3B-NEO Premium Test

For Guardian

Comprehensive Genetic Screening for Your Newborn

NEWBORN DETAILS

Unique ID	[Unique ID]	**Physician**	[Physician]	**Sample type**	DBS
3billion ID	[3billion ID]	**Department**	Obstetrics & Gynecology	**Collected on**	yyyy-mm-dd
DOB* / Sex	yyyy-mm-dd / Male	**Institution**	[Institution]	**Ordered on**	yyyy-mm-dd
Ethnicity	Latino/Admixed American			**Accessioned on**	yyyy-mm-dd

* (YYYY-MM-DD)

RESULT SUMMARY

DETECTED **Further confirmatory testing required**

- A pathogenic variant was identified in the ALDH7A1 gene.
- Related Condition: Epilepsy, early-onset, 4, vitamin B6-dependent (OMIM: 266100)

WHAT DOES THIS RESULT MEAN?

1. Your newborn's screening result suggests a possible problem with the brain and nervous system, related to a gene called ALDH7A1. The condition detected is known as Pyridoxine-dependent epilepsy. Without treatment, this could lead to serious health problems. This finding is not caused by anything you did during pregnancy.
2. The test detected a genetic change that increases the risk for the condition listed above. **It is important to note that many of the conditions screened, including this one, are manageable when identified and treated early.** Please understand that this is a screening result, not a definitive clinical diagnosis. Further evaluation by a medical specialist is required to confirm these findings and determine the most appropriate care plan for your baby.

WHAT SHOULD I DO?

1. 

Specialist Consultation and Additional Testing

Meet with a specialist in pediatric neurology to discuss these results. Following the specialist's guidance, confirmatory testing (such as specialized blood or urine analysis) may be conducted to reach a final diagnosis.

2. 

Consider Parental Genetic Testing

Testing both parents is recommended to determine if the identified variant was inherited. This helps medical professionals more accurately assess the clinical significance of the finding and its potential impact on newborn's health.

3. 

Monitor Clinical Symptoms

Even before a final diagnosis, closely observe the newborn for signs of excessive irritability (being overly sensitive to external stimuli or difficult to soothe) or seizures (such as body tremors or staring spells). If any of these symptoms occur, notify your medical team immediately for prompt evaluation.

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HOW DOES EARLY DETECTION HELP?

1. **Proactive Management**
   Early identification allows for proactive medical management, which aims to minimize the risk of severe neurological emergencies such as sudden seizures.
2. **Optimal Development**
   Timely medical intervention supports the best possible outcomes for the child's cognitive and motor development.
3. **Lifelong Health Foundation**
   Understanding the genetic condition facilitates tailored medical and nutritional strategies, establishing a strong foundation for the child's long-term well-being.

VARIANT INFORMATION

Epilepsy, early-onset, 4, vitamin B6-dependent (OMIM:266100)

Gene	Variant		Classification
ALDH7A1	Genomic Position	5-126552059-C-G (GRCh38)	Pathogenic
	cDNA	NM_001182.5:c.1279G>C	
	Protein	NP_001173.2:p.Glu427Gln	
	Zygosity	Homozygous	
	Inheritance	Unknown	

See the next page for term definitions and explanations →

ABOUT THIS SCREENING

This screening provides a comprehensive analysis of **704 genes** associated with serious, early-onset childhood conditions. It spans all medical specialties, including **Metabolism, Neurology, Immunology, Cardiology**, and more, to ensure a thorough genetic assessment for your newborn.

For the complete list of genes and associated conditions, please click here.

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INTERPRETING VARIANT INFORMATION

The table above shows the specific genetic change identified in your newborn. The explanations below are provided to help you understand what each term means. The example used here is for illustration purposes only.

Marfan syndrome (OMIM:154700) Disease name

Gene	Variant		❹ Classification
FBN1 Gene name	❶ Genomic Position	15-48779599-G-A (GRCh37)	Pathogenic
	cDNA	NM_000138.5:c.3373C>T	
	Protein	NP_000129.3:p.Arg1125Ter	
	❷ Zygosity	Heterozygous	
	❸ Inheritance	Unknown	

- The human genome consists of 3 billion base pairs stored across 22 pairs of autosomes and 1 pair of sex chromosomes.
- Just as the English language is composed of 26 letters, the genome is written using 4 nitrogenous bases (A/T/G/C).

❶ **Genomic Position:** Indicates the specific location within the total genome sequence where the change occurred.

Example:

5 - 48779599 - G - A

Chromosome | Position | Reference | Patient

Think of the genome like a very long book. This tells you exactly which page and which letter contains the change — in this case, on Chromosome 15, at a specific location, the letter G was changed to A.

❷ **Zygosity:** We each carry two copies of every gene — one from each parent. Zygosity tells you whether the change was found in one copy or both.

- **Heterozygous:** The change is present in only one of the two copies. Think of it as one working copy and one altered copy.
- **Homozygous:** The same change is present in both copies.

❸ **Inheritance:** Indicates whether the same variant is present in one or both parents. This helps determine if the finding was inherited or occurred for the first time in your newborn. Depending on the case, parental testing may be required.

❹ **Classification:** Indicates the clinical grade/significance of the variant.

- **Pathogenic:** A variant that has a very high probability of causing disease.
- **Likely Pathogenic:** A variant that is likely to cause disease.
- **VUS** (Variant of Uncertain Significance): A variant whose significance is currently unclear. It may or may not be related to the condition, and further evidence or testing may be needed over time.

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TEST METHODS

Sample Collection  › Genomic Analysis  › Expert Review  › Result Reporting 

1. **Sample Collection**
   A Dried Blood Spot (DBS) sample was safely collected from your newborn and sent to our laboratory for analysis.
2. **Genomic Analysis**
   Your newborn's DNA was analyzed using Genome Sequencing (GS), a cutting-edge technology that reads through the most critical parts of the genetic code to identify changes that may affect health.
3. **Expert Review**
   The identified genetic changes were reviewed and classified by our specialists using our proprietary software, EVIDENCE, and internationally recognized guidelines from the American College of Medical Genetics and Genomics (ACMG).
4. **Result Reporting**
   This report focuses on genetic variants associated with serious conditions that begin in childhood, where early intervention and immediate medical care can prevent irreversible harm.

TEST LIMITATION

To ensure a correct understanding of your results, please review the following:

1. **Technical Scope**
   This test is highly accurate but focuses on specific genomic regions. Certain complex changes (e.g., mosaic variants or non-coding regions) may not be detectable. Specialized testing may be needed if these are clinically suspected.
2. **Medical Updates**
   Interpretations are based on data available at the time of reporting and not subject to automatic reanalysis. As genomic science evolves, please consult a specialist if new symptoms arise to determine if updated testing or re-interpretation is needed.
3. **Screening Nature**
   This is a screening tool, not a final diagnosis. A "Detected" result requires confirmation, and "Not Detected" does not 100% rule out a condition (potential for false negatives).
4. **Follow-up Care**
   If symptoms or family history are present, consult a specialist regardless of these results. Final diagnosis may require additional clinical evaluation and confirmatory tests (e.g., biochemical assays). Note: For certain genes including SMN1 and CYP21A2, confirmatory testing is especially recommended due to technical limitations inherent to these genomic regions.

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DISCLAIMER

This test was developed by 3billion for the purpose of identifying single nucleotide variants, small insertions and deletions, and structural variants from the [exome/genome] sequence. This laboratory is certified under the College of American Pathologists (CAP#: 8750906) and Clinical Laboratory Improvement Amendments (CLIA#: 99D2274041) as qualified to perform high complexity clinical laboratory testing.Assay validation and clinical validation were performed following the Korea Institute of Genetic Testing Evaluation, the American College of Medical Genetics and Genomics (ACMG) Technical Standards and Guidelines Section G (https://www.acmg.net/PDFLibrary/Standards-Guidelines-Clinical-Molecular-Genetics.pdf) and the CAP Next Generation Sequencing (NGS) Worksheets (Santani A et al. J Mol Diagn. 2019 May;21(3):369-374; https://www. cap.org/member-resources/precision-medicine/next-generation-sequencing-ngs-worksheets). This test is designed for newborn screening purposes only and is not intended as a standalone diagnostic tool. If low-level mosaicism or variants within regions that are incompletely sequenced due to technical difficulties with amplification, sequencing, or alignment are suspected, it is recommended to perform appropriate testing specifically designed to detect such variants. This report may not be copied or reproduced except in its totality.

ACCREDITATIONS AND CERTIFICATIONS

CAP License #	CLIA ID #
8750906, AU-ID# 2052626	99D2274041

This case has been comprehensively reviewed by our clinical team of physicians, geneticists and informaticists.
Report electronically signed by:

Go Hun Seo, M.D, Ph.D.
Chief Medical Officer & Laboratory Director