Welcome!

This toolkit is designed for people affected by rare conditions called ***long-chain fatty acid oxidation disorders*** (LC-FAOD, also called FAOD). The ten resources included will support your journey whether you are living with or caring for someone with LC-FAOD.

It includes information on how to:

- ***Understand LC-FAOD.*** Learn about the causes, impacts, signs, and symptoms.
- ***Build Your Support Network.*** Learn about organizations that can help you.
- ***Communicate with Healthcare Providers.*** Make the most of your appointments.
- ***Prepare an LC-FAOD Medical History.*** Gather your important information.
- ***Live Well While Caring for Someone with LC-FAOD.*** Prepare others to help and get the respite you need.
- ***Share Your Rare Journey and Craft Your Story.*** Learn to educate and advocate.
- ***Learn What to Expect with LC-FAOD.*** Prepare for what's ahead with three unique booklets focused on age: Infants & Children, Pre-Teen & Teen, and Young Adult & Beyond.

ABOUT LC-FAOD

LC-FAOD are a group of rare, autosomal recessive genetic conditions. This means that the disorder is inherited when each parent is a carrier. In people with LC-FAOD, an enzyme that transports or breaks down dietary long-chain fat is either very low or does not work properly. The signs and symptoms seen in people with LC-FAOD occur because they are unable to properly break down long-chain fatty acids for energy. Therefore, they must find alternative energy sources.

TYPES OF LC-FAOD

There are different types of LC-FAOD. Each type results from a different gene mutation.

Fats in our diet are an important source of energy production during times of metabolic stress or prolonged fasting. Long-chain fatty acids need to be transported into the mitochondrion (energy house of the cell) by three different enzymes (CPT I, CACT, CPT II), and then once in the mitochondrion, the fatty acids undergo further metabolism for energy (VLCAD, TFP, LCHAD).

CPT I (Carnitine Palmitoyltransferase I) Deficiency

A mutation in the *CPTIA* gene causes the CPT I enzyme to not function properly, which results in CPT I deficiency. This means that long-chain fatty acids cannot begin the first step in the carnitine shuttle to bring long-chain fatty acids into the mitochondrion.

There are approximately 14 babies born with LC-FAOD in Canada per year. A 2020 estimate indicated there are 455 people living with LC-FAOD in Canada.

We would like to acknowledge and thank the Ultragenyx LC-FAOD Patient Leadership Council and the healthcare providers who provided substantive feedback and input on the development of these materials. We would also like to thank those community members who provided specific feedback to help ensure relevance for those living in Canada.

CACT (Carnitine-Acylcarnitine Translocase) Deficiency

A mutation in the *SLC25A20* gene causes CACT deficiency. This means that the middle step of the carnitine shuttle, transporting the long-chain fatty acid into the mitochondrion, cannot be performed properly.

CPT II (Carnitine Palmitoyltransferase II) Deficiency

A mutation in the *CPTII* gene causes CPT II deficiency. This means that the last step in the carnitine shuttle cannot be completed. Therefore, the long-chain fat cannot enter the mitochondrion.

John, living with TFP deficiency, and his mom, Eileen.

VLCAD (Very Long Chain Acyl-CoA Dehydrogenase) Deficiency

A mutation in the *ACADVL* gene causes VLCAD deficiency. This enzyme is part of the long-chain beta oxidation spiral. Once long-chain fats enter the mitochondria after transportation via the carnitine shuttle, they are processed by the long-chain beta oxidation spiral. If the VLCAD enzyme is not functioning properly, then long-chain fatty acids are not broken down properly, resulting in lower energy and damage from incomplete processing of fatty acids.

TFP (Trifunctional Protein) Deficiency

TFP deficiency occurs when a person has a mutation in both the *HADHA* gene and *HADHB* gene. TFP is a three enzyme complex and performs the last three steps in the breakdown of long-chain fatty acids. One of these enzymes is LCHAD. If the TFP enzyme complex is not working properly, long-chain fats cannot be broken down for energy and unused fatty acids can build up in the body and cause issues.

LCHAD (Long-chain 3-hydroxy-acyl-CoA Dehydrogenase) Deficiency

LCHAD deficiency occurs when a person has a mutation in the *HADHA* gene. This is part of the TFP complex, but the mutation is just in the *HADHA* gene, causing LCHAD. If there is a deficiency in this step, long-chain fatty acids are not properly broken down so they cannot be used for energy.

Ultragenyx is a biopharmaceutical company committed to bringing to patients novel products for the treatment of serious rare and ultra-rare genetic diseases.

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