

Stuttering via *GNPTAB*, *GNPTG* and *NAGPA* Gene Sequencing (Test #315)

Brief Description of Clinical Features: 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 the *GNPTAB*, *GNPTG*, and *NAGPA* genes, all located on autosomes, have been associated with stuttering (Kang et al. N Engl J Med 362:677-685, 2010). These three genes encode enzymes involved in the lysosomal enzyme-targeting pathway. Nearly all mutations in the three genes were missense. The great majority of the stuttering patients were heterozygous for the mutations, although a few homozygous individuals in consanguineous kindreds were also reported. Penetrance of the mutations does not appear to be complete. *GNPTAB* and *GNPTG* mutations have also been reported in patients with mucopolidosis. In contrast to stuttering, mucopolidosis appears to be a solely autosomal recessive disorder.

Description of This Particular Test: This test involves bidirectional DNA sequencing of all coding exons of the three genes. The full coding region of each exon plus ~50 bp of flanking non-coding DNA on either side are sequenced. All three genes are sequenced *simultaneously* in this Test. PreventionGenetics also offers sequencing of the genes individually.

Reference Sequences:

Gene:	Genomic: NC_	mRNA: NM_	Protein: NP_	CCDS:
<i>GNPTAB</i>	000012.11	024312.3	077288.2	9088.1
<i>GNPTG</i>	000016.9	032520.3	115909.1	10436.1
<i>NAGPA</i>	000016.9	016256.2	057340.2	10527.1

Indications for Testing: 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.

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

Specimen Requirements: Refer to page 4 of the Test Requisition form.

Price: Sequencing of *GNPTAB*, *GNPTG* and *NAGPA* Genes: \$ 1,790

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x39	83898 \$ 570	Sequencing x39	83904 \$ 850
Separation x1	83894 \$ 160	Interpretation/Report x1	83912 \$ 140

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