell lymphomas and 5 to 10% of follicular lymphomas are associated with chromosomal translocations that deregulate expression of BCL6 by juxtaposing heterologous promoters to the BCL6 coding domain. Translocation t(3;14)(q27;q32). Translocation t(3;22)(q27;q11) with immunoglobulin gene regions. Translocation t(3;7)(q27;p12) with IKZF1 gene 5'non-coding region. Translocation t(3;6)(q27;p21) with Histone H4. Translocation t(3;16)(q27;p11) with IL21R. Translocation t(3;13)(q27;q14) with LCP1.; Note=A chromosomal aberration involving BCL6 may be a cause of a form of B-cell leukemia. Translocation t(3;11)(q27;q23) with POU2AF1/OBF1.; Note=A chromosomal aberration involving BCL6 may be a cause of lymphoma. Translocation t(3;4)(q27;p11) with ARHH/TTF.
Q9NYV4	Note=Chromosomal aberrations involving CDK12 may be a cause gastric cancer. Deletions within 17q12 region producing fusion transcripts with ERBB2, leading to CDK12-ERBB2 fusion leading to trunctated CDK12 protein not in-frame with ERBB2.
O76039	Note=Chromosomal aberrations involving CDKL5 are found in patients manifesting early-onset seizures and spams and psychomotor impairment. Translocation t(X;6)(p22.3;q14); translocation t(X;7)(p22.3;p15).; Epileptic encephalopathy, early infantile, 2 (EIEE2) [MIM:300672]: A severe form of epilepsy characterized by seizures or spasms beginning in infancy. Patients with epileptic encephalopathy early infantile type 2 manifest features resembling Rett syndrome such as microcephaly, lack of speech development, stereotypic hand movements. However, EIEE2 and Rett syndrome are considered two distinct entities. {ECO:0000269|PubMed:12736870, ECO:0000269|PubMed:15492925,

	ECO:0000269|PubMed:15499549, ECO:0000269|PubMed:15689447, ECO:0000269|PubMed:15917271, ECO:0000269|PubMed:16015284, ECO:0000269|PubMed:16611748, ECO:0000269|PubMed:17993579, ECO:0000269|PubMed:18790821, ECO:0000269|PubMed:18809835, ECO:0000269|PubMed:19241098, ECO:0000269|PubMed:19253388, ECO:0000269|PubMed:24564546}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q92793	Note=Chromosomal aberrations involving CREBBP may be a cause of acute myeloid leukemias. Translocation t(8;16)(p11;p13) with KAT6A; translocation t(11;16)(q23;p13.3) with KMT2A/MLL1; translocation t(10;16)(q22;p13) with KAT6B. KAT6A-CREBBP may induce leukemia by inhibiting RUNX1-mediated transcription.; Rubinstein-Taybi syndrome 1 (RSTS1) [MIM:180849]: A disorder characterized by craniofacial abnormalities, postnatal growth deficiency, broad thumbs, broad big toes, mental retardation and a propensity for development of malignancies. {ECO:0000269|PubMed:11331617, ECO:0000269|PubMed:12114483, ECO:0000269|PubMed:12566391, ECO:0000269|PubMed:15706485, ECO:0000269|PubMed:20684013, ECO:0000269|PubMed:25388907}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q96DH6	Note=Chromosomal aberrations involving MSI2 may contribute to disease progression in chronic myeloid leukemia. Translocation t(7;17)(p15;q23) with HOXA9; translocation t(7;17)(q32-34;q23).
P62424	Note=Chromosomal recombination involving RPL7A activates the receptor kinase domain of the TRK oncogene.
P50750	Note=Chronic activation of CDK9 causes cardiac myocyte enlargement leading to cardiac hypertrophy, and confers predisposition to heart failure.
O15523	Note=DDX3Y is located in the 'azoospermia factor a' (AZFa) region on chromosome Y which is deleted in Sertoli cell-only syndrome. This is an infertility disorder in which no germ cells are visible in seminiferous tubules leading to azoospermia.
P31751	Note=Defects in AKT2 are a cause of susceptibility to breast cancer (BC). AKT2 promotes metastasis of tumor cells without affecting the latency of tumor development. With AKT3, plays also a pivotal role in the biology of glioblastoma.; Diabetes mellitus, non-insulin-dependent (NIDDM) [MIM:125853]: A multifactorial disorder of glucose homeostasis caused by a lack of sensitivity to the body's own insulin. Affected individuals usually have an obese body habitus and manifestations of a metabolic syndrome characterized by diabetes, insulin resistance, hypertension and hypertriglyceridemia. The disease results in long-term complications that affect the eyes, kidneys, nerves, and blood vessels. {ECO:0000269|PubMed:15166380, ECO:0000269|PubMed:19164855}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Hypoinsulinemic hypoglycemia with hemihypertrophy (HIHGHH) [MIM:240900]: A disorder characterized by hypoglycemia, low insulin levels, low serum levels of ketone bodies and branched-chain amino acids, left-sided hemihypertrophy, neonatal macrosomia, reduced consciousness and hypoglycemic seizures. {ECO:0000269|PubMed:21979934}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P15056	Note=Defects in BRAF are found in a wide range of cancers. {ECO:0000269|PubMed:18974108}.; Colorectal cancer (CRC) [MIM:114500]: A complex disease characterized by malignant lesions arising from the inner wall of the large intestine (the colon) and the rectum. Genetic alterations are often associated with progression from premalignant lesion (adenoma) to invasive adenocarcinoma. Risk factors for cancer of the colon and rectum include colon polyps, long-standing ulcerative colitis, and genetic family history. {ECO:0000269|PubMed:12198537, ECO:0000269|PubMed:23263490, ECO:0000269|PubMed:24455489}. Note=The disease may be caused by mutations affecting the gene represented in this entry.; Lung cancer (LNCR) [MIM:211980]: A common malignancy affecting tissues of the lung. The most common form of lung cancer is non-small cell lung cancer (NSCLC) that can be divided into 3 major histologic subtypes: squamous cell carcinoma, adenocarcinoma, and large cell lung cancer. NSCLC is often diagnosed at an advanced stage and has a poor prognosis. {ECO:0000269|PubMed:12460919}. Note=The gene represented in this entry is involved in disease pathogenesis.; Familial non-Hodgkin lymphoma (NHL) [MIM:605027]: Cancer that starts in cells of the lymph system, which is part of the body's immune system. NHLs can occur at any age and are often marked by enlarged lymph nodes, fever and weight loss. {ECO:0000269|PubMed:14612909}. Note=The gene represented in this entry is involved in disease pathogenesis.; Cardiofaciocutaneous syndrome 1 (CFC1) [MIM:115150]: A multiple congenital anomaly disorder characterized by a distinctive facial appearance, heart defects and mental retardation. Heart defects include pulmonic stenosis, atrial septal defects and hypertrophic cardiomyopathy. Some affected individuals present with ectodermal abnormalities such as sparse, friable hair, hyperkeratotic skin lesions and a generalized ichthyosis-like condition. Typical facial features are similar to Noonan syndrome. They include high forehead with bitemporal constriction, hypoplastic supraorbital ridges, downslanting palpebral fissures, a depressed nasal bridge, and posteriorly angulated ears with prominent helices. {ECO:0000269|PubMed:16439621,

	ECO:0000269|PubMed:16474404, ECO:0000269|PubMed:18042262, ECO:0000269|PubMed:19206169}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Noonan syndrome 7 (NS7) [MIM:613706]: A form of Noonan syndrome, a disease characterized by short stature, facial dysmorphic features such as hypertelorism, a downward eyeslant and low-set posteriorly rotated ears, and a high incidence of congenital heart defects and hypertrophic cardiomyopathy. Other features can include a short neck with webbing or redundancy of skin, deafness, motor delay, variable intellectual deficits, multiple skeletal defects, cryptorchidism, and bleeding diathesis. Individuals with Noonan syndrome are at risk of juvenile myelomonocytic leukemia, a myeloproliferative disorder characterized by excessive production of myelomonocytic cells. {ECO:0000269|PubMed:19206169}. Note=The disease is caused by mutations affecting the gene represented in this entry.; LEOPARD syndrome 3 (LPRD3) [MIM:613707]: A disorder characterized by lentigines, electrocardiographic conduction abnormalities, ocular hypertelorism, pulmonic stenosis, abnormalities of genitalia, retardation of growth, and sensorineural deafness. {ECO:0000269|PubMed:19206169}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Note=A chromosomal aberration involving BRAF is found in pilocytic astrocytomas. A tandem duplication of 2 Mb at 7q34 leads to the expression of a KIAA1549-BRAF fusion protein with a constitutive kinase activity and inducing cell transformation. {ECO:0000269|PubMed:18974108}.
Q09472	Note=Defects in EP300 may play a role in epithelial cancer.; Note=Chromosomal aberrations involving EP300 may be a cause of acute myeloid leukemias. Translocation t(8;22)(p11;q13) with KAT6A.; Rubinstein-Taybi syndrome 2 (RSTS2) [MIM:613684]: A disorder characterized by craniofacial abnormalities, postnatal growth deficiency, broad thumbs, broad big toes, mental retardation and a propensity for development of malignancies. Some individuals with RSTS2 have less severe mental impairment, more severe microcephaly, and a greater degree of changes in facial bone structure than RSTS1 patients. {ECO:0000269|PubMed:15706485}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8IYU2	Note=Defects in HACE1 are a cause of Wilms tumor (WT). WT is a pediatric malignancy of kidney and one of the most common solid cancers in childhood. HACE1 is epigenetically down-regulated in sporadic Wilms tumor. Moreover, a t(5;6)(q21;q21) translocation that truncates HACE1 has been found in a child with bilateral, young-onset Wilms tumor.
P46734	Note=Defects in MAP2K3 may be involved in colon cancer.
Q14680	Note=Defects in MELK are associated with some cancers, such as brain or breast cancers. Expression is dramatically increased in aggressive undifferentiated tumors, correlating with poor patient outcome in breast and brain cancers, suggesting a role in tumor-initiating cells and proliferation via its function in cell proliferation regulation.
P53350	Note=Defects in PLK1 are associated with some cancers, such as gastric, thyroid or B-cell lymphomas. Expression is cancer increased in tumor tissues with a poor prognosis, suggesting a role in malignant transformations and carcinogenesis.
Q99575	Note=Defects in POP1 may be the cause of a severe skeletal dysplasia reminiscent of anauxetic dysplasia. Affected individuals show severe growth retardation of prenatal onset, a bone dysplasia affecting the epiphyses and metaphyses of the long bones particularly in the lower limbs, and abnormalities of the spine including irregularly shaped vertebral bodies and marked cervical spine instability.
Q9H3S3	Note=Defects in TMPRSS5 may be a cause of deafness.
P47974	Note=Defects in ZFP36L2 may be a cause of leukemias. Frameshfits mutations disrupting ZFP36L2 have been found in a patient with acute myeloid leukemia (PubMed:21109922). {ECO:0000269|PubMed:21109922}.
Q96GD4	Note=Disruptive regulation of expression is a possible mechanism of the perturbation of chromosomal integrity in cancer cells through its dominant-negative effect on cytokinesis.
Q15056	Note=EIF4H is located in the Williams-Beuren syndrome (WBS) critical region. WBS results from a hemizygous deletion of several genes on chromosome 7q11.23, thought to arise as a consequence of unequal crossing over between highly homologous low-copy repeat sequences flanking the deleted region. Haploinsufficiency of EIF4H may be the cause of certain cardiovascular and musculo-skeletal abnormalities observed in the disease.
Q12955	Note=Genetic variations in ANK3 may be associated with autism spectrum disorders susceptibility.; Mental retardation, autosomal recessive 37 (MRT37) [MIM:615493]: A disorder characterized by significantly below average general intellectual functioning associated with impairments in adaptive behavior and manifested during the developmental period. MRT37 patients manifest delayed global development with speech delay, hypotonia, spasticity, and a sleep disorder. Severe behavioral abnormalities include aggression, hyperactivity, and grinding of the teeth. Note=The disease is caused by

	mutations affecting the gene represented in this entry. A homozygous deletion in ANK3 predicted to result in frameshift and premature truncation, has been shown to be the cause of moderate intellectual disability, an ADHD-like phenotype and behavioral problems in a consanguineous family (PubMed:23390136). {ECO:0000269|PubMed:23390136}.
Q9P0L2	Note=Genetic variations in MARK1 may be associated with susceptibility to autism. MARK1 is overexpressed in the prefrontal cortex of patients with autism and causes changes in the function of cortical dendrites.
Q5U5Q3	Note=Genetic variations in MEX3C may be associated with susceptibility to essential hypertension.
P00750	Note=Increased activity of TPA results in increased fibrinolysis of fibrin blood clots that is associated with excessive bleeding. Defective release of TPA results in hypofibrinolysis that can lead to thrombosis or embolism.
P53778	Note=MAPK is overexpressed in highly metastatic breast cancer cell lines and its expression is preferentially associated with basal-like and metastatic phenotypes of breast tumor samples.
P80192	Note=May play a role in esophageal cancer susceptibility and/or development.
P26927	Note=MST1 variant Cys-689 may be associated with inflammatory bowel disease (IBD), a chronic, relapsing inflammation of the gastrointestinal tract with a complex etiology. It is unsure whether Cys-689 itself or a variation in linkage disequilibrium with Cys-689 is responsible for the association with IBD. {ECO:0000269|PubMed:19079170, ECO:0000269|PubMed:20228799}.
O00423	Note=Mutations in this gene are associated with atypical heterotopia, epilepsy and mental retardation. Patients present giant bilateral periventricular and ribbon-like subcortical heterotopia with polymicrogyria and agenesis of the corpus callosum.
Q9Y4P3	Note=TBL2 is located in the Williams-Beuren syndrome (WBS) critical region. WBS results from a hemizygous deletion of several genes on chromosome 7q11.23, thought to arise as a consequence of unequal crossing over between highly homologous low-copy repeat sequences flanking the deleted region. Haploinsufficiency of TBL2 may be the cause of certain cardiovascular and musculo-skeletal abnormalities observed in the disease.
Q8WVM0	Note=Variations in TFB1M may influence the clinical expression of aminoglycoside-induced deafness caused by the A1555G mutation in the mitochondrial 12S rRNA.
Q86U42	Oculopharyngeal muscular dystrophy (OPMD) [MIM:164300]: A form of late-onset slowly progressive myopathy characterized by eyelid ptosis, dysphagia and, sometimes by other cranial and limb-muscle involvement. {ECO:0000269|PubMed:12673802}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q5T1V6	Orofaciodigital syndrome 5 (OFD5) [MIM:174300]: A form of orofaciodigital syndrome, a group of heterogeneous disorders characterized by malformations of the oral cavity, face and digits, and associated phenotypic abnormalities that lead to the delineation of various subtypes. OFD5 patients show the core features of cleft palate, lobulated tongue, and polydactyly. Additional features include frontal bossing and intellectual disability. {ECO:0000269|PubMed:23972372}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9BXN1	Osteoarthritis 3 (OS3) [MIM:607850]: A degenerative disease of the joints characterized by degradation of the hyaline articular cartilage and remodeling of the subchondral bone with sclerosis. Clinical symptoms include pain and joint stiffness often leading to significant disability and joint replacement. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry. Susceptibility to osteoarthritis is conferred by a triplet repeat expansion polymorphism. ASPN allele having 14 aspartic acid repeats in the N-terminal region of the protein (D14), is overrepresented relative to the common allele having 13 aspartic acid repeats (D13). The frequency of the D14 allele increases with disease severity. The D14 allele is also overrepresented in individuals with hip osteoarthritis.; Intervertebral disc disease (IDD) [MIM:603932]: A common musculo-skeletal disorder caused by degeneration of intervertebral disks of the lumbar spine. It results in low-back pain and unilateral leg pain. {ECO:0000269|PubMed:18304494}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry. Susceptibility to intervertebral disk disease, particularly lumbar disk degeneration, is conferred by a triplet repeat expansion polymorphism. ASPN allele having 14 aspartic acid repeats in the N-terminal region of the protein (D14), is associated with the disorder in some populations (PubMed:18304494). {ECO:0000269|PubMed:18304494}.
Q9BXB1	Osteoporosis (OSTEOP) [MIM:166710]: A systemic skeletal disorder characterized by decreased bone mass and deterioration of bone microarchitecture without alteration in the composition of bone. The result is fragile bones and an increased risk of fractures, even after minimal trauma. Osteoporosis is a chronic condition of multifactorial etiology and is usually clinically silent until a fracture occurs. {ECO:0000269|PubMed:23644456}. Note=Disease susceptibility may be associated with variations affecting the gene represented in this entry. A LGR4 nonsense mutation creating a stop codon after

	position 126 (c.376C>T) is strongly associated with low bone mineral density and osteoporotic fractures (PubMed:23644456). This mutation probably causes degradation of the transcript by nonsense-mediated decay (NMD). The c.376C>T mutation is also associated with electrolyte imbalance, late onset of menarche and reduced testosterone levels, as well as an increased risk of squamous cell carcinoma of the skin and biliary tract cancer (PubMed:23644456). {ECO:0000269|PubMed:23644456}.
P07477	Pancreatitis, hereditary (PCTT) [MIM:167800]: A disease characterized by pancreas inflammation, permanent destruction of the pancreatic parenchyma, maldigestion, and severe abdominal pain attacks. {ECO:0000269|PubMed:10204851, ECO:0000269|PubMed:10381903, ECO:0000269|PubMed:10930381, ECO:0000269|PubMed:11073545, ECO:0000269|PubMed:11788572, ECO:0000269|PubMed:11866271, ECO:0000269|PubMed:14695529, ECO:0000269|PubMed:15776435, ECO:0000269|PubMed:8841182, ECO:0000269|PubMed:9322498, ECO:0000269|PubMed:9633818}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
Q99895	Pancreatitis, hereditary (PCTT) [MIM:167800]: A disease characterized by pancreas inflammation, permanent destruction of the pancreatic parenchyma, maldigestion, and severe abdominal pain attacks. {ECO:0000269|PubMed:18059268, ECO:0000269|PubMed:18172691, ECO:0000269|PubMed:22580415, ECO:0000269|PubMed:22942235}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry. Loss-of-function CTRC variants predispose to pancreatitis by diminishing its protective trypsin-degrading activity (PubMed:18059268). They cause loss of function by one or more of three mechanisms: reduced secretion, catalytic defect and increased degradation by trypsin (PubMed:22942235). {ECO:0000269|PubMed:18059268, ECO:0000269|PubMed:22942235}.
Q04637	Parkinson disease 18 (PARK18) [MIM:614251]: An autosomal dominant, late-onset form of Parkinson disease. Parkinson disease is a complex neurodegenerative disorder characterized by bradykinesia, resting tremor, muscular rigidity and postural instability, as well as by a clinically significant response to treatment with levodopa. The pathology involves the loss of dopaminergic neurons in the substantia nigra and the presence of Lewy bodies (intraneuronal accumulations of aggregated proteins), in surviving neurons in various areas of the brain. {ECO:0000269|PubMed:21907011}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q5S007	Parkinson disease 8 (PARK8) [MIM:607060]: A slowly progressive neurodegenerative disorder characterized by bradykinesia, rigidity, resting tremor, postural instability, neuronal loss in the substantia nigra, and the presence of neurofibrillary MAPT (tau)-positive and Lewy bodies in some patients. {ECO:0000269|PubMed:15541308, ECO:0000269|PubMed:15541309, ECO:0000269|PubMed:15680455, ECO:0000269|PubMed:15680456, ECO:0000269|PubMed:15680457, ECO:0000269|PubMed:15726496, ECO:0000269|PubMed:15732108, ECO:0000269|PubMed:15811454, ECO:0000269|PubMed:15852371, ECO:0000269|PubMed:15880653, ECO:0000269|PubMed:15925109, ECO:0000269|PubMed:15929036, ECO:0000269|PubMed:16102999, ECO:0000269|PubMed:16157901, ECO:0000269|PubMed:16157908, ECO:0000269|PubMed:16157909, ECO:0000269|PubMed:16172858, ECO:0000269|PubMed:16240353, ECO:0000269|PubMed:16247070, ECO:0000269|PubMed:16250030, ECO:0000269|PubMed:16251215, ECO:0000269|PubMed:16272164, ECO:0000269|PubMed:16272257, ECO:0000269|PubMed:16298482, ECO:0000269|PubMed:16333314, ECO:0000269|PubMed:16533964, ECO:0000269|PubMed:18213618, ECO:0000269|PubMed:22956510}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8IYB7	Perlman syndrome (PRLMNS) [MIM:267000]: An autosomal recessive congenital overgrowth syndrome. Affected children are large at birth, are hypotonic, and show organomegaly, characteristic facial dysmorphisms (inverted V-shaped upper lip, prominent forehead, deep-set eyes, broad and flat nasal bridge, and low-set ears), renal anomalies (nephromegaly and hydronephrosis), frequent neurodevelopmental delay, and high neonatal mortality. Perlman syndrome is associated with a high risk of Wilms tumor. Histologic examination of the kidneys in affected children shows frequent nephroblastomatosis, which is a precursor lesion for Wilms tumor. {ECO:0000269|PubMed:22306653, ECO:0000269|PubMed:23486540, ECO:0000269|PubMed:23576526}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O00628	Peroxisome biogenesis disorder complementation group 11 (PBD-CG11) [MIM:614879]: A peroxisomal disorder arising from a failure of protein import into the peroxisomal membrane or matrix. The peroxisome biogenesis disorders (PBD group) are genetically heterogeneous with at least 14 distinct genetic groups as concluded from complementation studies. Include disorders are: Zellweger syndrome (ZWS), neonatal adrenoleukodystrophy (NALD), infantile Refsum disease (IRD), and classical rhizomelic chondrodysplasia punctata (RCDP). ZWS, NALD and IRD are distinct from RCDP and constitute a clinical continuum of overlapping phenotypes known as the Zellweger spectrum (PBD-ZSS). Note=The disease is caused by mutations affecting the gene represented in this entry.; Rhizomelic chondrodysplasia punctata 1 (RCDP1) [MIM:215100]: A peroxisome biogenesis disorder. It is

	characterized by rhizomelic shortening of femur and humerus, vertebral disorders, cataract, cutaneous lesions and severe mental retardation. {ECO:0000269|PubMed:9090381}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Peroxisome biogenesis disorder 9B (PBD9B) [MIM:614879]: A peroxisome biogenesis disorder with unusually mild clinical and biochemical manifestations. Affected individuals manifest a variable phenotype similar to, and in some cases indistinguishable from, classic Refsum disease. Variable features include ocular abnormalities, sensorimotor neuropathy, ichthyosis, deafness, chondrodysplasia punctata without rhizomelia or growth failure. {ECO:0000269|PubMed:12522768}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P49590	Perrault syndrome 2 (PRLTS2) [MIM:614926]: A sex-influenced disorder characterized by sensorineural deafness in both males and females and ovarian dysgenesis in females. Affected females have primary amenorrhea, streak gonads, and infertility, whereas affected males show normal pubertal development and are fertile. {ECO:0000269|PubMed:21464306}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q15031	Perrault syndrome 4 (PRLTS4) [MIM:615300]: A sex-influenced disorder characterized by sensorineural deafness in both males and females, and ovarian dysgenesis in females. Affected females have primary amenorrhea, streak gonads, and infertility, whereas affected males show normal pubertal development and are fertile. {ECO:0000269|PubMed:23541342}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q15831	Peutz-Jeghers syndrome (PJS) [MIM:175200]: An autosomal dominant disorder characterized by melanocytic macules of the lips, multiple gastrointestinal hamartomatous polyps and an increased risk for various neoplasms, including gastrointestinal cancer. {ECO:0000269|PubMed:10408777, ECO:0000269|PubMed:12372054, ECO:0000269|PubMed:21411391, ECO:0000269|PubMed:9425897, ECO:0000269|PubMed:9428765, ECO:0000269|PubMed:9760200, ECO:0000269|PubMed:9837816}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Testicular germ cell tumor (TGCT) [MIM:273300]: A common malignancy in males representing 95% of all testicular neoplasms. TGCTs have various pathologic subtypes including: unclassified intratubular germ cell neoplasia, seminoma (including cases with syncytiotrophoblastic cells), spermatocytic seminoma, embryonal carcinoma, yolk sac tumor, choriocarcinoma, and teratoma. {ECO:0000269|PubMed:9605748}. Note=The gene represented in this entry may be involved in disease pathogenesis.; Note=Defects in STK11 are associated with some sporadic cancers, especially lung cancers. Frequently mutated and inactivated in non-small cell lung cancer (NSCLC). Defects promote lung cancerigenesis process, especially lung cancer progression and metastasis. Confers lung adenocarcinoma the ability to trans-differentiate into squamous cell carcinoma. Also able to promotes lung cancer metastasis, via both cancer-cell autonomous and non-cancer-cell autonomous mechanisms.
P40337	Pheochromocytoma (PCC) [MIM:171300]: A catecholamine-producing tumor of chromaffin tissue of the adrenal medulla or sympathetic paraganglia. The cardinal symptom, reflecting the increased secretion of epinephrine and norepinephrine, is hypertension, which may be persistent or intermittent. {ECO:0000269|PubMed:12000816, ECO:0000269|PubMed:14500403, ECO:0000269|PubMed:9663592}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.; von Hippel-Lindau disease (VHLD) [MIM:193300]: VHLD is a dominantly inherited familial cancer syndrome predisposing to a variety of malignant and benign neoplasms, most frequently retinal, cerebellar and spinal hemangioblastoma, renal cell carcinoma (RCC), pheochromocytoma, and pancreatic tumors. VHL type 1 is without pheochromocytoma, type 2 is with pheochromocytoma. VHL type 2 is further subdivided into types 2A (pheochromocytoma, retinal angioma, and hemangioblastomas without renal cell carcinoma and pancreatic cyst) and 2B (pheochromocytoma, retinal angioma, and hemangioblastomas with renal cell carcinoma and pancreatic cyst). {ECO:0000269|PubMed:10408776, ECO:0000269|PubMed:10533030, ECO:0000269|PubMed:10627136, ECO:0000269|PubMed:10635329, ECO:0000269|PubMed:16502427, ECO:0000269|PubMed:7728151, ECO:0000269|PubMed:7987306, ECO:0000269|PubMed:8493574, ECO:0000269|PubMed:8592333, ECO:0000269|PubMed:8634692, ECO:0000269|PubMed:8730290, ECO:0000269|PubMed:8825918, ECO:0000269|PubMed:8956040, ECO:0000269|PubMed:9452032, ECO:0000269|PubMed:9452106, ECO:0000269|PubMed:9829911, ECO:0000269|PubMed:9829912, ECO:0000269|Ref.41}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Erythrocytosis, familial, 2 (ECYT2) [MIM:263400]: An autosomal recessive disorder characterized by an increase in serum red blood cell mass, hypersensitivity of erythroid progenitors to erythropoietin, increased erythropoietin serum levels, and normal oxygen affinity. Patients with ECYT2 carry a high risk for peripheral thrombosis and cerebrovascular events. {ECO:0000269|PubMed:12393546, ECO:0000269|PubMed:12844285}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Renal cell carcinoma (RCC) [MIM:144700]: Renal

	cell carcinoma is a heterogeneous group of sporadic or hereditary carcinoma derived from cells of the proximal renal tubular epithelium. It is subclassified into clear cell renal carcinoma (non-papillary carcinoma), papillary renal cell carcinoma, chromophobe renal cell carcinoma, collecting duct carcinoma with medullary carcinoma of the kidney, and unclassified renal cell carcinoma. Clear cell renal cell carcinoma is the most common subtype. {ECO:0000269|PubMed:11986208}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P00747	Plasminogen deficiency (PLGD) [MIM:217090]: A disorder characterized by decreased serum plasminogen activity. Two forms of the disorder are distinguished: type 1 deficiency is additionally characterized by decreased plasminogen antigen levels and clinical symptoms, whereas type 2 deficiency, also known as dysplasminogenemia, is characterized by normal, or slightly reduced antigen levels, and absence of clinical manifestations. Plasminogen deficiency type 1 results in markedly impaired extracellular fibrinolysis and chronic mucosal pseudomembranous lesions due to subepithelial fibrin deposition and inflammation. The most common clinical manifestation of type 1 deficiency is ligneous conjunctivitis in which pseudomembranes formation on the palpebral surfaces of the eye progresses to white, yellow-white, or red thick masses with a wood-like consistency that replace the normal mucosa. {ECO:0000269|PubMed:10233898, ECO:0000269|PubMed:1427790, ECO:0000269|PubMed:1986355, ECO:0000269|PubMed:6216475, ECO:0000269|PubMed:6238949, ECO:0000269|PubMed:8392398, ECO:0000269|PubMed:9242524, ECO:0000269|PubMed:9858247}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9UPY3	Pleuropulmonary blastoma (PPB) [MIM:601200]: A rare pediatric intrathoracic neoplasm. The tumor arises from the lung, pleura, or both, and appears to be purely mesenchymal in phenotype. It lacks malignant epithelial elements, a feature that distinguishes it from the classic adult-type pulmonary blastoma. It arises during fetal lung development and is often part of an inherited cancer syndrome. The tumor contain both epithelial and mesenchymal cells. Early in tumorigenesis, cysts form in lung airspaces, and these cysts are lined with benign-appearing epithelium. Mesenchymal cells susceptible to malignant transformation reside within the cyst walls and form a dense layer beneath the epithelial lining. In a subset of patients, overgrowth of the mesenchymal cells produces a sarcoma, a transition that is associated with a poorer prognosis. Some patients have multilocular cystic nephroma, a benign kidney tumor. {ECO:0000269|PubMed:19556464}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Goiter multinodular 1, with or without Sertoli-Leydig cell tumors (MNG1) [MIM:138800]: A common disorder characterized by nodular overgrowth of the thyroid gland. Some individuals may also develop Sertoli-Leydig cell tumors, usually of the ovary. {ECO:0000269|PubMed:21205968}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Rhabdomyosarcoma, embryonal, 2 (RMSE2) [MIM:180295]: A form of rhabdomyosarcoma, a highly malignant tumor of striated muscle derived from primitive mesenchymal cells and exhibiting differentiation along rhabdomyoblastic lines. Rhabdomyosarcoma is one of the most frequently occurring soft tissue sarcomas and the most common in children. It occurs in four forms: alveolar, pleomorphic, embryonal and botryoidal rhabdomyosarcomas. Note=The disease is caused by mutations affecting the gene represented in this entry.; Note=DICER1 mutations have been found in uterine cervix embryonal rhabdomyosarcoma, primitive neuroectodermal tumor, Wilms tumor, pulmonary sequestration and juvenile intestinal polyp (PubMed:21882293). Somatic missense mutations affecting the RNase IIIb domain of DICER1 are common in non-epithelial ovarian tumors. These mutations do not abolish DICER1 function but alter it in specific cell types, a novel mechanism through which perturbation of microRNA processing may be oncogenic (PubMed:22187960). {ECO:0000269|PubMed:21882293, ECO:0000269|PubMed:22187960}.
Q15928	Polydactyly, postaxial A6 (PAPA6) [MIM:615226]: A condition characterized by the occurrence of supernumerary digits in the upper and/or lower extremities. In postaxial polydactyly type A, the extra digit is well-formed and articulates with the fifth or a sixth metacarpal/metatarsal. {ECO:0000269|PubMed:23160277}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8TDJ6	Polyendocrine-polyneuropathy syndrome (PEPNS) [MIM:616113]: A progressive endocrine and neurodevelopmental disorder manifesting early in childhood with growth retardation and recurrent episodes of profound asymptomatic hypoglycemia. PEPNS is characterized by central hypothyroidism, hypogonadotropic hypogonadism, incomplete puberty, progressive non-autoimmune insulin-dependent diabetes mellitus, peripheral demyelinating sensorimotor polyneuropathy, and cerebellar and pyramidal signs. {ECO:0000269|PubMed:25248098}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q92989	Pontocerebellar hypoplasia 10 (PCH10) [MIM:615803]: A form of pontocerebellar hypoplasia, a disorder characterized by structural defects of the pons and cerebellum, evident upon brain imaging. PCH10 features include cortical dysgenesis marked by a simplified gyral pattern, cortical atrophy, mild or focal

	cerebellar vermian volume loss, delayed myelination, progressive microcephaly, global growth and developmental delays, severe intellectual disabilities, and seizures refractory to treatment. {ECO:0000269|PubMed:24766809, ECO:0000269|PubMed:24766810}. Note=The disease is caused by mutations affecting the gene represented in this entry. Neurodegeneration is due to defects in tRNA splicing (PubMed:24766809, PubMed:24766810). {ECO:0000269|PubMed:24766809, ECO:0000269|PubMed:24766810}.
Q96B26	Pontocerebellar hypoplasia 1C (PCH1C) [MIM:616081]: A severe autosomal recessive neurodegenerative disease characterized by cerebellar and corpus callosum hypoplasia, abnormal myelination of the central nervous system, and spinal motor neuron disease. Affected individuals manifest failure to thrive, severe muscle weakness, spasticity and psychomotor retardation. Vision and hearing are impaired. {ECO:0000269|PubMed:24989451}. Note=The disease is caused by mutations affecting the gene represented in this entry. EXOSC8 dysfunction causes myelin disruption through an imbalanced supply of myelin proteins due to dysregulation of their ARE-containing mRNAs (PubMed:24989451). {ECO:0000269|PubMed:24989451}.
Q8NCE0	Pontocerebellar hypoplasia 2B (PCH2B) [MIM:612389]: A disorder characterized by an abnormally small cerebellum and brainstem, and progressive microcephaly from birth combined with extrapyramidal dyskinesia. Severe chorea occurs and epilepsy is frequent. There are no signs of spinal cord anterior horn cells degeneration. {ECO:0000269|PubMed:18711368}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9BSV6	Pontocerebellar hypoplasia 2C (PCH2C) [MIM:612390]: A disorder characterized by an abnormally small cerebellum and brainstem, and progressive microcephaly from birth combined with extrapyramidal dyskinesia. Severe chorea occurs and epilepsy is frequent. There are no signs of spinal cord anterior horn cells degeneration. {ECO:0000269|PubMed:18711368}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9HD40	Pontocerebellar hypoplasia 2D (PCH2D) [MIM:613811]: A disorder characterized by postnatal onset of progressive atrophy of the cerebrum and cerebellum, microcephaly, profound mental retardation, spasticity, and variable seizures. {ECO:0000269|PubMed:20920667}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q5T160	Pontocerebellar hypoplasia 6 (PCH6) [MIM:611523]: A disorder characterized by an abnormally small cerebellum and brainstem, infantile encephalopathy, generalized hypotonia, lethargy and poor feeding. Recurrent apnea, intractable seizures occur early in the course of this condition. {ECO:0000269|PubMed:17847012}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P57078	Popliteal pterygium syndrome, lethal type (PPS-L) [MIM:263650]: An autosomal recessive disorder characterized by multiple popliteal pterygia leading to severe arthrogryposis, ankyloblepharon filiforme adnatum, filiform bands between the jaws, synostosis of the carpal/tarsal and phalangeal bones in the hands and feet, digital hypoplasia/aplasia, complete soft-tissue syndactyly, lack of nails, lack of scalp hair, eyebrows and eyelashes, blepharophimosis, cleft lip and/or palate, and hypoplastic external genitalia. Early lethality is common, although survival into childhood and beyond has been reported. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9Y5Q5	Pre-eclampsia/eclampsia 5 (PEE5) [MIM:614595]: A hypertensive disorder of pregnancy characterized by new hypertension (blood pressure 140/90 or greater) presenting after 20 weeks' gestation with clinically relevant proteinuria. It impacts 2 individuals, the mother and her child, both of whom can be severely affected. Preeclampsia is one of the causes of maternal mortality and morbidity worldwide. {ECO:0000269|PubMed:22437503}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q13064	Precocious puberty, central 2 (CPPB2) [MIM:615346]: A condition defined as the development of secondary sexual characteristics in boys and girls at a chronological age that is 2.5 standard deviations below the mean age at onset of puberty in the population. Central precocious puberty results from premature activation of the hypothalamic-pituitary-gonadal axis. {ECO:0000269|PubMed:23738509, ECO:0000269|PubMed:24438377, ECO:0000269|PubMed:24628548, ECO:0000269|PubMed:25011910, ECO:0000269|PubMed:25316453}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P03952	Prekallikrein deficiency (PKK deficiency) [MIM:612423]: This disorder is a blood coagulation defect. {ECO:0000269|PubMed:14652634, ECO:0000269|PubMed:17598838}. Note=The disease is caused by mutations affecting the gene represented in this entry.
A2PYH4	Premature ovarian failure 9 (POF9) [MIM:615724]: An ovarian disorder defined as the cessation of ovarian function under the age of 40 years. It is characterized by oligomenorrhea or amenorrhea, in the presence of elevated levels of serum gonadotropins and low estradiol. {ECO:0000303|PubMed:24597873}. Note=The disease may be caused by mutations affecting the gene

	represented in this entry.
P17612	Primary pigmented nodular adrenocortical disease 4 (PPNAD4) [MIM:615830]: A rare bilateral adrenal defect causing ACTH-independent Cushing syndrome. Macroscopic appearance of the adrenals is characteristic with small pigmented micronodules observed in the cortex. Adrenal glands show overall normal size and weight, and multiple small yellow-to-dark brown nodules surrounded by a cortex with a uniform appearance. Microscopically, there are moderate diffuse cortical hyperplasia with mostly nonpigmented nodules, multiple capsular deficits and massive circumscribed and infiltrating extra-adrenal cortical excrescences with micronodules. Clinical manifestations of Cushing syndrome include facial and truncal obesity, abdominal striae, muscular weakness, osteoporosis, arterial hypertension, diabetes. {ECO:0000269|PubMed:24571724, ECO:0000269|PubMed:24700472, ECO:0000269|PubMed:24747643, ECO:0000269|PubMed:24855271}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q05823	Prostate cancer, hereditary, 1 (HPC1) [MIM:601518]: A condition associated with familial predisposition to cancer of the prostate. Most prostate cancers are adenocarcinomas that develop in the acini of the prostatic ducts. Other rare histopathologic types of prostate cancer that occur in approximately 5% of patients include small cell carcinoma, mucinous carcinoma, prostatic ductal carcinoma, transitional cell carcinoma, squamous cell carcinoma, basal cell carcinoma, adenoid cystic carcinoma (basaloid), signet-ring cell carcinoma and neuroendocrine carcinoma. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
Q8NDI1	Prostate cancer, hereditary, 12 (HPC12) [MIM:611868]: A condition associated with familial predisposition to cancer of the prostate. Most prostate cancers are adenocarcinomas that develop in the acini of the prostatic ducts. Other rare histopathologic types of prostate cancer that occur in approximately 5% of patients include small cell carcinoma, mucinous carcinoma, prostatic ductal carcinoma, transitional cell carcinoma, squamous cell carcinoma, basal cell carcinoma, adenoid cystic carcinoma (basaloid), signet-ring cell carcinoma and neuroendocrine carcinoma. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
Q9BQ52	Prostate cancer, hereditary, 2 (HPC2) [MIM:614731]: A condition associated with familial predisposition to cancer of the prostate. Most prostate cancers are adenocarcinomas that develop in the acini of the prostatic ducts. Other rare histopathologic types of prostate cancer that occur in approximately 5% of patients include small cell carcinoma, mucinous carcinoma, prostatic ductal carcinoma, transitional cell carcinoma, squamous cell carcinoma, basal cell carcinoma, adenoid cystic carcinoma (basaloid), signet-ring cell carcinoma and neuroendocrine carcinoma. {ECO:0000269|PubMed:10986046, ECO:0000269|PubMed:11175785, ECO:0000269|PubMed:11507049, ECO:0000269|PubMed:11522646, ECO:0000269|PubMed:12515253, ECO:0000269|PubMed:12522685, ECO:0000269|PubMed:12783937, ECO:0000269|PubMed:15489334, ECO:0000269|PubMed:18987736, ECO:0000269|Ref.3}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Combined oxidative phosphorylation deficiency 17 (COXPD17) [MIM:615440]: An autosomal recessive disorder of mitochondrial dysfunction characterized by onset of severe hypertrophic cardiomyopathy in the first year of life. Other features include hypotonia, poor growth, lactic acidosis, and failure to thrive. The disorder may be fatal in early childhood. {ECO:0000269|PubMed:23849775}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q96J92	Pseudohypoaldosteronism 2B (PHA2B) [MIM:614491]: An autosomal dominant disorder characterized by hypertension, hyperkalemia, hyperchloremia, mild hyperchloremic metabolic acidosis, and correction of physiologic abnormalities by thiazide diuretics. {ECO:0000269|PubMed:11498583}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9H4A3	Pseudohypoaldosteronism 2C (PHA2C) [MIM:614492]: An autosomal dominant disorder characterized by severe hypertension, hyperkalemia, hyperchloremia, mild hyperchloremic metabolic acidosis in some cases, and correction of physiologic abnormalities by thiazide diuretics. {ECO:0000269|PubMed:11498583}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Neuropathy, hereditary sensory and autonomic, 2A (HSAN2A) [MIM:201300]: A form of hereditary sensory and autonomic neuropathy, a genetically and clinically heterogeneous group of disorders characterized by degeneration of dorsal root and autonomic ganglion cells, and by sensory and/or autonomic abnormalities. HSAN2A is an autosomal recessive disorder characterized by impairment of pain, temperature and touch sensation, onset of symptoms in infancy or early childhood, occurrence of distal extremity pathologies (paronychia, whitlows, ulcers, and Charcot joints), frequent amputations, sensory loss that affects all modalities of sensation (lower and upper limbs and perhaps the trunk as well), absence or diminution of tendon reflexes (usually in all limbs), minimal autonomic dysfunction, absence of sensory nerve action potentials, and virtual absence of myelinated fibers with decreased numbers of unmyelinated fibers in sural nerves. {ECO:0000269|PubMed:15060842, ECO:0000269|PubMed:15911806, ECO:0000269|PubMed:18521183}. Note=The disease is caused by

	mutations affecting the gene represented in this entry.
O95255	Pseudoxanthoma elasticum (PXE) [MIM:264800]: A multisystem disorder characterized by accumulation of mineralized and fragmented elastic fibers in the skin, vascular walls, and Burch membrane in the eye. Clinically, patients exhibit characteristic lesions of the posterior segment of the eye including peau d'orange, angioid streaks, and choroidal neovascularizations, of the skin including soft, ivory colored papules in a reticular pattern that predominantly affect the neck and large flexor surfaces, and of the cardiovascular system with peripheral and coronary arterial occlusive disease as well as gastrointestinal bleedings. {ECO:0000269|PubMed:10811882, ECO:0000269|PubMed:10835642, ECO:0000269|PubMed:10954200, ECO:0000269|PubMed:11427982, ECO:0000269|PubMed:11536079, ECO:0000269|PubMed:11702217, ECO:0000269|PubMed:15086542, ECO:0000269|PubMed:15098239, ECO:0000269|PubMed:15459974, ECO:0000269|PubMed:16086317, ECO:0000269|PubMed:17617515, ECO:0000269|PubMed:19339160, ECO:0000269|PubMed:20034067, ECO:0000269|PubMed:25615550}. Note=The disease is caused by mutations affecting the gene represented in this entry. Homozygous or compound heterozygous ABCC6 mutations have been found in the overwhelming majority of cases. Individuals carrying heterozygous mutations express limited manifestations of the pseudoxanthoma elasticum phenotype.; Arterial calcification of infancy, generalized, 2 (GACI2) [MIM:614473]: A severe autosomal recessive disorder characterized by calcification of the internal elastic lamina of muscular arteries and stenosis due to myointimal proliferation. The disorder is often fatal within the first 6 months of life because of myocardial ischemia resulting in refractory heart failure. {ECO:0000269|PubMed:22209248}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q99758	Pulmonary surfactant metabolism dysfunction 3 (SMDP3) [MIM:610921]: A rare lung disorder due to impaired surfactant homeostasis. It is characterized by alveolar filling with floccular material that stains positive using the periodic acid-Schiff method and is derived from surfactant phospholipids and protein components. Excessive lipoproteins accumulation in the alveoli results in severe respiratory distress. {ECO:0000269|PubMed:15044640}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9P2K8	Pulmonary venoocclusive disease 2, autosomal recessive (PVOD2) [MIM:234810]: A disease characterized by widespread fibrous obstruction and intimal thickening of septal veins and preseptal venules, a low diffusing capacity for carbon monoxide, occult alveolar hemorrhage, and nodular ground-glass opacities, septal lines and lymph node enlargement showed by high-resolution computed tomography of the chest. It is frequently associated with pulmonary capillary dilatation and proliferation, and is a rare and devastating cause of pulmonary hypertension. {ECO:0000269|PubMed:24135949, ECO:0000269|PubMed:24292273}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P00749	Quebec platelet disorder (QPD) [MIM:601709]: An autosomal dominant bleeding disorder due to a gain-of-function defect in fibrinolysis. Although affected individuals do not exhibit systemic fibrinolysis, they show delayed onset bleeding after challenge, such as surgery. The hallmark of the disorder is markedly increased PLAU levels within platelets, which causes intraplatelet plasmin generation and secondary degradation of alpha-granule proteins. {ECO:0000269|PubMed:20007542}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NWZ3	Recurrent isolated invasive pneumococcal disease 1 (IPD1) [MIM:610799]: Recurrent invasive pneumococcal disease (IPD) is defined as two episodes of IPD occurring at least 1 month apart, whether caused by the same or different serotypes or strains. Recurrent IPD occurs in at least 2% of patients in most series, making IPD the most important known risk factor for subsequent IPD. {ECO:0000269|PubMed:16950813}. Note=The disease is caused by mutations affecting the gene represented in this entry.; IRAK4 deficiency (IRAK4D) [MIM:607676]: Causes extracellular pyogenic bacterial and fungal infections in otherwise healthy children. {ECO:0000269|PubMed:12637671, ECO:0000269|PubMed:12925671, ECO:0000269|PubMed:17878374, ECO:0000269|PubMed:19663824, ECO:0000269|PubMed:21057262, ECO:0000269|PubMed:24316379}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9BYW2	Renal cell carcinoma (RCC) [MIM:144700]: Renal cell carcinoma is a heterogeneous group of sporadic or hereditary carcinoma derived from cells of the proximal renal tubular epithelium. It is subclassified into clear cell renal carcinoma (non-papillary carcinoma), papillary renal cell carcinoma, chromophobe renal cell carcinoma, collecting duct carcinoma with medullary carcinoma of the kidney, and unclassified renal cell carcinoma. Clear cell renal cell carcinoma is the most common subtype. {ECO:0000269|PubMed:20054297, ECO:0000269|PubMed:23622243, ECO:0000269|PubMed:23792563}. Note=The disease may be caused by mutations affecting the gene represented in this entry. Defects of SETD2 are associated with loss of DNA methylation at non-promoter regions (PubMed:23792563). {ECO:0000269|PubMed:23792563}.

Q9H694	Renal dysplasia, cystic (CYSRD) [MIM:601331]: An anomaly of the kidney characterized by numerous renal cysts and apparent disorder of differentiation of the renal parenchyma. Kidney of affected individuals lack the normal renal bean shape, and the collection drainage system. The cystic, dysplastic kidney contains undifferentiated mesenchyme, cartilaginous tissue, and immature collecting ducts. {ECO:0000269|PubMed:21922595}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
P54819	Reticular dysgenesis (RDYS) [MIM:267500]: Most severe form of inborn severe combined immunodeficiencies (SCID) and is characterized by absence of granulocytes and almost complete deficiency of lymphocytes in peripheral blood, hypoplasia of the thymus and secondary lymphoid organs, and lack of innate and adaptive humoral and cellular immune functions, leading to fatal septicemia within days after birth. In bone marrow of individuals with reticular dysgenesis, myeloid differentiation is blocked at the promyelocytic stage, whereas erythro- and megakaryocytic maturation is generally normal. In addition, affected newborns have bilateral sensorineural deafness. Defects may be due to its absence in leukocytes and inner ear, in which its absence can not be compensated by AK1. {ECO:0000269|PubMed:19043416, ECO:0000269|PubMed:19043417}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8WWY3	Retinitis pigmentosa 11 (RP11) [MIM:600138]: A retinal dystrophy belonging to the group of pigmentary retinopathies. Retinitis pigmentosa is characterized by retinal pigment deposits visible on fundus examination and primary loss of rod photoreceptor cells followed by secondary loss of cone photoreceptors. Patients typically have night vision blindness and loss of midperipheral visual field. As their condition progresses, they lose their far peripheral visual field and eventually central vision as well. {ECO:0000269|PubMed:11545739, ECO:0000269|PubMed:12923864, ECO:0000269|PubMed:8808602}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q6P2Q9	Retinitis pigmentosa 13 (RP13) [MIM:600059]: A retinal dystrophy belonging to the group of pigmentary retinopathies. Retinitis pigmentosa is characterized by retinal pigment deposits visible on fundus examination and primary loss of rod photoreceptor cells followed by secondary loss of cone photoreceptors. Patients typically have night vision blindness and loss of midperipheral visual field. As their condition progresses, they lose their far peripheral visual field and eventually central vision as well. {ECO:0000269|PubMed:11468273, ECO:0000269|PubMed:11910553, ECO:0000269|PubMed:12714658, ECO:0000269|Ref.33}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O43395	Retinitis pigmentosa 18 (RP18) [MIM:601414]: A retinal dystrophy belonging to the group of pigmentary retinopathies. Retinitis pigmentosa is characterized by retinal pigment deposits visible on fundus examination and primary loss of rod photoreceptor cells followed by secondary loss of cone photoreceptors. Patients typically have night vision blindness and loss of midperipheral visual field. As their condition progresses, they lose their far peripheral visual field and eventually central vision as well. {ECO:0000269|PubMed:11773002, ECO:0000269|PubMed:12714658}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O75643	Retinitis pigmentosa 33 (RP33) [MIM:610359]: A retinal dystrophy belonging to the group of pigmentary retinopathies. Retinitis pigmentosa is characterized by retinal pigment deposits visible on fundus examination and primary loss of rod photoreceptor cells followed by secondary loss of cone photoreceptors. Patients typically have night vision blindness and loss of midperipheral visual field. As their condition progresses, they lose their far peripheral visual field and eventually central vision as well. {ECO:0000269|PubMed:16723661, ECO:0000269|PubMed:19710410, ECO:0000269|PubMed:19878916, ECO:0000269|PubMed:21618346, ECO:0000269|PubMed:23029027, ECO:0000269|PubMed:23887765, ECO:0000269|PubMed:24319334}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O94906	Retinitis pigmentosa 60 (RP60) [MIM:613983]: A retinal dystrophy belonging to the group of pigmentary retinopathies. Retinitis pigmentosa is characterized by retinal pigment deposits visible on fundus examination and primary loss of rod photoreceptor cells followed by secondary loss of cone photoreceptors. Patients typically have night vision blindness and loss of midperipheral visual field. As their condition progresses, they lose their far peripheral visual field and eventually central vision as well. {ECO:0000269|PubMed:21549338}. Note=The disease may be caused by mutations affecting the gene represented in this entry. Cells from RP60 patients show intron retention for pre-mRNA bearing specific splicing signals.
P20794	Retinitis pigmentosa 62 (RP62) [MIM:614181]: A retinal dystrophy belonging to the group of pigmentary retinopathies. Retinitis pigmentosa is characterized by retinal pigment deposits visible on fundus examination and primary loss of rod photoreceptor cells followed by secondary loss of cone photoreceptors. Patients typically have night vision blindness and loss of midperipheral visual field. As

	their condition progresses, they lose their far peripheral visual field and eventually central vision as well. {ECO:0000269|PubMed:21825139, ECO:0000269|PubMed:21835304}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P51955	Retinitis pigmentosa 67 (RP67) [MIM:615565]: A retinal dystrophy belonging to the group of pigmentary retinopathies. Retinitis pigmentosa is characterized by retinal pigment deposits visible on fundus examination and primary loss of rod photoreceptor cells followed by secondary loss of cone photoreceptors. Patients typically have night vision blindness and loss of midperipheral visual field. As their condition progresses, they lose their far peripheral visual field and eventually central vision as well. {ECO:0000269|PubMed:24043777}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O43172	Retinitis pigmentosa 70 (RP70) [MIM:615922]: A retinal dystrophy belonging to the group of pigmentary retinopathies. Retinitis pigmentosa is characterized by retinal pigment deposits visible on fundus examination and primary loss of rod photoreceptor cells followed by secondary loss of cone photoreceptors. Patients typically have night vision blindness and loss of midperipheral visual field. As their condition progresses, they lose their far peripheral visual field and eventually central vision as well. {ECO:0000269|PubMed:24419317}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P38919	Richieri-Costa-Pereira syndrome (RCPS) [MIM:268305]: A syndrome characterized by a unique pattern of anomalies consisting of microstomia, micrognathia, abnormal fusion of mandible, cleft palate/Robin sequence, absence of central lower incisors, minor ears anomalies, hypoplastic first ray, abnormal tibiae, hypoplastic halluces, and clubfeet. Learning disability is also a common finding. {ECO:0000269|PubMed:24360810}. Note=The disease is caused by mutations affecting the gene represented in this entry. EIF4A3 mutations resulting in Richieri-Costa-Pereira syndrome include a repeat expansion of 18 or 20 nucleotides in the 5' untranslated region. Affected individuals have 14 to 16 repeats, while healthy individuals have 3 to 12 repeats (PubMed:24360810). {ECO:0000269|PubMed:24360810}.
O94761	Rothmund-Thomson syndrome (RTS) [MIM:268400]: Characterized by dermatological features such as atrophy, pigmentation, and telangiectasia and frequently accompanied by juvenile cataract, saddle nose, congenital bone defects, disturbances of hair growth, and hypogonadism. {ECO:0000269|PubMed:10552928}. Note=The disease is caused by mutations affecting the gene represented in this entry.; RAPADILINO syndrome (RAPADILINOS) [MIM:266280]: Disease characterized by radial and patellar aplasia or hypoplasia. {ECO:0000269|PubMed:12952869}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Baller-Gerold syndrome (BGS) [MIM:218600]: An autosomal recessive syndrome characterized by short stature, craniosynostosis, absent or hypoplastic radii, short and curved ulna, fused carpal bones and absent carpals, metacarpals and phalanges. Some patients manifest poikiloderma. Cases reported as Baller-Gerold syndrome have phenotypic overlap with several other disorders, including Saethre-Chotzen syndrome. {ECO:0000269|PubMed:15964893}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9H9Q4	Severe combined immunodeficiency due to NHEJ1 deficiency (NHEJ1-SCID) [MIM:611291]: SCID refers to a genetically and clinically heterogeneous group of rare congenital disorders characterized by impairment of both humoral and cell-mediated immunity, leukopenia and low or absent antibody levels. Patients with SCID present in infancy with recurrent, persistent infections by opportunistic organisms. The common characteristic of all types of SCID is absence of T-cell-mediated cellular immunity due to a defect in T-cell development. NHEJ1-SCID is characterized by a profound T- and B-lymphocytopenia associated with increased cellular sensitivity to ionizing radiation, microcephaly and growth retardation. Some patients may manifest SCID with sensitivity to ionizing radiation without microcephaly and mild growth retardation, probably due to hypomorphic NHEJ1 mutations. {ECO:0000269|PubMed:16439204, ECO:0000269|PubMed:16439205}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Note=A chromosomal aberration involving NHEJ1 is found in a patient with polymicrogyria. Translocation t(2;7)(q35;p22). {ECO:0000269|PubMed:12604777}.
Q8NBT0	Short stature, onychodysplasia, facial dysmorphism, and hypotrichosis (SOFT) [MIM:614813]: A syndrome characterized by severely short long bones, peculiar facies associated with paucity of hair, and nail anomalies. Growth retardation is evident on prenatal ultrasound as early as the second trimester of pregnancy, and affected individuals reach a final stature consistent with a height age of 6 years to 8 years. Relative macrocephaly is present during early childhood but head circumference is markedly low by adulthood. Psychomotor development is normal. Facial dysmorphism includes a long, triangular face with prominent nose and small ears, and affected individuals have an unusual high-pitched voice. Clinodactyly, brachydactyly, and hypoplastic distal phalanges and fingernails are present in association with postpubertal sparse and short hair. Typical skeletal findings include short and thick long bones with mild irregular metaphyseal changes, short femoral necks, and hypoplastic pelvis and sacrum. All long bones of

	the hand are short, with major delay of carpal ossification and cone-shaped epiphyses. Vertebral body ossification is also delayed. {ECO:0000269|PubMed:22840363, ECO:0000269|PubMed:22840364}. Note=The disease is caused by mutations affecting the gene represented in this entry. Cells derived from affected individuals have abnormal mitotic mechanics with multipolar spindles, in addition to clearly impaired ciliogenesis.
Q9P2H3	Short-rib thoracic dysplasia 2 with or without polydactyly (SRTD2) [MIM:611263]: A form of short-rib thoracic dysplasia, a group of autosomal recessive ciliopathies that are characterized by a constricted thoracic cage, short ribs, shortened tubular bones, and a 'trident' appearance of the acetabular roof. Polydactyly is variably present. Non-skeletal involvement can include cleft lip/palate as well as anomalies of major organs such as the brain, eye, heart, kidneys, liver, pancreas, intestines, and genitalia. Some forms of the disease are lethal in the neonatal period due to respiratory insufficiency secondary to a severely restricted thoracic cage, whereas others are compatible with life. Disease spectrum encompasses Ellis-van Creveld syndrome, asphyxiating thoracic dystrophy (Jeune syndrome), Mainzer-Saldino syndrome, and short rib-polydactyly syndrome. {ECO:0000269|PubMed:17468754}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q96PY6	Short-rib thoracic dysplasia 6 with or without polydactyly (SRTD6) [MIM:263520]: A form of short-rib thoracic dysplasia, a group of autosomal recessive ciliopathies that are characterized by a constricted thoracic cage, short ribs, shortened tubular bones, and a 'trident' appearance of the acetabular roof. Polydactyly is variably present. Non-skeletal involvement can include cleft lip/palate as well as anomalies of major organs such as the brain, eye, heart, kidneys, liver, pancreas, intestines, and genitalia. Some forms of the disease are lethal in the neonatal period due to respiratory insufficiency secondary to a severely restricted thoracic cage, whereas others are compatible with life. Disease spectrum encompasses Ellis-van Creveld syndrome, asphyxiating thoracic dystrophy (Jeune syndrome), Mainzer-Saldino syndrome, and short rib-polydactyly syndrome. {ECO:0000269|PubMed:22499340}. Note=The disease is caused by mutations affecting the gene represented in this entry. In some cases NEK1 mutations result in disease phenotype in the presence of mutations in DYNC2H1 indicating digenic inheritance (digenic short rib-polydactyly syndrome 3/6 with polydactyly) (PubMed:21211617). {ECO:0000269|PubMed:21211617}.
Q9Y3A5	Shwachman-Diamond syndrome (SDS) [MIM:260400]: Autosomal recessive disorder characterized by pancreatic exocrine insufficiency, hematologic dysfunction, and skeletal abnormalities. {ECO:0000269|PubMed:12496757, ECO:0000269|PubMed:24898207}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q96Q11	Sideroblastic anemia with B-cell immunodeficiency, periodic fevers, and developmental delay (SIFD) [MIM:616084]: An autosomal recessive disease characterized by severe sideroblastic anemia with onset in the neonatal period or infancy, recurrent periodic fevers without an infectious etiology, B-cell lymphopenia and hypogammaglobulinemia. Affected individuals show delayed psychomotor development with variable neurodegeneration. Additional variable features include sensorineural hearing loss, retinitis pigmentosa, nephrocalcinosis, and cardiomyopathy. {ECO:0000269|PubMed:25193871}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O95786	Singleton-Merten syndrome 2 (SGMRT2) [MIM:616298]: A form of Singleton-Merten syndrome, an autosomal dominant disorder characterized by marked aortic calcification, dental anomalies, osteopenia, acro-osteolysis, and to a lesser extend glaucoma, psoriasis, muscle weakness, and joint laxity. Additional clinical manifestations include particular facial characteristics and abnormal joint and muscle ligaments. SGMRT2 is an atypical form characterized by variable expression of glaucoma, aortic calcification, and skeletal abnormalities, without dental anomalies. {ECO:0000269|PubMed:25620203}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q05516	Skeletal defects, genital hypoplasia, and mental retardation (SGYMR) [MIM:612447]: A disorder characterized by mental retardation, craniofacial dysmorphism, microcephaly and short stature. Additional features include absence of the thumbs, hypoplasia of the radii and ulnae, additional vertebrae and ribs, retarded bone age and genital hypoplasia. {ECO:0000269|PubMed:18611983}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Note=A chromosomal aberration involving ZBTB16 may be a cause of acute promyelocytic leukemia (APL). Translocation t(11;17)(q32;q21) with RARA.
Q96GW9	Spastic ataxia 3, autosomal recessive (SPAX3) [MIM:611390]: A neurologic disorder characterized by cerebellar ataxia, ataxic gait, spasticity, and hyperreflexia. Other variable features include dysarthria, dysmetria, mild cognitive impairment, urinary urgency and dystonic positioning. {ECO:0000269|PubMed:22448145}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Combined oxidative phosphorylation deficiency 25 (COXPD25) [MIM:616430]: A mitochondrial disorder resulting in developmental delay, growth failure, and sensorineural hearing loss. {ECO:0000269|PubMed:25754315}. Note=The disease is caused by mutations

	affecting the gene represented in this entry.
Q8WY41	Spermatogenic failure 12 (SPGF12) [MIM:615413]: An infertility disorder caused by spermatogenesis defects. It results in decreased sperm motility, concentration, and multiple sperm structural defects. Non-obstructive azoospermia, oligozoospermia and oligo-astheno-teratozoospermia are features observed in SPGF12 patients. {ECO:0000269|PubMed:23315541}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9UQB9	Spermatogenic failure 5 (SPGF5) [MIM:243060]: An infertility disorder caused by spermatogenesis defects. Semen from affected men show close to 100% morphologically abnormal multiflagellar spermatozoa with low motility, oversized irregular heads, and abnormal midpiece and acrosome. {ECO:0000269|PubMed:17435757, ECO:0000269|PubMed:21733974}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q13117	Spermatogenic failure Y-linked 2 (SPGFY2) [MIM:415000]: A disorder resulting in the absence (azoospermia) or reduction (oligozoospermia) of sperm in the semen, leading to male infertility. {ECO:0000269|PubMed:11095434, ECO:0000269|PubMed:11870237, ECO:0000269|PubMed:12801575}. Note=The disease may be caused by mutations affecting the gene represented in this entry. AZFc deletions in the Yq11.23 region including the DAZ genes are the most common known genetic cause of human male infertility.
Q9NQZ3	Spermatogenic failure Y-linked 2 (SPGFY2) [MIM:415000]: A disorder resulting in the absence (azoospermia) or reduction (oligozoospermia) of sperm in the semen, leading to male infertility. {ECO:0000269|PubMed:11095434, ECO:0000269|PubMed:11870237, ECO:0000269|PubMed:12801575}. Note=The disease may be caused by mutations affecting the gene represented in this entry. AZFc deletions in the Yq11.23 region including the DAZ genes are the most common known genetic cause of human male infertility.
Q86SG3	Spermatogenic failure Y-linked 2 (SPGFY2) [MIM:415000]: A disorder resulting in the absence (azoospermia) or reduction (oligozoospermia) of sperm in the semen, leading to male infertility. {ECO:0000269|PubMed:11095434, ECO:0000269|PubMed:12801575}. Note=The disease may be caused by mutations affecting the gene represented in this entry. AZFc deletions in the Yq11.23 region including the DAZ genes are the most common known genetic cause of human male infertility.
Q9NR90	Spermatogenic failure Y-linked 2 (SPGFY2) [MIM:415000]: A disorder resulting in the absence (azoospermia) or reduction (oligozoospermia) of sperm in the semen, leading to male infertility. {ECO:0000269|PubMed:11095434, ECO:0000269|PubMed:12801575}. Note=The disease may be caused by mutations affecting the gene represented in this entry. AZFc deletions in the Yq11.23 region including the DAZ genes are the most common known genetic cause of human male infertility.
P16157	Spherocytosis 1 (SPH1) [MIM:182900]: Spherocytosis is a hematologic disorder leading to chronic hemolytic anemia and characterized by numerous abnormally shaped erythrocytes which are generally spheroidal. SPH1 is characterized by severe hemolytic anemia. Inheritance is autosomal recessive. {ECO:0000269|PubMed:11102985, ECO:0000269|PubMed:8640229}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q16637	Spinal muscular atrophy 1 (SMA1) [MIM:253300]: A form of spinal muscular atrophy, a group of neuromuscular disorder characterized by degeneration of the anterior horn cells of the spinal cord, leading to symmetrical muscle weakness and atrophy. Autosomal recessive forms are classified according to the age of onset, the maximum muscular activity achieved, and survivorship. The severity of the disease is mainly determined by the copy number of SMN2, a copy gene which predominantly produces exon 7-skipped transcripts and only low amount of full-length transcripts that encode for a protein identical to SMN1. Only about 4% of SMA patients bear one SMN1 copy with an intragenic mutation. SMA1 is a severe form, with onset before 6 months of age. SMA1 patients never achieve the ability to sit. {ECO:0000269|PubMed:10732817, ECO:0000269|PubMed:15249625, ECO:0000269|PubMed:15580564, ECO:0000269|PubMed:7813012, ECO:0000269|PubMed:9147655}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Spinal muscular atrophy 2 (SMA2) [MIM:253550]: An autosomal recessive form of spinal muscular atrophy, a neuromuscular disorder characterized by degeneration of the anterior horn cells of the spinal cord, leading to symmetrical muscle weakness and atrophy. It has intermediate severity, with onset between 6 and 18 months. Patients do not reach the motor milestone of standing, and survive into adulthood. {ECO:0000269|PubMed:10732802, ECO:0000269|PubMed:9158159, ECO:0000269|PubMed:9837824}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Spinal muscular atrophy 3 (SMA3) [MIM:253400]: An autosomal recessive form of spinal muscular atrophy, a neuromuscular disorder characterized by degeneration of the anterior horn cells of the spinal cord, leading to symmetrical muscle weakness and atrophy. Onset is after 18 months. Patients develop ability to stand and walk and survive into adulthood. {ECO:0000269|PubMed:10732817,

	ECO:0000269|PubMed:9158159, ECO:0000269|PubMed:9837824}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Spinal muscular atrophy 4 (SMA4) [MIM:271150]: An autosomal recessive form of spinal muscular atrophy, a neuromuscular disorder characterized by degeneration of the anterior horn cells of the spinal cord, leading to symmetrical muscle weakness and atrophy. Onset is in adulthood, disease progression is slow, and patients can stand and walk. Note=The disease is caused by mutations affecting the gene represented in this entry.
P54253	Spinocerebellar ataxia 1 (SCA1) [MIM:164400]: Spinocerebellar ataxia is a clinically and genetically heterogeneous group of cerebellar disorders. Patients show progressive incoordination of gait and often poor coordination of hands, speech and eye movements, due to cerebellum degeneration with variable involvement of the brainstem and spinal cord. SCA1 belongs to the autosomal dominant cerebellar ataxias type I (ADCA I) which are characterized by cerebellar ataxia in combination with additional clinical features like optic atrophy, ophthalmoplegia, bulbar and extrapyramidal signs, peripheral neuropathy and dementia. SCA1 is caused by expansion of a CAG repeat in the coding region of ATXN1. Longer expansions result in earlier onset and more severe clinical manifestations of the disease. {ECO:0000269|PubMed:7647801, ECO:0000269|PubMed:7951322, ECO:0000269|PubMed:8634720}. Note=The disease is caused by mutations affecting the gene represented in this entry. The disease is caused by expansion of the polyglutamine tract to about 40-83 repeats, causing accumulation in neurons and exerting toxicity. {ECO:0000269|PubMed:7647801, ECO:0000269|PubMed:8634720}.
P05129	Spinocerebellar ataxia 14 (SCA14) [MIM:605361]: Spinocerebellar ataxia is a clinically and genetically heterogeneous group of cerebellar disorders. Patients show progressive incoordination of gait and often poor coordination of hands, speech and eye movements, due to degeneration of the cerebellum with variable involvement of the brainstem and spinal cord. SCA14 is an autosomal dominant cerebellar ataxia (ADCA). {ECO:0000269|PubMed:12644968}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P20226	Spinocerebellar ataxia 17 (SCA17) [MIM:607136]: Spinocerebellar ataxia is a clinically and genetically heterogeneous group of cerebellar disorders. Patients show progressive incoordination of gait and often poor coordination of hands, speech and eye movements, due to degeneration of the cerebellum with variable involvement of the brainstem and spinal cord. SCA17 is an autosomal dominant cerebellar ataxia (ADCA) characterized by widespread cerebral and cerebellar atrophy, dementia and extrapyramidal signs. The molecular defect in SCA17 is the expansion of a CAG repeat in the coding region of TBP. Longer expansions result in earlier onset and more severe clinical manifestations of the disease. {ECO:0000269|PubMed:11313753, ECO:0000269|PubMed:11448935, ECO:0000269|PubMed:11939898}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P13639	Spinocerebellar ataxia 26 (SCA26) [MIM:609306]: A form of spinocerebellar ataxia, a clinically and genetically heterogeneous group of cerebellar disorders. Patients show progressive incoordination of gait and often poor coordination of hands, speech and eye movements, due to degeneration of the cerebellum with variable involvement of the brainstem and spinal cord. {ECO:0000269|PubMed:23001565}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O00567	Spinocerebellar ataxia 36 (SCA36) [MIM:614153]: A form of spinocerebellar ataxia, a clinically and genetically heterogeneous group of cerebellar disorders. Patients show progressive incoordination of gait and often poor coordination of hands, speech and eye movements, due to degeneration of the cerebellum with variable involvement of the brainstem and spinal cord. SCA36 is characterized by complicated clinical features, with ataxia as the first symptom, followed by characteristic late-onset involvement of the motor neuron system. Ataxic symptoms, such as gait and truncal instability, ataxic dysarthria, and uncoordinated limbs, start in late forties to fifties. Characteristically, affected individuals exhibit tongue atrophy with fasciculation. Progression of motor neuron involvement is typically limited to the tongue and main proximal skeletal muscles in both upper and lower extremities. {ECO:0000269|PubMed:21683323}. Note=The disease is caused by mutations affecting the gene represented in this entry. Caused by large hexanucleotide CGCCTG repeat expansions within intron 1. These expansions induce RNA foci and sequester the RNA-binding protein SRSF2. In addition, the transcription of MIR1292, a microRNA gene located just 19 bp 3' of the GGCCTG repeat, is significantly decreased.
Q69YN2	Spinocerebellar ataxia, autosomal recessive, 17 (SCAR17) [MIM:616127]: Spinocerebellar ataxia defines a clinically and genetically heterogeneous group of cerebellar disorders. Patients show progressive incoordination of gait and often poor coordination of hands, speech and eye movements, due to degeneration of the cerebellum with variable involvement of the brainstem and spinal cord. SCAR17 features include non-progressive congenital cerebellar ataxia, mildly delayed walking with an unsteady gait and frequent falls, dysarthria, dysmetria, hypotonia in the extremities, truncal ataxia, increased reflexes in the lower extremities, and intellectual disability. {ECO:0000269|PubMed:25361784}. Note=The disease is caused by mutations affecting the gene represented in this entry. A disease-causing

	mutation has been reported that affects an intronic splice donor site and causes exon 9 skipping, this leads to an out-of-frame stop codon after 60 aberrant amino acids. Patients carrying this mutation exhibit much lower mRNA and protein levels compared to unaffected controls, probably due to mRNA nonsense-mediated decay (PubMed:25361784). {ECO:0000269|PubMed:25361784}.
P57775	Split-hand/foot malformation 3 (SHFM3) [MIM:246560]: A limb malformation involving the central rays of the autopod and presenting with syndactyly, median clefts of the hands and feet, and aplasia and/or hypoplasia of the phalanges, metacarpals, and metatarsals. Some patients have been found to have mental retardation, ectodermal and craniofacial findings, and orofacial clefting. {ECO:0000269|PubMed:12913067}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P78363	Stargardt disease 1 (STGD1) [MIM:248200]: A common hereditary macular degeneration. It is characterized by decreased central vision, atrophy of the macula and underlying retinal pigment epithelium, and frequent presence of prominent flecks in the posterior pole of the retina. {ECO:0000269|PubMed:10090887, ECO:0000269|PubMed:10206579, ECO:0000269|PubMed:10612508, ECO:0000269|PubMed:10634594, ECO:0000269|PubMed:10711710, ECO:0000269|PubMed:10746567, ECO:0000269|PubMed:10958763, ECO:0000269|PubMed:11328725, ECO:0000269|PubMed:11385708, ECO:0000269|PubMed:11527935, ECO:0000269|PubMed:11594993, ECO:0000269|PubMed:18977788, ECO:0000269|PubMed:24444108, ECO:0000269|PubMed:9054934, ECO:0000269|PubMed:9490294, ECO:0000269|PubMed:9503029, ECO:0000269|PubMed:9781034, ECO:0000269|PubMed:9973280}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Fundus flavimaculatus (FFM) [MIM:248200]: Autosomal recessive retinal disorder very similar to Stargardt disease. In contrast to Stargardt disease, FFM is characterized by later onset and slowly progressive course. {ECO:0000269|PubMed:11379881, ECO:0000269|PubMed:11385708, ECO:0000269|PubMed:9781034}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Macular degeneration, age-related, 2 (ARMD2) [MIM:153800]: A form of age-related macular degeneration, a multifactorial eye disease and the most common cause of irreversible vision loss in the developed world. In most patients, the disease is manifest as ophthalmoscopically visible yellowish accumulations of protein and lipid that lie beneath the retinal pigment epithelium and within an elastin-containing structure known as Bruch membrane. {ECO:0000269|PubMed:19028736, ECO:0000269|PubMed:9295268}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.; Cone-rod dystrophy 3 (CORD3) [MIM:604116]: An inherited retinal dystrophy characterized by retinal pigment deposits visible on fundus examination, predominantly in the macular region, and initial loss of cone photoreceptors followed by rod degeneration. This leads to decreased visual acuity and sensitivity in the central visual field, followed by loss of peripheral vision. Severe loss of vision occurs earlier than in retinitis pigmentosa. {ECO:0000269|PubMed:10958761, ECO:0000269|PubMed:11385708, ECO:0000269|PubMed:11527935}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Retinitis pigmentosa 19 (RP19) [MIM:601718]: A retinal dystrophy belonging to the group of pigmentary retinopathies. Retinitis pigmentosa is characterized by retinal pigment deposits visible on fundus examination and primary loss of rod photoreceptor cells followed by secondary loss of cone photoreceptors. Patients typically have night vision blindness and loss of midperipheral visual field. As their condition progresses, they lose their far peripheral visual field and eventually central vision as well. RP19 is characterized by choroidal atrophy. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q86WV6	STING-associated vasculopathy, infantile-onset (SAVI) [MIM:615934]: An autoinflammatory disease characterized by early-onset systemic inflammation and cutaneous vasculopathy, resulting in severe skin lesions. Violaceous, scaling lesions of fingers, toes, nose, cheeks and ears progress to acral necrosis in most of the patients. Some patients have severe interstitial lung disease. {ECO:0000269|PubMed:25029335}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O60602	Systemic lupus erythematosus 1 (SLEB1) [MIM:601744]: A chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys and serosal membranes. It is of unknown etiology, but is thought to represent a failure of the regulatory mechanisms of the autoimmune system. The disease is marked by a wide range of system dysfunctions, an elevated erythrocyte sedimentation rate, and the formation of LE cells in the blood or bone marrow. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
Q13043	T-cell immunodeficiency, recurrent infections, and autoimmunity with or without cardiac malformations (TIIAC) [MIM:614868]: A primary T-cell immunodeficiency syndrome characterized by progressive loss of naive T-cells, recurrent bacterial, viral, and fungal infections, warts, and abscesses, autoimmune

	manifestations, and cardiac malformations, including atrial septal defect. {ECO:0000269|PubMed:22294732}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P98175	TARP syndrome (TARPS) [MIM:311900]: A disorder characterized by the Robin sequence (micrognathia, glossoptosis and cleft palate), talipes equinovarus and cardiac defects. {ECO:0000269|PubMed:20451169}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O94804	Testicular germ cell tumor (TGCT) [MIM:273300]: A common malignancy in males representing 95% of all testicular neoplasms. TGCTs have various pathologic subtypes including: unclassified intratubular germ cell neoplasia, seminoma (including cases with syncytiotrophoblastic cells), spermatocytic seminoma, embryonal carcinoma, yolk sac tumor, choriocarcinoma, and teratoma. {ECO:0000269|PubMed:16175573}. Note=The disease may be caused by mutations affecting the gene represented in this entry.
O60938	The autosomal recessive cornea plana 2 (CNA2) [MIM:217300]: In CNA2, the forward convex curvature is flattened, leading to a decrease in refraction, reduced visual activity, extreme hyperopia (usually plus 10 d or more), hazy corneal limbus, opacities in the corneal parenchyma, and marked arcus senilis (often detected at an early age). CNA2 is a rare disorder with a worldwide distribution, but a high prevalence in the Finnish population. {ECO:0000269|PubMed:10802664, ECO:0000269|PubMed:11726611}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q96GX5	Thrombocytopenia 2 (THC2) [MIM:188000]: Thrombocytopenia is defined by a decrease in the number of platelets in circulating blood, resulting in the potential for increased bleeding and decreased ability for clotting. {ECO:0000269|PubMed:12890928}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P04070	Thrombophilia due to protein C deficiency, autosomal dominant (THPH3) [MIM:176860]: A hemostatic disorder characterized by impaired regulation of blood coagulation and a tendency to recurrent venous thrombosis. Individuals with decreased amounts of protein C are classically referred to as having type I protein C deficiency and those with normal amounts of a functionally defective protein as having type II deficiency. {ECO:0000269|PubMed:1301959, ECO:0000269|PubMed:1347706, ECO:0000269|PubMed:1511989, ECO:0000269|PubMed:1868249, ECO:0000269|PubMed:2437584, ECO:0000269|PubMed:25618265, ECO:0000269|PubMed:2602169, ECO:0000269|PubMed:7792728, ECO:0000269|PubMed:7865674, ECO:0000269|PubMed:8292730, ECO:0000269|PubMed:8398832, ECO:0000269|PubMed:8499568, ECO:0000269|PubMed:8560401, ECO:0000269|PubMed:8829639, ECO:0000269|PubMed:9798967}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Thrombophilia due to protein C deficiency, autosomal recessive (THPH4) [MIM:612304]: A hemostatic disorder characterized by impaired regulation of blood coagulation and a tendency to recurrent venous thrombosis. It results in a thrombotic condition that can manifest as a severe neonatal disorder or as a milder disorder with late-onset thrombophilia. The severe form leads to neonatal death through massive neonatal venous thrombosis. Often associated with ecchymotic skin lesions which can turn necrotic called purpura fulminans, this disorder is very rare. {ECO:0000269|PubMed:1511988, ECO:0000269|PubMed:1593215, ECO:0000269|PubMed:1611081, ECO:0000269|PubMed:25618265, ECO:0000269|PubMed:7841323, ECO:0000269|PubMed:7841324, ECO:0000269|PubMed:7878626}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q8N1B3	Toe syndactyly, telecanthus, and anogenital and renal malformations (STAR) [MIM:300707]: A syndrome characterized by anal, genital and renal tract anomalies, facial dysmorphism and syndactyly. Features include anal stenosis, a rectovaginal fistula, clitoral hypertrophy, a pelvic right kidney, toe syndactyly, and telecanthus. {ECO:0000269|PubMed:18297069}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q9NSC2	Townes-Brocks syndrome (TBS) [MIM:107480]: Rare, autosomal dominant malformation syndrome with a combination of imperforate anus, triphalangeal and supernumerary thumbs, malformed ears and sensorineural hearing loss. Note=The disease is caused by mutations affecting the gene represented in this entry. Some individuals with SALL1 mutations manifest a phenotype overlapping with TBS and bronchio-oto-renal syndrome. Clinical features include dysplastic ears, hypoplastic kidneys with impaired renal function, gastroesophageal reflux, hypermetropia, hypospadias, and mild developmental delay. Affected individuals lack the characteristic anal or hand malformations of TBS.
Q9Y2S0	Treacher Collins syndrome 2 (TCS2) [MIM:613717]: A form of Treacher Collins syndrome, a disorder of craniofacial development. Treacher Collins syndrome is characterized by a combination of bilateral downward slanting of the palpebral fissures, colobomas of the lower eyelids with a paucity of eyelashes medial to the defect, hypoplasia of the facial bones, cleft palate, malformation of the external ears, atresia of the external auditory canals, and bilateral conductive hearing loss. {ECO:0000269|PubMed:21131976}. Note=The disease is caused by mutations affecting the gene

	represented in this entry.
O15160	Treacher Collins syndrome 3 (TCS3) [MIM:248390]: A form of Treacher Collins syndrome, a disorder of craniofacial development. Treacher Collins syndrome is characterized by a combination of bilateral downward slanting of the palpebral fissures, colobomas of the lower eyelids with a paucity of eyelashes medial to the defect, hypoplasia of the facial bones, cleft palate, malformation of the external ears, atresia of the external auditory canals, and bilateral conductive hearing loss. {ECO:0000269|PubMed:21131976}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q15477	Trichohepatoenteric syndrome 2 (THES2) [MIM:614602]: A syndrome characterized by intrauterine growth retardation, severe diarrhea in infancy requiring total parenteral nutrition, facial dysmorphism, immunodeficiency, and hair abnormalities, mostly trichorrhexis nodosa. Hepatic involvement contributes to the poor prognosis of affected patients. {ECO:0000269|PubMed:22444670}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O94898	Urofacial syndrome 2 (UFS2) [MIM:615112]: A rare autosomal recessive disorder characterized by facial grimacing when attempting to smile and failure of the urinary bladder to void completely despite a lack of anatomical bladder outflow obstruction or overt neurological damage. Affected individuals often have reflux of infected urine from the bladder to the upper renal tract, with a risk of kidney damage and renal failure. {ECO:0000269|PubMed:23313374}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P12081	Usher syndrome 3B (USH3B) [MIM:614504]: A syndrome characterized by progressive vision and hearing loss during early childhood. Some patients have the so-called 'Charles Bonnet syndrome,' involving decreased visual acuity and vivid visual hallucinations. USH is a genetically heterogeneous condition characterized by the association of retinitis pigmentosa with sensorineural deafness. Age at onset and differences in auditory and vestibular function distinguish Usher syndrome type 1 (USH1), Usher syndrome type 2 (USH2) and Usher syndrome type 3 (USH3). USH3 is characterized by postlingual, progressive hearing loss, variable vestibular dysfunction, and onset of retinitis pigmentosa symptoms, including nyctalopia, constriction of the visual fields, and loss of central visual acuity, usually by the second decade of life. {ECO:0000269|PubMed:22279524}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Note=HARS mutations may be involved in peripheral neuropathy, a disease mainly characterized by distal motor and sensory dysfunction. Inherited peripheral neuropathies are clinically and genetically heterogeneous with variable age of onset and reduced penetrance associated with specific loci. HARS mutations may directly predispose patients to peripheral neuropathy or may modify a peripheral neuropathy phenotype by contributing to the genetic and environmental load in a given patient (PubMed:22930593). {ECO:0000269|PubMed:22930593}.
O14896	Van der Woude syndrome 1 (VWS1) [MIM:119300]: An autosomal dominant developmental disorder characterized by lower lip pits, cleft lip and/or cleft palate. {ECO:0000269|PubMed:12219090, ECO:0000269|PubMed:12920575, ECO:0000269|PubMed:14618417, ECO:0000269|PubMed:14640121, ECO:0000269|PubMed:15300989, ECO:0000269|PubMed:17122170, ECO:0000269|PubMed:18478600}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Popliteal pterygium syndrome (PPS) [MIM:119500]: An autosomal dominant disorder characterized by oro-facial, skin and genital anomalies. Expressivity is variable. Clinical features include cleft lip/palate, lower lip cysts, syngnathia, congenital ankyloblepharon filiforme in some cases, bifid scrotum, hypoplastic scrotum, hypoplastic uterus, talipes equinovarus. Note=The disease is caused by mutations affecting the gene represented in this entry.; Non-syndromic orofacial cleft 6 (OFC6) [MIM:608864]: A birth defect consisting of cleft lips with or without cleft palate. Cleft lips are associated with cleft palate in two-third of cases. A cleft lip can occur on one or both sides and range in severity from a simple notch in the upper lip to a complete opening in the lip extending into the floor of the nostril and involving the upper gum. {ECO:0000269|PubMed:15317890, ECO:0000269|PubMed:21082654}. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
Q9UHX1	Verheij syndrome (VRJS) [MIM:615583]: A syndrome characterized by growth retardation, delayed psychomotor development, dysmorphic facial features, and skeletal, mainly vertebral, abnormalities. Additional variable features may include coloboma, renal defects, and cardiac defects. {ECO:0000269|PubMed:24140112}. Note=The disease is caused by mutations affecting the gene represented in this entry.
O43623	Waardenburg syndrome 2D (WS2D) [MIM:608890]: WS2 is a genetically heterogeneous, autosomal dominant disorder characterized by sensorineural deafness, pigmentary disturbances, and absence of dystopia canthorum. The frequency of deafness is higher in WS2 than in WS1. {ECO:0000269|PubMed:12444107}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Piebald trait (PBT) [MIM:172800]: Autosomal dominant genetic developmental

	abnormality of pigmentation characterized by congenital patches of white skin and hair that lack melanocytes. {ECO:0000269|PubMed:12955764}. Note=The disease is caused by mutations affecting the gene represented in this entry.
P31483	Welander distal myopathy (WDM) [MIM:604454]: An autosomal dominant disorder characterized by adult onset of distal muscle weakness predominantly affecting the distal long extensors of the hands, with slow progression to involve all small hand muscles and the lower legs. Skeletal muscle biopsy shows myopathic changes and prominent rimmed vacuoles. Rare homozygous patients showed earlier onset, faster progression, and proximal muscle involvement. {ECO:0000269|PubMed:23348830, ECO:0000269|PubMed:23401021}. Note=The disease is caused by mutations affecting the gene represented in this entry.
Q14191	Werner syndrome (WRN) [MIM:277700]: A rare autosomal recessive progeroid syndrome characterized by the premature onset of multiple age-related disorders, including atherosclerosis, cancer, non-insulin-dependent diabetes mellitus, ocular cataracts and osteoporosis. The major cause of death, at a median age of 47, is myocardial infarction. {ECO:0000269|PubMed:16673358}. Note=The disease is caused by mutations affecting the gene represented in this entry.; Colorectal cancer (CRC) [MIM:114500]: A complex disease characterized by malignant lesions arising from the inner wall of the large intestine (the colon) and the rectum. Genetic alterations are often associated with progression from premalignant lesion (adenoma) to invasive adenocarcinoma. Risk factors for cancer of the colon and rectum include colon polyps, long-standing ulcerative colitis, and genetic family history. Note=The disease may be caused by mutations affecting the gene represented in this entry.
Q92466	Xeroderma pigmentosum complementation group E (XP-E) [MIM:278740]: An autosomal recessive pigmentary skin disorder characterized by solar hypersensitivity of the skin, high predisposition for developing cancers on areas exposed to sunlight and, in some cases, neurological abnormalities. The skin develops marked freckling and other pigmentation abnormalities. XP-E patients show a mild phenotype with minimal or no neurologic features. {ECO:0000269|PubMed:8798680}. Note=The disease is caused by mutations affecting the gene represented in this entry.