PREVENTION GENETICS
DISEASE PREVENTION THROUGH GENETIC TESTING

CLIA #: 52D1027685 ● CAP #: 7185561
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Stuttering via *GNPTAB* Gene Sequencing (Test #316)

Brief Description of Disorder: Stuttering (also called stammering) is speech that is characterized by frequent repetition and/or prolongation of sounds, syllables or words, or by frequent hesitations or pauses that disrupt the rhythmic flow of speech. Stuttering affects ~1% of the population and has a mean onset around 30 months of age (Yairi et al. J Speech Hear Res 35:782-788, 1992). Stuttering often resolves spontaneously before adulthood, particularly in females. In rare cases stuttering can occur in adulthood as a result of brain injury (Fawcett CNS Spectrums 10:94-95, 2005) or drug use (Krishnakanth et al. Prim Care Companion J Clin Psychiatry 10:333-334, 2008). Secondary behaviors, such as eye blinking or other involuntary head movements, are not uncommon (Prasee and Kikano Am Fam Physician 77:1271-1276, 2008).

Genetics: Mutations in *GNPTAB*, located on chromosome 12q, have been associated with stuttering (Kang et al. N Engl J Med 362:677-685, 2010). *GNPTAB* encodes the α and β subunits of GlcNAc-phosphotransferase, a protein involved in the lysosomal enzyme-targeting pathway. Four *GNPTAB* missense mutations were reported in stuttering patients. Most patients were heterozygous for the mutations, although a few were homozygous. Penetrance of the mutations does not appear to be complete. Mutations in the *GNPTG* and *NAGPA* genes, also involved in the lysosomal enzyme-targeting pathway, were similarly reported in stuttering patients. PreventionGenetics offers testing of all three genes.
GNPTAB mutations have also been reported in patients with mucolipidosis. In contrast to stuttering, mucolipidosis appears to be a solely autosomal recessive disorder. Mucolipidosis mutations are mostly nonsense, frameshift and splicing in contrast to the missense mutations found in stuttering patients.

Description of This Particular Test: This test involves bidirectional DNA sequencing of all 21 coding exons of the *GNPTAB* gene. The full coding region of each exon plus ~50 bp of flanking non-coding DNA on either side are sequenced.

Reference Sequences: **Genomic: NC_000012.11** **mRNA: NM_024312.3**
Protein: NP_077288.2 **mRNA and Protein: CCDS 9088.1**

Indications for Test: All stuttering patients are candidates for this test, although it is expected that test yield will be higher for patients with a family history of stuttering and/or speech characterized by more than 4% stuttering dysfluencies, as measured by instruments such as the Stuttering Severity Instrument, 3rd Edition (Riley Stuttering Severity Instrument for Children and Adults. 3rd ed. Los Angeles: Western Psychological Services 1980)

Sensitivity of Test: Kang et al. 2010 reported that 25 of 393 patients (6 %) had mutations in one of the three genes (*GNPTAB, GNPTG,* and *NAGPA*). About half of the 25 patients had mutations in *GNPTAB.*

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

Specimen Requirements: See page 4 of the Requisition form.

Price: **Sequencing of *GNPTAB* Gene** **$ 1,240**

CPT Codes:

Sample Ascertainment x1	83890	$ 30	DNA Isolation x1	83891	$ 40
Amplification x24	83898	$ 380	Sequencing x24	83904	$ 580
Separation x1	83894	$ 90	Interpretation/Report x1	83912	$ 120

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