LABHORIZONS
A NEWSLETTER FOR CLIENTS
Volume XIX, No. 9 — September 2019

New Procedures

Alpha Aminoadipic Semialdehyde (Urine) 620046

CPT 82542
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 10 - 14 days
Specimen Urine, **frozen**
Volume 1.0 mL
Minimum Volume 0.5 mL
Container Sterile cup
Storage Instructions Freeze as soon as possible after collection; ship within 24 hours.
Stability

Temperature	Period
Room temperature	Unstable (stability determined by manufacturer or literature reference)
Refrigerated	Unstable (stability determined by manufacturer or literature reference)
Frozen	Indefinite (stability determined by manufacturer or literature reference)

Causes for Rejection Thawed sample
Use Urine Alpha aminoadipiv semialdehyde is useful for diagnosing pyridoxine-dependent seizures (PDS) and folinic acid-responsive seizures (FRS). Elevation of alpha aminoadipic semialdehyde can also occur in molybdenum cofactor deficiency. Urine Alpha aminoadipic semialdehyde may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing Testing). Pyridoxine dependent seizures is a genetic disorder characterized by seizures in neonates or infants up to 3 years of age, which in general, respond to a pharmacologic dose of pyridoxine (vitamin B6). Alpha- aminoadipic seminaldehyde dehyrogenase (antiquin) deficiency is the underlying defect. Piperideine-6-Carboxylate (P6C) is the cyclic isomer of alpha-aminoadipic semialdehyde (AASA) and the equilibrium between P6C and Alpha aminoadipic semialdehyde is PH dependent. P6P reacts with pyridoxal 5'-phosphate and leads to deficiency of this cofactor. Folinic responsive seizures and PDS are allelic, and caused mutations in the *ALDH7A1* gene. Biochemical testing should be done prior to gene sequencing, and can be done regardless of pyridoxine therapy.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Liquid chromatography/tandem mass spectrometry (LC/MS-MS)

Cannabidiol (CBD)/Tetrahydrocannabinol (THC) Ratio, Urine 701907

CPT 80349
Special Instructions Testing is referred to MedTox Laboratories Inc.
Expected Turnaround Time 3 - 5 days
Specimen Urine (random)
Volume 30 mL
Minimum Volume 3 mL
Container Plastic urine container without preservative
Collection Collect urine in a plastic urine container without preservative.
Storage Instructions ***Submission/transport (<3 days):*** Room temperature. For storage beyond three days, specimen should be refrigerated or frozen.
Causes for Rejection Urine from preservative tube
Use To assist in distinguishing whether a positive urine THC test is exclusively the result of CBD use.
Methodology Liquid chromatography/tandem mass spectrometry (LC/MS-MS)

Coenzyme Q10 (Leukocytes) 620043

CPT 82542
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 10 - 14 days
Specimen Whole blood
Volume 5 mL
Container Yellow-top (ACD) tube
Storage Instructions Ship within 24 hours.
Causes for Rejection Hemolyzed sample; incorrect collection tube; received frozen
Use Coenzyme Q10 (Leukocytes) is used for diagnosis of Coenzyme Q10 (CoQ10) deficiency that is inherited or acquired. Coenzyme Q10 (Leukocytes) (MET04) may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing testing).
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology High-pressure liquid chromatography (HPLC)

Comprehensive Spinocerebellar Ataxia Repeat Expansion Panel 620167

CPT 82542
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Methodology See individual test components.

These new/revised publications are now available:

- CBD/THC Testing flyer (L21522)
- Diabetes Testing Services brochure (L21172)
- TMAO (Trimethylamine N-oxide) Test technical review (L20370)
- Whole Exome Sequencing flyer (L21409)

Please ask your LabCorp service representative for these titles.

Creatine and Guanidinoacetate (Plasma) 620180

CPT Call client services.
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 10 - 14 days
Specimen Plasma, **frozen**
Volume 1.0 mL
Minimum Volume 0.5 mL
Container Lavender-top (EDTA) tube, green-top (sodium heparin) tube
Collection Collect 2-4 mL blood in sodium heparin (green-top) or EDTA (purple-top) tube.
Storage Instructions Remove plasma and freeze at -20°C. Store frozen at -20°C and ship **frozen.**
Stability

Temperature	Period
Room temperature	Unstable
Refrigerated	Unstable
Frozen	Inderinitely

Causes for Rejection Thawed sample
Use Evaluation of patients with a clinical suspicion of inborn errors of creatine metabolism including arginine:glycine amidinotransferase deficiency, guanidinoacetate methyltransferase deficiency, and creatine transporter (SLC6A8) defect. Plasma/serum creatine and guanidinoacetate testing may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing testing). Disorders of creatine synthesis (deficiency of arginine:glycine amidinotransferase [AGAT] and guanidinoacetate methyltransferase [GAMT]) and creatine transporter (SLC6A8) deficiency are collectively described creatine deficiency syndromes (CDS). AGAT and GAMT deficiencies are inherited in an autosomal recessive manner, while the creatine transporter defect is X-linked. Diagnosis is possible by measuring guanidinoacetate (GAA), creatine (Crn) in plasma and urine. The profiles are specific for each clinical entity. Patients with GAMT deficiency typically exhibit normal to low Cr, very elevated GAA, and low Crn. Patients with AGAT deficiency typically exhibit normal to low Cr, low GAA, and normal to low Crn. In comparison, elevated Cr, normal GAA, normal to low Crn, and an elevated Cr:Crn ratio characterize patients with creatine transporter defect. AGAT, GAMT and the creatine transporter defect result in a depletion of of cerebral creatine and typically present with global developmental delays, intellectual disability, and severe speech delay. Some patients with CDS develop seizures. Patients with GAMT and the creatine transporter deficiency exhibit behavioral problems and features of autism. Female carriers for the creatine transporter deficiency can have intellectual disability and behavioral problems, and some develop seizures. Treatment with oral supplementation of creatine monohydrate is available and effective for the AGAT and GAMT deficiencies. Creatine supplementation has not been shown to improve outcomes in males with the creatine transporter defect. Female carriers of creatine transporter deficiency who have symptoms, however, have been reported to benefit from creatine supplementation.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Liquid chromatography/tandem mass spectrometry (LC/MS-MS)

Creatine and Guanidinoacetate (Urine) 620170

CPT 82017; 82570
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 10 - 14 days
Specimen Urine, **frozen**
Volume 1.0 mL
Minimum Volume 0.5 mL
Container Sterile cup
Collection Collect entire sample into a single sterile cup.
Storage Instructions Freeze as soon as possoble after collection; ship within 24 hours.
Stability

Temperature	Period
Room temperature	Unstable
Refrigerated	Unstable
Frozen	Inderinitely

Causes for Rejection Thawed sample
Use Evaluation of patients with a clinical suspicion of inborn errors of creatine metabolism including arginine:glycine amidinotransferase deficiency, guanidinoacetate methyltransferase deficiency, and creatine transporter (SLC6A8) defect. Urine creatine and guanidinoacetate testing may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing testing). Disorders of creatine synthesis (deficiency of arginine:glycine amidinotransferase [AGAT] and guanidinoacetate methyltransferase [GAMT]) and creatine transporter (SLC6A8) deficiency are collectively described creatine deficiency syndromes (CDS). AGAT and GAMT deficiencies are inherited in an autosomal recessive manner, while the creatine transporter defect is X-linked. Diagnosis is possible by measuring guanidinoacetate (GAA), creatine (Crn) in plasma and urine. The profiles are specific for each clinical entity. Patients with GAMT deficiency typically exhibit normal to low Cr, very elevated GAA, and low Crn. Patients with AGAT deficiency typically exhibit normal to low Cr, low GAA, and normal to low Crn. In comparison, elevated Cr, normal GAA, normal to low Crn, and an elevated Cr:Crn ratio characterize patients with creatine transporter defect. AGAT, GAMT and the creatine transporter defect result in a depletion of of cerebral creatine and typically present with global developmental delays, intellectual disability, and severe speech delay. Some patients with CDS develop seizures. Patients with GAMT and the creatine transporter deficiency exhibit behavioral problems and features of autism. Female carriers for the creatine transporter deficiency can have intellectual disability and behavioral problems, and some develop seizures. Treatment with oral supplementation of creatine monohydrate is available and effective for the AGAT and GAMT deficiencies. Creatine supplementation has not been shown to improve outcomes in males with the creatine transporter defect. Female carriers of creatine transporter deficiency who have symptoms, however, have been reported to benefit from creatine supplementation.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Liquid chromatography/tandem mass spectrometry (LC/MS-MS)

C9orf72 Genetic Testing (Repeat Expansion) 620017

CPT 81479
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Container Lavender-top (EDTA) tube
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Causes for Rejection Frozen blood EDTA tube
Use Varients in the C9orf72 gene have been found to cause amyotrophic lateral sclerosis (ALS), a condition characterized by progressive muscle weakness, a loss of muscle mass, and an inability to control movement
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Repeat-Primed PCR (QP-PCR)

DRPLA (ATN1) Genetic Testing (Repeat Expansion) . . . 620158

CPT 81177
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use Spinocerebellar ataxias (SCAs), and episodic ataxias are the most common types of ADCAs. SCAs are numbered based upon their time of identification. SCA3 is the most common type of SCA worldwide, followed by SCA2, SCA1, and SCA6. Some of the complicated forms have not been given a SCA number, like Dentatorubral Pallidoluysian Atrophy (DRPLA). Anticipation can be observed in the autosomal dominant ataxias in which CAG trinucleotide repeats occur. Anticipation results from expansion in the number of CAG repeats with transmission of the gene to subsequent generations. Most ADCAs have an overlap in clinical presentation, which makes it hard to differentiate. The most frequent clinical symptoms in all ADCAs are progressive adult-onset gait ataxia (often with hand dysmetria), and dysarthria associated with cerebellar atrophy. The episodic ataxias are characterized by periods of unsteady gait and often associated with nystagmus or dysarthria. Myokymia, vertigo, or hearing loss may occur in some of the subtypes. Permanent ataxia and even cerebellar atrophy may result late in the disease course.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Repeat-Primed PCR (QP-PCR)

dsDNA Antibody by IFA, *Crithidia luciliae,* with Reflex to Titer 096346

CPT 86225
Synonyms Crithidia
Specimen Serum
Volume 1 mL
Minimum Volume 0.3 mL (**Note:** This volume does **not** allow for repeat testing.)
Storage Instructions Room temperature
Stability

Temperature	Period
Room temperature	14 days
Refrigerated	14 days
Frozen	14 days
Freeze/thaw cycles	Stable x3

Causes for Rejection Bacterially contaminated samples
Use Used as an aid in the diagnosis of systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings.
Limitations Certain drugs, including procainamide and hydralazine, may induce a lupus erythematosus-like disease. Patients with drug-induced LE may demonstrate ANA commonly directed against nuclear histones, although antibody to dsDNA has also been reported.
Methodology Indirect fluorescent antibody (IFA)

Friedreich Ataxia Genetic Testing (Trinucleotide Repeat Expansion) 620077

CPT 81284
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Container Lavender-top (EDTA) tube
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze
Causes for Rejection Frozen blood EDTA tube
Use Friedreich ataxia is a genetic condition that affects the nervous system and causes movement problems.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Repeat-Primed PCR (QP-PCR)

GeneSeq®PLUS 630068

CPT Call client services.
Synonyms Follow-up gene sequencing; Full gene sequencing; Partner gene sequencing
Special Instructions This assay is not currently available in New York state. Contact an Integrated Genetics laboratory genetic coordinator at 800-255-7357 with any questions. Indicate the specific gene(s) to be analyzed on the test request form. Failure to indicate gene(s) will result in testing delays.
Expected Turnaround Time 14 - 21 days
Specimen Whole blood
Volume 10 mL
Container Yellow-top (ACD-A) tube or lavender-top (EDTA) tube
Storage Instructions Maintain at room temperature or refrigerate at 4°C.
Causes for Rejection Frozen specimen; quantity not sufficient for analysis; improper container; yellow-top (ACD-B) tube
Use Full gene sequencing is available for genes included in the Inheritest®500 PLUS panel. See related Inheritest® test codes: Inheritest® Carrier Screen, Comprehensive (144 genes) (451950); Inheritest® Carrier Screen, Ashkenazi Jewish (48 genes) (451920); Inheritest® Carrier Screen, Society-guided (14 genes) (451960).
For *HBA1* and *HBA2* (alpha-thalassemis) see α-Thalassemia, DNA Analysis (511172); for *SMN1* see Spinal Muscular Atrophy (SMA) Carrier Testing (450010); and for *FRM1* see Fragile X Syndrome, PCR with Reflex to Southern Blot (511919).
Limitations Technologies used do not detect germline mosaicism and do not rule out the presence of large chromosomal aberrations, including rearrangements, gene fusions, or variants in regions or genes not included in this test, or possible inter/intragenic interactions between variants. Variant classification and/or interpretation may change over time if more information becomes available. False positive or false negative results may occur for reasons that include: rare genetic variants, sex chromosome abnormalities, pseudogene interference, blood transfusions, bone marrow transplantation, somatic or tissue-specific mosaicism, mislabeled samples, or erroneous representation of family relationships.
Methodology
Single Nucleotide Polymorphism and Small Indel Sequencing Assessment: Genomic regions of interest are selected using a custom capture reagent for target enrichment and sequenced via the Illumina® next generation sequencing platform. Sequencing reads are aligned with the human genome reference GRCh37/hg19 build. Regions of interest include all exons and intron/exon junctions (+/-20 nucleotides) for each gene analyzed. A minimum of 99% of bases are covered at >15X. Analytical sensitivity is estimated to be >99% for single nucleotide variants, >97% for insertions/deletions less than six base pairs, and >95% for insertions/deletions between six and fifteen base pairs. Uncovered regions with known pathogenic variants are sequenced in a targeted manner. All

reported variants are confirmed by a second method.

Copy Number Variant Assessment: Next Generation Sequencing is performed and the data are assessed with Illumina's DRAGEN (Dynamic Read Analysis for GENomics) Bio-IT Platform. Reported variants are confirmed by a second method. Analytical sensitivity is estimated to be >95%.

Spinal Muscular Atrophy: This analysis will detect the copy number of exon 7 of the *SMN1* gene. When no copies of *SMN1* exon 7 are detected, *SMN2* exon 7 copy number is assessed and reported. This test is unable to differentiate between two copies of the *SMN1* gene on one allele (in cis) versus two copies of the gene on different alleles (in trans). When two copies of SMN1 exon 7 are detected, the data are assessed for the presence of the c.*3+80T>G "silent carrier" variant.

Congenital Adrenal Hyperplasia: This analysis will detect most large rearrangements/deletions/duplications within the *CYP21A2* gene, as well as the presence of seven of the most common pathogenic variants in the gene: 1) c.518T>A (p.Ile173Asn), Chr6:32007203; 2) c.713T>A (p.Val238Glu); Chr6:32007587; 3) c.719T>A (p.Met240Lys); Chr6:32007593; 4) c.923dup (p.Leu308Phefs); Chr6:32007966; 5) c.293-13C/A>G; Chr6:32006858; 6) c.332_339delGAGACTAC (p.Gly111Valfs); Chr6:32006910-32006917; 7) c.-113G>A; Chr6:32006087. Other point mutations and small indels and reciprocal changes between *CYP21A2* and *CYP21A1P* are not detected by this analysis. The analytical sensitivity of this assay is estimated to be >99%.

Alpha thalassemia: Variants included in the analysis of the alpha-globin (HBA) gene cluster are the Constant Spring non-deletion variant and the following deletions: -alpha3.7, -alpha4.2, --alpha20.5, --SEA, --FIL, --THAI, --MED, and the HS-40 regulatory region.

Reported Variants: Pathogenic variants, likely pathogenic variants, and variants of uncertain significance are reported after confirmation by an appropriate technology. NEB variants occurring in exons 82-105 may not be reliably detected by this analysis and are not reported. Nondeletion variants are specified using the numbering and nomenclature recommended by the Human Genome Variation Society. Benign and likely benign variants are not reported. Variant classification is consistent with ACMG standards and guidelines.

References

den Dunnen JT. Describing Sequence Variants Using HGVS Nomenclature. *Methods Mol Biol.* 2017;1492:243-251. PubMed 27822869

Monaghan KG, Lyon E, Spector EB; American College of Medical Genetics and Genomics. ACMG Standards and Guidelines for fragile X testing: a revision to the disease-specific supplements to the Standards and Guidelines for Clinical Genetics Laboratories of the American College of Medical Genetics and Genomics. *Genet Med.* 2013 Jul;15(7):575-586. PubMed 23765048

Richards S, Aziz N, Bale S. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015 May;17(5):405-424. PubMed 25741868

GeneSeq®PLUS, Prenatal 630119

CPT Call client services.

Synonyms Follow-up gene sequencing; Full gene sequencing

Special Instructions This assay is not currently available in New York state. Contact an Integrated Genetics laboratory genetic coordinator at 800-255-7357 with any questions.

Expected Turnaround Time 14 - 21 days

Specimen Amniotic fluid, chorionic villus sample (CVS), cultured amniocytes, cultured villi. Submission of maternal blood is required for analysis of Maternal Cell Contamination (511402), which should be ordered on a separate test request form.

Volume Amniotic fluid: 20 cc; CVS: 20 mg; or amniotic fluid and CVS Culture: two confluent flasks

Container Sterile plastic conical tube or two confluent T-25 flasks

Storage Instructions Maintain specimen at room temperature or refrigerate at 4ºC.

Causes for Rejection Frozen specimen; quantity not sufficient for analysis; improper container

Use Full gene sequencing is available for genes included in the Inheritest®500 PLUS panel. See related Inheritest® test codes: Inheritest® Carrier Screen, Comprehensive (144 genes) (451950); Inheritest® Carrier Screen, Ashkenazi Jewish (48 genes) (451920); Inheritest® Carrier Screen, Society-guided (14 genes) (451960).

For *HBA1* and *HBA2* (alpha-thalassemis) see α-Thalassemia, DNA Analysis (511172); for *SMN1* see Spinal Muscular Atrophy (SMA) Carrier Testing (450010); and for *FRM1* see Fragile X Syndrome, PCR with Reflex to Southern Blot (511919).

Limitations Technologies used do not detect germline mosaicism and do not rule out the presence of large chromosomal aberrations, including rearrangements, gene fusions, or variants in regions or genes not included in this test, or possible inter/intragenic interactions between variants. Variant classification and/or interpretation may change over time if more information becomes available. False positive or false negative results may occur for reasons that include: rare genetic variants, sex chromosome abnormalities, pseudogene interference, blood transfusions, bone marrow transplantation, somatic or tissue-specific mosaicism, mislabeled samples, or erroneous representation of family relationships.

Methodology

Single Nucleotide Polymorphism and Small Indel Sequencing Assessment: Genomic regions of interest are selected using a custom capture reagent for target enrichment and sequenced via the Illumina® next generation sequencing platform. Sequencing reads are aligned with the human genome reference GRCh37/hg19 build. Regions of interest include all exons and intron/exon junctions (+/-20 nucleotides) for each gene analyzed. A minimum of 99% of bases are covered at >15X. Analytical sensitivity is estimated to be >99% for single nucleotide variants, >97% for insertions/deletions less than six base pairs, and >95% for insertions/deletions between six and fifteen base pairs. Uncovered regions with known pathogenic variants are sequenced in a targeted manner. All reported variants are confirmed by a second method.

Copy Number Variant Assessment: Next Generation Sequencing is performed and the data are assessed with Illumina's DRAGEN (Dynamic Read Analysis for GENomics) Bio-IT Platform. Reported variants are confirmed by a second method. Analytical sensitivity is estimated to be >95%.

Spinal Muscular Atrophy: This analysis will detect the copy number of exon 7 of the *SMN1* gene. When no copies of *SMN1* exon 7 are detected, *SMN2* exon 7 copy number is assessed and reported. This test is unable to differentiate between two copies of the *SMN1* gene on one allele (in cis) versus two copies of the gene on different alleles (in trans). When two copies of *SMN1* exon 7 are detected, the data are assessed for the presence of the c.*3+80T>G "silent carrier" variant.

Congenital Adrenal Hyperplasia: This analysis will detect most large rearrangements/deletions/duplications within the *CYP21A2* gene, as well as the presence of seven of the most common pathogenic variants in the gene: 1) c.518T>A (p.Ile173Asn), Chr6:32007203; 2) c.713T>A (p.Val238Glu); Chr6:32007587; 3) c.719T>A (p.Met240Lys); Chr6:32007593; 4) c.923dup (p.Leu308Phefs); Chr6:32007966; 5) c.293-13C/A>G; Chr6:32006858; 6) c.332_339delGAGACTAC (p.Gly111Valfs); Chr6:32006910-32006917; 7) c.-113G>A; Chr6:32006087. Other point mutations and small indels and reciprocal changes between *CYP21A2* and *CYP21A1P* are not detected by this analysis. The analytical sensitivity of this assay is estimated to be >99%.

Alpha thalassemia: Variants included in the analysis of the alpha-globin (HBA) gene cluster are the Constant Spring non-deletion variant and the following deletions: -alpha3.7, -alpha4.2, --alpha20.5, --SEA, --FIL, --THAI, --MED, and the HS-40 regulatory region.

Reported Variants: Pathogenic variants, likely pathogenic variants, and variants of uncertain significance are reported after confirmation by an appropriate technology. NEB variants occurring in exons 82-105 may not be reliably detected by this analysis and are not reported. Nondeletion variants are specified using the numbering and nomenclature recommended by the Human Genome Variation Society. Benign and likely benign variants are not reported. Variant classification is consistent with ACMG standards and guidelines.

References

den Dunnen JT. Describing Sequence Variants Using HGVS Nomenclature. *Methods Mol Biol.* 2017;1492:243-251. PubMed 27822869

Monaghan KG, Lyon E, Spector EB; American College of Medical Genetics and Genomics. ACMG Standards and Guidelines for fragile X testing: a revision to the disease-specific supplements to the Standards and Guidelines for Clinical Genetics Laboratories of the

American College of Medical Genetics and Genomics. *Genet Med.* 2013 Jul;15(7):575-586. PubMed 23765048

Richards S, Aziz N, Bale S. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015 May;17(5):405-424. PubMed 25741868

GeneSeq®PLUS without VUS 630085

CPT Call client services.

Synonyms Follow-up gene sequencing; Full gene sequencing; Partner gene sequencing

Special Instructions This assay is not currently available in New York state. Contact an Integrated Genetics laboratory genetic coordinator at 800-255-7357 with any questions.

Expected Turnaround Time 14 - 21 days

Specimen Whole blood

Volume 10 mL

Container Yellow-top (ACD-A) tube or lavender-top (EDTA) tube

Storage Instructions Maintain at room temperature or refrigerate at 4°C.

Causes for Rejection Frozen specimen; quantity not sufficient for analysis; improper container; yellow-top (ACD-B) tube

Use Full gene sequencing is available for genes included in the Inheritest®500 PLUS panel. See related Inheritest® test codes: Inheritest® Carrier Screen, Comprehensive (144 genes) (451950); Inheritest® Carrier Screen, Ashkenazi Jewish (48 genes) (451920); Inheritest® Carrier Screen, Society-guided (14 genes) (451960).

For *HBA1* and *HBA2* (alpha-thalassemis) see α-Thalassemia, DNA Analysis (511172); for *SMN1* see Spinal Muscular Atrophy (SMA) Carrier Testing (450010); and for *FRM1* see Fragile X Syndrome, PCR with Reflex to Southern Blot (511919).

Limitations Technologies used do not detect germline mosaicism and do not rule out the presence of large chromosomal aberrations, including rearrangements, gene fusions, or variants in regions or genes not included in this test, or possible inter/intragenic interactions between variants. Variant classification and/or interpretation may change over time if more information becomes available. False positive or false negative results may occur for reasons that include: rare genetic variants, sex chromosome abnormalities, pseudogene interference, blood transfusions, bone marrow transplantation, somatic or tissue-specific mosaicism, mislabeled samples, or erroneous representation of family relationships.

Methodology

Single Nucleotide Polymorphism and Small Indel Sequencing Assessment: Genomic regions of interest are selected using a custom capture reagent for target enrichment and sequenced via the Illumina® next generation sequencing platform. Sequencing reads are aligned with the human genome reference GRCh37/hg19 build. Regions of interest include all exons and intron/exon junctions (+/-20 nucleotides) for each gene analyzed. A minimum of 99% of bases are covered at >15X. Analytical sensitivity is estimated to be >99% for single nucleotide variants, >97% for insertions/deletions less than six base pairs, and >95% for insertions/deletions between six and fifteen base pairs. Uncovered regions with known pathogenic variants are sequenced in a targeted manner. All reported variants are confirmed by a second method.

Copy Number Variant Assessment: Next Generation Sequencing is performed and the data are assessed with Illumina's DRAGEN (Dynamic Read Analysis for GENomics) Bio-IT Platform. Reported variants are confirmed by a second method. Analytical sensitivity is estimated to be >95%.

Spinal Muscular Atrophy: This analysis will detect the copy number of exon 7 of the *SMN1* gene. When no copies of *SMN1* exon 7 are detected, *SMN2* exon 7 copy number is assessed and reported. This test is unable to differentiate between two copies of the *SMN1* gene on one allele (in cis) versus two copies of the gene on different alleles (in trans). When two copies of *SMN1* exon 7 are detected, the data are assessed for the presence of the c.*3+80T>G "silent carrier" variant.

Congenital Adrenal Hyperplasia: This analysis will detect most large rearrangements/deletions/duplications within the *CYP21A2* gene, as well as the presence of seven of the most common pathogenic variants in the gene: 1) c.518T>A (p.Ile173Asn), Chr6:32007203; 2) c.713T>A (p.Val238Glu); Chr6:32007587; 3) c.719T>A (p.Met240Lys); Chr6:32007593; 4) c.923dup (p.Leu308Phefs); Chr6:32007966; 5) c.293-13C/A>G; Chr6:32006858; 6) c.332_339delGAGACTAC (p.Gly111Valfs); Chr6:32006910-32006917; 7) c.-113G>A; Chr6:32006087. Other point mutations and small indels and reciprocal changes between *CYP21A2* and *CYP21A1P* are not detected by this analysis. The analytical sensitivity of this assay is estimated to be >99%.

Alpha thalassemia: Variants included in the analysis of the alpha-globin (HBA) gene cluster are the Constant Spring non-deletion variant and the following deletions: -alpha3.7, -alpha4.2, --alpha20.5, --SEA, --FIL, --THAI, --MED, and the HS-40 regulatory region.

Reported Variants: Pathogenic and likely pathogenic variants are reported after confirmation by an appropriate technology. NEB variants occurring in exons 82-105 may not be reliably detected by this analysis and are not reported. Nondeletion variants are specified using the numbering and nomenclature recommended by the Human Genome Variation Society. Variants of uncertain significance, likely benign, and benign variants are not reported. Variant classification is consistent with ACMG standards and guidelines.

References

den Dunnen JT. Describing Sequence Variants Using HGVS Nomenclature. *Methods Mol Biol.* 2017;1492:243-251. PubMed 27822869

Monaghan KG, Lyon E, Spector EB; American College of Medical Genetics and Genomics. ACMG Standards and Guidelines for fragile X testing: a revision to the disease-specific supplements to the Standards and Guidelines for Clinical Genetics Laboratories of the American College of Medical Genetics and Genomics. *Genet Med.* 2013 Jul;15(7):575-586. PubMed 23765048

Richards S, Aziz N, Bale S. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015 May;17(5):405-424. PubMed 25741868

GeneSeq®PLUS without VUS, Prenatal 630102

CPT Call client services.

Synonyms Follow-up gene sequencing; Full gene sequencing

Special Instructions This assay is not currently available in New York state. Contact an Integrated Genetics laboratory genetic coordinator at 800-255-7357 with any questions.

Expected Turnaround Time 14 - 21 days

Specimen Amniotic fluid, chorionic villus sample (CVS), cultured amniocytes, cultured villi. Submission of maternal blood is required for analysis of Maternal Cell Contamination (511402), which should be ordered on a separate test request form.

Volume Amniotic fluid: 20 cc; CVS: 20 mg; or amniotic fluid and CVS Culture: two confluent flasks

Container Sterile plastic conical tube or two confluent T-25 flasks

Storage Instructions Maintain specimen at room temperature or refrigerate at 4ºC

Causes for Rejection Frozen specimen; quantity not sufficient for analysis; improper container

Use Full gene sequencing is available for genes included in the Inheritest®500 PLUS panel. See related Inheritest® test codes: Inheritest® Carrier Screen, Comprehensive (144 genes) (451950); Inheritest® Carrier Screen, Ashkenazi Jewish (48 genes) (451920); Inheritest® Carrier Screen, Society-guided (14 genes) (451960).

For *HBA1* and *HBA2* (alpha-thalassemis) see α-Thalassemia, DNA Analysis (511172); for *SMN1* see Spinal Muscular Atrophy (SMA) Carrier Testing (450010); and for *FRM1* see Fragile X Syndrome, PCR with Reflex to Southern Blot (511919).

Limitations Technologies used do not detect germline mosaicism and do not rule out the presence of large chromosomal aberrations, including rearrangements, gene fusions, or variants in regions or genes not included in this test, or possible inter/intragenic interactions between variants. Variant classification and/or interpretation may change over time if more information becomes available. False positive or false negative results may occur for reasons that include: rare genetic variants, sex chromosome abnormalities, pseudogene interference, blood transfusions, bone marrow transplantation, somatic or tissue-specific mosaicism, mislabeled samples, or erroneous representation of family relationships.

Methodology

Single Nucleotide Polymorphism and Small Indel Sequencing Assessment: Genomic regions of interest are selected using a custom

capture reagent for target enrichment and sequenced via the Illumina® next generation sequencing platform. Sequencing reads are aligned with the human genome reference GRCh37/hg19 build. Regions of interest include all exons and intron/exon junctions (+/-20 nucleotides) for each gene analyzed. A minimum of 99% of bases are covered at >15X. Analytical sensitivity is estimated to be >99% for single nucleotide variants, >97% for insertions/deletions less than six base pairs, and >95% for insertions/deletions between six and fifteen base pairs. Uncovered regions with known pathogenic variants are sequenced in a targeted manner. All reported variants are confirmed by a second method.

Copy Number Variant Assessment: Next Generation Sequencing is performed and the data are assessed with Illumina's DRAGEN (Dynamic Read Analysis for GENomics) Bio-IT Platform. Reported variants are confirmed by a second method. Analytical sensitivity is estimated to be >95%.

Spinal Muscular Atrophy: This analysis will detect the copy number of exon 7 of the SMN1 gene. When no copies of SMN1 exon 7 are detected, SMN2 exon 7 copy number is assessed and reported. This test is unable to differentiate between two copies of the SMN1 gene on one allele (in cis) versus two copies of the gene on different alleles (in trans). When two copies of SMN1 exon 7 are detected, the data are assessed for the presence of the c.*3+80T>G "silent carrier" variant.

Congenital Adrenal Hyperplasia: This analysis will detect most large rearrangements/deletions/duplications within the *CYP21A2* gene, as well as the presence of seven of the most common pathogenic variants in the gene: 1) c.518T>A (p.Ile173Asn), Chr6:32007203; 2) c.713T>A (p.Val238Glu); Chr6:32007587; 3) c.719T>A (p.Met240Lys); Chr6:32007593; 4) c.923dup (p.Leu308Phefs); Chr6:32007966; 5) c.293-13C/A>G; Chr6:32006858; 6) c.332_339delGAGACTAC (p.Gly111Valfs); Chr6:32006910-32006917; 7) c.-113G>A; Chr6:32006087. Other point mutations and small indels and reciprocal changes between *CYP21A2* and *CYP21A1P* are not detected by this analysis. The analytical sensitivity of this assay is estimated to be >99%.

Alpha thalassemia: Variants included in the analysis of the alpha-globin (HBA) gene cluster are the Constant Spring non-deletion variant and the following deletions: -alpha3.7, -alpha4.2, --alpha20.5, --SEA, --FIL, --THAI, --MED, and thse HS-40 regulatory region.

Reported Variants: Pathogenic and likely pathogenic variants are reported after confirmation by an appropriate technology. NEB variants occurring in exons 82-105 may not be reliably detected by this analysis and are not reported. Nondeletion variants are specified using the numbering and nomenclature recommended by the Human Genome Variation Society. Variants of uncertain significance, likely benign, and benign variants are not reported. Variant classification is consistent with ACMG standards and guidelines.

References

den Dunnen JT. Describing Sequence Variants Using HGVS Nomenclature. *Methods Mol Biol.* 2017;1492:243-251. PubMed 27822869

Monaghan KG, Lyon E, Spector EB; American College of Medical Genetics and Genomics. ACMG Standards and Guidelines for fragile X testing: a revision to the disease-specific supplements to the Standards and Guidelines for Clinical Genetics Laboratories of the American College of Medical Genetics and Genomics. *Genet Med.* 2013 Jul;15(7):575-586. PubMed 23765048

Richards S, Aziz N, Bale S. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015 May;17(5):405-424. PubMed 25741868

GM1 IgG Autoantibody 140385

CPT 83520

Special Instructions This assay is not approved for patients of New York State physicians.

Expected Turnaround Time 7 days

Specimen Serum, **frozen**

Volume 0.3 mL

Minimum Volume 0.1 mL (**Note:** This volume does **not** allow for repeat testing.)

Container Gel-barrier tube or red-top tube

Collection Separate serum from cells. Transfer the serum into a LabCorp PP transpak frozen purple tube with screw cap (LabCorp No. 49482). Freeze immediately and maintain frozen at ≤ -20°C until tested. To avoid delays in turnaround time when requesting multiple tests on frozen samples, **please submit separate frozen specimens for each test requested.**

Storage Instructions Freeze

Stability

Temperature	Period
Frozen	4 months (stability determined by manufacturer or literature reference)
Freeze/thaw cycles	Stable x2 (stability determined by manufacturer or literature reference)

Patient Preparation Lipemic samples can be avoided by having the patient fast for 12 hours prior to collection.

Causes for Rejection Non-serum sample received; non-frozen serum received; grossly lipemic, hemolytic or icteric sample received

Use The BUHLMANN™ Anti-GM1 IgG ELISA is intended for the qualitative determination of human IgG autoantibodies directed against monosialo-tetrahexosylganglioside (GM1) in human serum.[1]

Limitations This test by itself is not diagnostic and should be used in conjunction with other clinical parameters to confirm disease. Due to lack of standardization of assays employed in various clinical studies, published findings might not be directly transferable to patients result interpretation.

Results of this test are labeled for research purposes only by the assay's manufacturer. The performance characteristics of this assay have not been established by the manufacturer. The result should not be used for treatment or for diagnostic purposes without confirmation of the diagnosis by another medically established diagnostic product or procedure. The performance characteristics were determined by LabCorp.

Methodology Enzyme Linked Immunoassay (ELISA) for IgG antibodies to the ganglioside GM1

Reference Interval 0 - 30%

Additional Information The ganglioside GM1 is expressed in the peripheral nervous system in the nodes of Ranvier, outer myelin, and the end plates of motor neurons.[2] IgG antibodies against GM1 (Anti-GMI IgG) are strongly associated with motor axonal variants of Guillain-Barre syndrome.[3,4]

GBS is a rapid-onset, immune-mediated demyelinating polyneuropathy associated with acute flaccid paralysis.[5,7] The initial symptoms of GBS typically involve symmetrical limb weakness and loss of tendon reflexes. Two major symptoms of GBS are defined by electrophysiological and pathological criteria.[4,6-8] The classical, demyelinating form of GBS associated with impairment of the motor or sensory nerve fibers is referred to as Acute Inflammatory Demyelinating Polyneuropathy (AIDP). A second subtype of GBS associated with the myelin or the axonal impairment is referred to as Acute Motor Axonal Neuropathy (AMAN).[6,9] AMAN is characterized by acute paralysis and loss of reflexes without sensory loss. AMAN is the most common GBS variant, accounting for as many as 5-10% of cases with much higher incidence in Asia.[10]

Multiple studies have found an association between AMAN and Anti-GM1 IgG seropositivity.[8,9,11-18] Certain electrophysiologic features, such as reversible conduction failure, have been associated with the presence of Anti-GM1 IgG.[13,18-21] It is thought that antibodies to GM1 bind to at the nodes of Ranvier activating complement and disrupting sodium-channel clusters and axoglial junctions, leading to nerve conduction failure and muscle weakness.[8]

The recognition that diarrheal illness can precede GBS has led some to hypothesize that an infectious agent may cause the development of Anti-GM1 IgG, possibly due to molecular mimicry resulting from antecedent infection.[15] Campylobacter jejuni infection has been associated with the development of AMAN.[8,22] Several other antecedent infectious agents have been recognized including the most recently identified, Zika virus.[23]

Footnotes

1. Anti-GM1 Autoantibodies ELISA [package insert]. Switzerland: BUHLMANN Labs; Sep. 12, 2016.

2. Steck A, Yuki N, Graus F. Antibody testing in peripheral nerve disorders. *Handb Clin Neurol.* 2013;115:189-212. PubMed 23931781

3. Arcila-Londono X, Lewis RA. Guillain-Barré syndrome. *Semin Neurol.* 2012 Jul;32(3):179-186. PubMed 23117942

4. Emilien D, Hugh W. Diagnostic Utility of Auto Antibodies in Inflammatory Nerve Disorders. *J Neuromuscul Dis.* 2015 Jun;2(2):107-112. PubMed 27858733

5. Hughes RA, Cornblath DR. Guillain-Barré syndrome. *Lancet.* 2005 Nov 5;366(9497):1653-1666. PubMed 16271648
6. Goodfellow JA, Willison HJ. Guillain-Barré syndrome: A century of progress. *Nat Rev Neurol.* 2016 Dec;(12):723-731. PubMed 27857121
7. Wijdicks EF, Klein CJ. Guillain-Barré Syndrome. *Mayo Clin Proc.* 2017 Mar;92(3):467-479. PubMed 28259232
8. Kuwabara S, Yuki N. Axonal Guillain-Barré syndrome: Concepts and controversies. *Lancet Neurol.* 2013 Dec;12(12):1180-1188. PubMed 24229616
9. Shahrizaila N, Yuki N. Antiganglioside antibodies in Guillain-Barré syndrome and its related conditions. *Expert Rev Neurother.* 2011 Sep;11(9):1305-1313. PubMed 21864076
10. Bourque PR, Chardon JW, Massie R. Autoimmune peripheral neuropathies. *Clin Chim Acta.* 2015 Sep 20;449:37-42. PubMed 25748038
11. Sekiguchi Y, Uncini A, Yuki N, et al. Antiganglioside antibodies are associated with axonal Guillain-Barré syndrome: a Japanese-Italian collaborative study. *J Neurol Neurosurg Psychiatry.* 2012 Jan;83(1):23-28. PubMed 22010183
12. Capasso M, Notturno F, Mazoli C, Uncini A. Involvement of sensory fibres in axonal subtypes of Guillain-Barré syndrome. *J Neurol Neurosurg Psychiatry.* 2011 Jun;82(6):664-670. PubMed 21444320
13. Capasso M, Caporale CM, Pomilio F, Gandolfi P, Lugaresi A, Uncini A. Acute motor conduction block neuropathy: another Guillain-Barré syndrome variant. *Neurology.* 2003 Sep 9;61(5):617-622. PubMed 12963751
14. Gregson NA, Jones D, Thomas PK, Willison HJ. Acute motor neuropathy with antibodies to GM1 ganglioside. *J Neurol.* 1991 Dec;238(8):447-451. PubMed 1779252
15. Yuki N, Hartung HP. Guillain-Barré syndrome. *N Engl J Med.* 2012 Jun 14;366(24):2294-2304. PubMed 22694000
16. Ogawara K, Kuwabara S, Mori M, Hattori T, Koga M, Yuki N. Axonal Guillain-Barré syndrome: relation to anti-ganglioside antibodies and Campylobacter jejuni infection in Japan. *Ann Neurol.* 2000 Oct;48(4):624-631. PubMed 11026446
17. Ogawara K, Kuwabara S, Koga M, Mori M, Yuki N, Hattori T. Anti-GM1b IgG antibody is associated with acute motor axonal neuropathy and Campylobacter jejuni infection. *J Neurol Sci.* 2003 Jun 15;210(1-2):41-45. PubMed 12736086
18. Shahrizaila N, Kokubun N, Sawai S, et al. Antibodies to single glycolipids and glycolipid complexes in Guillain-Barré syndrome subtypes. *Neurology.* 2014 Jul 8;83(2):118-124. PubMed 24920848
19. Kuwabara S, Yuki N, Koga M, et al. IgG anti-GM1 antibody is associated with reversible conduction failure and axonal degeneration in Guillain-Barré syndrome. *Ann Neurol.* 1998 Aug;44(2):202-208. PubMed 9708542
20. Kokubun N, Nishibayashi M, Uncini A, Odaka M, Hirata K, Yuki N. Conduction block in acute motor axonal neuropathy. *Brain.* 2010 Oct;133(10):2897-2908. PubMed 20855419
21. Susuki K, Johkura K, Yuki N, Hasegawa O, Kuroiwa Y. Rapid resolution of nerve conduction blocks after plasmapheresis in Guillain-Barré syndrome associated with anti-GM1b IgG antibody. *J Neurol.* 2001 Feb;248(2):148-150. PubMed 11284136
22. van den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, van Doorn PA. Guillain-Barré syndrome: pathogensis, diagnosis, treatment and prognosis. *Nat Rev Neurol.* 2014 Aug;10(8):469-482. PubMed 25023340
23. Cao-Lormeau VM, Blake A, Mons S, et al. Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. *Lancet.* 2016 Apr 9; 387(10027):1531-1539. PubMed 26948433

References

Chalah MA, et al. A comparison of four commercial tests for detecting anti-ganglioside antibodies in patients with well-characterized dysimmune peripheral neuropathies. 2016.
Han TH, Kim DY, Park DW, Moon JH. Transient Isolated Lower Bulbar Palsy With Elevated Serum Anti-GM1 and Anti-GD1b Antibodies During Aripiprazole Treatment. *Pediatr Neurol.* 2017 Jan;66:96-99. PubMed 28341090
Islam Z, Jacobs BC, van Belkum A, et al. Axonal variant of Guillain-Barré syndrome associated with Campylobacter infection in Bangladesh. *Neurology.* 2010 Feb 16;74(7):581-587. PubMed 20157160
Kollewe K, Wurster U, Sinzenich T, et al. Anti-ganglioside antibodies in amyotrophic lateral sclerosis revisited. *PLoS One.* 2015 Apr 14;10(4):e0125339. PubMed 25875836
Lei T, Siu KL, Kok KH, et al. Anti-ganglioside antibodies were not detected in human subjects infected with or vaccinated against 2009 pandemic influenza A (H1N1) virus. *Vaccine.* 2012 Mar 30;30(16):2605-2610. PubMed 22342549
Mani B, et al. The Frequency of anti-Ganglioside Antibodies in Blood Donors Compared to Control Groups and Guillain-Barré Syndrome Patients. Poster presented at DAS, Dresden (GE). 2010.
Sharma MB, Chaudhry R, Tabassum I, et al. The presence of Mycoplasma pneumonia infection and GM1 ganglioside antibodies in Guillain-Barré syndrome. *J Infect Dev Ctries.* 2011 Jul 4;5(6):459-464. PubMed 21727645
Uncini A, Yuki N. Electrophysiologic and immunopathologic correlates in Guillain-Barré syndrome subtypes. *Expert Rev Neurother.* 2009 Jun;9(6):869-884. PubMed 19496690
Uysalol M, Tatli B, Uzel N, Citak A, Aygün E, Kayaoğlu S. A Rare Form of Guillain-Barré Syndrome: A Child Diagnosed with Anti-GD1a and Anti-GD1b Positive Pharyngeal-Cervical-Brachial Variant. *Balkan Med J.* 2013 Sep;30(3):337-341. PubMed 25207134
Wurster U, et al. Ganglioside Antibodies in Amyotrophic Lateral Sclerosis. Poster presented at DAS, Dresden (GE). 2009.

GM1 IgM Autoantibodies 140280

CPT 83520

Special Instructions This assay is not approved for patients of New York State physicians.

Expected Turnaround Time 7 days

Specimen Serum, **frozen**

Volume 0.3 mL

Minimum Volume 0.1 mL (**Note:** This volume does **not** allow for repeat testing.)

Container Gel-barrier tube or red-top tube

Collection Separate serum from cells. Transfer the serum into a LabCorp PP transpak frozen purple tube with screw cap (LabCorp No. 49482). Freeze immediately and maintain frozen at ≤ -20°C until tested. To avoid delays in turnaround time when requesting multiple tests on frozen samples, **please submit separate frozen specimens for each test requested.**

Storage Instructions Freeze

Stability

Temperature	Period
Frozen	4 months (stability determined by manufacturer or literature reference)
Freeze/thaw cycles	Stable x2 (stability determined by manufacturer or literature reference)

Patient Preparation Lipemic samples can be avoided by having the patient fast for 12 hours prior to collection.

Causes for Rejection Non-serum sample received; non-frozen serum received; grossly lipemic, hemolytic or icteric sample received

Use The BUHLMANN™ Anti-GM1 IgM ELISA is intended for the qualitative determination of human IgM autoantibodies directed against monosialotetrahexosylganglioside (GM1) in human serum.[1]

Limitations Anti-GM1 IgM seropositivity is supportive but not sufficient to confirm the diagnosis of MMN and the diagnosis of cannot be excluded by seronegativity for Anti-GM1.[15,24,25] Anti-GM1 may also be found in patients with Guillain-Barr syndrome,[4,26] acute motor axonal neuropathy, and chronic inflammatory demyelinating polyneuropathy as well as in normal individuals but these are mainly IgG type antibodies.[5,15,27] This test, by itself, is not diagnostic and should be used in conjunction with other clinical parameters to confirm disease.

Results of this test are labeled for research purposes only by the assay's manufacturer. The performance characteristics of this assay have not been established by the manufacturer. The result should not be used for treatment or for diagnostic purposes without confirmation of the diagnosis by another medically established diagnostic product or procedure. The performance characteristics were determined by LabCorp.

Methodology Enzyme Linked Immunoassay (ELISA) for antibodies to the ganglioside GM1[1]

Reference Interval 0 - 30%

Additional Information GM1 is expressed in the peripheral nervous system in the nodes of Ranvier, outer myelin, and the end plates of motor neurons.[2] Measurement of IgM antibodies to GM1 (Anti-GM1) has been employed in the evaluation of with chronic neuropathies that affect the motor nerves. IgM Anti-GM1 seropositivity is significantly associated with multifocal motor neuropathy (MMN).[2-6] MMN is a purely motor neuropathy (without sensory loss) that is characterized by progressive, asymmetric muscle weakness and atrophy of limbs.[6-12] The hallmark of MMN is the presence of conduction block CB with normal sensory nerve conduction across the region of block.[8] The reported prevalence of IgM Anti-GM1 positivity in MMN varies widely (25% to 85%) in the literature, depending on the clinical definition and detection techniques used in various studies.[2,13-16] Testing for Anti-GM1 was included among the possible supportive laboratory test for the diagnosis of MMN by the Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society.[17] Higher titers of Anti-GM1 are associated with greater clinical severity in MMN patients but are rare in most other neurological disorders such as ALS and chronic inflammatory demyelinating polyneuropathy.[15-16]

The underlying cause of MMN is poorly understood but clinical studies suggest that Anti-GM1 autoantibodies directed against myelin antigens, along with autoreactive T cells and macrophages that invade myelin sheath play a causative role.[11,18,19] Anti-GM1 antibodies have been shown to bind to the surface of motor neurons, the nodes of Ranvier, and at the neuromuscular junction, where they may exert their effects.[2] An autoimmune etiology is further supported the fact that immune modulating

therapy improves symptoms for most patients.[7,11,18] Approximately 80% of patients with MMN respond to intravenous mmunoglobulins (IVIg). It is important to distinguish MMN from other motor neuron diseases with similar symptoms that are unresponsive to this treatment.[8-10] The clinical presentation of MMN can closely mimic several neurological conditions including those with more malignant prognoses such as motor neuron disease.[20] There is further value in distinguishing MMN from other immune mediated neuropathies that are responsive to plasma exchanges and steroids, as correct diagnosis is required for choosing the appropriate treatment, with the aim of preventing progressive neuropathy.[10,21-23] Testing for anti-GM1 can be useful in cases where MMN is clinically suspected but conduction block is not evident or is in less accessible nerve segments.[24]

Footnotes

1. Anti-GM1 Autoantibodies ELISA [package insert]. Switzerland: BUHLMANN Labs; Sep. 12, 2016.

2. Steck A, Yuki N, Graus F. Antibody testing in peripheral nerve disorders. *Handb Clin Neurol.* 2013;115:189-212. PubMed 23931781

3. Whitesell J. Inflammatory neuropathies. *Semin Neurol.* 2010 Sep;30(4):356-364. PubMed 20941668

4. Kuijf ML, van Doorn PA, Tio-Gillen AP, et al. Diagnostic value of anti-GM1 ganglioside serology and validation of the INCAT-ELISA. *J Neurol Sci.* 2005 Dec 15; 239(1):37-44. PubMed 16154154

5. McCombe PA, Wilson R, Prentice RL. Results of testing for anti-GM1 antibodies. *J Clin Neurosci.* 2000 May;7(3):209-212. PubMed 10833617

6. Leger JM, Guimares-Costa R, Iancu Ferfoglia R. The pathogenesis of multifocal motor neuropathy and an update on current management options. *Ther Adv Neurol Disord.* 2015 May;8(3):109-122. PubMed 25941538

7. Bayrak AO, Ulusoy H, Bolat N, Dogan B, Ozbenli T. Multifocal Motor Neuropathy Associated With Infliximab: A Case Report and a Literature Review. *Neurologist.* 2017 Jul;22(4):144-146. PubMed 28644258

8. Garg N, Park SB, Vucic S, et al. Differentiating lower motor neuron syndromes. *J Neurol Neurosurg Psychiatry.* 2017 Jun;88(6):474-483. PubMed 28003344

9. Querol L, Devaux J, Rojas-Garcia R, Illa I. Autoantibodies in chronic inflammatory neuropathies: diagnostic and therapeutic implications. *Nat Rev Neurol.* Epub 2017 Jul 14. PubMed 28708133

10. Rajabally YA. Multifocal motor neuropathy: Review of a treatable immune mediated disorder. *Postgrad Med J.* 2008 Jun;84(992):287-292. PubMed 18644918

11. Vlam L, van der Pol WL, Cats EA, et al. Multifocal motor neuropathy: diagnosis, pathogenesis and treatment strategies. *Nat Rev Neurol.* 2011 Nov 22;8(1):48-58. PubMed 22105211

12. Bourque PR, Chardon JW, Massie R. Autoimmune peripheral neuropathies. *Clin Chim Acta.* 2015 Sep 20;449:37-42. PubMed 25748038

13. Koski CL. Treatment of multifocal motor neuropathy with intravenous immunoglobulin. *J Clin Immunol.* 2014 Jul;34 Suppl 1:S127-131. PubMed 24699885

14. Chavada G, Willison HJ. Autoantibodies in immune- mediated neuropathies. *Curr Opin Neurol.* 2012 Oct;25(5):550-555. PubMed 22941260

15. Nobile-Orazio E, Gallia F, Terenghi F, Allaria S, Giannotta C, Carpo M. How useful are anti-neural IgM antibodies in the diagnosis of chronic immune-mediated neropathies? *J Neurol Sci.* 2008 Mar 15;266(1-2):156-163. PubMed 17915254

16. Cats EA, Jacobs BC, Yuki N, et al. Multifocal motor neuropathy: association of anti-GM1 IgM antibodies with clinical features. *Neurology.* 2010 Nov 30;75(22):1961-1967. PubMed 20962291

17. Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society--first revision. *J Peripher Nerv Syst.* 2010 Dec;15(4):295-301. PubMed 21199100

18. Dalakas MC. Pathogenesis of immune-mediated neuropathies. *Biochim Biophys Acta.* 2015 Apr;1852(4):658-666. PubMed 24949885

19. Harschnitz O, Jongbloed BA, Franssen H, Straver DC, van der Pol WL, van den Berg LH. MMN: from immunological cross-talk to conduction block. *J Clin Immunol.* 2014 Jul;34 Suppl 1:S112-119. PubMed 24728842

20. Lawson VH, Arnold WD. Multifocal motor neuropathy: A review of pathogenesis, diagnosis, and treatment. *Neuropsychiatr* Dis Treat. 2014 Apr 5;10:567-576. PubMed 24741315

21. Latov N. Diagnosis and treatment of chronic acquired demyelinating polyneuropathies. Nat Rev Neurol. 2014 Aug;10(8):435-446. PubMed 24980070

22. Nowacek DG, Teener JW. Multifocal motor neuropathy. *Semin Neurol.* 2012 Nov;32(5):500-505. PubMed 23677657

23. Nobile-Orazio E, Giannotta C. Testing for anti-glycolipid IgM antibodies in chronic immune-mediated demyelinating neuropathies. *J Peripher Nerv Syst.* 2011 Jun;16 Suppl 1:18-23. PubMed 21696492

24. Huan MC, Bromberg M. Advances in the laboratory evaluation of peripheral neuropathies. Curr Neurol Neurosci Rep. 2012 Feb;12(1):84-91. PubMed 22147264

25. Franciotta D, Gastaldi M, Benedetti L, et al. Diagnostics of dysimmune peripheral neuropathies. Neurol Sci. 2017 Oct;38(Suppl 2):243-247. PubMed 29030769

26. Cats EA, van der Pol WL, Tio-Gillen AP, Diekstra FP, van den Berg LH, Jacobs BC. Clonality of anti-GM1 IgM antibodies in multifocal motor neuropathy and the Guillain- Barré syndrome. J Neurol Neurosurg Psychiatry. 2015 May;86(5):502-504. PubMed 25157033

27. Caudie C, Quittard Pinon A, Taravel D, et al. Preceding infections and anti-ganglioside antibody profiles assessed by a dot immunoassay in 306 French Guillain-Barré syndrome patients. *J Neurol.* 2011 Nov;258(11):1958-1964. PubMed 21516465

References

Cao-Lormeau VM, Blake A, Mons S, et al. Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. Lancet. 2016 Apr 9;387(10027):1531-1539. PubMed 26948433

Emilien D, Hugh W. Diagnostic Utility of Auto Antibodies in Inflammatory Nerve Disorders. J Neuromuscul Dis. 2015 Jun;2(2):107-112. PubMed 27858733

Han TH, Kim DY, Park DW, Moon JH. Transient Isolated Lower Bulbar Palsy With Elevated Serum Anti-GM1 and Anti-GD1b Antibodies During Aripiprazole Treatment. Pediatr Neurol. 2017 Jan;66:96-99. PubMed 28341090

Kollewe K, Wurster U, Sinzenich T, et al. Anti-ganglioside antibodies in amyotrophic lateral sclerosis revisited. PLoS One. 2015 Apr 14;10(4):e0125339. PubMed 25875836

Lei T, Siu KL, Kok KH, et al. Anti-ganglioside antibodies were not detected in human subjects infected with or vaccinated against 2009 pandemic influenza A (H1N1) virus. Vaccine. 2012 Mar 30;30(16):2605-2610. PubMed 22342549

Sharma MB, Chaudhry R, Tabassum I, et al. The presence of Mycoplasma pneumonia infection and GM1 ganglioside antibodies in Guillain-Barré syndrome. J Infect Dev Ctries. 2011 Jul 4;5(6):459-464. PubMed 21727645

Hepatitis B Surface Antigen, Quantitative 007130

CPT 82397

Synonyms Quantitative HBsAg; Quantitative HBV surface antigen; Quantitative Hepatitis B Virus Surface Antigen

Specimen Serum (preferred) **or** plasma, **frozen**

Volume 2 mL

Minimum Volume 1 mL

Container Gel-barrier tube, PPT™ tube or lavender-top (EDTA) tube

Collection Draw blood in either a serum gel tube, a PPT™ or a lavender-top (EDTA) tube and centrifuge. If tube other than a gel-barrier tube is used, transfer separated serum or plasma to a plastic transport tube (not a "pop-top" or "snapcap"). Specimen must be refrigerated immediately and frozen within 3 hours of collection.

Storage Instructions Freeze at -20°C and ship frozen.

Stability

Temperature	Period
Room temperature	Unstable
Refrigerated	< 3 hours
Frozen	14 days
Freeze/thaw cycles	Stable x5

Causes for Rejection Incorrect anticoagulant; PPT™ or gel-barrier tube not centrifuged

Use Quantitative HBV surface antigen (HBsAg) testing is intended for use in individuals with a confirmed diagnosis of Hepatitis B Virus infection based on positive HBsAg, Anti-HBs antibody and/or Anti-core antigen (anti-HBc) antibody test results. Quantitative HBsAg testing has utility in assessing HBV replication in the absence and presence of antiviral therapy, which may inform monitoring treatment response and relapse in the setting of initial and proloned antiviral therapy, respectively. Recent studies indicate that rapid decay and loss of HBsAg expression are strong predictors of sustained HBV clearance.

Limitations Quantitative HBsAg testing is not intended for the diagnosis of HBV infection. THe relationship between HBsAg levels and ongoing HBV replication and/or persistent infection has not been fully defined. HBV DNA viral load measurements reflect the extent of ongoing HBV replication. HBsAg levels reflect the transcription and trranslational expression of HBV DNA. The clinical ramifications of detectable levels of HBsAg in the absence of detectable levels of HBV DNA are the subject of ongoing investigation.

Methodology Immunochemiluminometric assay (ICMA)

Additional Information Hepatitis B is an infectious disease caused by Hepatitis B Virus (HBV). Worldwide, more than 350 million persons are chronically infected with HBV. Chronic HBV infection often leads to premature death as a result of liver cirrhosis and cancer. An estimated 3,000 to 4,000 persons die of hepatitis B-related cirrosis each year in the United States. The risk of hepatocellular carcinoma is significantly higher in persons with chronic HBV infection, which results in 1,000 to 1,500 deaths

each year in the United States.

HBV virions consist of a DNA genome that is packaged within an icosahedral nucleocapsid, comprised of core antigen (HBcAg), surrounded by a lipid envelope containing surface antigens (HBsAg). There are four distinct HBV serotypes (adr, adw, ayr, ayw) and at least eight different genotypes (A-H).

HBV infection is characterized by the transient detection of HBsAg and HBV DNA in serum. The most reliable markers for infectivity are HBsAg and HBV "e" antigen (HBeAg). HBsAg is the first serolgic marker to appear following acute infection, with detection averaging one month after HBV exposure. HBeAg indicates active infection and the ability to spread the virus to others. Spontaneous recovery is characterized by undetectable HBsAg and HBV DNA apprximately 15 weeks after the appearance of symptoms. The presence of anti-HBs antibody is strongly associated with reduced infectivity and clearance. In contrast, the chronic carrier state is indicated by the persistence of HBsAg and/or HBeAg in the absence of seroconversion characterized by anti-HBs and/or anti-HBe antibody, respectively. This clinical condition has the potential to lead to serious liver damage, but may be an isolated asymptomatic serologic phenomenon. Persitence of HBsAg expression in the absence of anti-HBs antibody, in combination with anti-HBc, HBeAg, or anti-HBe reactivity is an indication of ongoing HBV replication and the need to investigate chronic persistent or chronic aggressive hepatitis.

References

Schillie S, Vellozzi C, Reingold A, et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep.* 2018 Jan 12;67(1):1-31. PubMed 29939980

Seto WK, Lo YR, Pawlotski JM, Yuen MF. Chronic hepatitis B virus infection. *Lancet.* 2018 Nov 24;392(10161):2313-2324. PubMed 30496122

World Health Organization. *Global Hepatitis Report,* 2017. Geneva, Switzerland: World Health Organiztion; 2017.

Huntington Disease (HTT) Genetic Testing (Repeat Expansion) 620016

CPT 81271

Special Instructions This assay is not currently available in New York state.

Expected Turnaround Time 2 - 4 weeks

Specimen Whole blood

Volume 4 mL

Container Lavender-top (EDTA) tube

Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do not freeze.

Causes for Rejection Frozen blood EDTA tube

Use Huntington disease (HD) is a neurodegenerative disease of mid-life onset that produces choreic movements and cognitive decline, often accompanied by psychiatric changes. The disease is caused by an expansion of the CAG repeats in 3-5 out of 100,000 individuals. However, the prevalence of HD exceeds 15 per 100,000 in some populations, mostly of Western European origin. Juvenile-onset HD occurs in approximately 5% of affected patients, is rapidly progressive, and presents with rigidity, spasticity, and intellectual decline before the age of 20 years. The symptoms result from the selective loss of neurons, most notably in the caudate nucleus and putamen, and there is currently no effective treatment.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Inheritest®500 PLUS Panel 630049

CPT Call client services.

Synonyms Pan-ethnic carrier screening; Universal Carrier Screening

Special Instructions This assay is not currently available in New York state. Contact an Integrated Genetics laboratory genetic coordinator at 800-255-7357 with any questions.

Expected Turnaround Time 12 - 16 days

Specimen Whole blood

Volume 10 mL

Container Yellow-top (ACD-A) tube (preferred) or lavender-top (EDTA) tube

Storage Instructions Maintain at room temperature or refrigerate at 4°C.

Causes for Rejection Frozen specimen; hemolysis; quantity not sufficient for analysis; improper container; yellow-top (ACD-B) tube

Use Carrier testing by analyzing 525 genes, each associated with a clinically relevant disorder, including fragile X syndrome and spinal muscular atrophy.

Limitations Technologies used do not detect germline mosaicism and do not rule out the presence of large chromosomal aberrations, including rearrangements, gene fusions, or variants in regions or genes not included in this test, or possible inter/intragenic interactions between variants. Variant classification and/or interpretation may change over time if more information becomes available. False positive or false negative results may occur for reasons that include: rare genetic variants, sex chromosome abnormalities, pseudogene interference, blood transfusions, bone marrow transplantation, somatic or tissue-specific mosaicism, mislabeled samples, or erroneous representation of family relationships.

Methodology

Single Nucleotide Polymorphism and Small Indel Sequencing Assessment: Genomic regions of interest are selected using a custom capture reagent for target enrichment and sequenced via the Illumina® next generation sequencing platform. Sequencing reads are aligned with the human genome reference GRCh37/hg19 build. Regions of interest include all exons and intron/exon junctions (+/-20 nucleotides) for each gene analyzed. A minimum of 99% of bases are covered at >15X. Analytical sensitivity is estimated to be >99% for single nucleotide variants, >97% for insertions/deletions less than six base pairs, and >95% for insertions/deletions between six and fifteen base pairs. Uncovered regions with known pathogenic variants are sequenced in a targeted manner. All reported variants are confirmed by a second method.

Copy Number Variant Assessment: Next Generation Sequencing is performed and the data are assessed with Illumina's DRAGEN (Dynamic Read Analysis for GENomics) Bio-IT Platform. Reported variants are confirmed by a second method. Analytical sensitivity is estimated to be >95%.

Spinal Muscular Atrophy: This analysis will detect the copy number of exon 7 of the *SMN1* gene. When no copies of *SMN1* exon 7 are detected, *SMN2* exon 7 copy number is assessed and reported. This test is unable to differentiate between two copies of the *SMN1* gene on one allele (in cis) versus two copies of the gene on different alleles (in trans). When two copies of *SMN1* exon 7 are detected, the data are assessed for the presence of the c.*3+80T>G "silent carrier" variant.

Congenital Adrenal Hyperplasia: This analysis will detect most large rearrangements/deletions/duplications within the *CYP21A2* gene, as well as the presence of seven of the most common pathogenic variants in the gene: 1) c.518T>A (p.Ile173Asn), Chr6:32007203; 2) c.713T>A (p.Val238Glu); Chr6:32007587; 3) c.719T>A (p.Met240Lys); Chr6:32007593; 4) c.923dup (p.Leu308Phefs); Chr6:32007966; 5) c.293-13C/A>G; Chr6:32006858; 6) c.332_339delGAGACTAC (p.Gly111Valfs); Chr6:32006910-32006917; 7) c.-113G>A; Chr6:32006087. Other point mutations and small indels and reciprocal changes between *CYP21A2* and *CYP21A1P* are not detected by this analysis. The analytical sensitivity of this assay is estimated to be >99%.

Alpha thalassemia: Variants included in the analysis of the alpha-globin (HBA) gene cluster are the Constant Spring non-deletion variant and the following deletions: -alpha3.7, -alpha4.2, --alpha20.5, --SEA, --FIL, --THAI, --MED, and the HS-40 regulatory region.

Fragile X Syndrome: Repeat-primed PCR is used to detect the number of CGG repeats on each allele of the *FMR1* gene. The reportable range is 5-200 repeats. Alleles with expansions above 200 repeats are reported as >200. In females, excluding prenatal specimens, alleles between 55 and 90 repeats are assessed by a PCR assay to determine the number and position of AGG interruptions within the CGG repeats.

Reported Variants: Pathogenic and likely pathogenic variants are reported after confirmation by an appropriate technology. Variants in *GJB2, GJB6,* and *OPA3* that act in a dominant fashion are not reported. NEB variants occurring in exons 82-105 may not be reliably detected by this analysis and are not reported. Nondeletion variants are specified using the numbering and nomenclature recommended by the Human Genome Variation Society. Variants of uncertain significance, likely benign, and benign variants are not reported. Variant classification is consistent with

ACMG standards and guidelines.

References

den Dunnen JT. Describing Sequence Variants Using HGVS Nomenclature. *Methods Mol Biol.* 2017;1492:243-251. PubMed 27822869

Monaghan KG, Lyon E, Spector EB; American College of Medical Genetics and Genomics. ACMG Standards and Guidelines for fragile X testing: a revision to the disease-specific supplements to the Standards and Guidelines for Clinical Genetics Laboratories of the American College of Medical Genetics and Genomics. *Genet Med.* 2013 Jul;15(7):575-586. PubMed 23765048

Richards S, Aziz N, Bale S. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015 May;17(5):405-424. PubMed 25741868

Inheritest®500 PLUS with Repro Partners Report. . . . 630217

CPT Call client services.

Synonyms Pan-ethnic carrier screening; Universal Carrier Screening

Special Instructions This assay is not currently available in New York state. Contact an Integrated Genetics laboratory genetic coordinator at 800-255-7357 with any questions.

Expected Turnaround Time 12 - 16 days

Specimen Whole blood

Volume 10 mL

Container Yellow-top (ACD-A) tube (preferred) or lavender-top (EDTA) tube

Storage Instructions Maintain at room temperature or refrigerate at 4°C.

Causes for Rejection Frozen specimen; hemolysis; quantity not sufficient for analysis; improper container; yellow-top (ACD-B) tube

Use Carrier testing by analyzing 525 genes, each associated with a clinically relevant disorder, including Fragile X syndrome and spinal muscular atrophy.

Limitations Technologies used do not detect germline mosaicism and do not rule out the presence of large chromosomal aberrations, including rearrangements, gene fusions, or variants in regions or genes not included in this test, or possible inter/intragenic interactions between variants. Variant classification and/or interpretation may change over time if more information becomes available. False positive or false negative results may occur for reasons that include: rare genetic variants, sex chromosome abnormalities, pseudogene interference, blood transfusions, bone marrow transplantation, somatic or tissue-specific mosaicism, mislabeled samples, or erroneous representation of family relationships.

Methodology

Single Nucleotide Polymorphism and Small Indel Sequencing Assessment: Genomic regions of interest are selected using a custom capture reagent for target enrichment and sequenced via the Illumina® next generation sequencing platform. Sequencing reads are aligned with the human genome reference GRCh37/hg19 build. Regions of interest include all exons and intron/exon junctions (+/-20 nucleotides) for each gene analyzed. A minimum of 99% of bases are covered at >15X. Analytical sensitivity is estimated to be >99% for single nucleotide variants, >97% for insertions/deletions less than six base pairs, and >95% for insertions/deletions between six and fifteen base pairs. Uncovered regions with known pathogenic variants are sequenced in a targeted manner. All reported variants are confirmed by a second method.

Copy Number Variant Assessment: Next Generation Sequencing is performed and the data are assessed with Illumina's DRAGEN (Dynamic Read Analysis for GENomics) Bio-IT Platform. Reported variants are confirmed by a second method. Analytical sensitivity is estimated to be >95%.

Spinal Muscular Atrophy: This analysis will detect the copy number of exon 7 of the *SMN1* gene. When no copies of *SMN1* exon 7 are detected, *SMN2* exon 7 copy number is assessed and reported. This test is unable to differentiate between two copies of the *SMN1* gene on one allele (in cis) versus two copies of the gene on different alleles (in trans). When two copies of *SMN1* exon 7 are detected, the data are assessed for the presence of the c.*3+80T>G "silent carrier" variant.

Congenital Adrenal Hyperplasia: This analysis will detect most large rearrangements/deletions/duplications within the *CYP21A2* gene, as well as the presence of seven of the most common pathogenic variants in the gene: 1) c.518T>A (p.Ile173Asn), Chr6:32007203; 2) c.713T>A (p.Val238Glu); Chr6:32007587; 3) c.719T>A (p.Met240Lys); Chr6:32007593; 4) c.923dup (p.Leu308Phefs); Chr6:32007966; 5) c.293-13C/A>G; Chr6:32006858; 6) c.332_339delGAGACTAC (p.Gly111Valfs); Chr6:32006910-32006917; 7) c.-113G>A; Chr6:32006087. Other point mutations and small indels and reciprocal changes between *CYP21A2* and *CYP21A1P* are not detected by this analysis. The analytical sensitivity of this assay is estimated to be >99%.

Alpha thalassemia: Variants included in the analysis of the alpha-globin (HBA) gene cluster are the Constant Spring non-deletion variant and the following deletions: -alpha3.7, -alpha4.2, --alpha20.5, --SEA, --FIL, --THAI, --MED, and the HS-40 regulatory region.

Fragile X Syndrome: Repeat-primed PCR is used to detect the number of CGG repeats on each allele of the *FMR1* gene. The reportable range is 5-200 repeats. Alleles with expansions above 200 repeats are reported as >200. In females, excluding prenatal specimens, alleles between 55 and 90 repeats are assessed by a PCR assay to determine the number and position of AGG interruptions within the CGG repeats.

Reported Variants and Risk Revisions: Pathogenic and likely pathogenic variants are reported after confirmation by an appropriate technology. Variants in *GJB2, GJB6,* and *OPA3* that act in a dominant fashion are not reported. NEB variants occurring in exons 82-105 may not be reliably detected by this analysis and are not reported. Nondeletion variants are specified using the numbering and nomenclature recommended by the Human Genome Variation Society. Variants of uncertain significance, likely benign, and benign variants are not reported. Variant classification is consistent with ACMG standards and guidelines. When provided, carrier rates and detection rates are derived from gnomAD and ClinVar. For unknown or mixed ethnicities, the ethnic background with the most conservative risk estimate is used. For a complete list of residual risks for all genes on this panel, visit www.integratedgenetics.com.

References

den Dunnen JT. Describing Sequence Variants Using HGVS Nomenclature. *Methods Mol Biol.* 2017;1492:243-251. PubMed 27822869

Monaghan KG, Lyon E, Spector EB; American College of Medical Genetics and Genomics. ACMG Standards and Guidelines for fragile X testing: a revision to the disease-specific supplements to the Standards and Guidelines for Clinical Genetics Laboratories of the American College of Medical Genetics and Genomics. *Genet Med.* 2013 Jul;15(7):575-586. PubMed 23765048

Richards S, Aziz N, Bale S. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015 May;17(5):405-424. PubMed 25741868

Lactate (CSF) 620044

CPT 83605

Expected Turnaround Time 10 - 14 days

Specimen Cerebrospinal fluid (CSF)

Volume 1.0 mL

Minimum Volume 0.5 mL

Container Sterile screw capped vial

Collection Collect entire sample into a single sterile tube.

Storage Instructions Freeze as soon as possibe after collection.

Stability

Temperature	Period
Room temperature	Unstable (stability determined by manufacturer or literature reference)
Refrigerated	24 hours (stability determined by manufacturer or literature reference)
Frozen	-20°C = 72 hours; -80°C = Indefinite (stability determined by manufacturer or literature reference)

Causes for Rejection Bloody CSF; received thawed

Use CSF Lactate is useful for investigating possible disorders of mitochondrial metabolims, when used in conjenction with cerebrospinal fluid pyruvate collected at the same time to determine the Lactate:Pyruvate ratio. The CSF Lactate:Pyruvate ratio is considered a helpful (not diagnostic) tool in the evaluation of patients with possible disorders of mitochondrial metabolism, especially in patients with neurolofic dysfunction and normal blood Lactate:Pyruvate ratios. Pyruvic acid levels alone have little

clinical utility. The Lactate:Pyruvate ratio is elevated in several, but not all, mitochondrial disorders vary widely in presentation and age of onset. Many mitochondral disorders have neurologic and myopathic features and may involve multiple organ systems. Determination of lactate, pyruvate, and L:P ratio in cerebrospinal fluid is helpful in directing attention toward a possible mitochondrial disorder in cases with predominately neurologic dysfunction and normal blood lactate levels. An elevated Lactate:Pyruvate ratio may indicate inherited disorders of the respiratory chain complex, tricarboxylic acide cycle disorders and pyruvate carboxylase deficiency. Respiratory chain defects usually result in Lactate:Pyruvate ratios >20. A low Lactate:Pyruvate raio (disproportionately elevated pyruvic acid) may indicate an inherited disorder of pyruvate metabolism. Defects of the pyruvate dehydrogenase complex result in Lactate:Pyruvate ratios <10. The Lactate:Pyruvate ratio is characteristically normal in other patients. An artifactually high ratio can be found in acutely ill patients.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Enzyme/UV

Maturity-Onset Diabetes of the Young (MODY) Genetic Profile 504603

CPT 81404; 81405(x2); 81406(x2)

Test Includes This profile detects pathogenic variants and copy number variants in the coding sequence and exon-intron junctions of the four genes most commonly involved in MODY: *HNF1A, GCK, HNF4A,* and *HNF1B*.

Special Instructions This assay is currently **not** available in New York.

Specimen Whole blood

Volume 3.0 mL

Minimum Volume 1.0 mL

Container Lavender-top (EDTA) tube

Storage Instructions Room temperature

Stability

Temperature	Period
Room temperature	14 days
Refrigerated	14 days

Causes for Rejection Improper specimens; frozen samples; hemolyzed samples

Use Maturity-onset diabetes of the young (MODY) is a suspected diagnosis in young non-obese patients who lack an autoimmune cause for diabetes and who have a family history of diabetes in successive generations. The majority of MODY cases are due to mutations in one of four genes. Identifying a mutation in one of these MODY genes can lead to improved treatment, increased surveillance for related symptoms, and earlier detection in currently asymptomatic family members. *GCK* encodes the enzyme glucokinase, a key regulator of glucose metabolism in pancreatic beta cells. The three *HNF* (hepatic nuclear factor) genes encode transcription factors that regulate gene expression in the pancreas.

Mody #	Gene	Chromosome Location	RefSeq (Gene)	Transcript
MODY 3	*HNF1A*	12q24.31	NG_011731.2	NM_000545.6
MODY 5	*HNF4A*	20q13.12	NG_009818.1	NM_175914.4
MODY 1	*HNF1B*	17q12	NG_013019.2	NM_000458.3
MODY 2	*GCK*	7p13	NG_008847.2	NM_000162.5

Limitations Mutation analysis is performed using bidirectional Sanger sequencing of the exons and splice junctions for each gene analyzed. Copy number variants (CNVs) are detected by semi-quantitative PCR. Analytical sensitivity is estimated to be >99% for single nucleotide variants and small insertions/deletions, while clinical sensitivity can vary with the selection criteria and is predicted to be at least 85%. Variant classification is consistent with ACMG standards and guidelines. A variant of uncertain significance (VUS) is a classification based on inadequate or conflicting evidence and should not be used in clinical decision making. This assay reports pathogenic or likely pathogenic mutations and VUS's, while benign or likely benign variants are not reported. Numbering and nomenclature use the recommendations of the Human Genome Variation Society (HGVS: http://www.hgvs.org) and the transcript versions listed above.

This analysis does not detect germline mosaicism, large chromosomal rearrangements that do not alter copy number, and regions or genes not included in this test. Variant classification and/or interpretation may change with time if more information becomes available. False positive or negative results may occur for reasons that include: genetic variants that affect the assay, blood transfusions, mosaicism, mislabeled samples, or erroneous representation of family relationships.

Methodology Sanger sequencing and MLPA

References

Bellanne-Chantelot C, Clauin S, Chauveau D, et al. Large genomic rearrangements in the hepatocyte nuclear factor-1beta (TCF2) gene are the most frequent cause of maturity-onset diabetes of the young type 5. *Diabetes.* 2005 Nov;54(11):3126-3132. PubMed 16249435

Ellard S, Thomas K, Edghill EL, et al. Partial and whole gene deletion mutations of the GCK and HNF1A genes in maturity-onset diabetes of the young. *Diabetologia.* 2007 Nov;50(11):2313-2317. PubMed 17828387

Ellard S, Colclough K. Mutations in the genes encoding the transcription factors hepatocyte nuclear factor 1 alpha (HNF1A) and 4 alpha (HNF4A) in maturity-onset diabetes of the young. *Hum Mutat.* 2006 Sep;27(9):854-869. PubMed 16917892

Gloyn AL. Glucokinase (GCK) mutations in hyper- and hypoglycemia: maturity-onset diabetes of the young, permanent neonatal diabetes, and hyperinsulinemia of infancy. *Hum Mutat.* 2003 Nov;22(5):353-362. PubMed 14517946

Hattersley AT, Patel KA. Precision diabetes: learning from monogenic diabetes. *Diabetologia.* 2017 May;60(5):769-777. PubMed 28314945

Osbak KK, Colclough K, Saint-Martin C, et al. Update on mutations in glucokinase (GCK), which cause maturity-onset diabetes of the young, permanent neonatal diabetes, and hyperinsulinemic hypoglycemia. *Hum Mutat.* 2009 Nov;30(11):1512-1526. PubMed 19790256

Medication Assisted Treatment (MAT) Buprenorphine, Norbuprenorphine, and Naloxone MS Confirmation, Urine 701279

CPT 80362

Synonyms Opioid Use Disorder; Suboxone™ MAT, Opioid Use Disorder, Buprenorphine/Norbuprenorphine, Naloxone; Suboxone™ MAT

Special Instructions This profile is designed for Suboxone™/buprenorphine medication assisted treatment. It is not intended for workplace testing and does not comply with state regulatory workplace testing programs.

Expected Turnaround Time 4 - 7 days

Specimen Urine (random)

Volume 30 mL

Minimum Volume 15 mL

Container Urine container

Collection Random urine

Storage Instructions ***Submission/Transport (<3 days):*** Room temperature. For storage beyond three days, specimen should be refrigerated or **frozen.**

Stability Room Temperature: 5 days

Causes for Rejection Insufficient volume; no ID on container; urine from preservative tube

Use Detect and confirm presence of prescribed and illicit drugs for monitoring Suboxone™/buprenorphine medication assisted treatment (MAT).

Please note: This testing is designed specifically for monitoring patients who are on Suboxone™/buprenorphine only. This testing should not be used for monitoring chronic pain patients (medical drug monitoring) or methadone medication assisted treatment.

Methodology LC/MS-MS or GC/MS

Mitochondrial DNA Depletion Testing (Leukocyte) . . . 620108

CPT 81479

Special Instructions This assay is not currently available in New York state.

Expected Turnaround Time 2 - 4 weeks

Specimen Whole blood

Volume 4 mL

Minimum Volume 1 mL

Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use To diagnose the mitochondrial DNA depletion syndrome (MDS). The test is also useful in assessing variants of uncertain significance in nuclear DNA genes that cause MDS. MDS is a clinically heterogeneous group of mitochondrial disorders characterized by a reduction of the mtDNA copy number in affected tissues without mutations or rearrangements in the mtDNA. MDS is phenotypically heterogeneous, and can affect a specific organ or a combination of organs, with the main presentations described being either hepatocerebral (i.e. hypotonia, muscle weakness, bulbar weakness), encephalomyopathic (i.e. hypotonia, muscle weakness, psychomotor delay) or neurogastrointestinal (i.e. gastrointestinal dysmotility, peripheral neuropathy). Additional phenotypes include fatal infantile lactic acidosis with methylmalonic aciduria, spastic ataxia (early-onset spastic ataxia-neuropathy syndrome), and Alpers syndrome (see these terms).
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Real-time Quantitative PCR Analysis

Mitochondrial DNA Depletion Testing (Muscle) 620094

CPT 81479
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Muscle; extracted DNA - muscle
Volume 200 ng of DNA **or** 75 mg muscle
Minimum Volume 100 ng of DNA **or** 50 mg muscle
Container Sterile screw capped vial
Collection Collect biopsy per established policy.
Storage Instructions DNA: Ship at room temperature after extraction. Muscle: Ship in insulated container with 5-7 lbs of dry ice.
Stability

Temperature	Period
Room temperature	DNA: 30 days; Muscle: 0 days (stability provided by manufacturer or literature reference)
Refrigerated	DNA: 30 days; Muscle: 0 days (stability provided by manufacturer or literature reference)
Frozen	DNA: Indefinitely; Muscle: Indefinitely (stability provided by manufacturer or literature reference)

Causes for Rejection Extracted DNA A260:A280 ratio outside of 1.8-2.0 range; frozen blood EDTA tube; thawed and/or fatty muscle sample
Use To diagnose the mitochondrial DNA depletion syndrome (MDS). The test is also useful in assessing variants of uncertain significance in nuclear DNA genes that cause MDS. MDS is a clinically heterogeneous group of mitochondrial disorders characterized by a reduction of the mtDNA copy number in affected tissues without mutations or rearrangements in the mtDNA. MDS is phenotypically heterogeneous, and can affect a specific organ or a combination of organs, with the main presentations described being either hepatocerebral (i.e. hepatic dysfunction, psychomotor delay), myopathic (i.e. hypotonia, muscle weakness, bulbar weakness), encephalomyopathic (i.e. hypotonia, muscle weakness, psychomotor delay) or neurogastrointestinal (i.e. gastrointestinal dysmotility, peripheral neuropathy). Additional phenotypes include fatal infantile lactic acidosis with methylmalonic aciduria, spastic ataxia (early-onset spastic ataxia-neuropathy syndrome), and Alpers syndrome (see these terms).
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Real-time Quantitative PCR Analysis

Myelin Associated Glycoprotein (MAG) IgM Autoantibodies 140120

CPT 83520
Special Instructions This assay is not approved for patients of New York State physicians.
Expected Turnaround Time 7 days
Specimen Serum, **frozen**
Volume 0.3 mL
Minimum Volume 0.1 mL (**Note:** This volume does **not** allow for repeat testing.)
Container Gel-barrier tube or red-top tube
Collection Separate serum from cells. Transfer the serum into a LabCorp PP transpak frozen purple tube with screw cap (LabCorp No. 49482). Freeze immediately and maintain frozen at ≤ -20°C until tested. To avoid delays in turnaround time when requesting multiple tests on frozen samples, **please submit separate frozen specimens for each test requested.**
Storage Instructions Freeze
Stability

Temperature	Period
Frozen	1 year (stability determined by manufacturer or literature reference)
Freeze/thaw cycles	Stable x2 (stability determined by manufacturer or literature reference)

Patient Preparation Lipemic samples can be avoided by having the patient fast for 12 hours prior to collection.
Causes for Rejection Non-serum sample received; non-frozen serum received; grossly lipemic, hemolytic or icteric sample received; cryoglobulin present
Use The BUHLMANN Anti-MAG™ ELISA is intended for the quantitative in vitro diagnostic determination of human IgM autoantibodies directed against Myelin Associated Glycoprotein (MAG).[1]
Limitations Results of this test are labeled for research purposes only by the assay's manufacturer. The performance characteristics of this assay have not been established by the manufacturer. The result should not be used for treatment or for diagnostic purposes without confirmation of the diagnosis by another medically established diagnostic product or procedure. The performance characteristics were determined by LabCorp.
Methodology BUHLMANN™ anti-MAG ELISA. This assay measures antibodies to purified human MAG.[1,2,12-25]
Reference Interval 0-999 BTU
Additional Information MAG is a transmembrane lectin that preferentially binds to alpha-2,3-linked sialic acid terminal carbohydrates on cell surface molecules. It is localized in the oligodendroglial membranes of myelin sheaths and Schwann cells. Several different forms of motor and sensory neuropathies are associated with antibodies against the sulphated glucuronic acid moieties of MAG. The clinical picture of anti-MAG neuropathy is characterized by a distal and symmetric, mostly sensory neuropathy.[2-6] The clinical course of anti- MAG neuropathy is usually slowly progressive with evidence of demyelination and a variable degree of axonal loss associated with gait ataxia.[7] However, the clinical presentation of these patients can be variable, suggesting autoimmunity to other components of myelin may play a role in the disease.[8]

Anti-MAG autoantibodies frequently occur with IgM paraproteinemia. Approximately half the patients with Monoclonal Gammopathy of Uncertain Significance (MGUS) of IgM type with peripheral neuropathies have antibodies against MAG.[2,6] Anti-MAG IgM has also been identified in Waldenstrom's macroglobulinemia and IgM secreting lymphoma. These MAG autoantibodies are believed to be pathogenic.[2,9] A joint task force of

the European Federation of Neurological Societies (EFNS) and Peripheral Nerve Society (PNS) have constructed clinically useful guidelines for the diagnosis, investigation and treatment of patients with both, a demyelinating neuropathy and a paraprotein.[10]

Patients with anti-MAG antibodies may respond favorably to therapeutic intervention but to date there is no consensus on the treatment of this disease.[2,11,12] Testing for the presence of these autoantibodies is useful for diagnosis as well as for monitoring of therapy.[13,14] Historically, clinicians have applied a variety of approaches to treatment of anti-MAG neuropathy including:

- Reduction of circulating IgM anti-MAG antibodies by removal by [plasma exchange],
- Inhibition with Intravenous Immunoglobulin (IVIg), or
- Reduction of their synthesis by corticosteroids, immunosuppressive agents, cytotoxic agents or interferon alpha.[9,15]

Recent reports suggest Rituximab may be effective in some patients with anti-MAG neuropathy.[4,7,16-20] However, the effectiveness of this approach has not been confirmed in all cases.[12,21,22]

Footnotes

1. Anti-MAG Elisa [package insert]. Switzerland: BUHLMANN Labs; Nov. 16, 2012.

2. Franciotta D, Gastaldi M, Benedetti L, et al. Diagnostics of anti-MAG antibody polyneuropathy. *Neurol Sci.* 2017 Oct;38(Suppl 2):249-252. PubMed 29030772
3. Lozeron P, Ribrag V, Adams D, et al. Is distal motor and/or sensory demyelination a distinctive feature of anti-MAG neuropathy? *J Neurol.* 2016 Sep;263(9):1761-1770. PubMed 27314957
4. Campagnolo M, Ferrari S, Dalla Torre C, et al. Polyneuropathy with anti-sulfatide and anti-MAG antibodies: clinical, neurophysiological, pathological features and response to treatment. *J Neuroimmunol.* 2015 Apr 15;281:1-4. PubMed 25867460
5. Quarles RH. Myelin-associated glycoprotein (MAG): past, present and beyond. *J Neurochem.* 2007 Mar;100(6):1431-1448. PubMed 17241126
6. Pruppers MHJ, Merkies ISJ, Lunn MPT, Notermans NC; IMAGiNe Study Group. 230th ENMC International Workshop: Improving future assessment and research in IgM anti-MAG peripheral neuropathy: A consensus collaborative effort, Naarden, The Netherlands, 24-26 February 2017. *Neuromuscul Disord.* 2017 Nov;27(11):1065-1072. PubMed 28927829
7. Svahn J, Petiot P, Antoine JC, et al. Anti-MAG antibodies in 202 patients: clinicopathological and therapeutic features. *J Neurol Neurosurg Psychiatry.* 2018 May;89(5):499-505. PubMed 29070644
8. Magy L, Kabore R, Mathis S, et al. Heterogeneity of Polyneuropathy Associated with Anti-MAG Antibodies. *J Immunol Res.* 2015;2015:450391. PubMed 26065001
9. Dalakas MC. Rituximab in anti-MAG neuropathy: More evidence for efficacy and more predictive factors. *J Neurol Sci.* 2017 Jun 15;377:224-226. PubMed 28477700
10. Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of paraproteinemic demyelinating neuropathies. Report of a Joint Task Force of the European Federation of Neurological Societies and the Peripheral Nerve Society--first revision. *J Peripher Nerv Syst.* 2010 Sep;15(3):185-195. PubMed 21040140
11. Vallat JM, Magy L, Ciron J, Corcia P, Le Masson G, Mathis S. Therapeutic options and management of polyneuropathy associated with anti-MAG antibodies. *Expert Rev Neurother.* 2016 Sep;16(9):1111-1119. PubMed 27267749
12. Lunn MP, Nobile-Orazio E. Immunotherapy for IgM anti- myelin-associated glycoprotein paraproteinassociated peripheral neuropathies. *Cochrane Database Syst Rev.* 2016 Oct 4;10:CD002827. PubMed 27701752
13. Emilien D, Hugh W. Diagnostic Utility of Auto Antibodies in Inflammatory Nerve Disorders. *J Neuromuscul Dis.* 2015 Jun 4;2(2):107-112. PubMed 27858733
14. Latov N. Diagnosis and treatment of chronic acquired demyelinating polyneuropathies. *Nat Rev Neurol.* 2014 Aug; 10(8):435-446. PubMed 24980070
15. Baron M, Lozeron P, Harel S, et al. Plasma exchanges for severe acute neurological deterioration in patients with IgM anti-myelin-associated glycoprotein (anti-MAG) neuropathy. *J Neurol.* 2017 Jun;264(6):1132-1135. PubMed 28484839
16. Campagnolo M, Zambello R, Nobile-Orazio E, et al. IgM MGUS and Waldenstrom-associated anti-MAG neuropathies display similar response to rituximab therapy. *J Neurol Neurosurg Psychiatry.* Epub 2017 May 13. PubMed 28501820
17. Gazzola S, Delmont E, Franques J, et al. Predictive factors of efficacy of rituximab in patients with anti-MAG neuropathy. *J Neurol Sci.* 2017 Jun 15;377:144-148. PubMed 28477685
18. Léger JM, Viala K, Nicolas G, et al. Placebo-controlled controlled trial of rituximab in IgM anti-myelin-associated glycoprotein neuropathy. *Neurology.* 2013 Jun 11;80(24):2217-2225. PubMed 23667063
19. Maurer MA, Rakocevic G, Leung CS, et al. Rituximab induces sustained reduction of pathogenic B cells in patients with peripheral nervous system autoimmunity. *J Clin Invest.* 2012 Apr;122(4):1393-1402. PubMed 22426210
20. Gruson B, Ghomari K, Beaumont M, et al. Long-term response to rituximab and fludarabine combination in IgM anti-myelin-associated glycoprotein neuropathy. *Peripher Nerv Syst.* 2011 Sep;16(3):180-185. PubMed 22003932
21. Sala E, Robert-Varvat F, Paul S, Camdessanche JP, Antione JC. Acute neurological worsening after Ritiximab treatment in patients with anti-MAG neuropathy. *J Neurol Sci.* 2014 Oct 15;345(1-2):224-227. PubMed 25115501
22. Stork AC, Notermans NC, Vrancken AF, Cornblath DR, van der Pol WL. Rapid worsening of IgM anti-MAG demyelinating polyneuropathy during rituximab treatment. *J Peripher Nerv Syst.* 2013 Jun;18(2):189-191. PubMed 23781968
23. Kuijf ML, Eurelings M, Tio-Gillen AP, et al. Detection of anti-MAG antibodies in polyneuropathy associated with IgM monoclonal gammopathy. *Neurology.* 2009 Sep 1;73(9):688-695. PubMed 19720975
24. Jaskowski TD, Prince HE, Greer RW, Litwin CM, Hill HR. Further comparisons of assays for detecting MAG IgM autoantibodies. *J Neuroimmunol.* 2007 Jul;187(1-2):175-178. PubMed 17537521
25. Caudie C, Kaygisiz F, Jaquet P, et al. Diagnostic value of autoantibodies to MAG by ELISA Buhlmann in 117 immune-mediated peripheral neuropathies associated with monoclonal IgM to SGPG/SGLPG. *Ann Biol Clin (Paris).* 2006 Jul-Aug;64(4):353-359. PubMed 16829480

References

Dalakas MC. Pathogenesis of immune-mediated neuropathies. *Biochim Biophys Acta.* 2015 Apr;1852(4):658-666. PubMed 24949885

Myotonic Dystrophy 1 (*DMPK*) Genetic Testing (Repeat Expansion) 620084

CPT 81234
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use Type 1 myotonic dystrophy results from a mutation in the DMPK gene known as a trinucleotide repeat expansion. This mutation increases in the size of then repeated CTG segment in the *DMPK* gene. People with type 1 myotonic dystrophy have from 50 to 5,000 CTG repeats in most cells. The number of repeats may be even greater in certain types of cells, such as muscle cells.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Repeat-Primed PCR (QP-PCR)

Myotonic Dystrophy 2 (*ZNF9/CNBP*) Genetic Testing (Repeat Expansion) 620087

CPT 81187
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use Type 2 myotonic dystrophy results from a mutation in the CNBP gene know as a tetranucleotide repeat expansion. This mutation increases in size of the repeated CCTG segment in the CNBP gene. People with type 2 myotonic dystrophy have from 75 to more than 11,000 CCTG repeats.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Repeat-Primed PCR (QP-PCR)

NeuroSURE™ Metabolites: Alpha Aminoadipic Semialdehyde, Cerebrospinal Fluid (CSF) 620037

CPT 84275
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 10 - 14 days
Specimen Cerebrospinal fluid (CSF)
Volume 1.0 mL
Minimum Volume 0.5 mL
Container Sterile screw capped vial
Collection Collect entire sample into a single sterile tube.
Storage Instructions Freeze as soon as possible after collection.
Stability

Temperature	Period
Room temperature	Unstable (stability provided by manufacturer or literature reference)
Refrigerated	24 hours (stability provided by manufacturer or literature reference)
Frozen	-20°C = 72 hours; -80°C = Indefinite (stability provided by manufacturer or literature reference)
Freeze/thaw cycles	None (stability provided by manufacturer or literature reference)

Causes for Rejection Bloody CSF; received thawed
Use CSF Alpha aminoadipic semialdehyde is useful for diagnosing pyridoxine-dependent seizures (PDS) and folinic acid-responsive seizures (FRS). This testing may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing testing). Pyridoxine dependent seizures is a genetic disorder characterized by seizures in neonates or infants up to 3 years of age, which in general, respond to a pharmacologic dose of pyridoxine (vitamin B6). Alpha - aminoadipic semialdehyde dehydrogenase (antiquin) deficiency is the underlying defect. Piperideine-6- Carboxylate (P6C) is the cyclic isomer of alpha aminoadipic semialdehyde (AASA) and the equilibrium between P6C and Alpha aminoadipic semialdehyde is pH dependent. Folinic responsive seizures and PDS are allelic, and caused by mutations in the ALDH7A1 gene. Biochemical testing should be done prior to gene sequencing, and can be done regardless of pyridoxine therapy.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Liquid chromatography/tandem mass spectrometry (LC/MS-MS)

NeuroSURE™ Metabolites: 5-Methyltetrahydrofolate (CSF) 620008

CPT 82542
Expected Turnaround Time 10 - 14 days
Specimen Cerebrospinal fluid (CSF)
Volume 1.0 mL
Minimum Volume 0.5 mL
Container Sterile screw capped vial
Collection Collect entire sample into a single sterile tube.
Storage Instructions Freeze as soon as possible after collection.
Stability

Temperature	Period
Room temperature	Unstable (stability provided by manufacturer or literature reference)
Refrigerated	24 hours (stability provided by manufacturer or literature reference)
Frozen	-20°C = 72 hours; -80°C = Indefinite (stability provided by manufacturer or literature reference)

Causes for Rejection Bloody CSF; received thawed
Use CSF 5-Methyltetrahydrofolate (NC01) is useful for determining a deficiency of folate in the central nervous system. CSF 5-Methyltetrahydrofolate (NC01) may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing Testing). 5-Methyltetrahydrofolate (5-MTFH) is the predominant form of folate in cerebrospinal fluid (CSF). Low CSF 5-MTHF levels are associated with inborn errors of metabolism affecting folate metabolism, dietary deficiency of folate, cerebral folate syndromes and Kearns-Sayre syndrome. Symptoms may include, anemia, developmental delay, seizures, depression and dementia.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology High-pressure liquid chromatography (HPLC)

NeuroSURE™ Metabolites: Neopterin (CSF) 620009

CPT 82542
Expected Turnaround Time 10 - 14 days
Specimen Cerebrospinal fluid (CSF)
Volume 1.0 mL
Minimum Volume 0.5 mL
Container Sterile screw capped vial
Collection Collect entire sample into a single sterile tube.
Storage Instructions Freeze as soon as possible after collection.
Stability

Temperature	Period
Room temperature	Unstable (stability provided by manufacturer or literature reference)
Refrigerated	24 hours (stability provided by manufacturer or literature reference)
Frozen	-20°C = 72 hours; -80°C = Indefinite (stability provided by manufacturer or literature reference)

Causes for Rejection Bloody CSF; received thawed
Use CSF Neopterin (NC02) is useful for diagnosis of certain disorders of neurotransmitter metabolism. Neopterin is also useful as a marker for immune system stimulation. This testing may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing testing). Tetrahydrobiopterin (BH4) serves as a cofactor fot the hydroxylation of phenylalanine and in the biosynthesis of biogenic amines. Deficiency of BH4 may occur as a result of mutations causing a reduction in on of the three biosynthetic enzymes, guanosine triphosphate cyclohydrolase, 6-pyruvoyl-tetrahydropterin synthase, sepiapterin reductase, or the two regenerating enzymes, pterin-4-carbinolamine dehydratase, and dihydropteridine reductase. Defects in BH4 metabolism can result in hyperphenylalaninemia and deficiency of the neurotransmitters dopamine and serotonin. Changes in CSF neopterin may also occur in deficiency of the BH4 synthesis pathway. Disorders of BH4 metabolism are characterized by a wide range of symptoms that may include devleopmental delay, mental disability, behavorial distrubances, dystonia, Parkinsonian symptoms, gait distrubances, speech delay, psychomotor retardation and ptosis. In guanosine triphosphate (GTP) cyclohydrolase I (GTPCH) deficiency, neopterin and biopterin levels are low. In 6-pyruvoyl- tetrahydropterin synthesis (PTPS) deficiency, the neopterin level is high and the

biopterin level is low. In dihydropteridine reductase (DHPR) deficiency, the neopterin level is in the reference range or slightly increased, and the biopterin level is high. In carbinolamine-4a-dehydratase (PCD) deficiency, the neopterin level is initially high, the biopterin level is in the subnormal range, and a primapterin level (7-substitued biopterin) is present. Neopterin is released from macrophages and astrocytes following stimulation by interferon gamma. It is a non-specific marker for immune system stimualtion. An elevation in cerebrospinal fluid can be useful to help differenciate between immune problems and other causes of neurological disease.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology High-pressure liquid chromatography (HPLC)

NeuroSURE™ Metabolites: Neopterin/Tetrahydrobiopterin (CSF) 620010

CPT 82542

Expected Turnaround Time 10 - 14 days

Specimen Cerebrospinal fluid (CSF)

Volume 1.0 mL

Minimum Volume 0.5 mL

Container Sterile screw capped vial

Collection Collect entire sample into a single sterile tube.

Storage Instructions Freeze as soon as possible after collection.

Stability

Temperature	Period
Room temperature	Unstable (stability provided by manufacturer or literature reference)
Refrigerated	24 hours (stability provided by manufacturer or literature reference)
Frozen	-20°C = 72 hours; -80°C = Indefinite (stability provided by manufacturer or literature reference)

Causes for Rejection Bloody CSF; received thawed

Use CSF Neopterin/Tetrahydrobiopterin (NC03) is useful for diagnosis of certain disorders of neurotransmitter metabolism. This testing may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing testing). Tetrahydrobiopterin (BH4) serves as a cofactor for the hydroxylation of phenylalanine and in the biosynthesis of biogenic amines. Deficiency of BH4 may occur as a result of mutations causing a reduction in one of the three biosynthetic enzymes, guanosine triphosphate cyclohydrolase. 6-pyruvoyl-tetrahydropterin synthase, sepiapterin reductase, or the two regenerating enzymes, pterin-4-carbinolamine dehydratase, and dihydropteridine reductase. Defects in BH4 metabolism can result in hyperphenylalaninemia and deficiency of the neurotransmitters dopamine and serotonin. Changes in CSF neopterin may also occur in deficiency of the BH4 synthesis pathway. Disorders of BH4 metabolism are characterized by a wide range of symptoms that may include developmental delay, mental disability, behavioral disturbances, dystonia, Parkinsonian symptoms, gait disturbances, speech delay, psychomotor retardation and ptosis.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology High-pressure liquid chromatography (HPLC)

NeuroSURE™ Metabolites: Neurotransmitter Metabolites (5 HIAA, HVA, 30MD) (CSF) 620011

CPT 82542; 83150; 83497

Expected Turnaround Time 10 - 14 days

Specimen Cerebrospinal fluid (CSF)

Volume 0.5 mL

Minimum Volume 0.25 mL

Container Sterile screw capped vial

Collection Collect from first drops of lumbar puncture into single sterile tube. Do not aliquot from a pooled sample.

Storage Instructions Freeze as soon as possible.

Stability

Temperature	Period
Room temperature	Unstable (stability provided by manufacturer or literature reference)
Refrigerated	24 hours (stability provided by manufacturer or literature reference)
Frozen	-20°C = 72 hours; -80°C = Indefinite (stability provided by manufacturer or literature reference)

Causes for Rejection Bloody CSF; received thawed

Use CSF Neurotransmitter Metabolites (5HIAA, HVA, 3OMD) (NC04) is useful for diagnosis of certain disorders of neurotransmitter metabolism. This testing may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing testing). Monoamine metabolite testing includes homovanillic acid (HVA), 3-O-methyl-Dopa (3-OMD), and 5-hydroxyindole acetic acid (5-HIAA). This test is useful in diagnosing pediatric neurotransmitter diseases affecting dopamine and serotonin metabolism in the brain. Inborn errors of metabolism and and various drugs may lead to severe imbalances and disturbances in these neurotransmitter systems that are reflected by changes in the concentration of monoamines metabolites in CSF. Primary inherited defects involve deficiencies in tyrosine and tryptophan hydroxylase, aromatic amino acid decarboxylase, monoamine oxidase, dopamine beta hydroxylase and the dopamine transwporter. Other defects in the biopterin synthesis pathway may also affect dopamine and serotonin metabolism. These disorders are characterized by a wide range of symptoms that may include developmental delay, mental disability, behavioral disturbances, dystonia, seizures, encephalopathy, athetosis and ptosis.

Limitations Qualitative results if received in pooled sample.

This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology High-pressure liquid chromatography (HPLC)

NeuroSURE™ Metabolites: Pyridoxal 5′-phosphate, Cerebrospinal Fluid (CSF) 620034

CPT 84207

Expected Turnaround Time 10 - 14 days

Specimen Cerebrospinal fluid (CSF)

Volume 1.0 mL

Minimum Volume 0.5 mL

Container Sterile screw capped vial

Collection Collect entire sample into a single sterile tube.

Storage Instructions Freeze immediately.

Stability

Temperature	Period
Room temperature	Unstable (stability provided by manufacturer or literature reference)
Refrigerated	Unstable (stability provided by manufacturer or literature reference)
Frozen	-20°C = 72 hours; -80°C = Indefinite (stability provided by manufacturer or literature reference)
Freeze/thaw cycles	None (stability provided by manufacturer or literature reference)

Causes for Rejection Bloody CSF; received thawed

Use CSF Pyridoxal 5′-phosphate is useful for diagnosis of disorders leading to low CSF levels of this cofactor. This testing may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (eg. Next Generation Sequencing or Capillary Sequencing testing). Pyridoxal 5′ phosphate (PLP) (a member of the vitamin B6 family) is required as a cofactor for more than 100 different enzymes in the

body. These may involve the metabolism of various neurotransmitters and amino acids. Inadequate PLP may occur due to genetic, nutritional deficiencies as well as reaction with various drugs. Inherited disorders that affect the CSF PLP level include pyriodx(am)ine phosphate oxidase (PNPO) deficiency, alpha amnioadipic semialdehyde dehydrogenase deficiency, hyperprolinermia type 2 and hypophoshatasia due to alkaline phosphatase deficiency.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology High-pressure liquid chromatography (HPLC)

NeuroSURE™ Metabolites: Sialic Acid, Cerebrospinal Fluid (CSF) 620036

CPT 84275

Special Instructions This assay is not currently available in New York state.

Expected Turnaround Time 10 - 14 days

Specimen Cerebrospinal fluid (CSF)

Volume 1.0 mL

Minimum Volume 0.5 mL

Container Sterile screw capped vial

Collection Collect entire sample into a single sterile tube.

Storage Instructions Freeze as soon as possible after collection.

Stability

Temperature	Period
Room temperature	Unstable (stability provided by manufacturer or literature reference)
Refrigerated	24 hours (stability provided by manufacturer or literature reference)
Frozen	-20°C = 72 hours; -80°C = Indefinite (stability provided by manufacturer or literature reference)
Freeze/thaw cycles	None (stability provided by manufacturer or literature reference)

Causes for Rejection Bloody CSF; received thawed

Use CSF Sialic Acid is useful for diagnosing free sialic acid storage diseases. This testing may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing testing). Mutations in the SLC17A5 gene encoding the lysosomal transporter sialin are associated with the free sialic acid storage diseases (SASD): Salla disease (or the Finish type of sialuria), the more severe infantile free sialic acid storage disease (ISSD), and intermediate phenotypes with clinical findings of both Salla disease and ISSD. 1 SASD are characterized by the abnormal retention of free sialic acid in the lysosome (OMIM 604369 and 269920). Patients with SASD usually present with nystagmus, progressive cerebellar ataxia, spasticity, and severe psychomotor delay. Cerebellar ataxia may be the primary symptom. These symptoms are associated with diffuse supratentorial hypomyelination, thin corpus callosum, and cortical and cerebellar atrophy. In some patients, sialic acid increases are indentified only in CSF.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Liquid chromatography/tandem mass spectrometry (LC/MS-MS)

NeuroSURE™ Metabolites: Succinyladenosine, Cerebrospinal Fluid (CSF) 620035

CPT 82542

Expected Turnaround Time 10 - 14 days

Specimen Cerebrospinal fluid (CSF)

Volume 1.0 mL

Minimum Volume 0.5 mL

Container Sterile screw capped vial

Collection Collect entire sample into a single sterile tube.

Storage Instructions Freeze as soon as possible after collection.

Stability

Temperature	Period
Room temperature	Unstable (stability provided by manufacturer or literature reference)
Refrigerated	Unstable (stability provided by manufacturer or literature reference)
Frozen	-20°C = 72 hours; -80°C = Indefinite (stability provided by manufacturer or literature reference)
Freeze/thaw cycles	None (stability provided by manufacturer or literature reference)

Causes for Rejection Bloody CSF; received thawed

Use CSF Succinyladenosine is useful for diagnosing Adenylosuccinate Lyase Deficiency. This testing may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing testing). Succinyladenosine is elevated in adenylosuccinate lyase (ADSL) deficiency and results in succinylpurinemic autism, intellectual disability, and, in some cases, growth retardation associated with muscle wasting and epilepsy. Adenylosuccinate lyase is involved in both de novo synthesis of purines and formation of adenosine monophosphate from inosine monophosphate by catalyzing two reactions in AMP biosynthesis: the removal of a fumarate from succinylaminoimidazole carboxamide (SAICA) ribotide to give aminoimidazole carboxamide ribotide (AICA) and removal of fumarate from adenylosuccinate to give AMP. In the absence of ADSL deficiency, succinyladenosine is either not detected or at very low levels in the CSF. Small elevations of succinyladenosine in spinal fluid have been reported in AICA-Ribosiduria (deficiency of AICAR transformylase) a devastating condition involving profound mental retardation, epilepsy, dysmorphic features and congenital blindness. Small elevations are also seen secondary to fumarase deficiency.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology High-pressure liquid chromatography (HPLC)

NeuroSURE™ Metabolites: Thymidine Phosphorylase Enzyme Analysis (Blood) 620038

CPT 82657

Special Instructions This assay is not currently available in New York state.

Expected Turnaround Time 3 weeks

Specimen Whole blood-ACD

Volume 5 mL

Container Yellow-top (ACD) tube

Storage Instructions Ship within 24 hours.

Causes for Rejection Hemolyzed sample; incorrect collection tube; received frozen

Use Thymidine phosphorylase Enzyme Analysis is used for the diagnosis of Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE). Thymidine phosphorylase Enzyme Analysis may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencung testing). MNGIE is an autosomal recessive disorder caused by mutations in the gene encoding thymidine phosphorylase (TP). The disease is characterized clinically by impaired eye movements, gastrointestinal dysmotility, cachexia, peripherl neuropathy, myopathy, and leukoencephalopathy. Molecular genetic studies of MNGIE patients' tissues have reveled mutlitple deletions, depletion, and site-specific point mutations of mitochondrial DNA. TP is a cytosolic enzyme required for nucleoside homeostasis. In MNGIE, TP activity is severely reduced and consequently levels of thymidine and deoxyuridine in plasma are drmatically elevated. MNGIE may benefit from hematopoietic stem cell transplantation.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology High-pressure liquid chromatography (HPLC)

3-O-Methyldopa (Plasma) 620176

CPT 82131
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 10 - 14 days
Specimen Plasma, **frozen**
Volume 1.0 mL
Minimum Volume 0.5 mL
Container Lavender-top (EDTA) tube, green-top (sodium heparin) tube
Collection Collect 2-4 mL blood in sodium heparin (green-top) or EDTA (purple-top) tube.
Storage Instructions Remove plasma and freeze at -20°C. Store frozen at -20°C and ship frozen.
Stability

Temperature	Period
Room temperature	Unstable
Refrigerated	Unstable
Frozen	Indefinitely

Causes for Rejection Thawed sample
Use Aromatic L-amino acid decarboxylase (AADC) is a pyridoxal 5'-phosphate dependent enzyme responsible for the formation of dopamine and serotonin. AADC deficiency is a congenital autosomal recessive metabolic disorder that causes hypotonia, hypokinesia, oculogyric crises, and signs of autonomic dysfunction beginning in infancy. In AADC deficiency, L-dopa accumulates and can be methylated by catechol O-methyltransferase using S-adenosylmethionine as the methyl donor to form 3-O-methyldopa (3-OMD). 3-OMD is more stable than L-dopa and can be detected in blood.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Liquid chromatography/tandem mass spectrometry (LC/MS-MS)

PD-L1 IHC, TECENTRIQ™ TNB 452909

CPT Call client services.
Special Instructions Please provide a copy of the pathology report. Testing will be delayed if the pathology report is not received. Please direct any questions regarding this test to Customer Service at 800-710-1800.
This test number is used for tracking oncology IHC specimens to the laboratory. Bill codes will be added when testing is complete, based on the processes performed in the laboratory.
Specimen Formalin-fixed, paraffin-embedded (FFPE) tissue block **or** slides
Volume At least two unstained slides sectioned at 4 microns, less than two month of sectioning if stored at 15°C - 30°C. Four slides ideal.
Minimum Volume Two unstained slides at 4 microns less than two month of sectioning if stored at 15°C - 30°C.
Container Paraffin block **or** unstained positive charged slides
Collection Paraffin block **or** unstained slides sectioned if stored at 15°C - 30°C for two months age.
Storage Instructions Refrigerate
Causes for Rejection Slides sectioned greater than two month prior to test request and not stored at 15°C - 30°C
Use PD-L1 SP142/TECENTRIQ is validated for use in triple negative breast cancer, urothelial carcinoma, and non-small cell lung cancer (NSCLC) only. If this specimen is not triple negative breast cancer, urothelial carcinoma, or non-small cell lung cancer (NSCLC), the FDA approval for this test is invalidated. The clinical validity of this test for any other tumor type is unknown and the results should therefore be interpreted with caution.
Methodology Immunohistochemistry using Ventana BenchMark Ultra
References

Dong H, Zhu G, Tamada K, Chen L. B7-H1, a third member of the B7 family, co-stimulates T-cell proliferation and interleukin-10 secretion. Nat Med. 1999 Dec;5(12):1365-1369. PubMed 10581077

PMP22 MLPA Deletion/Duplication Analysis 620081

CPT 81324
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use Mutations in the *PMP22* gene cause several forms of a neurological disorder called Charot-Marie-Tooth disease. This disorder damamges the peripheral nerves, which can result in loss of sensation and wasting (atrophy) of muscles in the feet, legs and hands.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Multiplex Ligation-dependent Probe Amplification

Pyruvate (CSF) 620045

CPT 84210
Expected Turnaround Time 10 - 14 days
Specimen Cerebrospinal fluid (CSF)
Volume 1.0 mL
Minimum Volume 0.5 mL
Container Sterile screw capped vial
Collection Collect entire sample into a single sterile tube. Immediately after collection, add a 2:1 ratio (acid:sample) of cold 8% perchloric acid. Vortex for 30 seconds, and place on ice for 5 minutes. Store **frozen** at -20°C and ship **frozen.**
Storage Instructions Freeze as soon as possibe after collection.
Stability

Temperature	Period
Room temperature	Unstable (stability provided by manufacturer or literature reference)
Refrigerated	24 hours (stability provided by manufacturer or literature reference)
Frozen	-20°C = 72 hours; -80°C = Indefinite (stability provided by manufacturer or literature reference)

Causes for Rejection Bloody CSF; received thawed; sample received untreated
Use CSF Pyruvate is useful for investigating possible disorders of mitochondrial, metabolism, when used in conjunction with cerebrospinal fluid lactate collected at the same time to determine the Lactate:Pyruvate ratio. The CSF Lactate:Pyruvate ratio is considered a helpful (not diagnostic) tool in the evaluation of patients with possible disorders of mitochondrial metabolism, especially in patients with neurologic dysfunctin and normal blood Lactate:Pyruvate ratios. Pyruvic acid levels alone have little clinical utility. The Lactate:Pyruvate raio is elevated in several, but not all, mitochondrial respiratory chain disorders. Mitochondrial disorders vary widely in presentation and age of onset. Many mitochondrial disorders have neurologic and myopathic features and may involve multiple organ systems. Determination of lactate, pyruvate, and L:P ratio in cerebrospinal

fluid is helpful in directing attention toward a possible mitochondrial disorder in cases with predominatly neurologic dysfunction and normal blood lactate levels. An elevated Lactate:Pyruvate ratio may indicate inherited disorders of the respiratory chain complex, tricarboxylic acid cycle disorders and pyruvate carboxylase deficiency. Respiratory chain defects usually result in Lactate:Pyruvate ratios >20. A low Lactate: Pyruvate ratio (disproportionately elevated pyruvic acid) may indicate an inherited disorder of pyruvate metabolism. Defects of the pyruvate dehydrogenase complex result in Lactate:Pyruvate ratios <10. The Lactate:Pyruvate ratio is characteristically normal in other patients. An artifactually high ratio can be found in acutely ill patients.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Enzyme/UV

SCA1 (ATXN1) Genetic Testing (Repeat Expansion) . . . 620114

CPT 81178

Special Instructions This assay is not currently available in New York state.

Expected Turnaround Time 2 - 4 weeks

Specimen Whole blood

Volume 4 mL

Minimum Volume 1 mL

Container Lavender-top (EDTA) tube

Collection Draw blood into EDTA tube.

Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.

Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube

Use Spinocerebellar ataxias (SCAs), and episodic ataxias are the most common types of ADCAs. SCAs are numbered based upon their time of identification. SCA3 is the most common type of SCA worldwide, followed by SCA2, SCA1, and SCA6. Some of the complicated forms have not been given a SCA number, like Dentatorubral Pallidoluysian Atrophy (DRPLA). Anticipation can be observed in the autosomal dominant ataxias in which CAG trinucleotide repeats occur. Anticipation results from expansion in the number of CAG repeats with transmission of the gene to subsequent generations. Most ADCAs have an overlap in clinical clinical presentation, which makes it hard to differentiate. The most frequent clinical symptoms in all ADCAs are progressive adult-onset gait ataxia (often with hand dysmetria), and dysarthria associated with cerebellar atrophy. The episodic ataxias are characterized by periods of unsteady gait and often associated with nystagmus or or dysarthria. Myokymia, vertigo, or hearing loss may occur in some of the subtypes. Permanent ataxia and even cerebellar atrophy may result late in the disease course.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Repeat-Primed PCR (QP-PCR)

SCA2 (ATXN2) Genetic Testing (Repeat Expansion) . . . 620118

CPT 81179

Special Instructions This assay is not currently available in New York state.

Expected Turnaround Time 2 - 4 weeks

Specimen Whole blood

Volume 4 mL

Minimum Volume 1 mL

Container Lavender-top (EDTA) tube

Collection Draw blood into EDTA tube.

Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.

Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube

Use Spinocerebellar ataxias (SCAs), and episodic ataxias are the most common types of ADCAs. SCAs are numbered based upon their time of identification. SCA3 is the most common type of SCA worldwide, followed by SCA2, SCA1, and SCA6. Some of the complicated forms have not been given a SCA number, like Dentatorubral Pallidoluysian Atrophy (DRPLA). Anticipation can be observed in the autosomal dominant ataxias in which CAG trinucleotide repeats occur. Anticipation results from expansion in the number of CAG repeats with transmission of the gene to subsequent generations. Most ADCAs have an overlap in clinical presentation, which makes it hard to differentiate. The most frequent clinical symptoms in all ADCAs are progressive adult-onset gait ataxia (often with hand dysmetria), and dysarthria associated with cerebellar atrophy. The episodic ataxias are characterized by periods of unsteady gait and often associated with nystagmus or dysarthria. Myokymia, vertigo, or hearing loss may occur in some of the subtypes. Permanent ataxia and even cerebellar atrophy may result late in the disease course.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Repeat-Primed PCR (QP-PCR)

SCA3 (ATXN3) Genetic Testing (Repeat Expansion) . . . 620123

CPT 81180

Special Instructions This assay is not currently available in New York state.

Expected Turnaround Time 2 - 4 weeks

Specimen Whole blood

Volume 4 mL

Minimum Volume 1 mL

Container Lavender-top (EDTA) tube

Collection Draw blood into EDTA tube.

Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.

Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube

Use Spinocerebellar ataxias (SCAs), and episodic ataxias are the most common types of ADCAs. SCAs are numbered based upon upon their time of identification. SCA3 is the most common type of SCA worldwide, followed by SCA2, SCA1, and SCA6. Some of the complicated forms have not been given a SCA number, like Dentatorubral Pallidoluysian Atrophy (DRPLA). Anticipation can be observed in the autosomal dominant ataxias in which CAG trinucleotide repeats occur. Anticipation results from expansion in the number of CAG repeats with transmission of the gene to subsequent generations. Most ADCAs have an overlap in clinical presentation, which makes it hard to differentiate. The most frequent clinical symptoms in all ADCAs are progressive adult-onset gait ataxia (often with hand dysmetria), and dysarthria associated with cerebellar atrophy. The episodic ataxias are characterized by periods of unsteady gait and often associated with nystagmus or dysarthria. Myokymia, vertigo, or hearing loss may occur in some of the subtypes. Permanent ataxia and even cerebellar atrophy may result late in the disease course.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Repeat-Primed PCR (QP-PCR)

SCA6 (CACNA1A) Genetic Testing (Repeat Expansion) 620127

CPT 81184
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use Spinocerebellar ataxias (SCAs), and episodic ataxias are the most common types of ADCAs. SCAs are numbered based upon their time of identification. SCA3 is the most common type of SCA worldwide, followed by SCA2, SCA1, and SCA6. Some of the complicated forms have not been given a SCA number, like Dentatorubral Pallidoluysian Atrophy (DRPLA). Anticipation can be observed in the autosomal dominant ataxias in which CAG trinucleotide repeats occur. Anticipation results from expansion in the number of CAG repeats with transmission of the gene to subsequent generations. Most ADCAs have an overlap in clinical presentation, which makes it hard to differentiate. The most frequent clinical symptoms in all ADCAs are progressive adult-onset gait ataxia (often with hand dysmetria), and dysarthria associated with cerebellar atrophy. The episodic ataxias are characterized by periods of unsteady gait and often associated with nystagmus or dysarthria. Myokymia, vertigo, or hearing loss may occur in some of the subtypes. Permanent ataxia and even cerebellar atrophy may result late in the disease course.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Repeat-Primed PCR (QP-PCR)

SCA7 (ATXN7) Genetic Testing (Repeat Expansion) . . . 620131

CPT 81181
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use Spinocerebellar ataxias (SCAs), and episodic ataxias are the most common types of ADCAs. SCAs are numbered based upon their time of identification. SCA3 is the most common type of SCA worldwide, followed by SCA2, SCA1, and SCA6. Some of the complicated forms have not been given a SCA number, like Dentatorubral Pallidoluysian Atrophy (DRPLA). Anticipation can be observed in the autosomal dominant ataxias in which CAG trinucleotide repeats occur. Anticipation results from expansion in the number of CAG repeats with transmission of the gene to subsequent generations. Most ADCAs have an overlap in clinical presentation, which makes it hard to differentiate. The most frequent clinical symptoms in all ADCAs are progressive adult-onset gait ataxia (often with hand dysmetria), and dysarthria associated with cerebellar atrophy. The episodic ataxias are characterized by periods of unsteady gait and often associated with nystagmus or dysarthria. Myokymia, vertigo, or hearing loss may occur in some of the subtypes. Permanent ataxia and even cerebellar atrophy may result late in the disease course.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Repeat-Primed PCR (QP-PCR)

SCA8 (ATXN8) Genetic Testing (Repeat Expansion) . . . 620135

CPT 81182
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use Spinocerebellar ataxias (SCAs), and episodic ataxias are the most common types of ADCAs. SCAs are numbered based upon their time of identification. SCA3 is the most common type of SCA worldwide, followed by SCA2, SCA1, and SCA6. Some of the complicated forms have not been given a SCA number, like Dentatorubral Pallidoluysian Atrophy (DRPLA). Anticipation can be observed in the autosomal dominant ataxias in which CAG trinucleotide repeats occur. Anticipation results from expansion in the number of CAG repeats with transmission of the gene to subsequent generations. Most ADCAs have an overlap in clinical presentation, which makes it hard to differentiate. The most frequent clinical symptoms in all ADCAs are progressive adult-onset gait ataxia (often with hand dysmetria), and dysarthria associated with cerebellar atrophy. The episodic ataxias are characterized by periods of unsteady gait and often associated with nystagmus or dysarthria. Myokymia, vertigo, or hearing loss may occur in some of the subtypes. Permanent ataxia and even cerebellar atrophy may result late in the disease course.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Repeat-Primed PCR (QP-PCR)

SCA10 (ATXN10) Genetic Testing (Repeat Expansion) 620140

CPT 81183
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.

Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use Spinocerebellar ataxias (SCAs), and episodic ataxias are the most common types of ADCAs. SCAs are numbered based upon their time of identification. SCA3 is the most common type of SCA worldwide, followed by SCA2, SCA1, and SCA6. Some of the complicated forms have not been given a SCA number, like Dentatorubral Pallidoluysian Atrophy (DRPLA). Anticipation can be observed in the autosomal dominant ataxias in which CAG trinucleotide repeats occur. Anticipation results from expansion in the number of CAG repeats with transmission of the gene to subsequent generations. Most ADCAs have an overlap in clinical presentation, which makes it hard to differentiate. The most frequent clinical symptoms in all ADCAs are progressive adult-onset gait ataxia (often with hand dysmetria), and dysarthria associated with cerebellar atrophy. The episodic ataxias are characterized by periods of unsteady gait and often associated with nystagmus or dysarthria. Myokymia, vertigo, or hearing loss may occur in some of the subtypes. Permanent ataxia and even cerebellar atrophy may result late in the disease course.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Repeat-Primed PCR (QP-PCR)

SCA12 (PPP2R2B) Genetic Testing (Repeat Expansion) 620144

CPT 81343
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use Spinocerebellar ataxias (SCAs), and episodic ataxias are the most common types of ADCAs. SCAs are numbered based upon their time of identification. SCA3 is the most common type of SCA worldwide, followed by SCA2, SCA1, and SCA6. Some of the complicated forms have not been given a SCA number, like Dentatorubral Pallidoluysian Atrophy (DRPLA). Anticipation can be observed in the autosomal dominant ataxias in which CAG trinucleotide repeats occur. Anticipation results from expansion in the number of CAG repeats with transmission of the gene to subsequent generations. Most ADCAs have an overlap in clinical presentation, which makes it hard to differentiate. The most frequent clinical symptoms in all ADCAs are progressive adult-onset gait ataxia (often with hand dysmetria), and dysarthria associated with cerebellar atrophy. The episodic ataxias are characterized by periods of unsteady gait and often associated with nystagmus or dysarthria. Myokymia, vertigo, or hearing loss may occur in some of the subtypes. Permanent ataxia and even cerebellar atrophy may result late in the disease course.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Repeat-Primed PCR (QP-PCR)

SCA17 (TBP) Genetic Testing (Repeat Expansion) 620149

CPT 81344
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use Spinocerebellar ataxias (SCAs), and episodic ataxias are the most common types of ADCAs. SCAs are numbered based upon their time of identification. SCA3 is the most common type of SCA worldwide, followed by SCA2, SCA1, and SCA6. Some of the complicated forms have not been given a SCA number, like Dentatorubral Pallidoluysian Atrophy (DRPLA). Anticipation can be observed in the autosomal dominant ataxias in which CAG trinucleotide repeats occur. Anticipation results from expansion in the number of CAG repeats with transmission of the gene to subsequent generations. Most ADCAs have an overlap in clinical presentation, which makes it hard to differentiate. The most frequent clinical symptoms in all ADCAs are progressive adult-onset gait ataxia (often with hand dysmetria), and dysarthria associated with cerebellar atrophy. The episodic ataxias are characterized by periods of unsteady gait and often associated with nystagmus or dysarthria. Myokymia, vertigo, or hearing loss may occur in some of the subtypes. Permanent ataxia and even cerebellar atrophy may result late in the disease course.
Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
Methodology Repeat-Primed PCR (QP-PCR)

SCA36 (NOP56) Genetic Testing (Repeat Expansion) 620154

CPT 81479
Special Instructions This assay is not currently available in New York state.
Expected Turnaround Time 2 - 4 weeks
Specimen Whole blood
Volume 4 mL
Minimum Volume 1 mL
Container Lavender-top (EDTA) tube
Collection Draw blood into EDTA tube.
Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.
Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube
Use Spinocerebellar ataxias (SCAs), and episodic ataxias are the most common types of ADCAs. SCAs are numbered based upon their time

of identification. SCA3 is the most common type of SCA worldwide, followed by SCA2, SCA1, and SCA6. Some of the complicated forms have not been given a SCA number, like Dentatorubral Pallidoluysian Atrophy (DRPLA). Anticipation can be observed in the autosomal dominant ataxias in which CAG trinucleotide repeats occur. Anticipation results from expansion in the number of CAG repeats with transmission of the gene to subsequent generations. Most ADCAs have an overlap in clinical presentation, which makes it hard to differentiate. The most frequent clinical symptoms in all ADCAs are progressive adult-onset gait ataxia (often with hand dysmetria), and dysarthria associated with cerebellar atrophy. The episodic ataxias are characterized by periods of unsteady gait and often associated with nystagmus or dysarthria. Myokymia, vertigo, or hearing loss may occur in some of the subtypes. Permanent ataxia and even cerebellar atrophy may result late in the disease course.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Repeat-Primed PCR (QP-PCR)

Spinal Muscular Atrophy (*SMN1/SMN2*) MLPA Deletion/ Duplication Analysis 620091

CPT 81329

Special Instructions This assay is not currently available in New York state.

Expected Turnaround Time 2 - 4 weeks

Specimen Whole blood

Volume 4 mL

Minimum Volume 1 mL

Container Lavender-top (EDTA) tube

Collection Draw blood into EDTA tube.

Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.

Stability

Temperature	Period
Room temperature	5 days
Refrigerated	5 days
Frozen	Do **not** freeze

Causes for Rejection Frozen blood EDTA tube

Use Mutations in the *SMN1* gene cause all types of spinal muscular atrophy described above. The number of copies of the *SMN2* gene modifies the severity of the condition and helps determine which type develops.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Multiplex Ligation-dependent Probe Amplification

Thymidine and Deoxyuridine Analytes (Plasma) 620173

CPT 82017; 82570

Special Instructions This assay is not currently available in New York state.

Expected Turnaround Time 10 - 14 days

Specimen Plasma, **frozen**

Volume 1.0 mL

Minimum Volume 0.5 mL

Container Green-top (heparin) tube; lavender-top (EDTA) tube

Collection Collect 2-4 mL blood in sodium heparin (green-top) or EDTA (purple-top) tube.

Storage Instructions Remove plasma and freeze at -20°C. Store **frozen** at -20°C and ship **frozen.**

Stability

Temperature	Period
Room temperature	Unstable
Refrigerated	Unstable
Frozen	Indefinitely
Freeze/thaw cycles	Indefinitely

Causes for Rejection Thawed sample

Use Plasma Thymidine/Deoxyuridine analyte is used for diagnosis of Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE). Thymidine phosphorylase Enzyme Analysis (ENZ06) may also be used for assessment of Variants of Uncertain Significance (VUS) identified during genetic testing (e.g. Next Generation Sequencing or Capillary Sequencing testing). MNGIE is an autosomal recessive disorder caused by mutations in the gene encoding thymidine phosphorylase (TP). The disease is characterized clinically by impaired eye movements, gastrointestinal dysmotility, cachexia, peripheral neuropathy, myopathy and leukoencephalopathy. Molecular genetic studies of MNGIE patients\tissues have revealed multiple deletions, depletion, and site-specific point mutations of mitochrondrial DNA. TP is a cytosolic enzyme required for nucleoside homeostatis. In MNGIE, TP activity is severely reduced and consequently levels of thymidine and deoxyuridine in plasma are dramatically elevated. MNGIE patients may benefit from hematopoietic stem cell transplantation.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology High-pressure liquid chromatography (HPLC)

TMAO (Trimethylamine N-oxide) 123413

CPT 84999

Special Instructions This assay is not approved for patients of New York State physicians.

Specimen Spun NMR LipoTube, shipped refrigerated (preferred)

Volume 1 mL

Minimum Volume 0.5 mL

Container NMR LipoTube (black-and-yellow-top tube)

Collection Keep NMR LipoTube (black-and-yellow-top tube) upright at room temperature for 30 minutes and allow to clot. Centrifuge at 1800 to 2200g for 10 to 15 minutes immediately after clotting. If the sample cannot be centrifuged immediately, it must be refrigerated at (2°C to 8°C) and centrifuged within 24 hours of collection. The NMR tube should then be stored at (2°C to 8°C) until shipped. Do **not** open NMR LipoTube. Serum drawn in gel-barrier collection tubes other than the NMR LipoTube should not be used.

Storage Instructions Refrigerate

Stability

Temperature	Period
Room temperature	14 days
Refrigerated	14 days
Frozen	14 days
Freeze/thaw cycles	Stable x3

Patient Preparation TMAO levels are lower in humans who follow a vegetarian or vegan diet than in omnivores.[3] Because TMA and TMAO are naturally abundant in some fish,[7,8] patients should fast overnight and refrain from consuming fish and other marine food items the day before the blood draw. Fasting for 10 to 12 hours is recommended.

Causes for Rejection Unspun LipoTube; serum specimen drawn in gel-barrier collection tube other than the NMR LipoTube; sample older than 14 days; plasma samples

Use High levels of TMAO have been associated with an increased risk of heart disease.[1]

The TMAO test may be used as (1) an aid in the assessment of risk for cardiovascular disease (CVD), independent of established risk factors, (2) an aid in the determination of altered gut microbiome (gut dysbiosis) in individuals who may benefit from intensive dietary intervention, and (3) a monitor therapy aimed at reducing TMAO concentrations.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Nuclear magnetic resonance (NMR)

Additional Information TMAO is a dietary metabolite produced by a pathway involving gut microbiota. TMAO concentrations increase in the blood after ingestion of dietary choline and L-carnitine, which are abundant in meat, eggs, liver, and wheat germ and energy drinks. Choline and L-carnitine are metabolized in the gut by microbiota to form trimethylamine (TMA), which is subsequently oxidized in the liver into TMAO by flavin monooxygenases (FMOs). TMAO concentrations have been shown to be reduced in animals and humans treated with broad-spectrum oral antibiotics confirming the requirement for gut bacteria in the formation of TMA and TMAO.[2-6] TMAO has been hypothesized to promote atherosclerosis by upregulating macro-phage scavenger receptor activity and downregulating bile acid synthesis which together reduce reverse cholesterol transport.[2-6]

Footnotes

1. Garcia E, Wolak-Dinsmore J, Wang Z, et al. NMR quantification of trimethylamine-N-oxide in human serum and plasma in the clinical laboratory setting. *Clin. Biochem.* 2017 Nov;50(16-17):947-955. PubMed 28624482

2. Wang Z, Klipfell E, Bennett BJ, et al. Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. *Nature.* 2011 Apr 7;472(7341):57-63. PubMed 21475195

3. Koeth RA, Wang Z, Levison BS, et al. Intestinal microbiota metabolism of l-carnitine, a nutrient in red meat, promotes atherosclerosis. *Nat Med*. 2013 May;19(5):576-585. PubMed 23563705

4. Tang WH, Wang Z, Levison BS, et al. Intestinal microbial metabolism of phosphatidylcholine and cardiovascular risk. *New Eng J Med.* 2013 Apr 25;368(17):1575-1584. PubMed 23614584

5. Zhu W, Gregory JC, Org E, et al. Gut Microbial Metabolite TMAO Enhances Platelet Hyperreactivity and Thrombosis Risk. *Cell.* 2016 Mar 24;165(1):111-124. PubMed 26972052

6. Senthong V, Li XS, Hudec T, et al. Plasma Trimethylamine N-Oxide, a Gut Microbe-Generated Phosphatidylcholine Metabolite, Is Associated With Atherosclerotic Burden. *J Am Coll Cardiol.* 2016 Jun 7;67(22):2620-2628. PubMed 27256833

7. Lundstrom RC, Racicot LD. Gas chromatographic determination of dimethylamine and trimethylamine in seafoods. *J Assoc Off Anal Chem.* 1983 Sep;66(5):1158-1163. PubMed 6630129

8. Svensson BG, Akesson B, Nilsson A, Paulsson K. Urinary excretion of methylamines in men with varying intake of fish from the Baltic Sea. *J Toxicol Environ Health.* 1994 Apr;41(4):411-420. PubMed 8145282

Whole Exome Sequencing - DUO 620023

CPT 81415; 81416

Special Instructions This assay is not currently available in New York state. Samples must be accompanied by both a consent form and clinical questionnaire and/or supporting clinical documents or they will not be processed.

Expected Turnaround Time 2 - 4 weeks

Specimen Whole blood

Volume 4 mL

Container Lavender-top (EDTA) tube

Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.

Causes for Rejection Frozen blood EDTA tube

Use Whole Exome Sequencing (WES) is a genetic test used to identify a heritable cause of a disorder. WES searches through all coding regions of all genes currently identified; thus, it has a higher chance to find the cause of a heritable disease. WES can be used if a patient has symptoms, which, after exhaustive testing, cannot be linked to a diagnosis and corrective treatment is necessary to change the prognosis. WES can also be used if, upon clinical presentation, multiple disease states may be suspected and a clinician wishes to improve his/her testing approach. Once a genetic variant has been identified, this information can then be linked back to the phenotype of the patient, which will improve the pathway to a correct diagnosis and a suitable treatment plan can be administered. DUO testing consists of a proband or patient sample, and one biological parent or family member in the case that both parents are not available for testing.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Whole Exome Sequencing

Whole Exome Sequencing - Proband Only 620024

CPT 81415

Special Instructions This assay is not currently available in New York state. Samples must be accompanied by both a consent form and clinical questionnaire and/or supporting clinical documents or they will not be processed.

Expected Turnaround Time 2 - 4 weeks

Specimen Whole blood

Volume 4 mL

Container Lavender-top (EDTA) tube

Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.

Causes for Rejection Frozen blood EDTA tube

Use Whole Exome Sequencing (WES) is a genetic test used to identify a heritable cause of a disorder. WES searches through all coding regions of all genes currently identified; thus, it has a higher chance to find the cause of a heritable disease. WES can be used if a patient has symptoms, which, after exhaustive testing, cannot be linked to a diagnosis and corrective treatment is necessary to change the prognosis. WES can also be used if, upon clinical presentation, multiple disease states may be suspected and a clinician wishes to improve his/her testing approach. Once a genetic variant has been identified, this information can then be linked back to the phenotype of the patient, which will improve the pathway to a correct diagnosis and a suitable treatment plan can be administered. Proband Only testing is exome sequencing for the patient only. Proband-only samples are acceptable when parental or other family member samples are not available.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Whole Exome Sequencing

Whole Exome Sequencing - TRIO 620022

CPT 81415; 81416(x2)

Special Instructions This assay is not currently available in New York state. Samples must be accompanied by both a consent form and clinical questionnaire and/or supporting clinical documents or they will not be processed.

Expected Turnaround Time 2 - 4 weeks

Specimen Whole blood

Volume 4 mL

Container Lavender-top (EDTA) tube

Storage Instructions Ship ASAP, but stable up to 5 days post-collection at room temperature. Do **not** freeze.

Causes for Rejection Frozen blood EDTA tube

Use Whole Exome Sequencing (WES) is a genetic test used to identify a heritable cause of a disorder. WES searches through all coding regions of all genes currently identified; thus, it has a higher chance to find the cause of a heritable disease. WES can be used if a patient has symptoms, which, after exhaustive testing, cannot be linked to a diagnosis and corrective treatment is necessary to change the prognosis. WES can also be used if, upon clinical presentation, multiple disease states may be suspected and a clinician wishes to improve his/her testing approach. Once a genetic variant has been identified, this information can then be linked back to the phenotype of the patient, which will improve the pathway to a correct diagnosis and a suitable treatment plan can be administered. TRIO testing consists of a proband or patient sample, and both biological parents. In the case both parents are not available for testing, up to two family member samples are also accepted. Trios are preferred for better diagnostic sensitivity.

Limitations This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

Methodology Whole Exome Sequencing

Special Announcement

ICD-10-CM Diagnosis Code Updates: October 1, 2019

The annual ICD-10-CM coding update is effective for dates of service on or after October 1, 2019.

The following list contains ICD-10-CM diagnosis codes that are invalid after September 30, 2019. These codes must be provided at the highest level of specificity in order to be valid codes as of October 1, 2019. For a complete list of diagnosis code updates, please visit the following website: https://www.cms.gov/Medicare/Coding/ICD10/2020-ICD-10-CM.html.

ICD-10-CM Diagnosis Codes Invalid After September 30, 2019	
Description	**Diagnosis Code**
Adenosine deaminase [ADA] deficiency	D81.3
Vertigo of central origin, right ear	H81.41
Vertigo of central origin, left ear	H81.42
Vertigo of central origin, bilateral	H81.43
Vertigo of central origin, unspecified ear	H81.49
Persistent atrial fibrillation	I48.1
Chronic atrial fibrillation	I48.2
Congenital talipes equinovarus	Q66.Ø
Congenital talipes calcaneovarus	Q66.1
Congenital metatarsus (primus) varus	Q66.21
Congenital metatarsus adductus	Q66.22
Other congenital varus deformities of feet	Q66.3
Congenital talipes calcaneovalgus	Q66.4
Congenital pes cavus	Q66.7
Congenital deformity of feet, unspecified	Q66.9
Ehlers-Danlos syndromes	Q79.6
Congenital malformation syndromes predominantly associated with short stature	Q87.1
Abnormal findings on cytological and histological examination of urine	R82.8
Heatstroke and sunstroke	T67.Ø

Updates to the *Directory of Services and Interpretive Guide (DoS)*

Test Name	Test No.	Field/Change (Only fields that change are included here.)
Adult Acute Lymphoblastic Leukemia (ALL) Profile, FISH	**511077**	**Specimen** Blood, bone marrow, CSF, fixed-cell pellet from a cytogenetic analysis, slide with metaphase and/or interphase nuclei **or** bone marrow touch preparation slides are acceptable for testing. **Volume** 10 mL blood (pediatric), 3 mL bone marrow, fixed-cell pellet from a cytogenetic analysis, 8 slides with metaphase and/or interphase nuclei **or** 8 touch preparation slides. **Minimum Volume** 5 mL blood (pediatric), 1 mL bone marrow, fixed-cell pellet from a cytogenetic analysis, 4 slides with metaphase and/or interphase nuclei **or** 4 touch preparation slides. (**Note:** Minimum volumes may **not** allow for repeat testing.) **Container** Green-top (sodium heparin) tube; pediatric Vacutainer® is optimal **or** lavender-top (EDTA) tube (suboptimal). Adjust tube size to sample volume to avoid heparin toxicity. **Collection** Transport to the testing laboratory at room temperature, use of a cool pack or a LabCorp transport kit is acceptable. Do **not** allow samples to overheat or freeze. **Storage Instructions** Maintain the specimen at either room temperature or refrigerate. Do **not** freeze. **Causes for Rejection** Broken Vacutainer®; broken or stained slides; paraffin blocks; paraffin slides; decalcified bone cores; frozen specimen; quantity not sufficient for analysis **Methodology** Fluorescence in situ hybridization (FISH)
***BCR-ABL1* Kinase Domain Mutation Analysis**	**480510**	Volume 3 to 5 mL whole blood **or** 1 to 2 mL bone marrow
Flunitrazepam, Screen and Confirmation, Urine (Forensic)	**808417**	**Methodology** Initial presumptive testing by immunoassay at a testing threshold of 100 ng/mL; presumptive positives confirmed by chromatography with mass spectrometry
Gastrointestinal Profile, Stool, PCR	**183480**	**Causes for Rejection** Specimen not received in Cary-Blair preservative medium; specimen vial leaking; specimen >96 hours since collection; frozen specimen; rectal swab; specimen below fill line on container (underfilled)
Gastrointestinal Stromal Tumors (GISTs), *PDGFRA* Mutation Analysis	**510860**	**Minimum Volume** 4 unstained slides at 10µM with 2mm x 2mm tumor area
Hemophagocytic Lymphohistiocytosis (HLH) Genetic Panel	**830203**	**Synonyms** (Removed field)
Glutamic Acid Decarboxylase (GAD) Autoantibody	**143008**	**Synonyms** (added) GAD-65 Antibody
Hepatitis B Core Antibody, IgG, IgM, Differentiation	**098418**	**Storage Instructions** Room temperature **Stability** Temperature / Period: Room temperature / 14 days; Refrigerated / 14 days; Frozen / 14 days; Freeze/thaw cycles / Stable x3
Hepatitis B Surface Antibody, Quantitative, HBIG Assessment	**144072**	**Storage Instructions** Room temperature
Hepatitis Be Antigen	**006619**	**Storage Instructions** Refrigerate **Stability** Temperature / Period: Refrigerated / 7 days (stability provided by manufacturer or literature reference); Frozen / 1 year (stability provided by manufacturer or literature reference); Freeze/thaw cycles / Stable x3 (stability provided by manufacturer or literature reference) **Additional Information** HBeAg appears in acute B hepatitis with or shortly after HBsAg, when the patient is most infectious. HBeAg is found only in HBsAg-positive sera. During the HBeAg-positive state, usually three to six weeks, hepatitis B patients are at increased risk of transmitting the virus to their contacts, including babies born during this period. Exposure to serum or body fluid positive for HBeAg and HBsAg is associated with three to five times greater risk of infectivity than when HBsAg positivity occurs alone. Persistence of HBeAg is associated with chronic liver disease.
Hepatitis Profile IV (Hepatitis A and B Immune Status)	**058537**	**Storage Instructions** Room temperature **Stability** Temperature / Period: Room temperature / 14 days; Refrigerated / 14 days; Frozen / 14 days; Freeze/thaw cycles / Stable x3

Note: Please consult the online Directory of Services and Interpretive Guide at https://www.labcorp.com/tests for the most current test information.

Test Name	Test No.	Field/Change (Only fields that change are included here.)
***IDH1/IDH2* Mutation Analysis**	**481484**	**Volume** 3 to 5 mL whole blood, 1 to 2 mL bone marrow, four pre-cut unstained slides at 5 micron with one matching H&E reference slide, **or** formalin-fixed, paraffin-embedded tissue (FFPE) block
Immunoglobulin A (IgA) Heavy and Light Chain (HLC) Pairs, κ and λ With Ratio	**123540**	**Use** (Removed statement announcing tests were made nonorderable. These tests are now orderable again.)
Immunoglobulin G (IgG) Heavy and Light Chain (HLC) Pairs, κ and λ With Ratio	**123550**	
Immunoglobulin M (IgM) Heavy and Light Chain (HLC) Pairs, κ and λ With Ratio	**123560**	
InSight: Prenatal Amnio Aneuploid (FISH) Testing for Chromosomes 13, 18, 21, and XY	**511894**	**Special Instructions** Pertinent medical findings should accompany request for FISH. It is recommended that InSight FISH testing be performed concurrently with prenatal chromosome analysis or microarray. Abnormal results should have banded chromosome confirmation. **Volume** 5 mL amniotic fluid **Storage Instructions** Maintain specimen at room temperature and transport to the cytogenetics laboratory immediately. Do not freeze. Refrigerate if sterility is questioned or if sample cannot be shipped within 24 hours. **Causes for Rejection** Frozen amniotic fluid; wrong specimen type; low specimen volume; specimen in fixative; glass containers and/or rubber stoppered tubes (rubber is toxic to amniocytes); hypocellular specimen **Use** Fluorescence in situ hybridization (FISH), Prenatal aneuploid evaluation FISH targeting numerical changes in 13, 18, 21, X, Y. If specimen volume is too small, then direct FISH may not be performed and results may be obtained if cultured chromosome studies are ordered. **Limitations** Molecular mutations below the resolution of FISH will not be detected; will not detect aneuploidy that is not targeted by FISH probes in this panel. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.
***KRAS* Gene Mutation Analysis, Colorectal Cancer (CRC)**	**480875**	**Storage Instructions** Maintain specimen at room temperature up to 4 weeks at 15-30°C.
Lead, Blood, Filter Paper	**791280**	**Special Instructions** This assay currently is not available in New York state.
Lead, Capillary (Fingerstick) Blood Pediatric	**717016**	**Name** Changed from "Lead, Blood (Pediatric), Capillary (Fingerstick)"
Lead, Venous Blood Pediatric	**717009**	**Name** Changed from "Lead, Blood (Pediatric), Venous"
Lyme Disease, Antibody Total With Reflex	**160325**	**Test Includes** Lyme disease total antibodies, EIA; supplementary Line blots for all positives from antibody test **Methodology** Enzyme immunoassay (EIA); Line blot
Lyme Disease Antibodies, Total and IgM, With Reflex to Line Blot	**258004**	**Name** Changed from "Lyme Disease Antibodies, Total and IgM, With Reflex to Western Blot on Positive" **Test Includes** ISR (immune status ratio) results for total antibodies; index results for IgM positives; Line blot analysis; result interpretation **Methodology** Enzyme immunoassay (EIA); Line Blot
Lyme Disease, Line Blot, Cerebrospinal Fluid	**160457**	**Name** Changed from "Lyme Disease, Western Blot, Cerebrospinal Fluid" **Test Includes** Line blot, CSF; analysis and interpretation for IgG-specific and IgM-specific antibodies **Methodology** Line blot
Magnesium, Urine	**003400**	**Storage Instructions** Room temperature (KBS tablet is acceptable)
Microsatellite Instability Analysis	**511855**	**Minimum Volume** Samples with ≥4 mm^2 tumor and normal tissue surface area and ≥50% tumor content are preferred; 3 mL whole blood
Myasthenia Gravis Complete Antibody Profile	**086005**	**Minimum Volume** 1.5 mL (**Note:** This volume does **not** allow for repeat testing.)
Oxidized Low-density Lipoprotein (OxLDL)	**123023**	**Container** Lavender-top (EDTA) tube (preferred) **or** gel-barrier tube **Collection** For plasma, draw blood into an EDTA tube and gently invert the tube 8 to 10 times to mix the anti-coagulant. Centrifuge the tube, remove the stopper and draw off approximately 2/3 of the upper plasma layer into a labeled transfer tube using a transfer pipet bulb. **Note:** This ensures the buffy coat of white cells and red cells remain undisturbed. Plasma must be separated from cells within 45 minutes of venipuncture. Send plasma in a plastic transfer tube.
Pediatric Acute Lymphoblastic Leukemia (ALL) Profile, FISH	**510324**	**Specimen** Blood, bone marrow, CSF, fixed-cell pellet from a cytogenetic analysis, slide with metaphase and/or interphase nuclei **or** bone marrow touch preparation slides are acceptable for testing. **Volume** 5 mL blood (pediatric), 3 mL bone marrow, fixed-cell pellet from a cytogenetic analysis, 12 slides with metaphase and/or interphase nuclei **or** 12 touch preparation slides. **Minimum Volume** 1 mL blood (pediatric), 1 mL bone marrow, fixed-cell pellet from a cytogenetic analysis, 6 slides with metaphase and/or interphase nuclei **or** 6 touch preparation slides. (**Note:** Minimum volumes may **not** allow for repeat testing.) **Container** Green-top (sodium heparin) tube; pediatric Vacutainer® is optimal **or** lavender-top (EDTA) tube (suboptimal). Adjust tube size to sample volume to avoid heparin toxicity. **Collection** Transport to the testing laboratory at room temperature, use of a cool pack or a LabCorp transport kit is acceptable. Do **not** allow samples to overheat or freeze. **Storage Instructions** Maintain the specimen at either room temperature or refrigerate. Do **not** freeze. **Causes for Rejection** Broken Vacutainer®; broken or stained slides; paraffin blocks; paraffin slides; decalcified bone cores; frozen specimen; quantity not sufficient for analysis
***PML-RARA* Transcript Detection for Acute Promyelocytic Leukemia, Quantitative**	**510840**	**Volume** 3 to 5 mL whole blood **or** 1 to 2 mL bone marrow

Note: Please consult the online Directory of Services and Interpretive Guide at https://www.labcorp.com/tests for the most current test information.

<table>
<tr><th>Test Name</th><th>Test No.</th><th>Field/Change (Only fields that change are included here.)</th></tr>
<tr><td>Postvasectomy Sperm Evaluation, Qualitative</td><td>519020</td><td>Stability
<table>
<tr><th>Temperature</th><th>Period</th></tr>
<tr><td>Room temperature</td><td>72 hours (stability provided by manufacturer or literature reference)</td></tr>
<tr><td>Refrigerated</td><td>Unstable (stability provided by manufacturer or literature reference)</td></tr>
<tr><td>Frozen</td><td>Unstable (stability provided by manufacturer or literature reference)</td></tr>
<tr><td>Freeze/thaw cycles</td><td>Unstable (stability provided by manufacturer or literature reference)</td></tr>
</table></td></tr>
<tr><td>Prenatal Aneuploid Evaluation, Chorionic Villus Sampling, FISH</td><td>510960</td><td>Special Instructions Pertinent medical findings should accompany request for FISH. It is recommended that InSight FISH testing be performed concurrently with prenatal chromosome analysis or microarray. Abnormal results should have banded chromosome confirmation.
Volume 30 mg chorionic villi
Minimum Volume 5 mg chorionic villi (Note: Minimum volumes may not allow for repeat testing.)
Causes for Rejection No villi submitted in specimen; low volume; wrong specimen type; frozen specimen; specimen placed in fixative
Use Fluorescence in situ hybridization (FISH), Prenatal Chorionic Villus Sampling, FISH targeting numerical changes in 13, 18, 21, X, Y.
Limitations Molecular mutations below the resolution of FISH will not be detected. Will not detect aneuploidy that is not targeted by FISH probes in this panel.
This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.</td></tr>
<tr><td>Products of Conception (POC) Aneuploid Evaluation, FISH Genetics</td><td>510963</td><td>Specimen Viable chorionic villi, fetal tissue, fixed-cell pellet from a cytogenetic analysis, slides from a fixed-cell pellet with metaphase and/or interphase nuclei, amniotic fluid from fetal demise.
Volume 30 mg chorionic villi, 4x4x4mm fetal tissue, fixed-cell pellet from a cytogenetic analysis, 8 slides from a fixed cell pellet with metaphase and/or interphase nuclei
Minimum Volume 5 mg chorionic villi, 2x2x2mm fetal tissue, fixed-cell pellet from a cytogenetic analysis, 4 slides from a fixed cell pellet with metaphase and/or interphase nuclei. (Note: Minimum volumes may not allow for repeat testing.)
Container For CVS samples: CVS transport tube available from the cytogenetics laboratory (call 800-533-0567, ext 4065 or 3300); sterile container with transport media. For fetal tissue samples: Sterile container with sterile Ringer's lactate or Hanks' balanced salt solution or transport medium provided by cytogenetics laboratory. Do not use urine containers for shipping.
Causes for Rejection Frozen or contaminated villi; maternal decidua received; frozen sample; absence of villi or fetal tissue; broken or stained slides; excessive cellular debris; low volume or quantity not sufficient for analysis
Use Fluorescence in situ hybridization (FISH), POC Aneuploid Evaluation, targeting numerical changes in 13, 16, 18, 21, 22, X, Y.
Limitations Molecular mutations below the resolution of FISH will not be detected; will not detect aneuploidy that is not targeted by FISH probes in this panel.
This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.</td></tr>
<tr><td>Semen Analysis (AUA Guidelines), Postvasectomy</td><td>519013</td><td rowspan="2">Stability
<table>
<tr><th>Temperature</th><th>Period</th></tr>
<tr><td>Room temperature</td><td>1 hour; keep sample close to body (inside shirt or coat) to avoid temperature extremes during transport. (stability provided by manufacturer or literature reference)</td></tr>
<tr><td>Refrigerated</td><td>Unstable (stability provided by manufacturer or literature reference)</td></tr>
<tr><td>Frozen</td><td>Unstable (stability provided by manufacturer or literature reference)</td></tr>
<tr><td>Freeze/thaw cycles</td><td>Unstable (stability provided by manufacturer or literature reference)</td></tr>
</table></td></tr>
<tr><td>Semen Analysis, Basic</td><td>519114</td></tr>
</table>

Note: Please consult the online Directory of Services and Interpretive Guide at https://www.labcorp.com/tests for the most current test information.

CPT Code Updates

Test Name	Test No.	CPT(s)
Gene Sequencing, ADAMTS-13	**825252**	81479
Gene Sequencing, aHUS	**825212**	81404; 81405; 81479
Gene Sequencing, Dysfibrinogenemia	**830113**	81479
Gene Sequencing, VWD-Complete	**830195**	81408; 81479
HER-2/CEP17 FISH, Breast With Reflex to Immunohistochemistry (IHC) if Group 2, 3, 4 by FISH	**483333**	88377
Plasminogen Gene Sequencing	**830145**	81479
PlateletGenex Thrombocytopenia Panel	**830160**	81334; 81406(x2); 81408; 81479

Deleted Procedures

Deleted Tests	Test No.	LabCorp Offers	Test No.
Propoxyphene Confirmation, Meconium	**808862**	Please contact your LabCorp representative for testing options.	

The CPT codes listed are in accordance with the current edition of Current Procedural Terminology, a publication of the American Medical Association. CPT codes are provided for the convenience of our clients; however, correct coding often varies from one carrier to another. Consequently, the codes presented here are intended as general guidelines and should not be used without confirming with the applicable payer that their use is appropriate in each case.

LOINC® Map. The Logical Observation Identifiers Names and Codes (LOINC®) corresponding to the individual LabCorp published assays is updated on a regular basis at www.labcorp.com.

LabCorp

www.LabCorp.com