SPONSORED GENETIC TESTING FOR LONG-CHAIN FATTY ACID OXIDATION DISORDERS (LC-FAOD)

Sponsored By:

ultragenyx
pharmaceutical

PROGRAM SUMMARY

The fatty acid oxidation disorders testing program provides sponsored, no-cost genetic testing for individuals suspected of having long-chain fatty acid oxidation disorders (LC-FAOD).

ELIGIBILITY

This program is available to patients in the US who meet at least 1 of the following criteria:

- Patient has a completed UltraCare Start Form for LC-FAOD

OR

- Patient is suspected of having, or has a known diagnosis of, a long-chain fatty acid oxidation disorder AND a plasma acylcarnitine test that either has been performed (regardless of result—abnormal or normal) or has been ordered
  - Carnitine palmitoyltransferase (CPT) I deficiency
  - Carnitine-acylcarnitine translocase (CACT) deficiency/ carnitine palmitoyltransferase (CPT) II deficiency
  - Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency/ mitochondrial trifunctional protein (TFP) deficiency
  - Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency

Providing a copy of plasma acylcarnitines results, or any other confirmatory tests, when available, is strongly encouraged. These results are helpful for variant interpretation and in some cases can make a difference in the final interpretation of the variant.

While Ultragenyx provides financial support for this program, the genetic testing and counseling services are performed by independent third parties. Healthcare professionals must confirm that patients meet certain criteria to use the program and shall not seek reimbursement for the testing or services provided under this program from any third party, including but not limited to federal healthcare programs. Ultragenyx receives de-identified patient data from this program, but at no time does Ultragenyx receive patient identifiable information. Ultragenyx receives contact information for healthcare professionals who use this program. Genetic testing and counseling services are available in the US only. Healthcare professionals who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use, or support any Ultragenyx product.

WHAT ARE LONG-CHAIN FATTY ACID OXIDATION DISORDERS?

Long-chain fatty acid oxidation disorders (LC-FAOD) are a group of 6 rare autosomal recessive disorders[1,2]:

- Carnitine palmitoyltransferase (CPT) I deficiency
- Carnitine-acylcarnitine translocase (CACT) deficiency
- Carnitine palmitoyltransferase (CPT) II deficiency
- Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency
- Mitochondrial trifunctional protein (TFP) deficiency
- Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency

LC-FAOD are caused by defects in the mitochondrial carnitine shuttle or β-oxidation enzymes that are involved in the conversion of long-chain fatty acids into energy to support the ongoing energy needs of major organ systems, including the heart, skeletal muscle, and liver.[2,3]

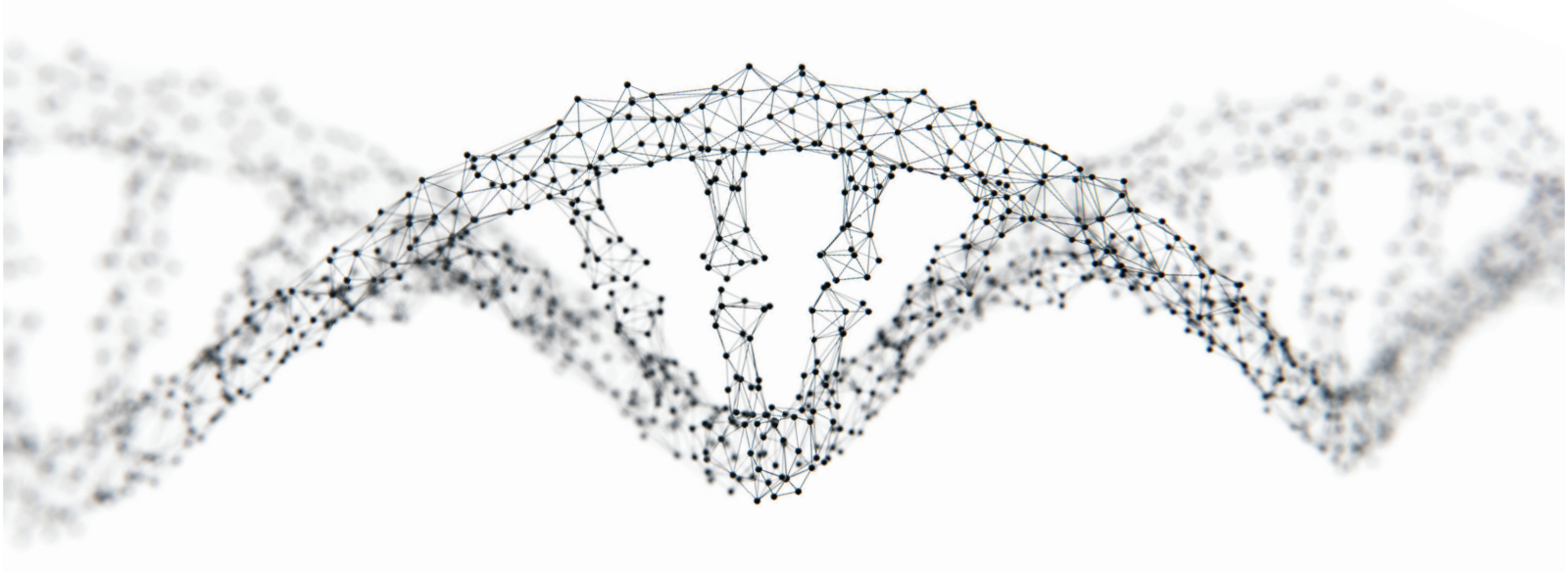
Clinical manifestations of LC-FAOD are heterogeneous, may be acute or chronic, and often phenotypically present as fatigue (physical and/or mental), and/or with episodic exacerbations of rhabdomyolysis, cardiomyopathy, and hypoketotic hypoglycemia, which often require hospitalization and can lead to death.[2,4]

WHY GENETIC TESTING FOR LC-FAOD?

Accurate diagnosis of LC-FAOD may have an impact on clinical management of the condition, including customizing care to a patient's specific needs, providing patients with the appropriate genetic counseling support, and connecting patients and their families to patient advocacy organizations and other resources.

GENETIC TEST RESULTS ARE USUALLY AVAILABLE WITHIN 10 TO 21 CALENDAR DAYS FROM WHEN SAMPLE PROCESSING BEGINS

Complete the enclosed test requisition form and include it with the patient sample in the prepaid mailer.



TEST OPTIONS

The fatty acid oxidation disorders testing program offers testing with the **Invitae Fatty Acid Oxidation Defects Panel**.

INVITAE FATTY ACID OXIDATION DEFECTS PANEL

Genes included: ACADM, ACADS, ACADSB, ACADVL, CPT1A, CPT2, ETFA, ETFB, ETFDH, HADH, HADHA, HADHB, HMGCL, HMGCS2, MLYCD, SLC22A5, SLC25A20

Add on: NADK2, SLC52A1, SLC52A2, SLC52A3

The Invitae Fatty Acid Oxidation Defects Panel includes up to 21 genes known to be associated with the β-oxidation of fatty acids, carnitine shuttle, carnitine transport, ketogenesis, and conditions that may cause similar abnormal profiles on plasma acylcarnitine analysis.

Once Invitae receives the sample, your results will be available in 10 to 21 calendar days, on average.

PARTNER CODE

FAOD

COUNTRIES

US Only

ABOUT ULTRAGENYX PHARMACEUTICAL INC.

Ultragenyx is a biopharmaceutical company committed to bringing to patients novel products for the treatment of serious rare and ultra-rare genetic diseases. The company has built a diverse portfolio of approved therapies and product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are no approved therapies.

The company is led by a management team experienced in the development and commercialization of rare disease therapeutics. The Ultragenyx strategy is predicated upon time- and cost-efficient drug development, with the goal of delivering safe and effective therapies to patients with the utmost urgency.

For more information on Ultragenyx, please visit the company's website at **www.ultragenyx.com**.

GENETIC TESTING FOR LC-FAOD

WHAT IS AND WHY CONDUCT CONFIRMATORY TESTING?

Some insurers require verification of an LC-FAOD diagnosis before determining patient eligibility for treatment coverage. In this situation, patients are eligible for the sponsored test if they have completed the UltraCare Start Form for LC-FAOD.

WHAT IS AND WHY CONDUCT SUSPECTED PATIENT TESTING?

Genetic testing helps facilitate an accurate diagnosis for patients suspected of having an LC-FAOD. In this situation, a patient is eligible for the sponsored test if:

- Patient is suspected of having, or has a known diagnosis of, a long-chain fatty acid oxidation disorder

AND

- Patient has a plasma acylcarnitine test that either has been performed (regardless of result—abnormal or normal) or has been ordered

HOW DO I SUBMIT A PATIENT TEST?

STEP 1	STEP 2	STEP 3
Complete both pages of the enclosed Invitae test requisition form.	Obtain a blood or saliva sample from your patient using the Invitae kit provided.	Mail the form and patient sample using the packaging provided and prepaid label.

Test results are usually available within 10 to 21 calendar days. You will be notified via email or fax to access results through the Invitae secure site. Obtain patient permission before sharing test results with the patient's insurance company.

QUESTIONS ABOUT GENETIC TESTING FOR LC-FAOD?

Contact UltraCare at **1-888-756-8657** or online at **ultracaresupport.com**.

Complete the enclosed test requisition form and include it with the patient sample in the prepaid mailer.

IS IT AN LC-FAOD? HELP CONFIRM THE DIAGNOSIS WITH SPONSORED TESTING.

FOR PATIENTS MEETING THE ELIGIBILITY CRITERIA, THIS PROGRAM IS PROVIDED AT NO COST.

References:

1. Roe CR, Brunengraber H. Anaplerotic treatment of long-chain fat oxidation disorders with triheptanoin: review of 15 years experience. *Mol Genet Metab*. 2015;116(4):260-268.
2. Knotternus SJG, Bleeker JC, Wust RCI, et al. Disorders of mitochondrial long-chain fatty acid oxidation and the carnitine shuttle. *Rev Endocr Metab Disord*. 2018;19(1):93-106.
3. Wanders RJ, Ruiter JP, IJlst L, Waterham HR, Houten SM. The enzymology of mitochondrial fatty acid beta-oxidation and its application to follow-up analysis of positive neonatal screening results. *J Inherit Metab Dis*. 2010;33(5):479-494.
4. Vavlukis M, Eftimov A, Zafirovska P, et al. Rhabdomyolysis and cardiomyopathy in a 20-year-old patient with CPT II deficiency. *Case Rep Genet*. 2014;2014:496410.

Sponsored By:

ultragenyx pharmaceutical

MRCP-UX007-00042 4/2020