Test Definition: PGDBS

Plasmalogens, Blood Spot

Overview

Useful For

Diagnosing patients with possible peroxisomal disorders, such as peroxisomal biogenesis disorders (Zellweger syndrome spectrum) and rhizomelic chondrodysplasia punctata (RCDP), including fatty acyl-CoA reductase 1 (FAR1) deficiency

Evaluating patients with abnormal newborn screen results for X-linked adrenoleukodystrophy who appear to have a different type of peroxisomal disorder, such as a Zellweger syndrome spectrum disorder

Aiding in the assessment of peroxisomal function

Genetics Test Information

This test measures plasmalogens and plasmalogen to fatty acid ratios for the purpose of diagnosis of peroxisomal biogenesis disorders (Zellweger syndrome spectrum) and rhizomelic chondrodysplasia punctata, including fatty acyl-CoA reductase 1 deficiency.

Special Instructions

- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions

Highlights

This test analyzes plasmalogens and plasmalogen to fatty acid ratios. Reports include concentrations of C16:0, C18:0, and C18:1 plasmalogens and the ratio of the C16:0 and C18:0 plasmalogens to the respective fatty acid.

Method Name

Gas Chromatography Mass Spectrometry (GC-MS)

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Additional Testing Requirements

If peroxisomal biogenesis disorders (Zellweger syndrome spectrum) are suspected, also order very long chain fatty acids (POX / Fatty Acid Profile, Peroxisomal [C22-C26], Serum; or POXP / Fatty Acid Profile, Peroxisomal [C22-C26], Plasma), bile acids (BAIPD / Bile Acids for Peroxisomal Disorders, Serum), and pipecolic acid (PIPU / Pipecolic Acid, Random,

Urine).

If rhizomelic chondrodysplasia punctata (RCDP) is suspected, also order very long chain fatty acids (POX / Fatty Acid Profile, Peroxisomal [C22-C26], Serum), which includes phytanic and pristanic acid analysis.

Necessary Information

1. **Reason for testing is required**
2. Date of blood transfusion, if performed.
3. Biochemical Genetics Patient Information (T602) is recommended, but not required, to be filled out and sent with the specimen to aid in the interpretation of test results.

Specimen Required

Submit only 1 of the following specimens:

Preferred:
Patient Preparation: Specimen must be collected either prior to or 6 weeks after a blood transfusion.
Specimen Type: Blood spot
Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Blood spot collection card
Acceptable: Local newborn screening card, PerkinElmer 226 filter paper, Munktell filter paper, Whatman Protein Saver 903 paper, or blood collected in tubes containing ACD, EDTA, or heparin spotted and dried on filter paper
Specimen Volume: 2 Blood spots
Collection Instructions:
1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect Dried Blood Spot Samples.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.
Specimen Stability Information: Ambient (preferred) 90 days/Refrigerated 90days/Frozen 90 days
Additional Information:
1. For collection instructions, see Blood Spot Collection Instructions.
2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777).
3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800).

Acceptable
Specimen Type: Whole Blood
Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Green top (sodium or lithium heparin), yellow top (ACD solution A or B)
Specimen Volume: 2 mL
Collection Instructions: Send whole blood specimen in original tube. **Do not** aliquot.
Specimen Stability Information: Refrigerate (preferred) 14 days/Ambient 11 days

Forms

1. Biochemical Genetics Patient Information (T602)
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

Blood spot: 1
Whole blood: 0.5 mL

Reject Due To

Shows serum rings Has multiple layers Insufficient specimen Unapproved filter papers	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Varies		

Clinical & Interpretive

Clinical Information

Peroxisomes are organelles that carry out essential metabolic functions, including beta-oxidation of very long-chain fatty acids (VLCFA), alpha-oxidation of phytanic acid, and biosynthesis of plasmalogen and bile acids. Peroxisomal disorders include disorders of peroxisomal biogenesis with defective assembly of the entire organelle, and disorders of peroxisome function with single peroxisomal enzyme/transporter defects where the organelle is intact but a specific function is disrupted.

Biochemical abnormalities in peroxisomal biogenesis disorders can include accumulations of VLCFA, phytanic acid, pristanic acid, pipecolic acid, bile acids, and reduced plasmalogens. The differential diagnosis of these disorders is based on recognition of clinical phenotypes combined with a series of biochemical tests to assess peroxisomal function and structure. These include measurements and ratios of VLCFA, phytanic acid, and its metabolite pristanic acid (POX / Fatty Acid Profile, Peroxisomal [C22-C26], Serum or POXP / Fatty Acid Profile, Peroxisomal [C22-C26], Plasma), pipecolic acid (PIPA / Pipecolic Acid, Serum or PIPU / Pipecolic Acid, Random, Urine), bile acids (BAIPD / Bile Acids for Peroxisomal Disorders, Serum), and plasmalogens.

Peroxisomal biogenesis disorders include Zellweger syndrome spectrum disorders, which are clinically diverse and range in severity from neonatal lethal (Zellweger syndrome) to more variable clinical courses in neonatal adrenoleukodystrophy and infantile Refsum disease. Affected children typically have hypotonia, poor feeding, distinctive

facial features, seizures, and liver dysfunction. Other features can include retinal dystrophy, hearing loss, developmental delays, and bleeding episodes.

Rhizomelic chondrodysplasia punctata (RCDP) is a malformation disorder characterized by rhizomelic shortening, chondrodysplasia punctata, cataracts, intellectual disability, and seizures, although it can have a milder phenotype with only cataracts and chondrodysplasia punctata. Currently, there are 5 clinical types of rhizomelic chondrodysplasia punctata: RCDP 1, 2, 3, 4 (also known as FAR1 deficiency) and 5. RCDP 1 is the classical form that presents in infancy with skeletal manifestations including rhizomelic shortening, cataracts, and severe to profound postnatal growth deficiency. Infants with RCDP 1 have developmental delay, and later, intellectually disability. The majority of children with RCDP 1 do not survive beyond the first decade of life. RCDP 1 is an autosomal recessive disorder caused by disease-causing variants in the *PEX7* gene. RCDP 2 and 3 have clinical phenotypes similar to RCDP 1 and may be distinguished by plasmalogen deficiency. RCDP 2 and 3 are autosomal recessive conditions caused by disease-causing variants in *GNPAT* and *AGPS* genes, respectively. Individuals with RCDP 5 have a milder phenotype when compared to classic RCDP 1, with most individuals able to achieve self-feeding, independent ambulation, and development of limited language skills. RCDP5 results in less pronounced reduction in plasmalogens compared to RCDP 1. This newly recognized subtype of RCDP is an autosomal recessive disorder caused by disease-causing variants in the *PEX5* gene.

The typical biochemical profile for RCDP shows reduced plasmalogens, elevated phytanic acid, and normal VLCFA. Confirmatory testing via molecular analysis for all types of RCDP is available (PDGP / Peroxisomal Disorder Gene Panel, Varies).

Fatty acyl-CoA reductase 1 (FAR1) deficiency, also known as RCDP type 4, is an autosomal recessive peroxisomal disorder caused by disease-causing variants in the *FAR1* gene that result in early-onset epilepsy, microcephaly, cataracts, postnatal growth deficiency, and intellectual disability. Unlike RCDP, however, infants with FAR1 deficiency have no skeletal abnormalities. The biochemical profile for FAR1 deficiency includes reduced plasmalogens, normal to elevated phytanic acid, and normal VLCFA.

Reference Values

Hexadecanal-Dimethylacetal, C16:0 DMA
> or =7.00 mcg/mL

Octadecanal-Dimethylacetal, C18:0 DMA
> or =12.00 mcg/mL

9Z-Octadecenal-Dimethylacetal C18:1DMA
> or =2.00 mcg/mL

C16:0 DMA/C16:0
> or =0.012

C18:0 DMA/C18:0
> or =0.050

Interpretation

Reports include concentrations of C16:0, C18:0 and C18:1 plasmalogens and the ratio of the C16:0 and C18:0 plasmalogens to the respective fatty acid. When no significant abnormalities are detected, a simple descriptive

interpretation is provided.

A profile of reduced plasmalogens and abnormal very long-chain fatty acids (VLCFA), as well as possible abnormalities in pipecolic acid and bile acids, can be consistent with a diagnosis of a peroxisomal biogenesis disorder (Zellweger syndrome spectrum).

A profile of reduced plasmalogens, elevated phytanic acid, and normal VLCFA is consistent with a diagnosis of rhizomelic chondrodysplasia punctata, such as RCDP type 1 or 2, FAR1 deficiency (RCDP type 4), or other types of RCDP.

Positive test results could be due to a genetic or nongenetic condition. Additional confirmatory testing would be required to differentiate between these causes.

Cautions

The results of testing performed in erythrocytes are invalid following a transfusion; therefore, collect specimen either prior to, or 6 weeks after, a blood transfusion.

Clinical Reference

1. Braverman NE, Moser AB, Steinberg SJ, Fallatah WF, Duker A, Bober M. Rhizomelic chondrodysplasia punctata type 1. In: Adam MP, Mirzaa GM, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2001. Updated January 30, 2020. Accessed May 25, 2023. Available at www.ncbi.nlm.nih.gov/books/NBK1270/
2. Buchert R, Tawamie H, Smith C, et al. A peroxisomal disorder of severe intellectual disability, epilepsy, and cataracts due to fatty acyl-CoA reductase 1 deficiency. Am J Hum Genet. 2014;95(5):602-610
3. Baroy T, Koster J, Stromme P, et al. A novel type of rhizomelic chondrodysplasia punctata, RCDP5, is caused by a loss of the PEX5 long isoform. Hum Mol Genet. 2015;24(20):5845-5854
4. Braverman NE, Moser AB. Functions of plasmalogen lipids in health and disease. Biochim Biophys Acta. 2012;1822(9):1442-1452

Performance

Method Description

This test measures C16:0, C18:1 and C18:0 plasmalogens in dried blood spots as a diagnostic marker for peroxisomal disorders as well as C16:0 and C18:0 fatty acid for normalization. Briefly, samples, standards, and quality control are mixed with internal standards, and derivatization and extraction are performed. Plasmalogens and fatty acids are then extracted from solution, transferred to a new tube, dried down under nitrogen, reconstituted, and analyzed by gas chromatography mass spectrometry.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Tuesday

Report Available

3 to 9 days

Specimen Retention Time

Normal result: 3 months; Abnormal result: Indefinitely

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PGDBS	Plasmalogens, BS	104687-9

Result ID	Test Result Name	Result LOINC® Value
609665	Hexadecanal-Dimethylacetal, C16 DMA	104682-0
609666	Octadecanal-Dimethylacetal, C18 DMA	104683-8
609667	9Z-Octadecenal-DiMe acetal C18:1DMA	104684-6
609670	C16 DMA/C16:0	104685-3
609671	C18 DMA/C18:0	104686-1
BG724	Reason for Referral	42349-1
609673	Reviewed By	18771-6
609674	Interpretation	59462-2