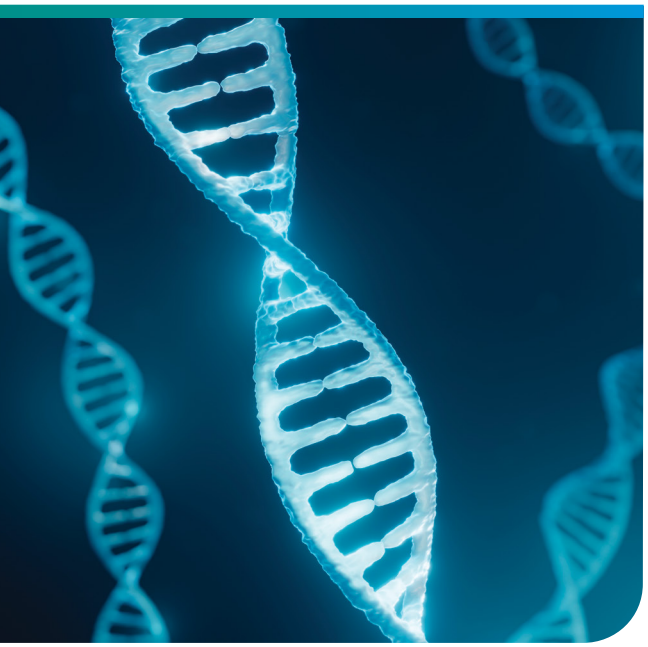
NOVODETECT™
Driving change in the diagnostic journey



Your guide to NovoDETECT™ genetic test results

Genetic test results from **NovoDETECT™**, sponsored by Novo Nordisk through **Blueprint Genetics**, can help you identify the possible underlying genetic cause of your patient's kidney stones.

Eligible patients supply a DNA sample (buccal or blood) for testing via a **3-gene primary hyperoxaluria (PH) panel** or **45-gene nephrolithiasis panel**. From these panels, results will determine if a variant is:

1. Negative
2. Variant of uncertain significance (VUS)
3. Likely pathogenic
4. Pathogenic

These results can help guide diagnostics and next steps for your patient. Learn more about interpreting results on the following pages.

For more information on genetic testing, visit NovoDETECT.com.

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Interpretation of key findings

Example of a NovoDETECT™ test result

Your patient's 3-gene PH panel or 45-gene nephrolithiasis panel report will analyze genes associated with nephrolithiasis and provide a high-level summary of genetic sequence alterations known as genetic variants (mutations).

The following example shows a **VUS test result** from a 3-gene PH panel. It is annotated to help you interpret the primary findings. Please see your patient's report for additional information.

VUS TEST RESULT

PRIMARY FINDINGS

The patient is homozygous for *AGXT* c.743C>T, p.(Ala248Val), which is a variant of uncertain significance (VUS).

PRIMARY FINDINGS: SEQUENCE ALTERATIONS

1	2	3	4	5	6	7
GENE AGXT	**TRANSCRIPT** NM_000030.2	**NOMENCLATURE** c.743C>T, p.(Ala248Val)	**GENOTYPE** HOM	**CONSEQUENCE** missense_variant	**INHERITANCE** AR	**CLASSIFICATION** Variant of uncertain significance

8	9	10	11
ID rs372482918	**ASSEMBLY** GRCh37/hg19	**POS** 2:241814588	**REF/ALT** C/T

12	13		14
gnomAD AC/AN 22/251364	**POLYPHEN** possibly damaging	**SIFT** deleterious	**MUTTASTER** disease causing	**PHENOTYPE**

Key findings of genetic analysis.

Report categories defined

1 GENE
Pathogenic variants in *AGXT* cause PH1[1,2]
- **PH1 is the most common subtype of a group of rare genetic disorders that cause hepatic oxalate overproduction, resulting in kidney stones that may lead to progressive kidney damage and systemic disease**

Examples of other potential reports:
- ***GRHPR*, causing PH2[1]**
- ***HOGA1*, causing PH3[1]**

For more information on the gene, click the link on the report.

2 TRANSCRIPT
Gene identification number

3 NOMENCLATURE
Position and type of nucleotide change within the gene; position and amino acid change

4 GENOTYPE
Genotype reported as homozygous (HOM) indicates that the same variant is present on both copies of the gene, which, if pathogenic, causes PH

Examples of other potential reports:
- Heterozygous (HET)[a]
- Hemizygous (HEM)[b]

5 CONSEQUENCE
Impact of the genetic variant on the amino acid sequence

6 INHERITANCE
Inheritance reported as autosomal recessive (AR), such as in a PH finding, indicates that both copies of the gene must have pathogenic variants to cause the disease

Examples of other potential reports:
- Autosomal dominant (AD)[c]
- X-linked (XL)[d]

7 CLASSIFICATION
Results are determined when compared to human genome assembly 37 with NovoDETECT™ genetic data on file

8 ID
Single nucleotide polymorphism (SNP) ID in SNP database

For more information on the ID number, click the link on the report.

9 ASSEMBLY
Genome build used for reference; GRCh37=genome reference consortium human build 37

10 POS
Genomic position of variant; chromosome: position

11 REF/ALT
Reference/variant nucleotide

12 gnomAD AC/AN
Allele count/allele number in the genome aggregation database

13 POLYPHEN, SIFT, AND MUTATIONTASTER
In silico prediction tools used to predict the significance of identified amino acid changes

14 PHENOTYPE
Phenotype, such as hyperoxaluria, will be stated in the instance of a positive classification

[a]HET=different variants are present on each copy of the gene.
[b]HEM=only 1 copy of the gene is present.
[c]AD=indicates the disease is caused by 1 pathogenic variant.
[d]XL=indicates that the disease is caused by pathogenic variants on the X chromosome(s).

Call NovoDETECT™ at (833) 472-2999 (Monday-Friday, 8 AM-8 PM EST)
to speak with a **Blueprint Genetics** support team member.

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Review test results with your patient

A negative test result means that the panel did not find any known disease-causing variant that explains the patient's current symptoms.

A negative test result may mean alternative diagnostic tools should be discussed with your patient to further understand what is causing their symptoms.

A likely pathogenic or pathogenic test result means that the panel found a genetic variant associated with kidney stone disease, confirming a diagnosis.

A result indicating a likely pathogenic or pathogenic variant may give you the information you need to potentially help manage your patient's symptoms and disease.

A VUS test result means that currently there is not enough evidence to support a positive or negative diagnosis.

While in silico tools like PolyPhen, SIFT, and MutationTaster report the predicted impact of a variant, clinical pathogenicity may be resolved with additional testing.

VUS Resolution Program in PH, sponsored by Novo Nordisk

- Working with **Quest Diagnostics**, a PH urine metabolite assay is conducted to help resolve a VUS result in PH-associated genes
- **ExamOne** will reach out to your patient directly and set up an at-home appointment for a urine sample collection
- Segregation studies are offered to investigate how PH was inherited and how it may impact family members

Actor portrayals.

Genetic counseling is available through Quest Diagnostics regardless of result, if you chose to opt your patient in for this feature when submitting the test requisition.

If your patient receives a **likely pathogenic or pathogenic test result for PH or has a PH VUS result**, family member testing may be suggested.

For more details on key findings,
refer to other sections throughout the report.

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What's next for your patient with NovoDETECT™

Have a question? A Blueprint Genetics support team member is available to answer clinical questions and, if needed, help you interpret genetic test results.

Call NovoDETECT™ at (833) 472-2999 (Monday-Friday, 8 AM-8 PM EST) to speak with a **Blueprint Genetics** support team member.

Email a **Blueprint Genetics** support team member via: **support.us@blueprintgenetics.com**.

Actor portrayals.

Visit **NovoDETECT.com** for more information.

NovoDETECT™ is not intended to and should not interfere in any way with a healthcare professional's or patient's independent judgment and choice in the treatment options for these diseases. Healthcare professionals and patients should always consider the full range of treatment options and select those most appropriate for the individual patient.

No patient-identifiable information or raw sequence data will be shared outside of the program. Examples of de-identified patient data are clinical diagnosis, age range, sex, and genetic variants associated with kidney stone diseases. Contact information of the healthcare professional associated with the patient may also be shared as needed.

No samples or identifiable research data will be shared with third parties without express permission from the patient.

No patients, healthcare professionals, or payers, including government payers, are billed for this program.

References: 1. Lai C, Pursell N, Gierut J, et al. Specific inhibition of hepatic lactate dehydrogenase reduces oxalate production in mouse models of primary hyperoxaluria. *Mol Ther*. 2018;26(8):1983-1995. **2.** Hoppe B, Beck BB, Milliner DS. The primary hyperoxalurias. *Kidney Int*. 2009;75(12):1264-1271.

Blueprint Genetics

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