Genetic Fact Sheets for Parents

Fatty Acid Oxidation Disorders

Screening, Technology, and Research in Genetics is a multi-state project to improve information about the financial, ethical, legal, and social issues surrounding expanded newborn screening and genetic testing – http:// www.newbornscreening.info

Disorder Name: **Carnitine palmitoyl transferase, type 1A arctic variant**
Acronym: **CPT1A arctic variant**

This fact sheet contains general information about CPT1A arctic variant. Every child is different and some of this information may not apply to your child specifically. Many children with CPT1A arctic variant never have any symptoms, but there is no way to tell who is at risk. Certain treatments may be recommended for some children but not others. Children with CPT1A arctic variant should be followed by their health care provider.

What is CPT1A arctic variant?

CPT1A arctic variant is a form of classic CPT1A deficiency. It is more common in the Inupiaq and Yu'pik populations in Alaska, and the Inuit population in Canada and Greenland. It is also seen in higher frequency among the indigenous people of Vancouver Island, northern coastal regions of Canada, Greenland, and northeast Siberia.

Like classic CPT1A deficiency, CPT1A arctic variant is a type of fatty acid oxidation disorder. People with CPT1A arctic variant have problems breaking down fat into energy for the body.

Fatty Acid Oxidation Disorders:

Fatty acid oxidation disorders (FAODs) are a group of rare inherited conditions. They are caused by enzymes that do not work properly.

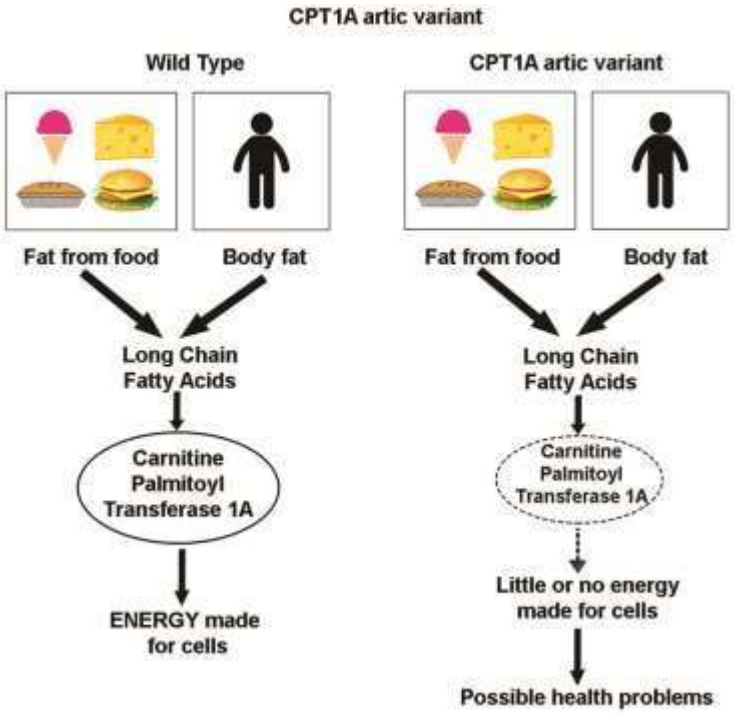
A number of enzymes are needed to break down fats in the body (a process called fatty acid oxidation). Problems with any of these enzymes can cause a fatty acid oxidation disorder. People with FAODs cannot properly break down fat from either the food they eat or from fat stored in their bodies.

The symptoms and treatments vary between different FAODs. They can also vary from person to person with the same FAOD. See the fact sheets for each specific FAOD.

FAODs are inherited in an autosomal recessive manner and affect both males and females.

What causes CPT1A arctic variant?

CPT1A arctic variant is caused by problems with the enzyme called "carnitine palmitoyl transferase 1A" (CPT1A). In people with CPT1A caused by the arctic variant, the CPT1A enzyme does not work properly. This enzyme's job is to help change certain fats in the food we eat into energy. It also helps break down fat already stored in the body. The difference between a wild type person and a person with CPT1A arctic variant can be seen below.



Energy from fat keeps us going whenever our bodies run low of their main source of energy, a type of sugar called glucose. Our bodies rely on fat when we do not eat for a stretch of time – like when we miss a meal or when we sleep.

The arctic variant causes the CPT1A enzyme to work more slowly than usual. This makes it harder for the body to make energy from fat. Most of the time, this does not cause any problems. However, when young children get sick and are not able to eat as much as usual, they may not be able to break down fat fast enough to provide all of the energy they need. At these times, children must be given a source of glucose (sugar) for energy.

What happens if CPT1A arctic variant is not treated?

Most infants and children with CPT1A arctic variant never have any symptoms. However, some children will have problems when they are sick and cannot eat or drink.

We can't be sure when children with CPT1A arctic variant will start showing symptoms, but we think this is most likely in children less than 2 years old. The most common symptom in young children, especially infants, is sleepiness. Older children may also get sleepy, but more often their first symptom is often irritability or other changes in behavior.

If children go too long without eating or drinking enough glucose-containing fluids (such as when they are sick), they can have an illness called a metabolic crisis. Some of the first signs of a metabolic crisis are:

- extreme sleepiness
- irritable mood
- poor appetite

If a metabolic crisis is not treated, a child with CPT1A arctic variant can develop:

- low blood sugar (hypoglycemia)
- high levels of ammonia in the blood
- breathing problems
- seizures
- coma, sometimes leading to death

If treated quickly and appropriately, these symptoms can be reversed. However, if a child has too many metabolic crises, they could develop brain damage. This brain damage can result in learning problems or intellectual disabilities. Therefore, it is important that infants and children with CPT1A arctic variant receive prompt treatment if they exhibit symptoms of metabolic crisis. Treatment should help to avoid potential long-term effects on development.

What is the treatment for CPT1A arctic variant?

The following are treatments sometimes recommended for children with CPT1A arctic variant:

1. **Avoid going a long time without food**
   Infants and young children with CPT1A arctic variant need to eat regularly to keep their energy level up. This helps to prevent a metabolic crisis. During the first few months of life, infants normally want to eat every 2-3 hours. This is enough to avoid any problems from the arctic variant. We generally recommend that parents not let their baby go more than 6-8 hours without eating, especially if their baby is sick.

   If your child is sick and not eating as well as usual, you should not let your child go too long without eating. This means you may need to wake your child up to feed them. This is especially important if the child is sick and seems sleepier than normal, is hard to wake up, seems confused, or is excessively irritable. If you have questions or concerns about how often your infant or child should eat, you should talk to your health care provider.

2. **Call your health care provider when your child is sick**
   Always call your health care provider right away when your child is sick and not able to eat or drink glucose-containing fluids (juices, Gatorade, etc.) for greater than 6-8 hours. Also call if your child has any of these symptoms:
   - poor appetite
   - low energy or excessive sleepiness
   - vomiting
   - diarrhea
   - an infection
   - a fever

Children with CPT1A arctic variant who are sick and not eating as much as normal need to drink fluids with glucose, even if they may not feel hungry. This is because they need to avoid low blood sugar (hypoglycemia) and other problems. Children who are sick are often unable to drink or do not want to drink. In this case, they may need to be treated in the hospital to prevent serious health problems.

What happens when CPT1A arctic variant is treated?

With prompt treatment, children with CPT1A arctic variant live healthy lives with good growth and development.

What happens when children with CPT1A arctic variant grow up?

Most children with CPT1A arctic variant will never have any symptoms. In those who do, prompt and careful treatment will prevent long-term problems in most children, allowing them to grow and develop normally, and live healthy lives. Some symptoms, such as feeling the need to eat frequently, may last into adulthood. However, a metabolic crisis or other severe problems usually do not happen after 2-3 years of age.

What causes the CPT1A enzyme to not work correctly?

Genes tell the body to make various enzymes. The CPT1A gene instructs the body to make the CPT-1A enzyme. Everyone has two copies of the CPT1A gene. People with CPT1A arctic variant have the same change in both copies of their CPT1A genes. The gene change (variant) is called C1436T or P479L and referred to as the arctic variant. This arctic variant makes the CPT1A enzyme work slower than usual, which makes it harder for the body to make energy from fats.

In science, we use the term "wild type" to describe a version of a gene that is the most common version found throughout the whole world. Therefore, if a person does not have the wild type version of the CPT1A gene, they might have the arctic variant version or other versions. This handout only describes the arctic variant version and the wild type version of the CPT1A gene.

How is CPT1A arctic variant inherited?

CPT1A arctic variant is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has two copies (a pair) of all of their genes, one that came from their mother, and one that came from their father. When someone has a child, they pass on one gene from each of their many pairs of genes to their child. Everyone has two copies of the CPT1A gene. In Alaska, there are two common forms of the CPT1A gene, one that contains the arctic variant, and one with the wild type. Some people have two copies with the arctic variant, some have two copies of the wild type, and others have one copy of each. **Only children with two copies of the arctic variant form of CPT1A are at risk for the symptoms that result from the reduced ability to use fats for energy that is caused by the arctic variant.**

The chances that a child will have one, two, or zero copies of the CPT1A arctic variant genes depend on how many CPT1A arctic variant copies their parents have.

To see all the different ways CPT1A arctic variant can be inherited, please see the last section of this handout "CPT1A Arctic Variant – Inheritance Patterns."

In the Inupiaq and Yu'pik populations in Alaska, the most common form of the CPT1A gene is the one with the arctic variant. About 50% of the people in the Inupiaq and Yu'pik populations carry two copies of the CPT1A arctic variant gene. The reason we think that CPT1A arctic variant is so common in Yu'pik and Inupiaq people and other indigenous populations is because it was advantageous to people eating the traditional diet consisting of mainly sea mammals. In other Alaska Native people who did not have this diet, as well as non-Native Alaskans, the CPT1A gene without the arctic variant is the most common.

The chance that a baby born to Inupiaq or Yu'pik parents will have two copies of the CPT1A arctic variant gene is about 50%. However, the chance that a baby born to parents who are not Inupiaq or Yi'pik will have two copies of the CPT1A arctic variant gene is much lower.

Can other members of the family have CPT1A arctic variant?

There is a very good chance that the brothers, sisters, and parents of a baby with two copies of the CPT1A arctic variant gene also carry one or two copies of the CPT1A arctic variant gene. This is particularly true in Yu'pik and Inupiaq Alaska Natives in whom the arctic variant is the normal form of the CPT1A gene.

CPT1A arctic variant and pregnancy

There is little known about how the CPT1A arctic variant may affect pregnancy. If you have CPT1A arctic variant in your family and you are pregnant or planning to become pregnant, make sure to talk to your healthcare provider about your family history.

How many people have CPT1A arctic variant?

CPT1A arctic variant is more common (and is considered to be the normal gene) among the Inupiaq and Yu'pik people of Alaska, and the Inuit people of Canada and Greenland. It is estimated that about 7 in every 100 infants (about 7% of infants) in Alaska are born with CPT1A arctic variant each year.

The reason that CPT1A arctic variant is more common in the Inupiaq and Yu'pik people of Alaska and the Inuit people of Canada and Greenland is not known. Many believe that the arctic variant is beneficial for people who eat a traditional native diet containing protein and fats from fish and sea and land animals.

Does CPT1A arctic variant go by any other names?

The name arctic variant refers to a specific change in the DNA of the gene for CPT1A. There are several other ways that this variant might be identified:

- CPT1A c.1436C→T
- CPT1A p.P479L
- CPT1A P479L
- CPT1A P479L

It might also be called the CPT1A P479L polymorphism, or CPT1A P479L mutation.

There is another type of CPT deficiency called CPT-1B, or “muscle type.” CPT- 1B is not discussed in this fact sheet.

Where can I find more information?

Fatty Oxidation Disorders (FOD) Family Support Group
http://www.fodsupport.org

Baby’s First Test
https://www.babysfirsttest.org/newborn-screening/conditions/carnitine-palmitoyltransferase-i-deficiency

Genetic Home Reference
https://ghr.nlm.nih.gov/condition/carnitine-palmitoyltransferase-i-deficiency

Organic Acidemia Association
http://www.oaanews.org

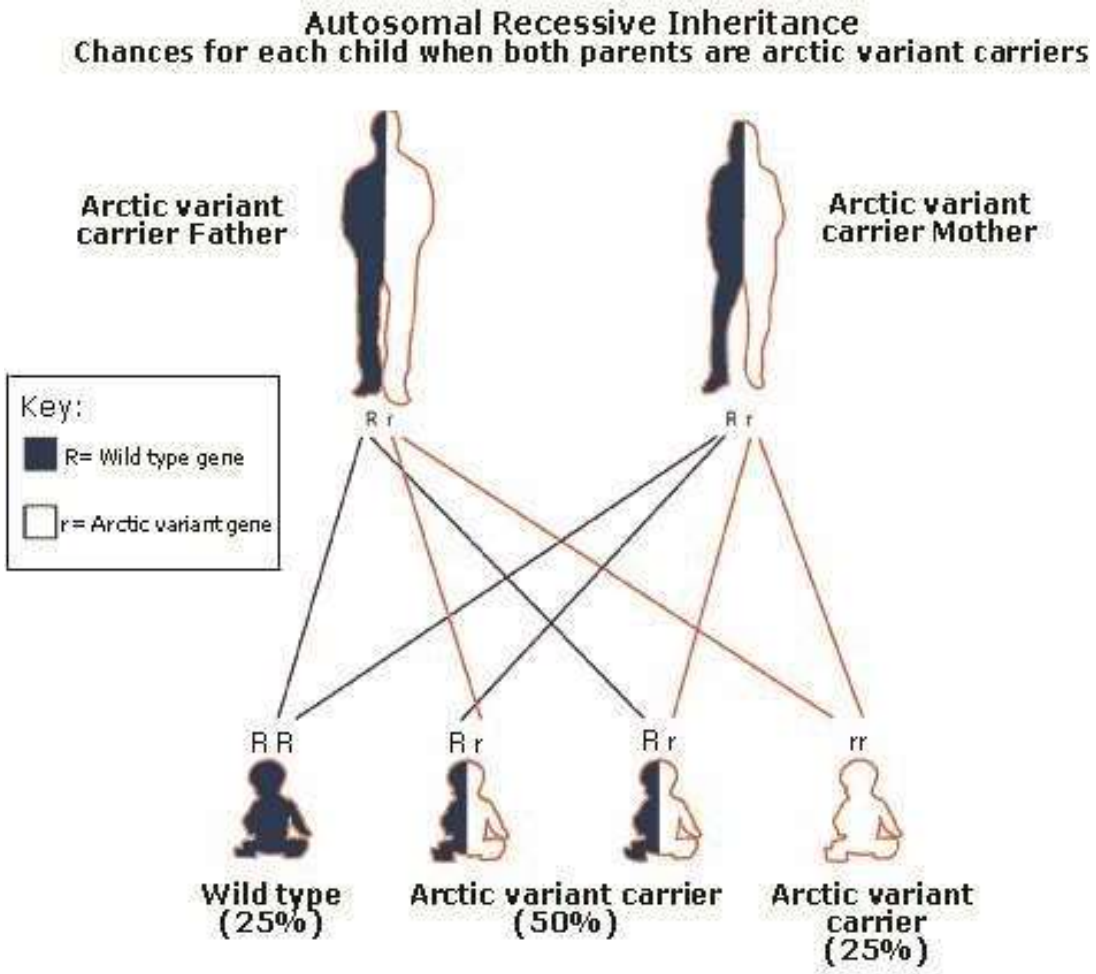
United Mitochondrial Disease Foundation
http://www.umdf.org

Genetic Alliance
http://www.geneticalliance.org

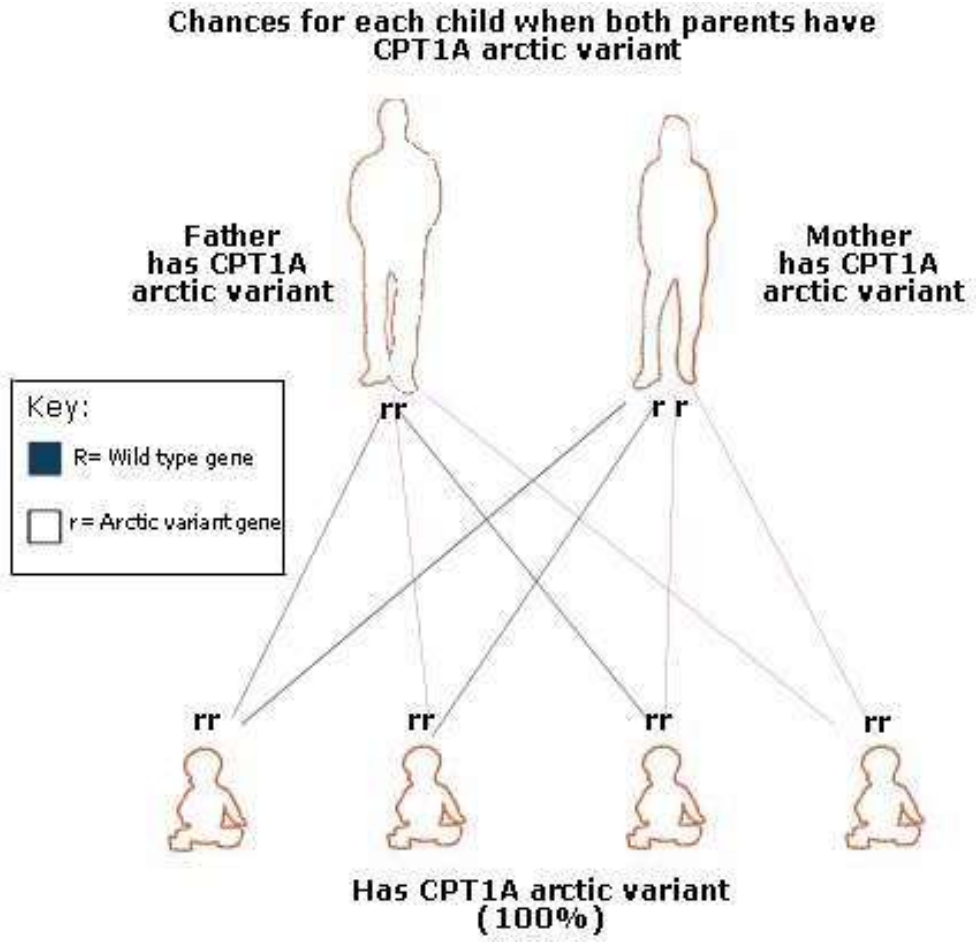
Mito Action
http://www.mitoaction.org

CPT1A Arctic Variant – Inheritance Patterns

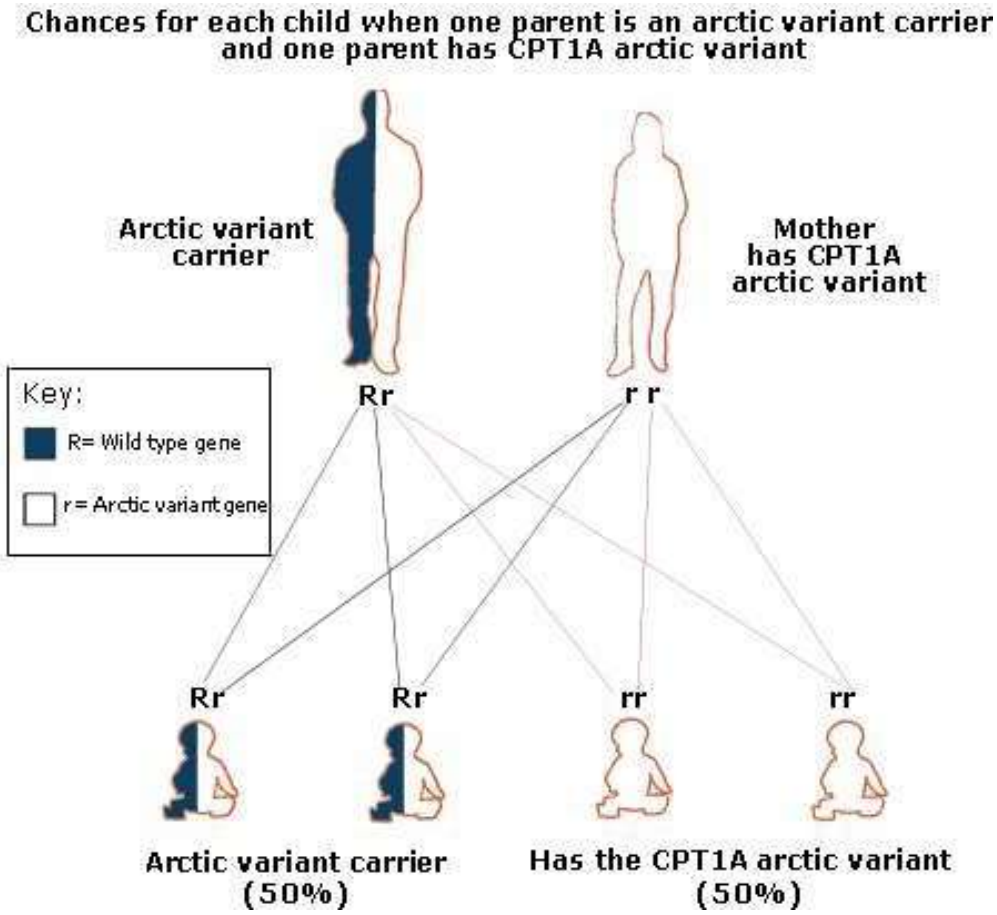
If both parents have one copy of the CPT1A arctic variant gene and one copy of the wild type CPT1A gene, they are called carriers. If this couple has children, 25% will have two copies with the arctic variant, 25% will have no copies of the arctic variant, and half (50%) will have one copy with the arctic variant. See diagram below.



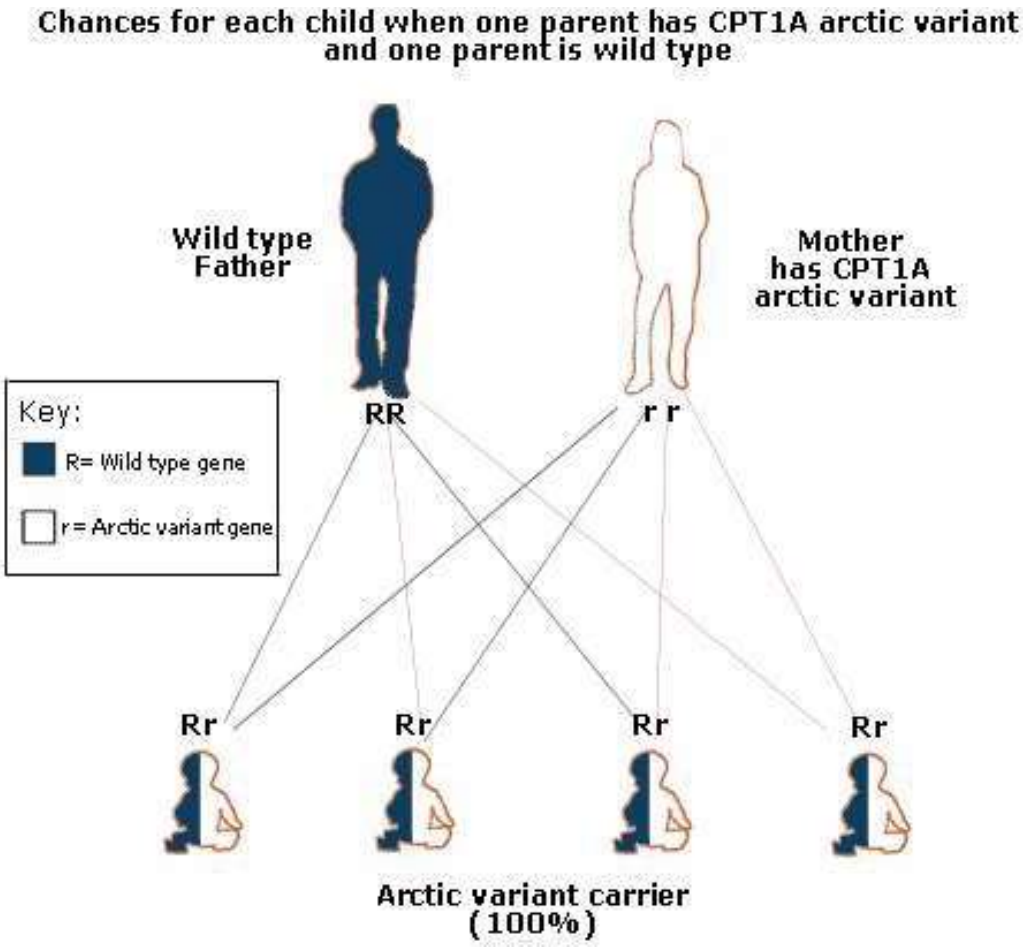
If both parents have two copies of the CPT1A arctic variant gene, then they both have CPT1A arctic variant. All of their children will also have two copies of the CPT1A arctic variant gene. See diagram below.



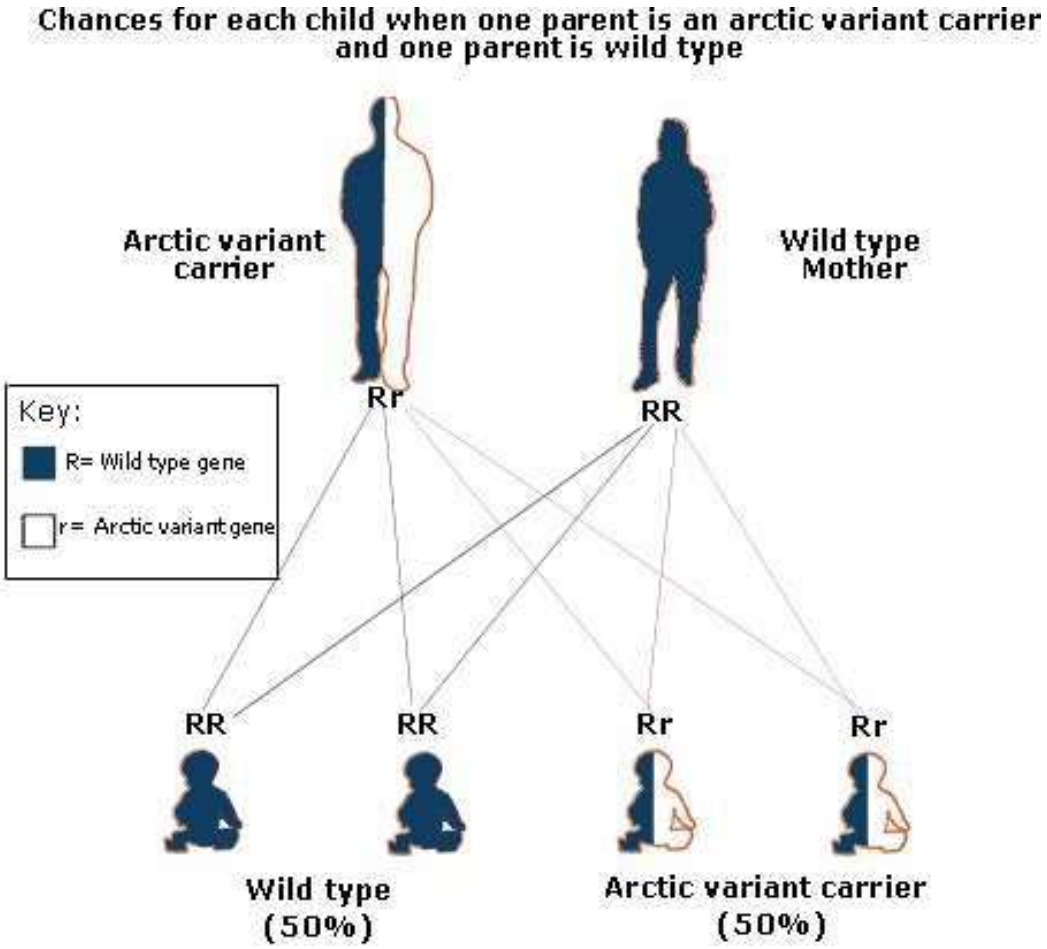
If one parent has two copies of the CPT1A arctic variant gene (has CPT1A arctic variant) and the other parent has only one copy of the CPT1A arctic variant gene (arctic variant carrier), then half of their children (50%) will have two copies of the CPT1A arctic variant gene, and the other half will have only one copy of the CPT1A arctic variant gene (arctic variant carriers). See diagram below.



If one parent has two copies of the CPT1A arctic variant gene (has CPT1A arctic variant) and the other parent has no copy of the CPT1A arctic variant gene (has wild type), then all of their children (100%) will have one copy with the arctic variant (arctic variant carriers). See diagram below.



If one parent has no copies of the CPT1A arctic variant gene (has wild type) and the other parent has one copy of the CPT1A arctic variant gene (arctic variant carrier), then 50% of their children will have one copy of the CPT1A arctic variant gene (arctic variant carriers) and 50% will have no copies (wild type). See diagram below.



If neither parent has a copy of the CPT1A gene with the arctic variant (both have wild type), then none of their children will have it either (all children will be wild type). No diagram provided.

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