

Maple Syrup Urine Disease Gene Sequencing Panel (Test #525)

Brief Description of Clinical Features: Maple syrup urine disease (MSUD; OMIM 248600) is a heterogeneous organic aciduria disorder caused by the impairment of the branched-chain α -keto acid dehydrogenase complex (BCKD). BCKD is a mitochondrial complex, encoded by four nuclear genes (*BCKDHA*, *BCKDHB*, *DBT* and *DLN*), which is involved in the metabolism of branched-chain amino acids (leucine, isoleucine, and valine) (Morton et al. Pediatrics 109:999-1008, 2002; Nellis et al. Molec Genet Metab 80:189-195, 2003; Chuang et al. J Biol Chem 279:17792-17800, 2004). Defective BCKD complex activity leads to the accumulation of the branch-chain amino acids to toxic levels (Chuang et al. 2004). MSUD, in untreated neonates, is characterized by mental and physical retardation, maple syrup odor in cerumen and urine, poor feeding, ketonuria, irritability, lethargy, intermittent apnea, opisthotonus, stereotyped movements such as “fencing” and “bicycling”, coma and respiratory failure. Biochemically, MSUD is characterized by elevated plasma concentrations of branched-chain amino acids (leucine, isoleucine, and valine) and allo-isoleucine, as well as a generalized disturbance of plasma amino acid concentration ratios (Schadewaldt et al. Clin Chem 45:1734-1740, 1999; Morton et al. 2002; Nellis et al. 2003; Chuang et al. 2004).

Genetics: MSUD is an autosomal recessive genetically heterogeneous disorder caused by mutations in one of the four BCKD complex encoded genes (*BCKDHA*, *BCKDHB*, *DBT* and *DLN*) (Zhang et al. Clin. Invest. 83:1425-1429, 1989; Zhang et al. Molec. Biol. Med. 8: 39-47, 1991). Of note, *DLN* gene sequencing is not included in this panel since mutations in *DLN* gene result in a clinically distinguishable phenotype. *DLN* sequencing may be ordered separately (Test #529).

Description of This Particular Test: The following genes will be tested in the order specified in the Table below, unless a different order is requested by the client. Testing is accomplished by amplifying and sequencing the coding exons and ~50 bp of adjacent non-coding sequence. See also the individual Test Descriptions for each gene.

Reference Sequences:

Gene	Disease	Percentage of reported mutation	Genomic: NC	mRNA: NM	Protein: NP	CCDS
<i>BCKDHB</i>	MSUD	~38%	000006.11	183050.2	898871.1	4994.1
<i>BCKDHA</i>	MSUD	~33%	000019.9	000709.3	000700.1	12581.1
<i>DBT</i>	MSUD	~19%	000001.10	001918.2	001909.2	767.1

Indications for Test: Candidates for this panel test are patients with symptoms consistent with MSUD.

Sensitivity of Test: Sensitivity for MSUD testing is approximately 85% overall.

Turnaround Time: Maximum of 60 calendar days.

Specimen Requirements: See page four of the Requisition Form.

CPT Codes and Prices

Codes	<i>BCKDHB</i>	<i>BCKDHA</i>	<i>DBT</i>	Panel
83890	\$ 30	\$ 30	\$ 30	\$ 30
83891	\$ 40	\$ 40	\$ 40	\$ 40
83898	\$210	\$170	\$240	\$ 590
83904	\$300	\$250	\$360	\$ 880
83894	\$ 40	\$ 40	\$ 40	\$ 90
83912	\$110	\$110	\$110	\$ 230
Totals:	\$730	\$640	\$820	*\$1860

*When two or three genes are tested, a 15% discount will apply to the total cost of the individual gene tests.

Accreditation: CLIA ID:52D1027685 (expires 1/18/13) CAP ID:7185561, AU ID:1407125 (expires 12/20/12)

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