

Pontocerebellar Hypoplasias Subtype 2 via *TSEN2* Gene Sequencing (Test #305)

Brief Description of Clinical Features: Pontocerebellar hypoplasias subtype 2 (PCH2; OMIM 277470) is a subset of neurodegenerative disorders, characterized by small cerebellum and brainstem, variable neocortical atrophy, and impaired cognitive and motor development (Barth Brain Dev 15:411-422, 1993; Budde et al. Nat Genet 40:1113-1118, 2008). In addition, patients with PCH2 exhibit progressive microcephaly from birth, extrapyramidal dyskinesia, chorea/dystonia or spasticity, and epilepsy (Barth 1993; Budde et al. 2008).

Genetics: PCH2 is inherited as an autosomal recessive disorder. PCH2 is caused by mutations primarily in the *TSEN54* gene, however mutations in the *TSEN2* and in the *TSEN34* genes have also been reported in few PCH2 cases (Budde et al. 2008). *TSEN2* protein, a product of the *TSEN2* gene, which encodes one of the two catalytic subunits of the tRNA-splicing endonuclease complex required in cytoplasmic tRNA splicing (Budde et al. 2008). *TSEN34* protein, a product of the *TSEN34* gene, represents the second catalytic subunit, while the two noncatalytic structural subunits of the tRNA-splicing endonuclease complex are encoded by the *TSEN54* and *TSEN15* genes (Budde et al. 2008). A missense mutation (p.Tyr309Cys) in the *TSEN2* gene has been reported in a consanguineous family from Pakistani origin (Budde et al. 2008).

Description of This Particular Test: This test involves bidirectional sequencing using genomic DNA of the 11 coding exons (exons 2-12) of the *TSEN2* gene. The full coding region of each exon plus ~50 bp of flanking non-coding DNA on each side are sequenced. As indicated, we will also perform sequencing of any single exon (Test #100) or pair of exons (Test #200) for family members of patients with known mutations and to confirm previous research results (\$190-340 charge).

Reference Sequences: Genomic: NC_00003.11 mRNA: NM_025265.3 Protein: NP_079541.1 (CCDS 2611.1)

Indications for Test: Candidates for this test are patients with symptoms consistent with Pontocerebellar hypoplasias subtype 2 (PCH2) and family members of patients who have known *TSEN2* mutations.

Sensitivity of Test: *TSEN2* mutations account for about 2% of PCH2 cases (Budde et al. 2008).

Turnaround Time: Maximum of 40 calendar days, although many tests are completed in 2-3 weeks.

Specimen Requirements: See page 4 of the Requisition Form.

Prices:	Sequencing of <i>TSEN2</i> gene	\$ 740
CPT Codes:		
Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1 83891 \$ 40
Amplification x12	83898 \$ 200	Sequencing x12 83904 \$ 290
Separation x1	83894 \$ 70	Interpretation/Report x1 83912 \$ 110

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

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