

## About Us

The Center for Inherited Disorders of Energy Metabolism (CIDEM), established in 1988, is comprised of interdisciplinary, 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.

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

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

The Center for Human Genetics Laboratory includes state-of-the-art facilities and has offered genetic screening and diagnostic testing for numerous genetic conditions for more than 25 years.

The Laboratory combines clinical practice with genetic research allowing it to offer physicians and their patients advanced, innovative diagnostic testing.

The CHG Laboratory Molecular Diagnostic section is directed by Dr. Shulin Zhang

**Locations:** University Hospitals of Cleveland Case Medical Center and Case Western Reserve University (CWRU) School of Medicine, Cleveland, Ohio.

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

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## The Center for Human Genetics Laboratory

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CLIA and CAP Certified

## Our Mission

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

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.

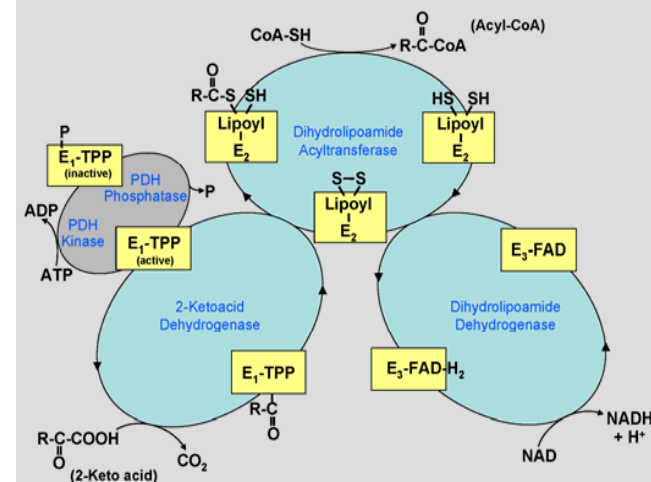


# CIDEM

## Center for Inherited Disorders of Energy Metabolism

www.case.edu/med/CIDEM

## Pyruvate Dehydrogenase Complex & Other Pyruvate Metabolism Disorders



## The Center for Human Genetics Laboratory

www.chglab.com



# Biochemical Analyses

(see CIDEM website for details)

## Metabolites in Body Fluids:

- Lactate and pyruvate (blood, CSF)
- $\beta$ -Hydroxybutyrate, acetoacetate, and free fatty acids (plasma)
- Total carnitine and acylcarnitine analysis (plasma and urine)

## Enzyme Assays:

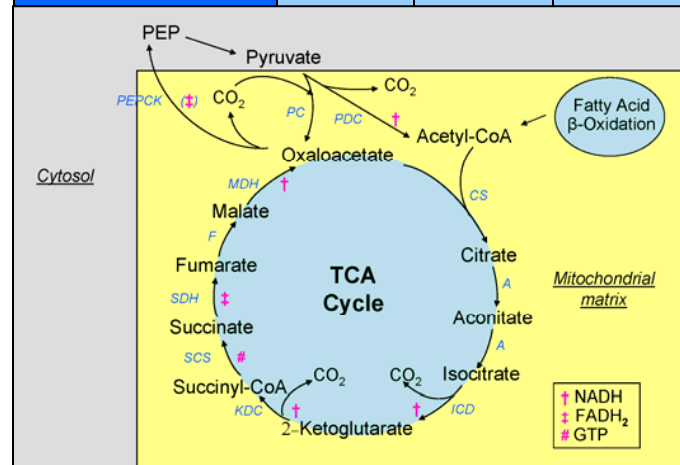
- Pyruvate dehydrogenase complex (PDC), including:
  - Activated/inactivated assays
  - Dihydrolipoamide dehydrogenase (E3)
  - Detection of TPP, lipoate and phosphatase deficiencies
- 2-Ketoglutarate dehydrogenase complex (KDC)
- Pyruvate carboxylase (PC)
- Phosphoenolpyruvate carboxykinase (PEPCK)
- Cell Tissue Samples:
  - Skin fibroblasts
  - Blood lymphocytes
  - Muscle biopsies, other tissues

## Whole Cell Assays:

- Permeabilized fibroblasts
- Rate of pyruvate oxidation and other substrates
- Oxidative phosphorylation

# Clinical & Metabolic Features

Deficiencies of			
Features	PDC	E3, TPP, lipoate	PC, PEPCK
<b>Clinical:</b>			
• Develop. delay	++	++	++
• Hypotonia	++	++	+
• Seizures	++	++	+
• Abnormal brain MRI	++	+	+
• Hepatomegaly	-	+/-	+
• Cardiomyopathy	-	+/-	-
<b>Metabolic:</b>			
• Lactate $\uparrow$ , L/P nl	++	++	++
• Alanine $\uparrow$	++	++	++
• Branch chain AA $\uparrow$	-	+	-
• Citrulline + $\text{NH}_3$ $\uparrow$	-	-	+/-
• 2-Ketoglutarate $\uparrow$	-	+	-
• Hypoglycemia	-	-	++
• Hyperglycinemia	-	+/-	-



# Genetic Analyses

(see CHG website for details)

## Pyruvate dehydrogenase complex genes:

- *PDHA1* (E1-alpha subunit)
- *PDHB* (E1-beta subunit)
- *DLAT* (E2, dihydrolipoamide transacetylase)
- *PDHX* (E3 binding protein)
- *DLD* (E3, dihydrolipoamide dehydrogenase)

## Pyruvate carboxylase:

- *PC*

## For all of the above:

- Exon sequence analyses
- Known mutation analysis
- Prenatal diagnosis

## Samples:

- Most sample types can be transferred between CIDEM and CHG labs

(Institutional discounts are available)  
For details see: [www.chglab.com](http://www.chglab.com)  
or [www.GeneTests.org](http://www.GeneTests.org)

## References:

1. Kerr D, Grahame G, and Nakouzi G. Assays of the Pyruvate Dehydrogenase Complex and Pyruvate Carboxylase, *in* Wong LJ, Biochemical and Molecular Methods in Mitochondrial Disorders, Humana Press, 2012.
2. DeBrosse SD, Okajima K, Zhang S, Nakouzi G, Schmotzer CL, Lusk-Kopp M, Frohnapfel MB, Grahame G, Kerr DS. Spectrum of neurological and survival outcomes in pyruvate dehydrogenase complex (PDC) deficiency: Lack of Correlation with Genotype. *Mol Genet Metab* 107:394-402, 2012.