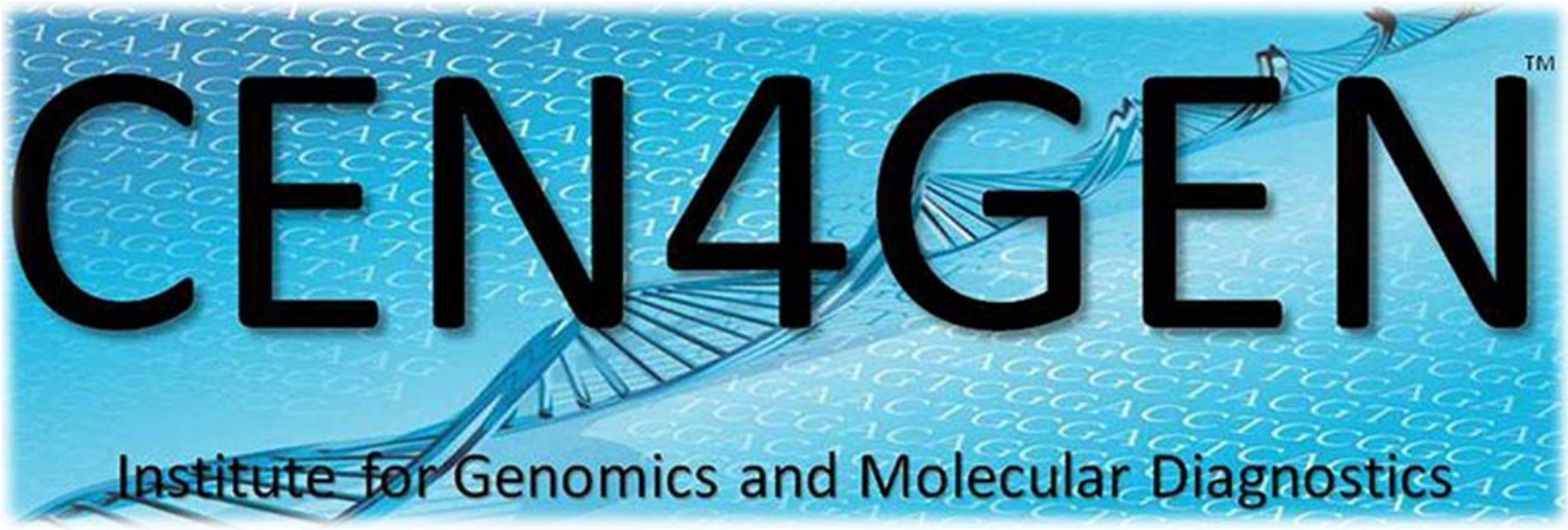

A GUIDE TO CEN4GEN PAN-ETHNIC CARRIER SCREENING

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This guide represents a "quick-reference manual" for the Pan-Ethnic Carrier Screen available at CEN4GEN, and may be used with patients to discuss the types of conditions included and if a positive result occurs, what that means in terms of expected clinical outcomes for an affected child. For each condition, a brief clinical description and corresponding gene is provided. Additional columns denote specific primary medical concerns related to each condition. Common features are included for each condition, however not all affected children will express each symptom mentioned. These symptoms may or may not be alleviated by treatment. It is important to note that those testing positive on the carrier screen are not expected to experience symptoms of the condition, but are at an increased risk for having a child who will be affected.

The list of conditions and genes is subject to change, so please refer to the CEN4GEN website for the most recent updates.

Clinical concern	Including, but not limited to:
Blood	Clotting disorders, excessive bleeding, anemia
Breathing	Difficulties as consequence of respiratory malfunction or muscular abnormalities of the chest
Cancer	Increased risk of cancer
Delays	Varying degrees of developmental and/or intellectual delays or learning disabilities when considered a primary feature versus a consequence of adverse event
Hearing	Deafness or reduced hearing (present at birth or progressive)
Heart	Damage, arrhythmias, failure, enlargement
Infections	Increased risk for infection
Kidneys	Damage, failure, malfunction
Liver	Damage, failure, enlargement, malfunction
Muscles	Weakness, abnormal tone, movement/balance/coordination difficulties
Seizures	When considered a primary feature versus a consequence of adverse event
Skeletal	General structural abnormalities, joint weakness, polydactyly, clubfoot, short stature
Vision	Blindness or reduced vision (present at birth or progressive)

CONDITION	GENE	SUMMARY	CLINICAL CONCERN												
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Achromatopsia	*CNGB3*	Achromatopsia is a condition that makes it hard for people to see color. The sharpness of images they see and the ability to see in brighter conditions is also affected.													●
Alpha-1 Antitrypsin Deficiency	*SERPINA1*	Alpha-1-antitrypsin is a condition that can cause tissue damage leading to liver disease in addition to lung damage, increased infection, and breathing difficulties (e.g. emphysema) due to the inability of the body to breakdown certain chemicals. Symptoms usually present after the 2nd decade of life. This condition is made worse by smoking.		●					●		●				
Alpha-Mannosidosis	*MAN2B1*	Alpha-mannosidosis is caused by an inability of the body to breakdown certain chemicals. The buildup of these chemicals can result in skeletal problems, hearing loss, and intellectual disability.				●	●				●			●	●
Andermann Syndrome	*SLC12A6*	In Andermann syndrome, the connection between the right and left side of the brain is absent, and there is damage to the nerves responsible for movement and the senses. People with this condition experience stiff joints, tremors, muscle weakness, and foot abnormalities, all of which lead to difficulties with walking.				●						●	●	●	
Argininosuccinate Lyase Deficiency	*ASL*	Argininosuccinate lyase deficiency causes the inability of the body to breakdown ammonia/ nitrogen. This chemical accumulates and is toxic to the nervous system and liver. It can result in problems with movement, body temperature control, liver disease, and seizures. Identification of this condition shortly after birth can help lessen the effects.		●		●					●				
Aspartylglycosaminuria	*AGA*	Aspartylglycosaminuria is caused by the inability of the body to breakdown certain chemicals in the body. Over time, this build-up affects the nerves and results in highly flexible joints, loose skin, seizures, weak bones (osteoporosis), and declining intellectual ability.				●			●				●	●	
Ataxia With Vitamin E Deficiency	*TTPA*	People with ataxia with vitamin E deficiency are unable to get enough of this vitamin to help protect the cells of the body. It can result in problems with coordination, speech, vision, and reflexes.				some						●			●
Ataxia-Telangiectasia	*ATM*	Ataxia-telangiectasia is a condition that results from increased DNA damage and abnormal cell division. People with this condition have problems with coordination, often have muscle twitches, high rates of infection, and enlarged blood vessels. They are extremely sensitive to X-ray exposure.			●				●			●			
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay (ARSACS)	*SACS*	ARSACS is a condition affecting the muscles. People with ARSACS have issues with coordination, muscle breakdown leading to problems walking, difficulty with speech, and loss of some sensation in the arms and legs.										●			
Bardet-Biedl Syndrome, Type 1	*BBS1*	Bardet-Biedl syndrome is a condition of progressive vision loss, obesity, coordination difficulties, behavioral problems, and kidney disease. If not treated, kidney failure will result in early death.				●		●		●	●	●		●	●
Bardet-Biedl Syndrome, Type 10	*BBS10*	Bardet-Biedl syndrome is a condition of progressive vision loss, obesity, coordination difficulties, behavioral problems, and kidney disease. If not treated, kidney failure will result in early death.				●		●		●	●	●		●	●
Bernard–Soulier Syndrome, Type B	*GP1BB*	Bernard-Soulier syndrome is a bleeding condition caused by defective platelets. The platelets are enlarged in this condition, causing them to be less effective and lower in overall availability. People with this condition suffer from easy bruising and prolonged bleeding from infancy on and are treated accordingly.	●												
Bernard–Soulier Syndrome, Type C	*GP9*	Bernard-Soulier syndrome is a bleeding condition caused by defective platelets. The platelets are enlarged in this condition, causing them to be less effective and lower in overall availability. People with this condition suffer from easy bruising and prolonged bleeding from infancy on and are treated accordingly.	●												

CONDITION	GENE	SUMMARY	CLINICAL CONCERN												
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Beta-Hemoglobinopathies (including Sickle Cell and Beta-Thalassemia)	*HBB*	Beta-hemoglobin disorders affect one of the building blocks of red blood cells, resulting either lower number of red blood cells or cells that are abnormally shaped and the tissues and cells of the body do not receive enough oxygen and nutrients. Some symptoms can be tiredness, muscle or bone pain, frequent infections, or liver damage. However, there are a wide spectrum of conditions, symptoms, and level of severity depending on how the gene is changed.	●						●		●				
Beta-Ketothiolase Deficiency	*ACAT1*	People with beta-ketothiolase deficiency have difficulty breaking down certain chemicals in the body causing the blood to be too acidic. Symptoms include excessive vomiting, dehydration, lack of energy, and breathing difficulties. If untreated, it could result in coma or death. Fasting, high protein diets, and infection can all trigger the onset of symptoms, so monitoring of diet and activity can help lessen the effects of this condition.		●		some							●		
Biotinidase Deficiency	*BTD*	People with biotinidase deficiency are unable to use biotin (a type of B vitamin) properly and are not able to breakdown food into the nutrients the body needs. It can result in seizures, low muscle tone, and breathing difficulties. If untreated, this condition can also lead to vision or hearing loss, balance and movement problems, and hair loss. Treatment with biotin supplements can prevent these symptoms.		●			●		●			●	●		●
Bloom Syndrome	*BLM*	Children with Bloom syndrome have extreme sensitivity to the sun often shown by enlarged blood vessels and red appearance of the nose and cheeks. Their DNA is relatively unstable and does not replicate properly, leading to highly increased cancer risks, which reduces their lifespan.			●				●						
Canavan Disease	*ASPA*	The protective covering of the nerves, called myelin, is not properly made in children with Canavan disease. As a result there is progressive nerve damage to the brain, leading to poor muscle control, seizures, intellectual disability, and difficulty with swallowing. Although most appear fine at birth, their health rapidly declines in the first few months. Most children do not live into adulthood.				●						●	●		
Carnitine Deficiency, Primary	*SLC22A5*	Primary carnitine deficiency prevents the body from using fat for energy. This results in dangerously low blood sugar, muscle weakness, and enlargement of the heart and liver. Without treatment, learning disabilities can also develop. Symptoms can be worsened during periods of fasting or infection. Eating at regular, frequent intervals and taking supplements of L-carnitine can help prevent the effects of this condition.				●		●			●	●			
Carnitine Palmitoyltransferase IA Deficiency	*CPT1A*	Carnitine palmitoyltransferase IA deficiency prevents the body from using fat for energy, so the fuel they need to function properly is lessened, especially in times of fasting or infection. People with this condition have low blood sugar, heart problems, an enlarged, malfunctioning liver, and often seizures. Diet changes can help lessen these symptoms.				●					●	●	●		
Carnitine Palmitoyltransferase II Deficiency	*CPT2*	Carnitine palmitoyltransferase II deficiency prevents the body from using fat for energy, so the fuel they need to function properly is lessened, especially in times of fasting, exercise, or infection. People with this condition have low blood sugar, an enlarged, malfunctioning liver, and often seizures. This condition also weakens the heart muscle				●		●			●	●	●		
Cartilage-Hair Hypoplasia	*RMRP*	Children with cartilage-hair hypoplasia have bone abnormality that causes short stature (3-5 feet all as adults) but also affects the nails, hair, and teeth. Some people with this condition also experience problems with their digestive tract. Due to the involvement of the immune system, there is also high risk for infections and various cancers.			●				●					●	
Choroideremia	*CHM**	People with choroideremia have loss of their vision over time due to a loss of cells in the eye and surrounding blood vessels.													●

CONDITION	GENE	SUMMARY	CLINICAL CONCERN												
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Citrullinemia Type 1	*ASS1*	Citrullinemia type I is caused by the body's inability to break down ammonia (nitrogen). This leads to a toxic build-up in the nervous system resulting in overall weakness, poor feeding, intellectual and developmental delay, and seizures. If untreated, pressure around the brain can increase, causing death. Special monitoring of the diet can help lessen these symptoms.				●						●	●		●
Cohen Syndrome	*VPS13B*	Children with Cohen syndrome experience intellectual and developmental disabilities as well as progressive nearsightedness that can result in blindness. They grow slowly at first, but can suffer from abdominal obesity later on. Due to a low white blood cell count, these children are also at high risk for infection.				●			●			●			●
Combined Pituitary Hormone Deficiency	*PROP1*	Combined pituitary hormone deficiency causes a shortage of all pituitary hormones (GH, TSH, LH, FSH, Prolactin, and ACTH) which results in failure to thrive, puberty and infertility issues, increased infection rates, weight gain, and fatigue. Medication can help lessen these symptoms.							●					●	
Congenital Adrenal Hyperplasia (CAH)	*CYP21A2*	In congenital adrenal hyperplasia (CAH), normal hormonal processing of the kidneys is affected and an excess of male hormones are produced. This can result in female genitalia looking more male, and also cause increased hair growth and fertility problems in females. Over 75% will also experience high loss of salt from the body leading to weight loss, severe dehydration, and vomiting which needs close medical attention.								●					
Congenital Disorder of Glycosylation Type Ia	*PMM2*	Congenital disorders of glycosylation (CDG) affects the body's ability to get the nutrients it needs from certain proteins which affects multiple parts of the body. Although the effects of this condition vary across many different organs, the main effect of CDG type Ia is on nervous system causing developmental and intellectual disabilities as well as problems with coordination and movement. If they children survive beyond the first year of life, they will require the use of a wheelchair.				●					●	●			●
Congenital Disorder of Glycosylation Type Ib	*MPI*	Congenital disorders of glycosylation (CDG) affect the body's ability to get the nutrients it needs from certain proteins which affects multiple parts of the body. Most notably, children with CDG type Ib can experience low blood sugar with failure to thrive, recurrent diarrhea, liver disease, and clotting issues. Unlike other CDG, this form does not affect the nervous system so movement and mental/physical development is normal.	●								●				
Costeff Optic Atrophy Syndrome	*OPA3*	Costeff optic atrophy syndrome causes a breakdown of the optic nerve that affects the sharpness of a person's vision. Children with this condition often have weak, twitchy muscles and problems remaining upright and wheelchair use is common. Intellectual disability, if present, is mild.				some						●			●
Cystic Fibrosis	*CFTR*	Cystic fibrosis is a condition that causes the mucus in the body to thicken. This abnormal mucous is sticky and becomes hard to breakdown, clogging-up and damaging certain organs, especially the lungs, pancreas, and intestines. Breathing difficulties, poor digestion, frequent infection, infertility, and poor weight gain are all symptoms of this condition.		●					●						
Cystinosis	*CTNS*	Cystinosis causes a high level of cystine in the blood that forms crystals and causes damage in multiple organs including kidneys, thyroid, pancreas, and eyes. Kidney failure is the most common cause of early death when the condition is untreated. The muscles are also affected causing slow growth and bowing of the legs. Medication and diet are important to lessen the symptoms of this condition.								●		●		●	●
D-Bifunctional Protein Deficiency	*HSD17B4*	Babies with D-bifunctional protein deficiency suffer from poor muscle tone, seizures, vision and hearing loss, as well as severe progressive intellectual and developmental disability. Most children with this condition do not live past the age of 2.				●	●				●	●	●		●

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Dihydrolipoamide Dehydrogenase Deficiency (a.k.a Maple Syrup Urine Disease Type 3)	*DLD*	Maple syrup urine disease type 3 (also called dihydrolipoamide dehydrogenase deficiency) is caused by an excess of lactic acid in the body giving a "maple syrup" smell to the urine. Early symptoms include vomiting, abdominal pain, rapid breathing, and lack of energy. Liver disease, vision loss, intellectual and developmental delays, and seizures can also occur. It is unclear if diet restrictions will help lessen symptoms of this condition.				●					●	●	●		●
Dihydropyrimidine Dehydrogenase Deficiency	*DPYD*	Although some people with hereditary thymine-uraciluria can have no symptoms at all, others will have weak muscles, small head size, autism, seizures, and intellectual and developmental delays. All people with this condition have a life-threatening reaction to certain medications, called fluoropyrimidines, used to treat cancer so exposure must be prevented.				●						●	●	●	
Fabry Disease	*GLA**	Fabry disease is caused by an abnormal build-up of certain fats on the body's cells. It causes a variety of problems including pain in the hands and feet, digestive issues, ringing in the ears or hearing loss, as well as increased risk of heart attack, and kidney damage. Another characteristic sign of this condition is the inability to sweat which causes the body to overheat.					●	●		●					●
Familial Dysautonomia	*IKBKAP*	Familial dysautonomia affects the development and survival of certain nerves that control involuntary actions like digestion, breathing, tear production, and blood pressure. It can also affect the body's response to pain and temperature. Although there is no cure, many people with this condition live into their 40s.		●		some						●			
Familial Mediterranean Fever	*MEFV*	Familial Mediterranean fever causes periodic episodes of painful swelling in the abdomen, chest, and joints along with fever, rash and headache. The first episode usually occurs by age 20, and each can last 12-72 hours and have days or years in between occurrences. The heart, brain, and testes can also be affected. Some people also have a build-up of in the kidneys that could cause kidney failure if untreated. Medication can help lessen the symptoms of this condition.						●		●					
Fanconi Anemia Type C	*FANCC*	Fanconi anemia type C causes uncontrolled cell growth and increased cell death which decreases the function of the bone marrow and increases the risk for infection and certain cancers. There can be a brown discoloring to the skin or thumb and lower arm abnormalities, but most people with this condition show no physical symptoms.	●		●			●		●				●	
Finnish Nephrosis (a.k.a Nephrotic Syndrome Type 1)	*NPHS1*	Congenital Finnish nephrosis is a condition that affects how the kidneys filter out protein. The babies with condition will be slow to gain weight and start to retain a lot of fluid as the kidneys malfunction. This usually leads to complete kidney failure and death by the age of 5 without a transplant.								●					
Fragile X Syndrome	*FMR1**	Synapses are the nerve connections throughout the body that help send messages to various cells. In Fragile X syndrome, the gene that helps to control these synapses is not working correctly. This results in intellectual disabilities (which can range from mild to severe), speech and/or language delays, and features of autism-spectrum disorders (such as autism, attention-deficit disorder, and high anxiety). About 15% of males and 5% of affected females also have seizures. Carriers are not at risk for intellectual or behavioral problems, but can be at risk for developing premature ovarian failure or fragile X-associated tremor/ataxia syndrome.				●							some		
Fumarase Deficiency	*FH*	In fumarase deficiency, the cells are unable to get the energy/nutrients they need. This results in multiple abnormalities, including a small head size, an enlarged liver and spleen, characteristic facial features, failure to thrive, and brain abnormalities that causes seizures. People with this condition also suffer from intellectual and developmental disabilities.	●			●					●	●	●		

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Galactosemia	*GALT*	Galactosemia is a condition reduces the body's ability to turn galactose (a certain sugar found in milk) into energy. Children with this condition have failure to thrive, recurrent vomiting, are prone to infection, and have can have liver damage. Without treatment, intellectual disabilities are possible. A change in diet will lessen the effects of this condition, but problems such as speech difficulties, cataracts, and learning disabilities are still possible.				●			●		●				●
Gaucher Disease	*GBA*	People with Gaucher disease cannot properly breakdown certain fatty substances which then build-up and damage organs like the spleen, liver, and bone marrow. There is a range in the age and severity of different symptoms, but most people will experience bone pain or fractures, anemia, tiredness, shorter height, frequent nosebleeds, and easy bruising. Medication can be used to help lessen many of the symptoms of this condition. There are different forms of the disease with varying levels of severity.	●								●			●	
Glaucoma, Primary Congenital	*CYP1B1*	Primary congenital glaucoma is a condition that causes damage to the eye over time. People with this condition experience excessive tears, sensitivity to light, cloudy eyes due to increased fluid pressure, and eventually vision loss. Surgery is often used to help correct the effects of this condition if it is caught early enough.													●
Glucose-6-Phosphate Dehydrogenase Deficiency	*G6PD**	In glucose-6-phosphate dehydrogenase deficiency, the red blood cells break down to early and cause anemia. Yellowed skin or eyes (jaundice), shortness of breath, and rapid heart rate are also possible side effects. Most people with this condition do not show symptoms unless triggered by certain medications, infections, or exposure to fava beans.	●	●							●				
Glutaric Acidemia Type 1	*GCDH*	With glutaric acidemia type I, the body cannot break down certain chemicals. This build-up leads to damage, specifically to a part of the nervous system called the basal ganglia which is responsible for movement. Muscles can be weak or stiff and experience involuntary twitching. The head size is also sometimes enlarged and there can be bleeding in the brain or eyes. Monitoring of the diet can help lessen the effects of this condition.				some						●			
Glycogen Storage Disease Type Ia (von Gierke)	*G6PC*	People with glycogen storage disorders cannot break down a certain type of sugar (glycogen) and turn it into the energy the body needs. The immediate result is low blood sugar and feelings of tiredness, irritability, and possibly seizures. If type Ia (also called von Gierke disease) is untreated, this condition can also affect the bones, liver and kidneys. Medication and close monitoring of the diet can help lessen the effects of this condition.								●	●		●	●	
Glycogen Storage Disease Type Ib (von Gierke)	*SLC37A4*	People with glycogen storage disorders cannot break down a certain type of sugar (glycogen) and turn it into the energy the body needs. The immediate result is low blood sugar and feelings of tiredness, irritability, and possibly seizures. If type Ib is untreated, this condition can also affect the bones, pancreas, small intestines, kidney, liver and the immune system. Medication and close monitoring of the diet can help lessen the effects of this condition.							●	●	●		●	●	
Glycogen Storage Disease Type III (Cori/Forbes)	*AGL*	People with glycogen storage disorders cannot break down a certain type of sugar (glycogen) and turn it into the energy the body needs. The most concerning effects of Type III are on the liver disease and muscle weakness, which can also affect the heart.						●			●	●			
Glycogen Storage Disease Type V (McArdle)	*PYGM*	People with glycogen storage disorders cannot break down a certain type of sugar (glycogen) and turn it into the energy the body needs. With type V (also called McArdle disease), the body turns to the muscles for energy causing them to break down. This can cause someone to become tired faster when exercising and create pain or soreness. A person's kidneys can also become overstressed during these times. Properly managing physical activity can help lessen these symptoms.								●		●			

** Genes marked with asterick are inherited in X-linked fashion and will not be reported on in males.*

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GRACILE Syndrome	*BCS1L*	GRACILE is an acronym for the various features of the condition (growth retardation amnioaciduria, cholestasis, iron overload, lactic acidosis, early death). Growth retardation is present from birth on. The other parts of the condition cause high amount of iron and acids to buildup damaging the liver and kidneys, which results in death within the first few months of life.								●	●				
Growth Hormone Deficiency, Isolated	*GHRHR*	Growth hormone deficiency 1B causes shorter stature starting in early to mid-childhood. Early treatment with medication can help lessen the effects of this condition.												●	
Hearing Loss, Non-syndromic (a.k.a Connexin 26)	*GJB2*	People with two mutations in the GJB2 gene (also called connexin 26) experience hearing loss prior to learning speech. No other physical or intellectual disabilities are related to this condition.					●								
Hearing Loss, Non-syndromic (a.k.a Connexin 30)	*GJB6*	People with two mutations in the GJB6 gene (also called connexin 30) or in combination with GJB2 (also called connexin 26) experience hearing loss prior to learning speech. No other physical or intellectual disabilities are related to this condition.					●								
Heme Oxygenase 1 Deficiency	*HMOX1*	Heme oxygenase deficiency causes a breakdown of the red blood cells and accumulation of iron in the kidneys and liver. Together, these create a signature rash, slow growth, liver damage, and anemia. People with this condition can also be missing their spleen.	●							●	●			●	
Hemochromatosis	*HFE*	Hereditary Hemochromatosis is caused by too much iron being absorbed from the diet which is then stored in tissues of the body causing damage as a person ages. People with this condition can experience tiredness along with joint and abdominal pain. Treatments are available to help reduce the amount of iron in the blood. If untreated, liver and heart disease can develop.	●					●			●				
Hemophilia B	*F9**	Due to a missing chemical, called factor 9, people with hemophilia B are not able to create effective clots and are prone to prolonged bleeding. Although this unusually long bleeding time is more likely after injury or surgery, there can also be spontaneous bleeding, seemingly for no reason, in the joints, muscles, or brain that could cause severe effects. Medication can help lessen the effects of this condition.	●												
Hereditary Fructose Intolerance	*ALDOB*	Hereditary fructose intolerance makes it difficult for the body to digest fructose, a sugar found in fruit, and use it for energy. Children have failure to thrive, abdominal pain, nausea, diarrhea, and vomiting. Repeated exposure can result in liver and kidney damage and lead to seizures and organ failure. Monitoring of the diet can help lessen the effects of this condition.								●	●		●		
Herlitz Junctional Epidermolysis Bullosa, LAMA3-Related	*LAMA3*	Herlitz junctional epidermolysis bullosa is a condition affecting the skin. The protein connecting the various layers of the skin is missing and creates a very fragile outer layer that will break or blister even with mild touch. Soft tissues like the inside of the mouth or digestive tract can also be affected leading to infections and difficulty eating or breathing.		●					●					●	
Herlitz Junctional Epidermolysis Bullosa, LAMB3-Related	*LAMB3*	Herlitz junctional epidermolysis bullosa is a condition affecting the skin. The protein connecting the various layers of the skin is missing and creates a very fragile outer layer that will break or blister even with mild touch. Soft tissues like the inside of the mouth or digestive tract can also be affected leading to infections and difficulty eating or breathing.		●					●					●	
Herlitz Junctional Epidermolysis Bullosa, LAMC2-Related	*LAMC2*	Herlitz junctional epidermolysis bullosa is a condition affecting the skin. The protein connecting the various layers of the skin is missing and creates a very fragile outer layer that will break or blister even with mild touch. Soft tissues like the inside of the mouth or digestive tract can also be affected leading to infections and difficulty eating or breathing.		●					●					●	

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Homocystinuria, CBS-deficient	*CBS*	Homocystinuria is caused by an inability of the body to breakdown certain chemicals due to a deficiency in cystathionine beta-synthase. This can lead to vision problems, osteoporosis, seizures, and a highly increased risk for blood clotting. Some people with condition may also have intellectual or developmental disabilities or suffer from depression, anxiety or other psychiatric illnesses. Diet and medication can help lessen the effects of this condition.	●			●							●		●
Hydatidiform Mole, Recurrent	*NLRP7*	People with two mutations in the NLRP gene experience recurrent miscarriage and infertility due to repeated development of complete molar pregnancies. These pregnancies will have abnormal placental growth without the presence of fetal tissue.													
Hyperinsulinism	*ABCC8*	Hyperinsulinism is a condition of low blood sugar due to the higher than normal amounts of insulin in the body. These low sugar levels deprive the body of necessary fuel and children can have seizures, low muscle tone, sleepiness, vision difficulties, and possible brain damage as a result. Treatment with diet and medical surveillance can help lessen the effects.										●	●		●
Hyperoxaluria, Primary Type 1	*AGXT*	Primary hyperoxaluria causes a build-up of salts in the body. The biggest effect of this is recurrent kidney stones and possible kidney failure. Fifty percent of children with type I have kidney failure by the age of 15. Bone pain, vision loss, abnormal sensations in the arms or legs, heart problems, and an enlarged liver or spleen can also be symptoms of this condition. Drinking plenty of water and taking B6 supplements can help reduce the effects of this condition. Some may need liver transplants to prevent the kidney damage.						●		●	●				●
Hyperoxaluria, Primary Type 2	*GRHPR*	Primary hyperoxaluria causes a build-up of salts in the body. The biggest effect of this is recurrent kidney stones and possible kidney failure. Bone pain, vision loss, abnormal sensations in the arms or legs, heart problems, and an enlarged liver or spleen can also be symptoms of this condition. People with type 2 have a milder form of the disease than type 1, but some may need liver transplants to prevent the kidney damage.						●		●	●				●
Hypohidrotic Ectodermal Dysplasia	*EDAR*	Hypohidrotic ectodermal dysplasia is a condition affecting the skin, hair, and teeth. Nails and hair are brittle, and growth is usually sparse. Teeth can be absent or appear small and pointed. People with this condition also have a reduced ability to sweat which can cause the body to overheat. Although there is no cure for this condition, lifespan is not usually reduced.													
Hypophosphatasia	*ALPL*	Hypophosphatasia is a condition that causes weak and softened bones. Children often are shorter with bowed appearance to the legs and are at high risk for fractures, osteoporosis, and arthritis. Due to weak rib bones, they often experience difficulty breathing and are at high risk for respiratory failure. Tooth formation is also affected and baby teeth are usually lost before the age of 5 and adult teeth are more prone to breakage or decay. In more severe cases, kidney damage and seizures are also possible. In milder cases, only the teeth are affected.		●						●			●	●	
Inclusion Body Myopathy 2	*GNE*	Inclusion body myopathy 2 is a condition that causes weakening of the muscles of the body. This weakness usually starts in the lower limbs and moves upward towards the arms and neck. Most people need the use of a wheelchair within 20 years of their first symptoms.										●			
Isovaleric Acidemia	*IVD*	Isovaleric acidemia is caused by an inability of the body to properly break down isovaleric acid into smaller substances. Although some people this condition do not show any symptoms, most start with poor feeding, vomiting, and problems staying warm. There can be period between episodes without any symptoms. If untreated, it could progress to seizures, learning disabilities, and organ failure. The excess isovaleric acid in the body can also cause a "sweaty feet" odor. Diet and medication can help lessen the effects of this condition.				●							●		

CONDITION	GENE	SUMMARY	CLINICAL CONCERN												
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Joubert Syndrome 2	*TMEM216*	An abnormality in the structure of the brain leads to Joubert syndrome. People with this condition have weak muscles, poor coordination, abnormal eye movement, breathing and feeding difficulties, and often kidney disease. Intellectual and developmental disabilities may also be present.		●		●				●		●			
Krabbe Disease	*GALC*	Krabbe disease is caused by a defect in the protective coating over the nerve cells. Without this protection, the nerves and brain cells begin to die. Early symptoms include feeding difficulties, unexplained fever, irritability, and muscle weakness. Breathing problems are the often the cause of death before age 2 in the more severe cases. Milder cases show difficulty with walking, movement, vision, and intellectual abilities over time.		●		●						●			●
Limb-Girdle Muscular Dystrophy Type 2A	*CAPN3*	Limb-girdle muscular dystrophy is a condition in which the muscles weaken over time. The areas most affected are the upper arms and legs, shoulders, and pelvic muscles. Type 2A does not progress rapidly, but can affect the walk and posture of those affected.										●			
Limb-Girdle Muscular Dystrophy Type 2C	*SGCG*	Limb-girdle muscular dystrophy is a condition in which the muscles weaken over time. The areas most affected are the upper arms and legs, shoulders, and pelvic muscles. Type 2C can also involve joint contractures and curving of the spine as well as heart and/or breathing problems.		●				●				●		●	
Limb-Girdle Muscular Dystrophy Type 2D	*SGCA*	Limb-girdle muscular dystrophy is a condition in which the muscles weaken over time. The areas most affected are the upper arms and legs, shoulders, and pelvic muscles. Type 2D can also involves joint contractures and curving of the spine. Heart and breathing problems are also present in about 20%.		●				●				●		●	
Limb-Girdle Muscular Dystrophy Type 2E	*SGCB*	Limb-girdle muscular dystrophy is a condition in which the muscles weaken over time. The areas most affected are the upper arms and legs, shoulders, and pelvic muscles. Type 2E can also involve joint contractures and curving of the spine. Heart and breathing problems are also present in about 20%.		●				●				●		●	
Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	*HADHA*	People with long chain 3-hydroxyacyl-coA dehydrogenase deficiency have difficulty converting certain foods to energy. It can also cause a build-up of certain chemicals in the body damaging certain organs and tissues. Early signs of this condition are low blood sugar, weak muscles, feeding difficulty, and liver problems. Without treatment this could progress to breathing difficulties, intellectual disability, heart problems, loss of sensation in the arms/legs or even death. Early alterations to the diet can help prevent the effects of this condition.		●				●	●		●	●			●
Maple Syrup Urine Disease Type 1A	*BCKDHA*	Maple syrup urine disease is caused by an excess of lactic acid in the body giving a "maple syrup" smell to the urine. Early symptoms include vomiting, abdominal pain, rapid breathing, and lack of energy. If untreated, neurological damage and seizures could occur, possibly resulting in death. Early alterations to the diet can help prevent the effects of this condition.				●						●	●		
Maple Syrup Urine Disease Type 1B	*BCKDHB*	Maple syrup urine disease is caused by an excess of lactic acid in the body giving a "maple syrup" smell to the urine. Early symptoms include vomiting, abdominal pain, rapid breathing, and lack of energy. If untreated, neurological damage and seizures could occur, possibly resulting in death. Early alterations to the diet can help prevent the effects of this condition.				●						●	●		
Maple Syrup Urine Disease Type 2	*DBT*	Maple syrup urine disease is caused by an excess of lactic acid in the body giving a "maple syrup" smell to the urine. Early symptoms include vomiting, abdominal pain, rapid breathing, and lack of energy. If untreated, neurological damage and seizures could occur, possibly resulting in death. Early alterations to the diet can help prevent the effects of this condition.				●						●	●		

CONDITION	GENE	SUMMARY	CLINICAL CONCERN													
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Medium Chain Acyl-CoA Dehydrogenase Deficiency	*ACADM*	People with medium chain acyl-coA dehydrogenase deficiency have difficulty converting certain foods to energy. It can also cause a build-up of certain chemicals in the body damaging certain organs and tissues. Early signs of this condition are low blood sugar, tiredness, and vomiting. Without treatment, this could progress to breathing difficulties, liver or brain damage, seizures or death. Early alterations to the diet can help prevent the effects of this condition.		●							●		●		
Megalencephalic Leukoencephalopathy With Subcortical Cysts	*MLC1*	In megalencephalic leukoencephalopathy with subcortical cysts, the white matter in the brain is swollen, cysts develop, and the protective coating of the nerves wastes away. Early symptoms include loss of coordination, muscle twitching, learning disabilities, and seizures. This progresses to include inability to walk, speech problems, and difficulty swallowing.				●						●	●		
Megaloblastic Anemia Syndrome	*SLC19A2*	People with megaloblastic anemia syndrome suffer from low number of red blood cells (anemia) that results in decreased energy, headaches, pale skin, and numbness or tingling sensation in the hands and feet. This condition also causes diabetes and hearing loss during childhood and adolescence. Although the anemia and diabetes show some improvement with vitamin B1 supplements, it is unclear if this treatment can affect hearing.	●				●								
Metachromatic Leukodystrophy	*ARSA*	The protective covering of the nerve cells is damaged in people with metachromatic leukodystrophy. People with this condition experience damage to the muscles over time where they become severely weakened and eventually rigid. Loss of sensation in the limbs is also common, and many experience vision and hearing loss as well as seizures. Although the majority of people with this condition show signs in infancy, childhood and adult forms have also been reported. Behavioral changes and psychiatric illnesses such as hallucinations can occur in the later onset forms. All forms progress to a stage of paralysis and unresponsiveness with shortened lifespan.				●	●					●	●		●
Methlymalonic Acidemia, cb1A-Type	*MMAA*	Methylmalonic acidemia is caused by the body's inability to breakdown certain proteins and fats. The build-up of these substances can damage organs such as the brain, liver, kidneys, and pancreas. Although there is a range in severity, most people with this condition experience extreme tiredness, dehydration, weak muscles, developmental delays, and failure to thrive. Recurrent vomiting, frequent infection, and low blood sugar that can cause seizures are also common. If untreated, this condition can lead to liver disease, breathing difficulties, and brain damage. Early diagnosis and treatment with diet and medication has shown to lessen the effects of this condition. Even with treatment, learning disabilities are still possible.		●		●		●	●	●	●	●	●		
Methlymalonic Acidemia, cblB-Type	*MMAB*	Methylmalonic acidemia is caused by the body's inability to breakdown certain proteins and fats. The build-up of these substances can damage organs such as the brain, liver, kidneys, and pancreas. Although there is a range in severity, most people with this condition experience extreme tiredness, dehydration, weak muscles, developmental delays, and failure to thrive. Recurrent vomiting, frequent infection, and low blood sugar that can cause seizures are also common. If untreated, this condition can lead to liver disease, breathing difficulties, and brain damage. Early diagnosis and treatment with diet and medication has shown to lessen the effects of this condition. Even with treatment, learning disabilities are still possible.		●		●		●	●	●	●	●	●		

CONDITION	GENE	SUMMARY	CLINICAL CONCERN												
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Methlymalonic Acidemia, mut-Type	*MUT*	Methylmalonic acidemia is caused by the body's inability to breakdown certain proteins and fats. The build-up of these substances can damage organs such as the brain, liver, kidneys, and pancreas. Although there is a range in severity, most people with this condition experience extreme tiredness, dehydration, weak muscles, developmental delays, and failure to thrive. Recurrent vomiting, frequent infection, and low blood sugar that can cause seizures are also common. If untreated, this condition can lead to liver disease, breathing difficulties, and brain damage. Early diagnosis and treatment with diet and medication has shown to lessen the effects of this condition. Even with treatment, learning disabilities are still possible.		●		●		●	●	●	●	●	●		
Methylmalonic Acidemia and Homocystinuria, cblC-Type	*MMACHC*	Methylmalonic acidemia with homocystinuria is caused by the body's inability to breakdown certain proteins and fats. The build-up of these substances can damage organs such as the brain, liver, kidneys, and pancreas. Although there is a range in severity, most people with this condition experience extreme tiredness, dehydration, weak muscles, developmental delays, and failure to thrive. Recurrent vomiting, frequent infection, and low blood sugar that can cause seizures are also common. This condition can lead to liver disease, breathing difficulties, and brain damage.				●			●	●	●	●	●		
Mucolipidosis Type II/IIIA	*GNPTAB*	Mucolipidosis is a condition affecting skeleton and nervous system. Children with this condition have muscle weakness and suffer from extremely slow growth. They also suffer from developmental, intellectual, and speech delays. Children with type II (also called I cell disease) suffer from several different bone abnormalities such as short stature, hip dislocation, abnormal curve to the spine, and clubfeet. The airway can be narrowed, and there is often a stiffening to the ribcage causing problems with breathing.		●		●	●		●			●		●	
Mucolipidosis Type IV	*MCOLN1*	Mucolipidosis is a condition affecting the development of the nerves. Children with this condition have extreme muscle weakness and stiffness, which is also accompanied by severe intellectual disability. The muscle problems in this condition cause difficulty with feeding and movement. Mucolipidosis type IV also affects the eyes, and vision usually starts to worsen drastically by the age of 5.	●			●	●					●			●
Mucopolysaccharidosis Type I (Hurler)	*IDUA*	Hurler syndrome (mucopolysaccharidosis type I), is caused by an inability of the body to breakdown certain chemicals called glycosaminoglycans, or GAGs. The build-up of these chemicals affects many different parts of the body. Although usually appearing normal and healthy at birth, these children will develop signs of the condition in early childhood including intellectual disability, hearing loss, skeletal abnormalities with short stature, restricted joint movement, increased infections, breathing difficulties, enlarged liver, and characteristic facial features. Heart problems are the common cause of death.		●		●	●	●	●		●			●	
Mucopolysaccharidosis Type II (Hunter)	*IDS**	Mucopolysaccharidosis type II (also known as Hunter syndrome or MPS II) is caused by an inability of the body to breakdown certain chemicals called glycosaminoglycans, or GAGs. The build-up of these chemicals occurs in many different parts of the body and causes damage. Although usually appearing normal and healthy at birth, these children begin to develop signs of the condition during early childhood. These include characteristic facial features, breathing difficulties, muscle weakness, skeletal abnormalities with short stature, stiff joints, vision loss, hearing loss, and an enlarged liver and/or heart. People with MPS II also have intellectual disabilities, a pebble-like feel to their skin, and can exhibit behavioral issues. Although some milder forms of the disease do not greatly affect lifespan, many children will die of respiratory or heart failure before the age of 16.		●		●	●	●				●		●	●

CONDITION	GENE	SUMMARY	CLINICAL CONCERN												
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Mucopolysaccharidosis Type IIIA (Sanfilippo A)	*SGSH*	Mucopolysaccharidosis type IIIA (also known as Sanfilippo syndrome A or MPS IIIA) is caused by an inability of the body to breakdown certain chemicals called glycosaminoglycans, or GAGs. The build-up of these chemicals occurs in many different parts of the body and causes damage. Although usually appearing normal and healthy at birth, these children begin to develop signs of the condition during early childhood such as slowed development or speech. Other features include mild characteristic facial features and mild skeletal abnormalities. Movement becomes clumsier over time and people with MPS IIIA will develop seizures and severe intellectual delay. Most children will die before their 20th birthday.				●						●	●	●	
Mucopolysaccharidosis Type IIIB (Sanfilippo B)	*NAGLU*	Mucopolysaccharidosis type IIIB (also known as Sanfilippo syndrome B or MPS IIIB) is caused by an inability of the body to breakdown certain chemicals called glycosaminoglycans, or GAGs. The build-up of these chemicals occurs in many different parts of the body and causes damage. Although usually appearing normal and healthy at birth, these children begin to develop signs of the condition during early childhood such as slowed development or speech. Other features include mild characteristic facial features and mild skeletal abnormalities. Movement becomes clumsier over time and people with MPS IIIB will develop seizures and severe intellectual delay. Most children will die before their 20th birthday.				●						●	●	●	
Mucopolysaccharidosis Type IVA (Morquio A)	*GALNS*	Mucopolysaccharidosis type IVA (also known as Morquio syndrome A or MPS IVA) is caused by an inability of the body to breakdown certain chemicals called glycosaminoglycans, or GAGs. The build-up of these chemicals occurs in many different parts of the body and causes damage. Although usually appearing normal and healthy at birth, these children begin to develop signs of the condition during early childhood. These include short stature with skeletal abnormalities involving the neck, chest, and joints. People with MPS IVA also have mild characteristic facial features, hearing and vision loss, tooth abnormalities, heart disease. Intellectual disability is usually not present in this form of the MPS. Compression of the spinal cord is the major medical complication of this condition can reduce life expectancy.		●			●	●	●					●	●
Mucopolysaccharidosis Type IVB (Morquio B)	*GLB1*	Mucopolysaccharidosis type IVB (also known as Morquio syndrome B or MPS IVB) is caused by an inability of the body to breakdown certain chemicals called glycosaminoglycans, or GAGs. The build-up of these chemicals occurs in many different parts of the body and causes damage. Although usually appearing normal and healthy at birth, these children begin to develop signs of the condition during early childhood. These include short stature with skeletal abnormalities involving the neck, chest, and joints. People with MPS IVB also have mild characteristic facial features, hearing and vision loss, tooth abnormalities, heart disease. Intellectual disability is usually not present in this form of the MPS. Compression of the spinal cord is the major medical complication of this condition can reduce life expectancy.		●			●	●	●					●	●
Mucopolysaccharidosis Type VI (Maroteaux-Lamy)	*ARSB*	Mucopolysaccharidosis type VI (also known as Maroteaux-Lamy syndrome or MPS VI) is caused by an inability of the body to breakdown certain chemicals called glycosaminoglycans, or GAGs. The build-up of these chemicals occurs in many different parts of the body and causes damage. Although usually appearing normal and healthy at birth, these children begin to develop signs of the condition during early childhood. These include typical facial features, skeletal issues like short stature, limited joint movement, vision and hearing loss, breathing problems, and an enlarged liver. People with MPS VI also have heart problems that often lead to heart failure.		●			●	●	●		●			●	●

CONDITION	GENE	SUMMARY	CLINICAL CONCERN												
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Mucopolysaccharidosis Type VII (Sly)	*GUSB*	Mucopolysaccharidosis type VII (also known as Sly syndrome or MPS VII) is caused by an inability of the body to breakdown certain chemicals called glycosaminoglycans, or GAGs. The build-up of these chemicals occurs in many different parts of the body and causes damage. Severe cases of MPS VII will have abnormal swelling throughout the body at or before birth (hydrops fetalis). Additional symptoms include characteristic facial features, mild skeletal abnormalities with short stature, hearing and vision loss, intellectual disabilities, and an enlarged liver. Heart and respiratory failure are main causes of death prior to the age of 30.		●		●	●	●			●			●	●
Muscle-Eye-Brain Disease	*POMGNT1*	Muscle-eye-brain disease is a form of congenital muscular dystrophy. In addition, the brain in people with this condition lacks the normal folds and is bumpier in appearance. The result is muscle weakness, involuntary muscle twitches, and intellectual disability. Vision loss due to extreme nearsightedness or glaucoma is also common and lifespan is often decreased.				●						●			●
Nemaline Myopathy	*NEB*	Nemaline myopathy is a condition of muscle weakness, particularly in the face, neck, and upper arms and legs, which can cause problems with movement, swallowing, and breathing.		●								●			
Nephrotic Syndrome Type 2	*NPHS2*	Steroid-resistant nephrotic syndrome is caused by a shortage of protein along with an excess of cholesterol in the blood. The biggest effect of this condition is kidney damage and possibly failure. This damage, along with increased fluid retention can create high blood pressure. Although medication can help lessen the problems of high cholesterol and blood pressure, a transplant is often needed to address the kidney complications.								●					
Neuronal Ceroid Lipofuscinosis Type 1	*PPT1*	Neuronal ceroid lipofuscinosis is a condition of progressive loss of nerve cells leading to mental and physical disabilities. These children suffer from involuntary muscle spasms and movements. There is also progressive loss of vision over time, resulting in blindness by the age of 2. Seizures, intellectual disability, and behavioral issues such as dementia also occur as the child ages. Most people with this condition do not live into their 30s.				●						●	●		●
Neuronal Ceroid Lipofuscinosis Type 2	*TPP1*	Neuronal ceroid lipofuscinosis is a condition of progressive brain damage leading to seizures, and a loss in the ability to walk and speak as the disease progresses. There is also progressive loss of intellectual abilities and vision over time, resulting in blindness by age 5. Most children with the severe form are bedridden by the age of 6, and most will not live past their 20s.				●						●	●		●
Neuronal Ceroid Lipofuscinosis Type 3	*CLN3*	Neuronal ceroid lipofuscinosis is a condition of progressive brain damage leading to mental and physical disabilities. There is also progressive loss of vision over time, resulting in blindness by the age of 5. Seizures and behavioral issues with possible dementia are also common as the child ages. Most people with this condition do not live into their 30s.				●						●	●		●
Neuronal Ceroid Lipofuscinosis Type 5	*CLN5*	Neuronal ceroid lipofuscinosis is a condition of progressive brain damage leading a loss in the ability to walk and speak as the disease progresses. There is also progressive loss of mental abilities and vision over time, resulting in blindness by the age of 10. Seizures are also very common. Most people with this condition do not live into their 30s.				●						●	●		●
Neuronal Ceroid Lipofuscinosis Type 8 (a.k.a Northern Epilepsy)	*CLN8*	People with northern epilepsy suffer from repeated convulsive seizures. Although these seizures may get less frequent over time, children with this condition can experience loss of intellectual ability over time, decline in sharpness of vision, and have problems with balance and coordination.				●						●	●		●

CONDITION	GENE	SUMMARY	CLINICAL CONCERN												
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Niemann-Pick Disease Type A & B (a.k.a. Acid Sphingomyelinase Deficiency)	*SMPD1*	Niemann-Pick disease affects the body's ability to breakdown certain chemicals in the body. The build-up can lead to failure to thrive, feeding issues, and enlarged liver and spleen. There is also a major effect on the nervous system in type A, and children with this condition experience problems with movement and intellectual and developmental disability and usually die in childhood. Type B is less severe, but tends to cause more problems with breathing, heart disease, and growth.	●	●		●		●	●		●	●			
Niemann-Pick Disease Type C1	*NPC1*	Niemann-Pick disease type C affects the body's ability to breakdown cholesterol and fat. Build-up of these substances in the body causes liver disease, learning disabilities, poor muscle tone and coordination, and seizures. Over time, people with this condition lose the ability to move many of their facial muscles making swallowing, speech, and vision difficult.		●		●			●		●	●	●		
Niemann-Pick Disease Type C2	*NPC2*	Niemann-Pick disease type C affects the body's ability to breakdown cholesterol and fat. Build-up of these substances in the body causes liver disease, learning disabilities, poor muscle tone and coordination, and seizures. Over time, people with this condition lose the ability to move many of their facial muscles making swallowing, speech, and vision difficult.		●		●			●		●	●	●		
Nijmegen Breakage Syndrome	*NBN*	The DNA of people with Nijmegen breakage syndrome damages more easily. This results in a higher chance of infection and over 50 times higher risk of cancer. Some people with this condition also suffer from mild to moderate intellectual disability.		●	●	●									
Oculocutaneous Albinism Type 1	*TYR*	Oculocutaneous albinism affects the ability of the body to make melanin, a chemical that is responsible for coloration of the skin, hair, and eyes. People with this condition have very light skin that is more likely to suffer damage from the sun and possible skin cancers. The eyes are sensitive to light and often shift rapidly from side to side. Intellectual ability is not affected by this condition.			●										●
Ornithine Transcarbamlyase Deficiency	*OTC**	Ornithine transcarbamylase deficiency is causes the inability of the body to breakdown ammonia/nitrogen. This chemical accumulates and is toxic to the nervous system and liver. It can result in problems with movement, body temperature control, liver disease, breathing difficulties, and seizures. Intellectual and developmental disabilities are also possible in some people with this condition.		●		●					●	●	●		
Pantothenate Kinase-associated Neurodegeneration	*PANK2*	In Hallervorden-Spatz syndrome, there is an excess of iron build-up in the brain. This results in problems with speech, vision, and movement. Muscle spasms, rigidity, and difficulty walking are usually present by the age of 10. Many also experience personality changes, depression or dementia.										●			●
Papillon-Lefevre Syndrome (also Haim-Munk Syndrome)	*CTSC*	Haim-Munk syndrome is a condition affecting teeth, skin, and nails. Infection of the gums that can destroy the teeth is often present along with thick overgrowth of the nails. There is also a reddened, thickening of the skin on the palms of the hands and soles of the feet accompanied by an increased risk of infection. This condition is also called Papillon-Lefevre syndrome.												●	
Pendred Syndrome	*SLC26A4*	Pendred syndrome is a condition resulting in severe hearing loss. People with this condition also have difficulty with maintaining balance, and many have an enlargement of the thyroid gland (also called a goiter).					●								
Phenylalanine Hydroxylase Deficiency (PKU)	*PAH*	People with phenylalanine hydroxylase deficiency have difficulty breaking down a chemical called phenylalanine. As this chemical builds-up, it becomes toxic to the brain and can cause intellectual disability, seizures, and behavioral issues. Early and continued changes to the diet can prevent further complications from this condition. This condition can also be referred to as phenylketonuria or PKU.				●		●					●		

** Genes marked with asterick are inherited in X-linked fashion and will not be reported on in males.*

CONDITION	GENE	SUMMARY	CLINICAL CONCERN												
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Polycystic Kidney Disease, Autosomal Recessive	*PKHD1*	The cysts present in autosomal recessive polycystic kidney disease affect the ability of the kidneys to fi out waste. Early on the kidneys become enlarged and eventually stop working, causing 30% of people with this condition to die in infancy. People with this condition suffer from high blood pressure, kidney stones, urinary tract infections, bulging of blood vessels (aneurysm) and liver disease.								●	●				
Polyglandular Autoimmune Syndrome Type 1	*AIRE*	Autoimmune conditions causes the system that usually helps fight off infection to attack healthy cells. In polyglandular autoimmune syndrome type I, this results in three main problems. The skin and mucous membranes of the nose and mouth will experience recurrent fungal infections. Malfunctioning glands in the kidneys will cause skin discoloration, weight loss, lower blood pressure, and muscle weakness. The parathyroid gland also malfunctions causing tiredness and tingling in the lips, fingers, or toes. Careful monitoring is needed to prevent these symptoms from becoming life-threatening.							●	●		●			
Pompe Disease (a.k.a Glycogen Storage Disease Type 2 or Acid Maltase Deficiency)	*GAA*	People with glycogen storage disorders cannot break down a certain type of sugar (glycogen). In Pompe disease (also called glycogen storage disorder type II) this build-up of sugar in the body results in muscle damage and weakness, often resulting in the need for a wheelchair. There is a range in how severe the condition can be, but other complications can include liver disease, heart problems, and trouble breathing. The immediate result is low blood sugar and feelings of tiredness, irritability, and possibly seizures. For those with severe onset at birth, there is also an enlarged heart and muscle weakness.		●		●		●			●	●				
Progressive Pseudorheumatoid Dysplasia	*WISP3*	Progressive pseudorheumatoid dysplasia causes a breakdown of cartilage, which is the protective layer between the bones. During childhood, this can result in pain, joint stiffness and swelling, short stature, abnormal curves to the lower spine, and movement limitations.												●	
Pycnodysostosis	*CTSK*	Pycnodysostosis is a condition that creates abnormally weak bones with multiple recurrent fractures. People with this condition are usually less than 5 feet in height and have additional bone problems such as scoliosis or osteoporosis. Delayed tooth development or missing teeth is also common along with an increased risk for cavities. Careful monitoring of activity can help minimize the fractures and lead to a normal lifespan.												●	
Retinoschisis, Juvenile	*RS1**	Retinoschisis is a condition that affects the eye. Sharpness of images is greatly affected. Peripheral, or side vision, is often reduced and can also worsen and lead to blindness.													●
Rhizomelic Chondrodysplasia Punctata Type 1	*PEX7*	Rhizomelic chondrodysplasia punctata type I causes a shortening of the upper arm and leg bones resulting in a shorter stature. This is often accompanied by stiff, painful joints, breathing difficulties, higher infection rates, and vision loss due to clouding (cataracts). Severe intellectual disability and seizures are also present and lifespan is greatly reduced.		●		●			●				●	●	●
Salla Disease (a.k.a Sialic Acid Storage Disease)	*SLC17A5*	Salla disease is a condition affecting the nervous system that gets worse over time. Early symptoms include weak muscles with developmental and intellectual delays. Coordination becomes difficult as muscle twitches and involuntary movements increase, which may or may not affect their ability to walk unassisted. Intellectual abilities also continue to decline over time and seizures can also develop.				●					●	●	●		
Sandhoff Disease	*HEXB*	Sandhoff disease causes an inability of the body to breakdown certain chemicals. The buildup of these chemicals in the brain and muscles becomes toxic and causes the destruction of nerves. This results in problems including seizures, enlarged liver, and loss of vision and hearing over time. There is also a loss of intellectual and physical abilities ending in paralysis. Although there can be milder, later onset forms of this condition, most children die before the age of 4 due to difficulties in breathing.		●		●	●				●	●	●		●

CONDITION	GENE	SUMMARY	CLINICAL CONCERN													
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Segawa Syndrome	*TH*	Stiff muscles and delay in reaching developmental milestones are the common symptoms of Segawa syndrome. Early signs include involuntary muscle twitches, and regulating normal body processes like temperature, blood sugar, and blood pressure are all problematic. Voluntary movements including facial expressions are rare. Milder forms of this condition can be treated well with medication, but has been less successful in the severe cases.				●						●			
Short Chain Acyl-CoA Dehydrogenase Deficiency	*ACADS*	People with short chain acyl-coA dehydrogenase deficiency have difficulty converting certain foods to energy, which is especially problematic in times of illness or fasting. It can also cause a build-up of certain chemicals in the body damaging certain organs and tissues. Early signs of this condition are weak muscles, low blood sugar, tiredness, and vomiting. Without treatment, this could result seizures with intellectual or developmental disability. Early alterations to the diet and frequent eating can help prevent the effects of this condition.				●			●			●	●		
Sjogren-Larsson Syndrome	*ALDH3A2*	The membranes that control water loss and the protective layers around nerves are affected by Sjogren-Larsson syndrome. Children with this condition are born with extremely dry and flaky skin. They often have problems with speech and suffer from extreme nearsightedness and light sensitivity. Over the first couple of years, these children will also be delayed in their development and show mild to moderate intellectual delay. Forty percent of children will have seizures and 50% will need a wheelchair due to extreme muscle stiffness, but most will live into adulthood with proper management of symptoms.				●						●	●		●
Skeletal Dysplasias, SLC26A2-related	*SLC26A2*	SLC26A2 is a gene that affects how our body makes cartilage. Cartilage is a tissue that acts as our skeleton very early on. Most of it later becomes bone, but some cartilage remains in ours ears, nose, and acts as a protective coating on the ends of certain bones. If this gene isn't working well, the cartilage doesn't form correctly and leads to conditions called skeletal (bone) dysplasias (abnormal formation). There are 4 different dysplasias that are each caused by different changes in the same gene: achondrogenesis type 1B, atelosteogenesis type 2, diastrophic dysplasia, and multiple epiphyseal dysplasia (MED). Even though they are separate conditions, many of the features are similar. With the exception of MED, people with these conditions will have very short arms and legs as well as a small overall body size. Their small size can cause problems with the joints, breathing, and possible foot abnormalities.		●										●		
Smith-Lemli-Opitz Syndrome	*DHCR7*	Smith-Lemli-Opitz syndrome (SLOS) causes the body to be unable to process cholesterol, which is important to many areas of the body. Children with SLOS grow slowly, have weak muscles, feeding difficulties, and over 90% will have some degree of intellectual disability. Cleft palate and abnormalities of the hands and/or feet are also common. The build-up of cholesterol also affects the kidneys and heart. Although some of these effects can be severe and lead to early death, proper medical attention and diet can often lengthen the lifespan of people with this condition.		●		●		●		●		●		●	
Spinal Muscular Atrophy	*SMN1*	Spinal muscular atrophy (SMA) is a condition that lowers the control people have over their muscles due to repeated death of certain nerve cells. People with SMA have muscle weakness, which gets worse over time. In addition to the leg muscles, SMA also weakens muscles controlling head movement, breathing, and swallowing. There are different types of SMA that will change how early someone shows signs and how severe the condition will be. Type 1 is most severe with earliest onset.		●								●			

CONDITION	GENE	SUMMARY	CLINICAL CONCERN												
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Tay-Sachs Disease (a.k.a. Hexosaminidase A Deficiency)	*HEXA*	Hexosaminidase A deficiency is causes an inability of the body to breakdown certain chemicals. The buildup of these chemicals in the brain and muscles becomes toxic and causes the destruction of nerves. This results in problems including seizures, and loss of vision and hearing over time. There is also a loss of intellectual and physical abilities over time leading to paralysis in the most severe forms. One type of this condition is Tay-Sachs disease with symptoms starting around 3-6 months of age while other forms start showing signs later.				●	●				●	●	●		●
Tricho-Hepato-Enteric Syndrome	*TTC37*	Tricho-hepato-enteric syndrome is a condition affecting the hair, liver, and intestines. Symptoms include patchy, brittle hair, recurrent diarrhea, feeding difficulty , failure to thrive, and short stature. Lifespan is reduced.				●				●	●			●	
Tyrosinemia Type I	*F11*	People with factor XI deficiency suffer from excessive bleeding following injury, surgery, or menstrual periods. Nosebleeds are especially common.	●												
Tyrosinemia Type I	*FAH*	People with tyrosinemia have difficulty breaking down a certain chemical in the body call tyrosine. The build-up of this chemical will damage certain organs such as the liver, kidneys and nervous system. Symptoms include excessive vomiting, diarrhea, failure to thrive, bone softening, and frequent nosebleeds. Liver damage can create a yellow appearance (jaundice) to the skin and eyes. If untreated, tyrosinemia could result in pain of the abdomen, arms, or legs, severe breathing difficulties, or cancer. Treatment with medication early in the process can prevent many of the symptoms of this condition.	●	●	●						●				
Usher Syndrome Type 1F	*PCDH15*	Severe hearing loss at birth followed by vision loss during childhood are the main features of Usher syndrome type 1F. Children with this condition often have issues with quick changes in speed or direction as well as problems with coordination and balance. Intellectual disability is not a finding in this condition.					●								●
Usher Syndrome Type 3	*CLRN1/ USH3A*	The main features of Usher syndrome type 3 are progressive hearing loss after the start of speech and vision loss in their teens. The severity of these symptoms will vary, but intellectual disability is not a finding in this condition.					●								●
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	*ACADVL*	People with very long chain acyl-coA dehydrogenase deficiency have difficulty converting certain foods to energy, which is especially problematic in times of exercise, illness or fasting. It can also cause a build-up of certain chemicals in the body damaging certain organs and tissues such as the heart or liver. Initial signs of this condition are weak muscles, low blood sugar, tiredness, and vomiting. Recurrent muscle cramps, breakdown of muscle tissue, and heart problems can also occur. The onset of symptoms and severity will vary from person to person. Early alterations to the diet and frequent eating can help prevent the effects of this condition.						●			●	●			
Von Willebrand Disease	*VWF*	Von Willebrand factor is a chemical that acts as a glue to hold clots together after injury. People with Von Willebrand disease are missing this factor and are prone to easy bruising, nosebleeds, heavy menstrual periods, and prolonged bleeding following injury, surgery, or giving birth. Medication can greatly lessen the effects of this condition.	●												
Walker- Warburg Syndrome, Type 4 (also Fukuyama Congenital Muscular Dystrophy)	*FKTN*	Walker-Warburg syndrome is a condition that affects the eyes, brain, and skeletal muscles. A chemical that helps to stabilize the fibers found in these muscles is missing and thus these muscles are more likely to damage with more and more use. Muscles become weak making movement more difficult. The change in brain structure will result in intellectual and physical disabilities, and some will have seizures. The eye problems often result in blindness. Most affected children will not live past the age of 3 years.		●		●		●				●	●		●

CONDITION	GENE	SUMMARY	CLINICAL CONCERN												
			BLOOD	BREATHING	CANCER	DELAYS	HEARING	HEART	INFECTION	KIDNEYS	LIVER	MUSCLES	SEIZURES	SKELETAL	VISION
Werner Syndrome	*WRN*	Werner syndrome is a condition of rapid aging after puberty. People with condition are usually shorter, have premature gray hair and hair loss, thin or hardened skin, cataracts, infertility, hardening of the arteries, osteoporosis, and cancer at significantly earlier ages than would be expected. Most symptoms become apparent in the early 20s and lifespan is reduced.			●			●							
Wilson Disease	*ATP7B*	People with Wilson disease are unable to effectively remove excess copper from their bodies. Although copper is used in many processes of the body, too much building up in organs like the liver, brain, and eyes will cause multiple medical problems. Symptoms of this condition include tiredness, loss of appetite, clumsiness, walking difficulties, speech problems, and yellowing of the skin or eyes (jaundice). Excess copper in the eyes can also cause restriction of movement, but does not usually affect vision. Certain behavioral or psychiatric illnesses such as depression, aggression or aggressive tendencies are also possible. Early treatment with copper reducers is shown to lessen the symptoms of this condition.									●	●			
Woolly Hair/Hypotrichosis Syndrome	*LIPH*	Woolly hair/hypotrichosis syndrome mainly affects the hair and skin. Hair is often dry, sparse, curly, and fragile. The hair on the head will often not grow more than a few inches. Eyebrows, eyelashes, and other body hair can also be affected. Itchy red skin or bumps on the skin are also common. Intellectual disability is not usually a feature with this condition.													
Zellweger Spectrum Disorder Type 1 (a.k.a Infantile Refsum Disease)	*PEX1*	Infantile refsum disease is part of the Zellweger syndrome spectrum which are a set of conditions with overlapping symptoms of weak muscles, feeding problems, hearing and vision loss, and seizures. These symptoms are caused by a breakdown of the protective coating to the nerve cells (called myelin) and part of the brain called white matter. There is also often damage to other organs like the liver, heart, and kidneys and can suffer from intellectual disabilities. Children with Infantile refsum disease are on the milder side of this spectrum having symptoms slightly later in childhood and worsening more slowly. Unlike other forms of this disease spectrum, they often live into adulthood.				●	●	●		●	●	●	●		●