There is a saying in medical school:
“When you hear hoofbeats, think horses not zebras.”
This means “think of common explanations first, not rare possibilities.”
When you encounter a zebra, think GeneDx.
We specialize in diagnosing rare genetic disorders.

References
We offer an extensive menu of testing options:

- cardiology
- cytogenetics
- dermatology
- endocrinology
- exome/genome sequencing
- gastroenterology
- immunology
- metabolic
- mitochondrial
- neurology
- oncology
- ophthalmology
- prenatal
- pulmonology
- rare disorders
- renal
- rheumatology
- skeletal disorders

We offer an extensive menu of testing options.

DNA is the instruction book that directs the production of proteins. Genes are the chapters of the instruction book and are made of two types of fragments:

- **Exons** are the pieces that come together to make proteins
- **Introns** are regions between exons that are cut out when proteins are made

Collectively, all of the exons in our body make up our *exome* and all the genes (exons and introns) make up our *genome*.

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**Clinical Genomic Testing**

When patients present with complex medical issues, a genetic diagnosis is likely. Clinical exome or genome sequencing is ideal for patients where identifying the underlying genetic diagnosis is not straightforward or may require time-consuming and costly evaluations.

**IMPACT OF DELAYED DIAGNOSIS**

The length of time from symptom onset to an accurate diagnosis is around 4.8 years for a rare disease. Genetic conditions account for more than 1/3 of deaths in U.S. Children’s Hospitals.

**INDICATIONS FOR CLINICAL EXOME/GENOME TESTING**

- Rapidly deteriorating clinical status
- Multiple congenital anomalies
- Genetically heterogeneous disease; pathogenic findings could be present in many different genes
- Long list of differential diagnoses
- Atypical presentation of a genetic disorder
- Currently available genetic testing has been exhausted

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Diagnostic yield for exome sequencing at GeneDx is:

- **~20%** for proband-only
- **~30%** for trios (proband-mother-father)

Candidate genes are reported in ~20% of our exome and genome results

~7% of exome results are CNVs; usually just a single exon

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www.genedx.com
Variant Interpretation

GeneDx classifies all variants according to the standards and guidelines put forth by the American College of Medical Genetics and Genomics and the Association for Molecular Pathology.  

POSSIBLE GENETIC TEST RESULTS:

Definitive
Pathogenic or likely pathogenic variant identified in gene known to be associated with the patient’s reported features

Possible

- Variant of uncertain significance (VUS) identified in gene known to be associated with the patient’s reported features OR
- Pathogenic/likely pathogenic variant in well-described gene where further clinical correlation is needed

Candidate
VUS identified in gene that has not yet been reported in association with disease, but data supports a possible association

Negative
No variants identified that are associated with reported clinical phenotype

ACMG Secondary Findings
Known or expected pathogenic variants in genes unrelated to the patient’s reported phenotype (unless the patient chooses to opt-out in writing)

EXOME REANALYSIS

- Clinician initiated: Two years after a non-diagnostic result, or sooner if patient’s features significantly evolve
- Laboratory initiated: as new disease genes are discovered and reported in the literature and through ongoing re-evaluation of accumulated internal data

External Databases
(ClinVar, Locus-specific Databases)

In Silico Predictors
(Provean, Alamut)

Internal Resources
(Familial Segregation, Co-Occurrence, Exome/Genome Database)

Detailed Phenotypic Information

Functional Studies/
RNA Analysis

Population
Data (gnomAD)

Publications
(PubMed, HGMD, Google)

SNAPSHOT OF GENE DX CLINICAL GENOMIC TESTING

Testing | Description
--- | ---
XomeDx® and XomeDx® Plus | Exome sequencing with or without mitochondrial genome sequencing

Trio testing available to aid in interpretation

XomeDxXpress® and XomeDx® Priority | Rapid exome sequencing for when timing is critical and results may direct or alter medical management

Rapid genome sequencing for when timing is critical and results may direct or alter medical management

XomeDx® Prenatal | Expedited exome sequencing specifically designed for ongoing pregnancies with abnormal fetal ultrasound findings

Slice | Custom gene list created by the ordering provider based on patient’s clinical presentation

Our custom Slice Tool and our clinical team can help you create the best gene list for your patient

Trio testing available to aid in interpretation for larger gene lists

GenomeSeqDx | Whole genome sequencing

GenomeXpress | Rapid genome sequencing for when timing is critical and results may direct or alter medical management

For a complete list of our genomic test options, please contact your GeneDx Sales Representative or see www.genedx.com.

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The GeneDx Difference

Founded in 2000 by two NIH scientists, GeneDx Inc. is a global leader in genomics, pioneering the identification of new disease-causing genes and the development of clinically-relevant genetic tests. Our team of experts includes well over a hundred genetic counselors and MD/PhD scientists with extensive clinical experience and peer-reviewed publications. We go the extra mile to find answers and provide useful information for clinicians, patients, and families. We work to end your patients’ diagnostic odyssey.

**WHAT WE DO**

<table>
<thead>
<tr>
<th>WHAT WE DO</th>
<th>WHY IT MATTERS</th>
</tr>
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<tbody>
<tr>
<td>Comprehensive Assessment</td>
<td>High Quality Testing</td>
</tr>
<tr>
<td>• Sequence at an average coverage of 100–120x for exomes and up to 500x for NGS panels</td>
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<tr>
<td>• Include mitochondrial sequencing alongside WES to increase the diagnostic yield (up to 3%)</td>
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<tr>
<td>Advanced Detection</td>
<td>Find More Answers</td>
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<tr>
<td>• Solve previously-undiagnosed cases by identifying:</td>
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<tr>
<td>• Difficult-to-detect variants such as MEIs using our SCRAMble Tool</td>
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<tr>
<td>• Clinically-relevant mosaicism down to single digit levels</td>
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<td>• CNVs as small as a single exon</td>
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<tr>
<td>• Heteroplasmacy as low as 1.5%</td>
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<tr>
<td>Check and Double-Check</td>
<td>Results You Can Trust</td>
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<tr>
<td>• Compare every case to our unparalleled database built over 20 years that includes close to a million tests performed</td>
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<tr>
<td>Customized Care</td>
<td>Your Patient is Our Patient</td>
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<tr>
<td>• On-call genetic counselors answer your clinical questions</td>
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<td>• Expedite analysis when timing is critical for management</td>
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<tr>
<td>• Thoroughly review every order for most appropriate testing strategy</td>
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<td>• Write clear, concise, and comprehensive reports individually for every patient</td>
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<tr>
<td>• Include recommendations for management or research studies for specific clinical situations</td>
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<tr>
<td>Expert Analysis</td>
<td>Cutting-Edge Knowledge</td>
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<tr>
<td>• Classify variants according to the most recent guidelines</td>
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<tr>
<td>• Search our internal database for additional evidence of causation when variants are found in candidate genes</td>
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<tr>
<td>• Proactively report new answers found for previously-negative or inconclusive cases</td>
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<tr>
<td>Advancing Genetics</td>
<td>Helping Future Patients</td>
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<tr>
<td>• Discover new disease-causing genes (Close to 200 genes published and more each year!)</td>
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<tr>
<td>• Contribute ~25% of all submissions to GeneMatcher</td>
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<tr>
<td>• Submit variants with full interpretations to ClinVar (over 120,000 so far!)</td>
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<tr>
<td>• Provide raw exome/genome data to clinicians (with proper consent) to further research</td>
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**WE’RE HERE TO HELP WITH COORDINATION OF TESTING!**

**Genetic Counselors**
- Easy access to genetic counselors who can help providers with test selection, answering clinical questions and discussing results
- Pre- and Post-test genetic counseling services for patients via MyGeneTeam (www.mygeneteam.com)

**Managed Care**
- GeneDx is committed to working with patients and offers numerous patient payment options
- GeneDx is in-network with the majority of commercial health plans

**Ease of Ordering**

**Ordering online**
- Register and/or sign in at www.genedx.com
- Select the appropriate test code

**Ordering on paper**
- Obtain a test requisition form from the GeneDx website (www.genedx.com/forms) or your sales representative

**Provide a sample**
- Order kits on our website (www.genedx.com/supplies) or email us (zebras@genedx.com)
- We accept the following specimens:
  - 4-6 mL blood in EDTA (lavender top) tube
  - Two buccal swabs
  - 20 ug DNA

**Get results**
- You will receive results in the online portal
- Result can also be sent via fax, mail, secure email or via EMR