

## About Us

The Center for Inherited Disorders of Energy Metabolism (CIDEM), established in 1988, is located at University Hospitals of Cleveland Case Medical Center and Case Western Reserve University (CWRU) School of Medicine. CIDEM is a group of inter-disciplinary, specialized laboratories focused on disorders of mitochondrial function. This includes defects of pyruvate metabolism, fatty acid oxidation, the TCA cycle, the electron transport chain, and oxidative phosphorylation.

Clinical conditions associated with these disorders include major disabilities affecting the central nervous system, sensory organs, skeletal muscle, heart, liver and kidney.

CIDEM is under the joint direction of Drs. Shawn McCandless, Charles Hoppel, and Douglas Kerr.

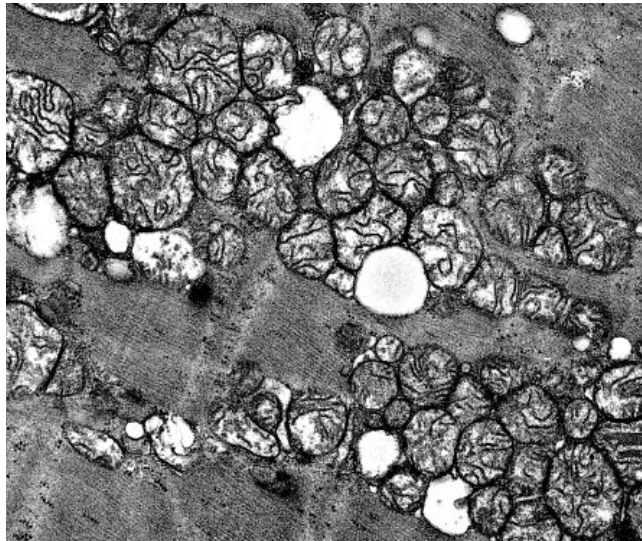
These laboratory services are accompanied, upon request, with relevant clinical specialty consultation and/or genetic evaluation for comprehensive approaches to diagnosis and treatment possibilities, including both children and adults.

## Center for Inherited Disorder of Energy Metabolism (CIDEM)

Wearn Bldg., Room 649  
University Hospitals Case Medical Center  
11100 Euclid Avenue, Cleveland OH 44106

Tel: 216-844-1286  
Fax: 216-844-8005  
cidem@case.edu  
[www.case.edu/med/CIDEM/](http://www.case.edu/med/CIDEM/)

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CLIA: 36D0925804  
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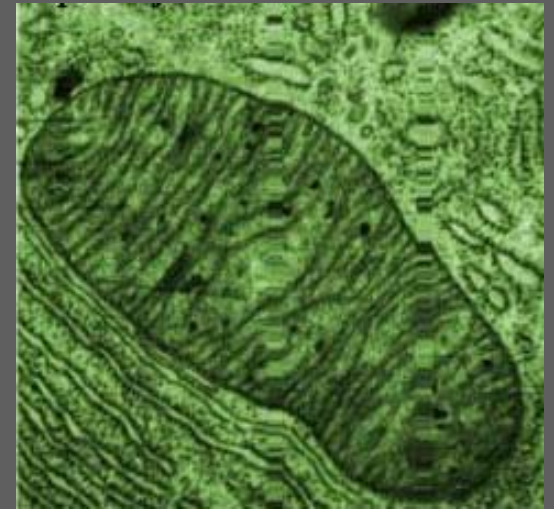


Among the nation's leading academic medical centers, University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine, a nationally recognized leader in medical research and education.



# CIDEM

## Center for Inherited Disorders of Energy Metabolism



### Our Mission

Is to provide comprehensive diagnostic laboratory services to facilitate the diagnosis and treatment of patients affected with mitochondrial disease.

[www.case.edu/med/CIDEM](http://www.case.edu/med/CIDEM)

## Test Information

(see CIDEM website for details)

### Metabolites in Body Fluids:

- $\beta$ -Hydroxybutyrate, acetoacetate, and free fatty acids: (plasma)
- Lactate and pyruvate: (blood, CSF)
- Urine organic acids: Gas chromatography with mass spectrometry
- Inclusive carnitine and acylcarnitine analysis: High-performance liquid chromatography with tandem mass spectrometry (see detail opposite page)
- Amino acids: Ultra-performance liquid chromatography

### Enzyme Assays:

- Pyruvate metabolism: Pyruvate dehydrogenase complex, pyruvate carboxylase, phosphoenolpyruvate carboxykinase, 3-MCC-CoA carboxylase, PCC-CoA carboxylase (blood lymphocytes, skin fibroblasts, tissues)
- Krebs Cycle: 2-ketoglutarate complex (including the E3 component), succinate dehydrogenase, and fumarase, citrate synthase (skin fibroblasts, tissues)
- Fatty Acid Oxidation: acyl-CoA dehydrogenases, enoyl-CoA hydratases, 3-hydroxy-acyl-CoA dehydrogenases; 3-ketothiolases (skin fibroblasts, tissues)
- Carnitine metabolism: carnitine palmitoyl transferases, carnitine acetyl transferase, carnitine translocase (skin fibroblasts, tissues)
- Electron Transport Chain: complexes II-IV (skin fibroblasts or liver); complexes I-IV (skeletal muscle, heart), plus components

**Genetic Analyses:** (in collaboration with the affiliated Center for Human Genetics lab)

- Pyruvate carboxylase (PC)
- Pyruvate dehydrogenase complex genes (*PDHA1*, *PDHB*, *DLAT*, *PDHX*, *DLD*) (see www.GeneTests.org for details.)

## Fresh Muscle Biopsies

(require on-site biopsy)

### Isolated intact (“live”) mitochondria

- Oxidative phosphorylation assay in isolated mitochondria with 18 different substrate combinations under various conditions to assess respiratory control, ATP formation, and to dissect functional activity of the intact respiratory chain.
- Electron transport chain activities and phosphorylation capacity in isolated mitochondria (complexes I-V) and homogenized whole fresh muscle.
- Blue native gel electrophoresis of mitochondrial super-complexes.
- Acylcarnitine/carnitine and coenzyme Q<sub>10</sub> analyses in fresh frozen muscle.
- Full histochemical and electron microscopic ultrastructural evaluation.

### Additional assays available as needed:

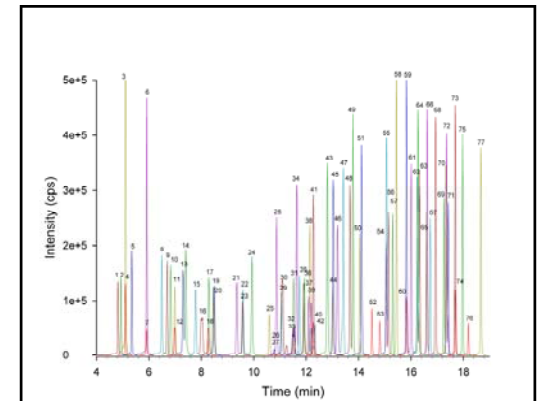
- nDNA and mtDNA gene sequencing.
- Carnitine palmitoyltransferases I&II and fatty acid oxidation enzyme activities.
- Selected confirmatory enzyme assays of pyruvate metabolism and the Krebs cycle (see listing to left).

## Cultured Skin Fibroblasts

- 1) Integrated Mitochondrial Function Oxidative Phosphorylation
- 2) Analysis of the Electron Transport Chain (ETC)
- 3) Acylcarnitine analysis during fatty acid oxidation

## Acylcarnitine Analysis by HPLC-MS/MS

- Validated HPLC-MS/MS method for the quantitative determination of Acylcarnitines
- Chromatographically removes isobaric contaminants
- Chromatographically resolves isomeric compounds
- MRM triple quadrupole detection
- Rigorously quantitative
- Standardized compounds
- Internal standards



HPLC-MS/MS chromatogram of a calibration curve high point of 65 acylcarnitines and 12 internal standards (colored red). All reference acylcarnitines are synthesized, characterized, and standardized.

### When should you use Acylcarnitine Analysis by HPLC-MS/MS?

- Follow-up to positive acylcarnitine Newborn Screening results
- Patients with disease
- False-negative Newborn Screening results
- Not tested by Newborn Screening
- Adolescent- or adult-onset disease
- Protocols for treatment and metabolism Research
- Accurate quantitation of carnitine and acylcarnitine biomarkers