Test Information Sheet

GeneDx, Inc.
207 Perry Parkway
Gaithersburg, MD 20877
Phone: 301-519-2100
Fax: 301-519-2892
E-mail: genedx@genedx.com
www.genedx.com

Mutation Confirmation for Genes not routinely offered by GeneDx, Inc

- **Mutation Confirmation of Mutations Identified in a Research Lab**
- **Custom Mutation-Specific Carrier or Pre-symptomatic Testing**
- **Custom Prenatal Diagnosis**

Clinical utility of this service:

GeneDx provides custom mutation-specific testing of *any* gene for a variety of indications. This specific service is offered so that results previously obtained in a research study can be confirmed in a CLIA certified diagnostic laboratory for inclusion in a patient's medical records and use in medical management. Results may also be used in genetic counseling and for prenatal, carrier, and pre-symptomatic testing of at-risk family members. This testing can be ordered for any genetic disease with Mendelian inheritance. Test accuracy is dependent on having unambiguous mutation descriptions as detailed below. NOTE: When submitting family members other than the proband, a positive control is required.

Required Mutation Information:

Mutation information should be provided to GeneDx in advance, in the form of a publication, lab report, or other communication from the laboratory in which the mutation was previously observed. To clearly identify the mutation, please provide:

1) The name of the gene
2) The mutation in cDNA-level notation (e.g. residue c.123 G to T, where c.1 is the A of the initiator ATG)
3) One of the following:
   a. The mutation given in protein-level notation
   b. The mutation given in gDNA-level notation, with reference to a specific public reference sequence
   c. A DNA sequence at least 30 bases long with the mutated base and mutation indicated

***Inheritance pattern*:**

Autosomal recessive, autosomal dominant, X-linked recessive and X-linked dominant disorders may all be tested using this approach. Once a mutation is confirmed in an affected individual, prenatal diagnosis, carrier testing, and pre-symptomatic testing can be performed on family members who are at risk for the mutation. In some cases, particularly those with time constraints such as prenatal diagnosis, mutation confirmation in an affected family member can be run concurrently with other samples from the same family.

***Reasons for referral*:**

1. Clinical laboratory confirmation of one or more mutations identified in a research lab
2. Carrier testing for a specific mutation previously identified in a family*
3. Pre-symptomatic testing for a specific mutation previously identified in a family*
4. Prenatal diagnosis for a specific mutation previously identified in a family*

**** In these situations a positive control is required with or prior to testing the new person***

***Test methods*:**

Using genomic DNA obtained from buccal (cheek) swabs or 1-5 mL blood in EDTA, GeneDx performs the analysis using information provided by the referring clinician or laboratory. Primers are designed and ordered by GeneDx based on the information provided. If prenatal or carrier testing on unaffected family members is desired, a sample from a related individual known to have the mutation(s) of interest must also be tested. PCR is used to amplify the region of interest in the gene and mutation-specific testing on the index case is performed by sequencing. Prenatal diagnosis or testing of other family members may be done by sequencing,

restriction digest analysis, heteroduplex analysis, or other molecular techniques known to have the ability to identify the specific mutation.

For prenatal diagnosis, we perform duplicate testing on a single specimen, which can be amniotic fluid cells, cultured amniocytes, or chorionic villus samples (CVS). Cultured CVS specimens are discouraged due to the increased risk of maternal cell contamination, but will be accepted. On all types of fetal specimens, we perform concurrent testing as needed to check for maternal cell contamination. ***For this reason, a maternal sample must accompany all prenatal samples.*** In specific circumstances, a paternal sample may also be required. One final report will be issued. Confirmation on cultured cells is not required following analysis of a direct sample.

***Mutational spectrum*:**

PCR and sequencing based methods can identify the majority of molecular mutations that are associated with genetic disease, but certain mutations such as deletions spanning one or more exons, complete gene deletions, gene rearrangements, or duplicationsand may not be detected. To evaluate for gene deletions or duplications, GeneDx offers quantitative gene copy number analysis, such as CopyDx (qPCR) or Muliplex Ligation-Dependent Probe Amplification (MLPA). However, please contact GeneDx in advance regarding the feasibility of quantitative deletion/duplication testing.

Specimen Requirements and Shipping/Handling:

- *Blood*: A single tube with 1-5 mL whole blood in EDTA. Ship overnight at ambient temperature, using a cool pack in hot weather. Specimens may be refrigerated for one week prior to shipping.
- *Buccal Brushes*: As an alternative to blood, use a GeneDx buccal kit (others not accepted). Submit by mail. Buccal brushes are not accepted on children under 6 months of age. **Note, we cannot accept buccal brush specimens for deletion/duplication analysis.**
- *Prenatal Diagnosis:* 10 mL amniotic fluid, 5 mg CVS, or 2 T25 flasks. Ship overnight at ambient temperature, using a cool pack in hot weather. Call to discuss requirements for parental blood. Keep backup cultures.

Required Forms:

- Sample Submission (Requisition) Form – complete all pages
- Payment Options Form or Institutional Billing Instructions

Prices and Turn-Around Time - *Fees are subject to change without notice:*

Test #9001: Confirmation for one specific mutation = $ 350; Approximately 3-4 weeks
Test #9002: Confirmation for two specific mutations = $ 500; Approximately 3-4 weeks
Test #905: Confirmation of a specific deletion/duplication in a custom gene = $800; Approx. 3-4 weeks
Test # 902: Prenatal diagnosis for a specific known mutation* = $2000; Approximately 2 weeks

***** Please see our website for CPT codes/prices for prenatal testing at http://www.genedx.com.

CPT Codes for One Specific Mutation

83891 x 2 units	= $ 20
83898 x 2 units	= $ 70
83894 x 2 units	= $ 40
83904 x 4 units	= $ 120
83892 x 2 units	= $ 40
83912 x 2 units	= $ 60
TOTAL =	**$ 350**

CPT Codes for Two Specific Mutations

83891 x 4 units	= $ 40
83898 x 4 units	= $ 120
83894 x 4 units	= $ 40
83904 x 8 units	= $ 200
83892 x 2 units	= $ 40
83912 x 2 units	= $ 60
TOTAL =	**$ 500**

CPT codes for confirmation of a deletion/duplication in a custom gene

83891 x 2 units	= $ 30
83898 x 12 units	= $ 670
83892 x 2 units	= $ 40
83912 x 2 units	= $ 60
TOTAL	**= $ 800**

Possible ICD Codes:

V18.9 Family member is a carrier of a genetic disease
655.2 Hereditary disease in family possibly affecting fetus