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MGL
MEDICAL GENETICS LABORATORIES

Biochemical Tests

Biochemical Tests

Baylor College of Medicine

AVAILABLE BIOCHEMICAL TESTS	ANALYTE ANALYSIS		ENZYME ASSAY		DNA ANALYSIS
Disease Name	Test Code	Specimen Type	Test Code	Specimen Type	Test Code Analysis
3-Methylcrotonyl-CoA Carboxylase Deficiency	4200	Urine			3635, 3638, 3639, 3640, 3643, 3644
3-Methylglutaconic Aciduria Type I	4200	Urine			3913, 3913, 3910
5-Oxoprolinuria	4200	Urine			
Acid Sphingomyelinase Deficiency | Niemann-Pick Disease Type A, B			4607, 4608	SFC/WBC	6942, 6944, 6047 | MA
Adenine Phosphoribosyltransferase Deficiency	4220	Urine			2825 | APRT
Adenosine Deaminase Deficiency	4220	Urine	4509	RBC	5010 | ADA
Adenylosuccinase Deficiency | ADSL	4220	Urine			3695 | ADSL SEQ
Alkaptonuria	4200	Urine			
Arginase Deficiency | Argininemia	4100	Plasma	4536	RBC	3425 | ARG1 SEQ
Arginine: Glycine Amidinotransferase (AGAT) Deficiency	4260, 4130	Urine /Plasma			3455 | GATM SEQ
Argininosuccinic Aciduria | Argininosuccinate Lyase Deficiency	4100	Plasma	4524	RBC	6360 | ASL SEQ
Arylsulfatase A Deficiency | Metachromatic Leukodystrophy			4537, 4538	WBC	6380 | ARSA SEQ
Aspartylglycosaminuria | Aspartylglucosaminuria			4514	SFC	2205 | AGA
Biotinidase Deficiency	4200	Urine	4555	Serum	3495 | BTD SEQ
Canavan Disease	4200	Urine			6942, 6944, 6070 | MA
Carbamoylphosphate Synthetase Deficiency | CPSI	4100	Plasma	4561	Liver	2085, 3345 | CPS1 SEQ
Carnitine Deficiency, Systemic | OCTN2	4300	Plasma			3360 | SLC22A5 SEQ
Carnitine Palmitoyltransferase I Deficiency | CPTI	4300	Plasma			3365 | CPT1A SEQ
Carnitine Palmitoyltransferase II Deficiency | CPTII	4300	Plasma			3160 | CPT2 SEQ
Carnitine-Acylcarnitine Translocase Deficiency	4300	Plasma			3435 | SLC25A20 SEQ
Cobalamin Disorders	4150, 4140	Plasma			2120 PANEL
Transcobalamin II Deficiency | TCN2	4150, 4140	Plasma			2120, 3695
Transcobalamin Binding Protein Deficiency | CD320	4150, 4140	Plasma			
Cobalamin a | MMAA	4150, 4140	Plasma			2120, 3575
Cobalamin b | MMAB	4150, 4140	Plasma			2120, 3580
Cobalamin c | MMACHC	4150, 4140	Plasma			2120, 3440
Cobalamin d | MMADHC	4150, 4140	Plasma			2120, 3885
Cobalamin e | MTRR	4150, 4140	Plasma			2120, 2565
Cobalamin f | LMBRD1 | Lysosomal B12 Transporter	4150, 4140	Plasma			2120, 2560
Cobalamin g | MTR | Methionine Synthase	4150, 4140	Plasma			2120, 2054
Cobalamin j | ABCD4	4150, 4140	Plasma			
Methylmalonyl-CoA Mutase Deficiency | MUT	4150, 4140	Plasma			2120, 3585
Citrin Deficiency	4100	Plasma			3155 | SLC25A13 SEQ

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Citrullinemia Type I	4100	Plasma	4545	SFC	6180 | ASS1 SEQ
Coenzyme Q10 Deficiency	4800	Muscle			3850, 3415, 3775, 3405, 3410 | CABC1, COQ2, COQ9, PDSS1, PDSS2 SEQ
Creatine Transporter Deficiency | CRTR	4260	Urine			3150 | SLC6A8 SEQ
Cystinosis	4627	WBC			
Dihydropyrimidinase (DHP) deficiency	4215	Urine			
Dihydropyrimidine Dehydrogenase (DPD) deficiency	4215	Urine			
Fabry Disease			4517	WBC	6063 | GLA SEQ
Fatty Acid Oxidation Disorders | FODs	4300	Plasma			2095 | 2300 | 2000
Fumarate Hydratase Deficiency | Fumaric Aciduria	4200	Urine			3740 | FH SEQ
Gaucher Disease			4554	WBC	6942, 6944, 6033 | MA
Glutaric Aciduria Type I	4200	Urine			3685
Glutaric Aciduria Type II | Multiple Acyl-CoA Dehydrogenase Deficiency	4300	Plasma			2349
Glycerol Kinase Deficiency | GK	4200	Urine			8466
Glycine Encephalopathy *	4100, 4160*	Plasma/CSF*			5034 | AMT
GM1 Gangliosidoses			4548, 4549	SFC/WBC	
Guanidinoacetate Methyltransferase (GAMT) Deficiency	4260, 4130	Urine /Plasma			3145 | GAMT SEQ
Hawkinsinuria	4200, 4100	Urine/Plasma			2075
Hexosaminidase A Deficiency | Tay-Sachs Disease | Sandhoff Disease			4569	Serum	6942, 6944, 6066 | MA
HMGCoA Lyase Deficiency	4300, 4200	Urine /Plasma			5064 | HMGCL COMP
Holocarboxylase Synthetase Deficiency	4200	Urine			3540 | HLCS SEQ
Homocystinuria caused by Cystathionine Beta-Synthase Deficiency	4140, 4100	Plasma			3970
Hyperornithinemia-Hyperammonemia-Homocitrullinemia Syndrome | HHH	4100	Plasma			3235 | SLC25A15 SEQ
Hyperprolinemia Type II	4100, 4240	Urine /Plasma			
Hypophosphatasia	4240	Urine			2250 | ALPL SEQ
Ichthyosis X-linked | Steroid Sulfatase Deficiency			4614, 4615	SFC/WBC	8485 | FISH
Isovaleric Acidemia	4200	Urine			3680 | IVD SEQ
Krabbe Disease			4565, 4566	SFC/WBC	6415 | GALC SEQ
Lesch Nyhan Syndrome	4220	Urine	4572, 4573	SFC/RBC	6240 | HPRT1 SEQ
Long Chain 3-Hydroxyaclyl-CoA Dehydrogenase Deficiency | LCHAD	4300	Plasma			3120, 3122 | HADHA SEQ, MA
Long Chain Acyl-CoA Dehydrogenase Deficiency | LCAD	4300	Plasma			3385 | ACADL SEQ
Lowe Syndrome			4585	SFC	6039 | OCRL SEQ
Lysinuric Protein Intolerance	4100	Urine /Plasma			
Malonyl-CoA Decarboxylase Deficiency	4200	Urine			

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Disease Name	Test Code	Specimen Type	Test Code	Specimen Type	Test Code Analysis
Maple Syrup Urine Disease	4100	Plasma			3460, 3865 | DLD, DBT SEQ
Medium Chain Acyl-CoA Dehydrogenase Deficiency | MCAD	4300, 4350	Urine /Plasma			3115, 3117 | ACADM SEQ, MA
Methylmalonic Acidemia | MMA	4150	Plasma			3575, 3580, 3585, 3885 | MMAA, MMAB, MUT, MMADHC SEQ
Methylmalonic Acidemia and Homocystinuria, cblC type	4150, 4140	Plasma			3440 | MMACHC SEQ
Mitochondrial Neurogastrointestinal Encephalopathy Disease | MNGIE	4330	Plasma			3060 | TYMP SEQ
Molybdenum Cofactor Deficiency	4220, 4225	Urine			MOCSI-3595 SEQ
Mucolipidosis I | Sialidosis			4603	SFC	MOCS2-3615 SEQ
Mucolipidosis II | I-cell Disease			4569	Serum	
Mucopolysaccharidosis Type I | Hurler Disease | MPS I			4575, 4576	SFC/WBC	6385 | IDUA SEQ
Multiple Acyl-CoA Dehydrogenase Deficiency	4300, 4200	Urine /Plasma			3840, 3855, 3860 | ETFDH, ETFA, ETFB SEQ
Ornithine Aminotransferase Deficiency | Gyrate Atrophy	4100	Plasma			
Ornithine Transcarbamylase Deficiency | OTC	4210, 4100	Urine /Plasma	4582	Liver	3140 | OTC SEQ
Orotic Aciduria	4210	Urine			
Phenylalanine Hydroxylase Deficiency | Phenylketonuria | PKU	4100	Plasma			3135 | PAH SEQ
Propionic Acidemia	4200, 4300, 4350	Urine/Plasma			3765, 3770 | PCCA, PCCB SEQ
Purine Nucleoside Phosphorylase Deficiency | PNP	4220	Urine	4592, 4593, 4594	SFC/RBC/ WBC	5025 | PNP SEQ
Pyridoxine-Dependent Seizures	4844, 4812	Plasma/CSF			6950 | ALDH7A1 SEQ
Pyruvate Dehydrogenase Deficiency | PDHA1	4200	Urine			3165 | PDHA1 SEQ
Ribose 5-Phosphate Isomerase Deficiency	4340	Urine			
Sandhoff Disease | Tay-Sachs Disease			4569	Serum	HEXA SEQ 6925
Succinic Semialdehyde Dehydrogenase Deficiency | SSADH	4200	Urine			
Sulfocysteinuria	4220	Urine			
Transaldolase Deficiency	4340	Urine			
Trifunctional Protein Deficiency | TFP	4300	Plasma			3120, 3630 | HADHA, HADHB SEQ
Tyrosinemia Types I, II, and III	4250	Urine			3445 | FAH SEQ
Very Long Chain Acly-CoA Dehydrogenase Deficiency | VLCAD	4300	Plasma			3355 | ACADVL SEQ
Wolman Disease | Lysosomal Acid Lipase Deficiency | Cholesterol Ester Storage Disease			4502, 4503, 4504	SFC/WBC/ Liver	6430 | LIPA SEQ
Xanthinuria, Type I	4220	Urine			
** Must send the both the plasma & CSF sample for clinical diagnosis.*	*RBC=Red Blood Cell WBC=White Blood Cell; SFC=Skin Fibroblast Culture CSF=Cerebrospinal Fluid*				*SEQ=Sequencing MA=Mutation Analysis*

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Neonatal and Infantile Metabolic Seizures Panel

Neonatal seizures are defined as occurring in the first 28 days of life, although they typically begin in the first week of life. With a prevalence of 1.5% in neonates, they represent an obvious clinical sign of neurologic dysfunction.[1,2] Clinically, they are primarily found to be subtle epileptic events; however, they can be more obvious and include seizures that are clonic, tonic, myoclonic or infantile spasms. Many etiologies exist, including hypoxic ischemic events, infectious, electrolyte abnormalities, or metabolic disorders. Metabolic conditions are found in ~4% of children presenting in status epilepticus and should be considered when initial evaluations for an infectious process or electrolyte abnormalities are unrevealing.[3] Identifying a metabolic etiology can have significant implications for treatment and also for prognosis.[4]

The Baylor MGL has a panel of tests to evaluate for an underlying metabolic cause for neonatal seizures:

Test Type/Name	Test Code
Plasma Amino Acid Analysis	4100
Plasma Acylcarnitine Profile	4300
Plasma Pyridoxine-Dependent Seizures	4811
Plasma Creatine and Guanidinoacetate	4130
Serum Biotinidase	4555
Urine Purines and Pyrimidines	4010
Urine Organic Acid Analysis	4200
Urine Sulfocysteine Determination	4225
CSF Pyridoxine-Dependent Seizures	4812
CSF Amino Acid Analysis	4160

Panel Test Code: 4400

Turn Around Time: 10 Days

References:

1. *Rahman S, Footitt EJ, Varadkar S, Clayton PT. Inborn errors of metabolism causing epilepsy. Dev Med Child Neurol. 2013 Jan;55(1):23-36.*
2. *Van Hove JL, Lohr NJ. Metabolic and monogenic causes of seizures in neonates and young infants. Mol Genet Metab. 2011;104(3):214-30.*
3. *Skjei KL, Dlugos DJ. The evaluation of treatment-resistant epilepsy. Semin Pediatr Neurol. 2011 Sep;18(3):150-70.*
4. *Stockler S, Plecko B, Gospe SM Jr, Coulter-Mackie M, Connolly M, van Karnebeek C, Mercimek-Mahmutoglu S, Hartmann H, Scharer G, Struijs E, Tein I, Jakobs C, Clayton P, Van Hove JL. Pyridoxine dependent epilepsy and antiquitin deficiency: clinical and molecular characteristics and recommendations for diagnosis, treatment and follow-up. Mol Genet Metab. 2011 Sep-Oct;104(1-2):48-60.*

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CREATINE DEFICIENCY SYNDROMES

Creatine deficiency syndromes are characterized by intellectual disability, severe disturbance of expressive and cognitive speech, seizures (often poorly controlled), and movement disturbances (1.2). A common hallmark is cerebral creatine depletion as detected by magnetic resonance spectroscopy (3).

Creatine deficiency syndromes include two autosomal recessive disorders, arginine:glycine amidinotransferase (AGAT) deficiency (OMIM 612718) and guanidinoacetate methyltransferase (GAMT) deficiency (OMIM 612736), as well as the X-linked creatine transporter deficiency (OMIM 300352).

In individuals with AGAT deficiency, both plasma and urine testing reveal extremely low guanidinoacetate (GAA) and creatine concentrations. In GAMT deficiency, high plasma GAA levels are characteristic. GAA is also mildly increased in urea cycle disorder patients with elevated arginine levels. In individuals with X-linked creatine transporter deficiency, urine is required for diagnosis, as plasma levels of GAA and creatine are typically normal in this disorder. The characteristic finding in the urine of individuals with creatine transporter deficiency is an elevated creatine/creatinine ratio (4).

To diagnose all three creatine deficiency syndromes, the Creatine Panel determines GAA and creatine in both plasma and urine by UPLC-tandem mass spectroscopy (5).

Turn around time: 10 days

Test codes: 4015 Creatine Panel or order individually
4130 plasma | 4260 urine

CPT codes: 82540x1, 82570x2, 82543x4

Related DNA tests:

AGAT Deficiency: GATM Sequence 3455 | Known Familial Mutation 3456 | Prenatal Diagnosis 3457

GAMT Deficiency: GAMT Sequence 3145 | Known Familial Mutation 3146 | Prenatal Diagnosis 3147

Creatine Transporter Deficiency: SLC6A8 Sequence 3150 | Known Familial Mutation 3151 | Prenatal Diagnosis 3152

References:

1. *Schulze, A. Creatine deficiency syndromes. Molec. Cell Biochem. 244: 143-150, 2003*

2. *Lion-Francois, L., Cheillan, D., Pitelet, G., Acquaviva-Bourdain, C., Bussy, G., Cotton, F., Guibaud, L., Gerard, D., Rivier, C., Vianey-Saban, C., Jakobs, C., Salomons, G. S., des Portes, V. High frequency of creatine deficiency syndromes in patients with unexplained mental retardation. Neurology 67: 1713-1714, 2006*

3. *Stöckler-Ipsiroglu S, Salomons GS (2006) Creatine deficiency syndromes In: Fernandes J, Saudubray JM, van den Berghe G, eds. Inborn Metabolic Diseases. Springer Verlag; 2006:211-7*

4. *Sylvia Stöckler-Ipsiroglu, Carmen Stromberger, Chike B. Item, Adolf Mühl Stöckler-Ipsiroglu S, Battini R, de Grauw T, Schulze A. Disorders of creatine metabolism. In: Blau N, DuranM, Blaskovics ME, Gibson KM eds. Physician's Guide to the Laboratory Diagnosis of Metabolic Diseases. Springer Verlag; 2003:467-80.*

5. *Sun, Q and O'brien, W. Diagnosis of creatine metabolism disorders by determining creatine and guanidinoacetate in plasma and urine. Methods Mol Biol. 2010; 603:175-85.*

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PYRIDOXINE-DEPENDENT EPILEPSY

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Autosomal recessive pyridoxine-dependent epilepsy disorder (PDE; OMIM 266100) has a frequency of 1/400,000 – 1/700,000 and can present as clonic, generalized tonic-clonic and/or myoclonic seizures. Onset of seizures is typically in the first hours of life, but may present as late as three weeks of age. Accurate diagnosis is critical for patient management as seizures are often unresponsive to standard anticonvulsants and good seizure control is typically achievable with administration of pyridoxine hydrochloride. Until recently, definitive diagnosis of PDE was based on successful control of epilepsy with pyridoxine therapy and recurrence of seizures after pyridoxine withdrawal (1).

Recent research has demonstrated that in PDE, pipecolic acid (PA) and alpha-amino adipic semialdehyde (AASA) are markedly elevated in urine, plasma, and cerebrospinal fluid, and thus are diagnostic biomarkers of the disorder (2, 3). The neurotoxic affects of AASA are thought to result from the accumulation of its cyclic derivative L-Δ1- piperideine-6-carboxylate (P6C). In PDE, excess P6C condenses with pyridoxal-5'-phosphate (PLP) and inactivates this essential cofactor in neurotransmitter metabolism (4).

This panel determines both P6C and PA concentrations in either cerebral spinal fluid (test code 4812) or plasma (test code 4811) by tandem mass spectroscopy (under our assay conditions a majority of AASA is converted to P6C). Note that determination of PA alone is not specific for diagnosis of PDE because PA is also found elevated in peroxisomal disorders (5).

Turn around time: 6 days

Test codes: 4811 PLASMA | 4812 CSF

CPT codes: 82543x4

Related tests: Pyridoxine-Dependent Seizures-ALDH7A1 Gene Sequence (6850)

Alternative disease title: Pyridoxine Dependency With Seizures; AASA Dehydrogenase Deficiency; Pyridoxine-Dependent Seizures

References:

1. *Gospe M. Pyridoxine-dependent seizures: findings from recent studies pose new questions. Pediatr Neurol 26:181–185. 2002.*

2. *Plecko, B., Paul, K., Paschke, E., Stoeckler-Ipsiroglu, S., Struys, E., Jakobs, C., Hartmann, H., Luecke, T., di Capua, M., Korenke, C., Hikel, C., Reutershahn, E., Freilinger, M., Baumeister, F., Bosch, F., Erwa, W. Biochemical and molecular characterization of 18 patients with pyridoxine-dependent epilepsy and mutations of the antiquitin (ALDH7A1) gene. Hum. Mutat. 28: 19-26, 2007.*

3. *Sadilkova K, Gospe SM Jr, Hahn SH. Simultaneous determination of alpha-aminoadipic semialdehyde, piperideine-6-carboxylate and pipecolic acid by LC-MS/MS for pyridoxine-dependent seizures and folinic acid-responsive seizures. J Neurosci Methods. 2009*

4. *Mills, P. B., Struys, E., Jakobs, C., Plecko, B., Baxter, P., Baumgartner, M., Willemsen, M. A. A. P., Omran, H., Tacke, U., Uhlenberg, B., Weschke, B., Clayton, P. T. Mutations in antiquitin in individuals with pyridoxine-dependent seizures. Nature Med. 12: 307-309, 2006.*

5. *Clayton, P. T. Pyridoxine-Dependent Epilepsy Due to α-Aminoadipic Semialdehyde Dehydrogenase (Antiquitin) Deficiency. The Online Metabolic & Molecular Bases of Inherited Disease.*

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VITAMIN D: 25-HYDROXYVITAMIN D2 AND D3 – PLASMA

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This test provides quantitative analysis of plasma 25-hydroxyvitamin D2 and 25-hydroxyvitamin D3 levels for diagnosis of vitamin D deficiency, differential diagnosis of causes of rickets, and management of vitamin D therapy/ patient compliance.

Vitamin D is a family of fat-soluble compounds derived either from cholesterol or ergosterol. Vitamin D is obtained from diet, and we can make it when exposed to ultraviolet radiation found in sunlight. The vitamin D that we make ourselves and that which we get from animal food sources is vitamin D3, or cholecalciferol, which is made from cholesterol. The vitamin D that we obtain from invertebrates and plants is vitamin D2, which is made from ergosterol. Once absorbed into the body, the vitamin D is rapidly hydroxylated by the liver, producing hydroxy vitamin D, which is then transported in the blood. The measurement of this plasma or serum 25-hydroxy vitamin D represents a good measure of the total vitamin D status of an individual.

Accumulating evidence demonstrates that vitamin D deficiency is highly prevalent worldwide. In its clinical practice guideline published in 2011, The Endocrine Society recommends using the serum 25-hydroxyvitamin D level to evaluate vitamin D status in patients who are at risk for vitamin D deficiency. Measurement of 25(OH)-vitamin D2 monitors the supplementation and exogenous intake of vitamin D; whereas 25(OH)-vitamin D3 is a measure of endogenous vitamin D.

Vitamin D levels have routinely been determined using immunoassays for many years and often provide inconsistent results. These assays suffer from cross-reactivity of the antibodies used and the inability to differentiate 25(OH)-D2 from 25(OH)-D3. Measurement of 25(OH)-vitamin D2 monitors the supplementation and exogenous intake of of vitamin D; whereas 25(OH)-vitamin D3 is a measure of endogenous vitamin D. This procedure uses Ultra Performance Liquid Chromatography (UPLC) coupled with multiple reaction monitoring (MRM) tandem mass spectrometry to differentiate and quantify the analytes. Our assay measures 25-hydroxyvitamin D2 and D3 by UPLC-MS/MS with an isotopic internal standard. Reference material (SRM 972 Vitamin D in Human Serum) from National Institute of Standard and Technology (NIST) is used for the assay calibration. This procedure is the gold standard for diagnosing vitamin D deficiency and monitoring vitamin D supplementation.

Turn around time: 8 days

Test Codes: 4360

CPT codes: 82306x1

References:

1. *Van den Ouweland JM, Vogeser M, Bächer S. Vitamin D and metabolites measurement by tandem mass spectrometry. Rev Endocr Metab Disord. 2013 Jun;14(2):159-84.*

2. *Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011 Jul;96(7):1911-30.*

3. *Stepman HC, Vanderroost A, Van Uytfanghe K, Thienpont LM. Candidate reference measurement procedures for serum 25-hydroxyvitamin D3 and 25-hydroxyvitamin D2 by using isotope-dilution liquid chromatography-tandem mass spectrometry. Clin Chem. 2011 Mar;57(3):441-8.*

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