Biochemical Genetics Laboratory

The Biochemical Genetics Laboratory in the Department of Pediatrics at the University of California San Diego has been in operation since the establishment of the UCSD Medical School in 1969. We offer tests not generally available which have been developed in the conduct of research or the care of our patients, and endeavor to assure the maximum quality and reliability. The goal of the UCSD Biochemical Genetics Laboratory is to provide comprehensive diagnostic laboratory services to assist in the diagnosis and treatment of inborn errors of metabolism. A special feature of our lab is our consultation services with health care professionals who specialize in inborn errors of metabolism, and these M.D., Ph.D.'s are available to you for interpretation. Please feel free to call if we can be of assistance in your diagnostic or therapeutic plans.

Shipping Address:

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San Diego, CA 92103

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General Information:

- Laboratory working hours are Monday through Friday, 08:00 to 16:00 PST. As our regular hours do not include weekends or holidays, we request that specimens be shipped routinely Monday-Thursday.
- In the event of medical emergency, special shipping arrangements can be made, and we are generally able to perform testing in the fastest possible time, including weekends and holidays.
- Use only guaranteed overnight carriers (U.S. Postal Express may take longer and specimens may be ruined).
- Please label each specimen with patient's name and date/time of collection, using permanent ink, and place in a resealable plastic biohazard bag, one per bag (gummed labels fall off frozen specimens). Please place completed test request form in separate plastic bag to avoid contamination from specimen.

Certification numbers:	CLIA ID # O5D0643075	Federal Tax ID # 33-0833316
	MediCal Lab # Lab 04102F	MediCare # 55L0008759
	California Dept. of Health Services Clinical Laboratory License, ID # CLE4102	
	College of American Pathologists (CAP) #2318702	
Proficiency Test Programs:	American Association of Bioanalysts, College of American Pathologists	
Physician Affiliations:	American Board of Medical Genetics, American Board of Pediatrics	

Following is a list of tests offered by our laboratory.

Test	Specimens
ACYLCARNITINE PROFILE	**Plasma**
AMINO ACIDS, QUANTITATIVE ANALYSIS	**Plasma, Urine, CSF**
CARBOXYLASES (PYRUVATE, PROPIONYL-COA, AND 3-METHYLCROTONYL-COA)	**Blood, Cultured Cells**
CARNITINE, QUANTITATIVE ANALYSIS	**Urine, Plasma, Tissue**
COENZYME Q10	**Plasma, Muscle**
FIBROBLAST/AMNIOCYTE CULTURE SERVICES	**Biopsy, Cultured Cells**
HOMOCYST(E)INE, TOTAL	**Plasma**
HYPOXANTHINE-GUANINE PHOSPHORIBOSYL TRANSFERASE	**Bloodspots**
MCAD (MEDIUM CHAIN ACYL COENZYME A DEHYDROGENASE) COMMON ALLELE DETECTION	**Blood, Cells**
METABOLIC PANEL (PLASMA QUANTITATIVE AMINO ACIDS AND URINE QUANTITATIVE ORGANIC ACIDS SCREEN)	**Urine and Plasma**
METHYLMALONIC ACID (MMA) QUANTITATION	**Urine, Plasma**
MITOCHONDRIAL DNA PANEL	**Blood, Muscle**
MITOCHONDRIAL DNA SINGLE POINT MUTATION	**Blood, Muscle**
MITOCHONDRIAL DNA SOUTHERN BLOT	**Blood, Muscle**
***N*-ACETYLASPARTATE QUANTITATION**	**Urine**
ORGANIC ACIDS, QUANTITATIVE COMPREHENSIVE	**Urine, Plasma, CSF**
PKU PANEL (PHENYLALANINE AND TYROSINE)	**Plasma, Bloodspots**
SCREEN, QUANTITATIVE ORGANIC ACIDS	**Urine**
OROTIC ACID QUANTITATION	**Urine**
SUCCINYLACETONE QUANTITATION	**Urine**
SUCCINYLPURINE SCREEN	**Urine**

The following pages summarize the individual tests and specify the sample requirements, turn-around times and prices.

ACYLCARNITINE ANALYSIS **(Plasma)**

Comments: Acylcarnitine is assayed by tandem mass spectrometry. Reported values are are accompanied with interpretation of profile. Acylcarnitines are very useful in diagnosing mitochondrial fatty acid beta oxidation disorders and several other organic acidemias.

Sample requirements: Plasma, ≥1 mL (0.5 mL) from heparinized blood (green top tube) supernatant from clinical centrifugation (within 20 minutes) promptly frozen and shipped frozen (packed with dry ice or lyophilized).

Turn-around time: Routine: less than 1 week.
Please provide information about carnitine therapy and clinical history to assist with interpretation.

AMINO ACID ANALYSIS, QUANTITATIVE **(Urine, Plasma, Cerebrospinal Fluid)**

Comments: Standard analysis using modern automated amino acid analyzer. Please be aware that for accurate determination of homocystine in blood, special handling is required - you may call our lab to arrange specifically for plasma homocystine.

Sample requirements: Urine, 10-20 mL (minimum 5 mL), frozen without preservatives and shipped frozen (packed with dry ice), .
Plasma, ≥1 mL (minimum 0.5 mL) from heparinized blood (green top tube) supernatant from clinical centrifugation (within 20 minutes) promptly frozen and shipped frozen (packed w/ dry ice) .
Cerebrospinal fluid, ≥1 mL (minimum 0.5 mL)[standard plastic LP tube or transferred to red top tube], frozen and shipped frozen (packed with dry ice).

Turn-around time: Routine: 3-5 working days, Stat: same day.

BENZOIC AND HIPPURIC, QUANTITATIVE **(Plasma)**

Comments: May be useful during treatment with benzoate and phenylacetate.

Sample requirements: Plasma, ≥2 mL (minimum 1.0 mL) from heparinized blood (green top tube) supernatant from clinical centrifugation (within 20 minutes) promptly frozen, shipped frozen (packed w/ dry ice).

Turn-around time: Routine: 5-7 working days.

CARBOXYLASE ACTIVITIES **(Lymphocytes, Fibroblasts, Amniocytes)**

(PYRUVATE, PROPIONYL-COA, AND 3-METHYLCROTONYL-COA CARBOXYLASES**)**

Comments: Radiochemical assays performed on cultured cells or isolated lymphocytes. For blood lymphocytes assay, please call to assure staff is available (specimens must be processed stat upon arrival).
Fibroblast/Amniocyte analysis will have an additional charge for culture (see fibroblast/amniocyte culture)

Sample requirements: Blood, 7-10 mL in ACD (yellow-top) tube (3 ml minimum on infants), kept at room temperature and shipped overnight at room temperature. For greater reliability, we **require** a simultaneous sample from a control individual (not a member of the patient's family).
Fibroblasts, Two T-25 flasks shipped overnight with medium at room temperature. Prenatal diagnosis of Multiple Carboxylase Deficiency or Isolated Carboxylase Deficiency is possible with Amniocytes: Please call lab to coordinate.

Turn-around time: Routine: 5-10 working days (not including growing cultured cells, if required).

PLEASE CONTACT LABORATORY TO ARRANGE FOR THIS ASSAY ON LYMPHOCYTES

CARNITINE ANALYSIS, QUANTITATIVE **(Urine, Plasma, Tissue)**

Comments: Carnitine is assayed by tandem mass spectrometry, with and without alkaline hydrolysis of esters. Reported values are total, free, and esterified carnitine.

Sample requirements: Urine, 10-20 mL (minimum 5 mL), frozen without preservatives and shipped frozen (packed with dry ice).
Plasma, ≥1 mL (0.5 mL) from heparinized blood (green top tube) supernatant from clinical centrifugation (within 20 minutes) promptly frozen and shipped frozen (packed with dry ice or lyophilized).
Tissue, ≥ 1 gram muscle, rapidly frozen/stored at -70°C, shipped frozen (packed with dry ice).

Turn-around time: Routine: 10-14 working days. Please provide information about carnitine therapy or a delay of an additional 10-14 working days could result for repeat analysis.

COENZYME Q10 **(Plasma, Muscle)**

Comments: Coenzyme Q10 is assayed by tandem mass spectrometry.

Sample requirements: Plasma, ≥1 mL (0.5 mL) from heparinized blood (green top tube) supernatant from clinical centrifugation (within 20 minutes) promptly frozen and shipped frozen (packed with dry ice).
Note: PROTECT FROM LIGHT
Muscle, ≥1 gram muscle, rapidly frozen/stored at -70°C, shipped frozen (packed w/ dry ice).

Turn-around time: Routine: 10-14 working days.

FIBROBLAST CULTURE, SET-UP **(Biopsy)**

Comments: We can establish a culture of your patient's fibroblasts in order to assay in our lab or to convey to a reference lab for a particular assay or genetic test.

Sample requirements: Biopsy (skin or other specimen with adequate connective tissue), usually a single 3 or 4 mm diameter piece of skin extending to the epidermal-dermal junction is sufficient, kept in sterile medium at room temperature and shipped overnight.

Turn-around time: Variable, depending on sample origin and condition, generally 4-6 week minimum.

FIBROBLAST/AMNIOCYTE CONTINUED CULTURE **(Cultured Cells)**

Comments: When we receive flasks of cultured cells, we continue to grow them until analysis is completed and then they are discarded, unless other arrangements are made.

Sample requirements: Cultured cells (fibroblasts or amniocytes), two T-25 flasks on hand in our lab or shipped overnight with medium at room temperature.

Turn-around time: Depends on analysis and on sample condition.

FIBROBLAST/AMNIOCYTE STORAGE **(Cultured Cells)**

Comments: Long-term storage of cultured cells in liquid nitrogen (9-12 ampules). Storage guaranteed for one year, unless other arrangements are made.

Sample requirements: Cultured cells previously grown in our lab.

Turn-around time: Not applicable.

FIBROBLAST/AMNIOCYTE RECULTURED FROM STORAGE **(Cultured Cells)**

Comments: Cultured cells which are stored can be thawed and recultured for further analysis.

Sample requirements: Cultured cells (previously grown and stored by our laboratory).

Turn-around time: Variable, depending on sample origin and condition, generally 4-6 week minimum.

HOMOCYST(E)INE, TOTAL **(Plasma)**

Comments: Elevation of homocysteine is diagnostic for homocystinuria, and has been associated with vaso-occlusive and thrombotic disease. Where older methods only measured free homocystine, this method by tandem massspectrometry detects total (free and protein-bound, reduced homocysteine and oxidized homocystine). Please note that this new method does detect homocyst(e)ine in healthy subjects, so the normal range is not directly comparable to that of older methods.

Sample requirements: Plasma, 1 mL (minimum 0.5 mL) (separated from heparinized or EDTA-treated blood (green or purple-top tube), promptly frozen and shipped frozen (packed with dry ice) by overnight carrier.

Turn-around time: 5-7 working days.

HYPOXANTHINE-GUANINE PHOSPHORIBOSYL TRANSFERASE **(Blood Spots)**

Comments: The diagnosis of Lesch-Nyhan syndrome and variant forms depends on the assay of HPRT. Our assay is radiochemical, and we also measure Adenine Phosphoribosyl Transferase as an internal control. It is helpful to have a clinical history of the patient provided.

Sample requirements: Blood Spots, PKU card (Guthrie Card Filter Paper) fill at least 3 spots, allow to air dry for >4 hours. Mail in envelope at room temperature.

Turn-around time: 10 working days.

MEDIUM CHAIN ACYL COENZYME A DEHYDROGENASE (MCAD) COMMON ALLELE DETECTION (WITH INTERPRETATION) **(Blood, Tissue, or Extracted DNA)**

Comments: MCAD is inherited as an autosomal recessive disorder which has been known to cause sudden infant death, hypoglycemia, and a Reye-like syndrome. Approximately 90% of all affected individuals examined to date have been shown to be homozygous for the A→G 985 mutation in MCAD gene. The test we offer is based on PCR analysis, and is specific for this mutation.

Sample requirements: Blood, 1 mL (minimum 250 µl) (in purple (EDTA), or yellow-top (ACD) tube or dried on small piece of clean filter paper). Blood must be kept in sealed original tubes at room temperature 8(NOT FROZEN) and sent at room temperature by overnight carrier.

Turn-around time: 1-3 weeks.

METABOLIC PANEL (PLASMA QUANTITATIVE AMINO ACIDS AND URINE QUANTITATIVE ORGANIC ACID SCREEN) **(Urine and Plasma)**

Comments: We offer these two tests at a special panel price. Please refer above for test details.

Sample requirements: Urine, 10-20 mL (min. 5 mL), frozen without preservatives, shipped frozen (packed w/ dry ice).
Plasma, ≥1 mL (minimum 0.5 mL) from heparinized blood (green top tube) supernatant from clinical centrifugation (within 20 minutes) promptly frozen, shipped frozen (packed w/ dry ice).

Turn-around time: Routine: 5-7 working days, Stat: 2 days.

METHYLMALONIC ACID (MMA) ANALYSIS, QUANTITATIVE **(Urine, Plasma)**

Comments: Quantitation of MMA excretion can be used to follow the clinical status and therapeutic response of patients with methylmalonic acidemia. We use gas chromatography-mass spectrometry for definitive identification and precise quantitation.

Sample requirements: Urine, 10-20 mL (minimum 5 mL), frozen without preservatives and shipped frozen (packed with dry ice).
Plasma, ≥2 mL (minimum 1.0 mL) from heparinized blood (green top tube) supernatant from clinical centrifugation (within 20 min) promptly frozen and shipped frozen (packed with dry ice).

Turn-around time: Routine: 5-7 working days, Stat: 2 days.

MITOCHONDRIAL DNA PANEL **(Blood, Muscle)**

Comments: Mutations in mitochondrial DNA give rise to various syndromes including lactic acidemia and encephalomyopathies, with maternal inheritance and remarkable variation in penetrance and expressivity. We perform PCR-based analysis of a set of the most common point mutations, and a Southern blot analysis to detect deletions, duplications and rearrangements in the mitochondrial genome. The point mutations which we routinely detect are: MELAS A3243G, MELAS T3271C, MERRF A8344G, MERRF T8356C, NARP T8993G, NARP T8993C. Our Southern blot methodology, using two restriction enzymes, achieves higher resolution than that by other methods.

Sample requirements: Blood, 5-9 mL (in purple (EDTA), or yellow-top (ACD) tube). Blood must be kept in sealed original tubes at room temperature (NOT FROZEN) and sent at room temperature by overnight carrier. Muscle, 0.1-0.25 gram fresh frozen, sent frozen on dry ice by overnight carrier.

WE ARE UNABLE TO BILL PATIENTS OR THEIR INSURANCE FOR THESE SERVICES; THE INSTITUTUION WILL BE BILLED.

Turn-around time: 4-6 weeks.

MITOCHONDRIAL DNA SINGLE POINT MUTATION ANALYSIS **(Blood, Muscle)**

Comments: We perform radiolabeled PCR-based analysis for individual point mutations in the mitochondrial genome. The point mutations for which we offer this service are: MELAS A3243G, MELAS T3271C, MERRF A8344G, MERRF T8356C, NARP T8993G, NARP T8993C.

Sample requirements: Blood, 5-9 mL (in purple (EDTA), or yellow-top (ACD) tube). Blood must be kept in sealed original tubes at room temperature (NOT FROZEN) and sent at room temperature by overnight carrier. Muscle, 0.1-0.25 gram fresh frozen, sent frozen on dry ice by overnight carrier.

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Turn-around time: 4-6 weeks.

MITOCHONDRIAL DNA SOUTHERN BLOT **(Blood, Muscle)**

Comments: Mutations in mitochondrial DNA give rise to various syndromes including lactic acidemia and encephalomyopathy, with maternal inheritance and remarkable variation in penetrance and expressivity. We perform a Southern blot analysis to detect deletions, duplications and rearrangements in the mitochondrial genome. Our Southern blot methodology, using two restriction enzymes, achieves higher resolution than other methods.

Sample requirements: Blood, 5-9 mL (in purple (EDTA), or yellow-top (ACD) tube). Blood must be kept in sealed original tubes at room temperature (NOT FROZEN) and sent at room temperature by overnight carrier. Muscle, 0.1-0.25 gram fresh frozen, sent frozen on dry ice by overnight carrier.

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Turn-around time: 4-6 weeks.

***N*-ACETYLASPARTATE ANALYSIS, QUANTITATIVE** **(Urine)**

Comments: Gross elevations of N-acetyl aspartate can be used to diagnose Canavan disease. We use gas chromatography-mass spectrometry for definitive identification.

Sample requirements: Urine, 10-20 mL (min. 5 mL), frozen without preservatives, shipped frozen (packed w/ dry ice).

Turn-around time: Routine: 5-7 working days, Stat: 2 days.

ORGANIC ACID COMPREHENSIVE, QUANTITATIVE **(Urine, Plasma, Cerebrospinal Fluid)**

Comments: Our organic acid analysis is based on a state-of-the-art application of gas chromatography-mass spectrometry. Identification of metabolites is definitive, and we fully quantitate more than 150 compounds. Note that other laboratories may give qualitative results only, or report results without mass spectral identification, which can lead to serious misinterpretation.

Sample requirements: Urine, 10-20 mL (minimum 5 mL), frozen without preservatives and shipped frozen (packed with dry ice).
Plasma, ≥2 mL (minimum 1.0 mL) from heparinized blood (green top tube) supernatant from clinical centrifugation (within 20 minutes) promptly frozen and shipped frozen (packed with dry ice).
Cerebrospinal fluid, ≥2 mL (minimum 1.0 mL)[standard plastic LP tube or transferred to red top tube], frozen and shipped frozen (packed with dry ice).

Turn-around time: Routine: 5-7 working days, Stat: 2 days.

ORGANIC ACID SCREEN, QUANTITATIVE **(Urine)**

Comments: We utilize the same gas chromatography-mass spectrometric technique as in our comprehensive organic acid analysis, but limit the analysis to a strategically selected group of compounds which should permit identification of patients with nearly all known organic acidemias. There are a limited number of known conditions which this screen will not detect, and complete diagnosis may require subsequent comprehensive analysis.

Sample requirements: Urine, 10-20 mL (minimum 5 mL), frozen without preservatives and shipped frozen (packed with dry ice) .

Turn-around time: Routine: 5-7 working days, Stat: 2 days.

OROTIC ACID ANALYSIS, QUANTITATIVE **(Urine)**

Comments: Orotic aciduria may be seen in deficiency of orotate decarboxylase, or following a single dose of allopurinol in females who are carriers for ornithine transcarbamylase deficiency. We use gas chromatography-mass spectrometry for definitive identification.

Sample requirements: Urine, 10-20 mL (minimum 5 mL), frozen without preservatives and shipped frozen (packed with dry ice).

Turn-around time: Routine: 5-7 working days, Stat: 2 days.

PKU PANEL (PHENYLALANINE AND TYROSINE) **(Plasma, Bloodspots)**

Comments: Standard analysis using modern automated amino acid analyzer or tandem mass spectrometry. Used to monitor dietary management of phenylketonuria.

Sample requirements: Plasma, ≥1 mL (minimum 0.3 mL) from heparinized blood (green top tube) supernatant from clinical centrifugation (within 20 minutes) promptly frozen and shipped frozen (packed with dry ice) .
Blood Spots, PKU card (Guthrie Card Filter Paper) fill at least 3 spots, allow to air dry for >4 hours. Mail in envelope at room temperature.

Turn-around time: Routine: 3-5 working days, Stat: same day.

SUCCINYLPURINE SCREEN (Urine)

Comments: Succinylpurine products (succinylAICAriboside and succinyladenosine) are elevated in the body fluids of patients with deficiency of adenylosuccinate lyase, a disorder which can present with mental retardation, seizures and autistic features. We use the colorimetric method of Bratton & Marshall to screen for succinylAICAriboside. The screen is subject to both false positive and false negative. Please do not send specimens from patients taking sulfonamides or vitamin C supplements , as SULFA DRUGS AND VITAMIN C SUPPLEMENTS CAUSE FALSE POSITIVES.

Sample requirements: Urine, filter paper pad (≥ 1 × 1 cm) soaked with urine and dried (will suffice for colorimetric screen ONLY), and/or
Urine, 10-20 mL (min 2) frozen and shipped on dry ice (required if confirmatory HPLC analysis wanted).

Turn-around time: 2-8 weeks.

SUCCINYLACETONE, QUANTITATIVE (Urine, Plasma)

Comments: Succinylacetone excretion can be used to follow the clinical status and therapeutic response of patients with tyrosinemia (type 1, hepatorenal). We use gas chromatography-mass spectrometry for definitive identification and precise quantitation.

Sample requirements: Urine, 10-20 mL (minimum 5 mL), frozen without preservatives and shipped frozen (packed with dry ice) .

Turn-around time: Routine: 5-7 working days, Stat: 2 days.