XomeDx*Xpress*: Frequently Asked Questions

1. What is the XomeDx*Xpress* test?

XomeDx*Xpress* is an expedited whole exome sequencing (WES) service offered by GeneDx. XomeDx*Xpress* uses the same methodology as XomeDx (our routine WES service). The primary difference is the personal, expedited handling of each case. We will verbally report pathogenic and/or expected pathogenic variants in known disease-causing genes (Human Genome Mutation Database genes) within 7 calendar days* after the start of testing. Variants of unknown significance will not be verbally reported. A written report, which includes confirmed variants of all clinically relevant genes in the exome, will be provided in approximately 2 weeks.

2. When is XomeDx*Xpress* useful?

XomeDx*Xpress* is available to critically ill patients (such as the NICU and PICU patients) for whom a rapid molecular diagnosis may direct or alter medical management. XomeDx*Xpress* can be used to identify the underlying molecular basis of a genetic disorder in an affected individual with:

- Rapidly deteriorating clinical status
- High-acuity illness manifesting with seizures, hypotonia, and morphological abnormalities of the central nervous system
- A genetic syndrome or underlying metabolic disorder for which a quick answer will impact management
- A clinical presentation for which a molecular diagnosis may replace the need for invasive testing
- A disease, which is highly genetically heterogeneous and no single gene or group of genes makes up a significant percentage of the mutation spectrum and for which a rapid result may change the patient's outcome

One small study of patients in an intensive care unit reported that sequencing had a diagnostic yield of 73% in the highly selected patient population that was tested (Soden et al., 2014).

3. What is the turn-around-time for this test?

A GeneDx geneticist will provide a verbal result of pathogenic variants in known disease-causing genes (HGMD genes) that may be related to the phenotype in the patient. This verbal result will be provided within 7 calendar days* after all three samples are received.

After the verbal result is discussed with the ordering provider, analysis will continue on all of the genes in the exome. A written report of all confirmed variants, including any variants of unknown significance, variants in novel (candidate) genes, and any secondary findings will be sent to the ordering provider in approximately 2 weeks.

4. What is required to proceed with XomeDx*Xpress* testing?

- We will only accept trios (specimens on the proband and both biological parents) for XomeDx*Xpress*. Exome sequencing will be performed on all three specimens; however, parental specimens will be used only for analysis and interpretation in the context of the proband's phenotype and molecular diagnosis. All individuals' samples must be received by GeneDx prior to beginning of testing. Only results on the proband will be reported.
- Detailed clinical information:
  - Complete clinical information is an essential part of identifying pathogenic variants with exome sequencing. We require clinical information with the specimens.
  - Please provide any updated lab results and clinical information as they become available.
  - We ask that any change in clinical presentation of the patient is reported to GeneDx. GeneDx may request additional clinical information on DAY 5 of testing to ensure any new clinical developments are included in analysis.
- Along with the ordering provider information on the test requisition, please provide contact information of a point person (physician) directly involved with the patient's care and the preferred method of contact during business and non-business hours. This is essential to ensuring timely communication.

5. How do I order XomeDx*Xpress*?

- Please contact GeneDx by email **(xpress@genedx.com)** to discuss a case or inform us that a sample is being sent.
- Complete the XomeDx*Xpress* requisition and informed consent (genedx.com/forms)
- Collect trio samples. Accepted specimen types: blood in EDTA (lavender top) tubes: 5-6 mL (3 mL minimum-proband only) or high quality extracted DNA: At least 15ug is requested (with a minimum concentration of 50ng/ul).
- Use dedicated XomeDx*Xpress* kit or label all tubes and boxes clearly visible as STAT
- Ship samples overnight at ambient temperature, using a cool pack in hot weather

6. What is the billing policy for XomeDx*Xpress*?

GeneDx cannot bill medical insurance companies for genetic testing we perform on inpatients; therefore, we will bill the institution for most cases. Self-pay will also be accepted. An expediting fee will apply. Your GeneDx sales representatives can work with your institution to determine pricing.

7. How does GeneDx identify variants that are associated with the patient's phenotype?

WES identifies hundreds to thousands of variants. Variants are filtered using a variety of factors including but not limited to population frequency, inheritance pattern, phenotype, presence of gene and/or mutation in the Human Gene Mutation Database (HGMD) or other databases, predicted severity of the sequence change, and pathway affected.

8. Will your analysis identify mutations in disease-associated genes that are not associated with the patient's reported phenotype?

GeneDx's XomeDxXpress service uses our clinical and molecular genetics expertise to identify variants that are associated with a patient's reported phenotype. However, as recommended by the American College of Medical Genetics (ACMG), all individuals whose samples were sent to GeneDx for whole exome sequencing (WES) testing will receive secondary findings, if present in the proband, as part of their result. Any secondary findings identified in the genes recommended by ACMG will be listed at the end of the report. In rare cases, GeneDx may also report an incidental finding in a gene that is not one of the genes recommended by the ACMG. These findings are pathogenic variants identified in genes that are considered medically actionable and the results are significant for the health of the proband.

GeneDx would like to honor patient preferences and therefore we will offer the choice to opt-out of receiving secondary findings. Patients can choose to opt-out of receiving secondary findings by selecting the opt-out option on the XomeDxXpress Test Requisition Form.

9. How can I get more information about XomeDx*Xpress* testing?

- To discuss this service in more detail, contact your product specialist or email us at **xpress@genedx.com**
- For a detailed general discussion of WES provided by GeneDx see XomeDx Frequently Asked Questions **(genedx.com/xomedx)**

References:

Soden et al. (2014) Science translational medicine 6 (265):265ra168 (PMID: 25473036)

*International clients will receive an email status update at 7 days and receive the written report in 2 weeks.

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