

CGT Bank v5.4.10

| Patient Information | | Sample Information | | Clinic Information | |
|---------------------|-------------------|--------------------|------------|--------------------|---------------------|
| Unique pat id.: | 0264386 | Sample type: | Blood | Clinic: | WeFIV |
| Patient name: | | Date of draw: | 30/10/2025 | Doctor: | FERNANDO NEUSPILLER |
| Patient DOB: | | Date of receipt: | 05/11/2025 | | |
| Ethnic group: | African American | Report date/time: | 02/04/2026 | | |
| Indication: | No family history | | | | |

TEST RESULTS

NEGATIVE

INTERPRETATION OF TEST RESULTS

For a negative test result, the risk of having children affected by the investigated conditions decreases significantly compared to the general population. This is also the case for a negative personal result when a partner or gamete donor is a carrier for one or more of these analyzed genes. However, due to test limitations associated with any genetic test, this low risk is not zero (see limitations section and informed consent)

TEST DESCRIPTION

The Carrier Genetic Test (CGT) is a preconception DNA screening test that aims to identify individuals and couples at increased risk of conceiving children affected by a monogenic disease. Knowledge of this risk may influence a couple's decision to conceive or encourage the couple to adopt preventive measures, including preimplantation genetic testing for the at risk disease (PGT-M) prenatal genetic testing, or to use donated gametes. The multigene CGT interrogates thousands of DNA variants using a high-throughput technology (Next Generation Sequencing, NGS).

COMMENTS

Report's language has been updated by clinic's request.

TEST METHODOLOGY

DNA is isolated from the sample, usually blood or saliva, and analyzed by whole exome sequencing by NGS. This includes capture and sequence of all human exons and other gene regions of interest where known disease-causing variants are located. Sequencing raw data is then analyzed using bioinformatics (bioinformatic pipeline v3.0), which includes sequence alignment against the GRCh37 human genome reference, variant calling, annotation, and real-time interpretation of variants. QC parameters include, all reported samples that will have a minimum of 7Gb of data, with minimal mean coverage greater than 75x, and a specific depth analysis for more than 68,000 DNA positions where known pathogenic variants are located. In addition, complementary tests (non-NGS techniques) are performed for the following genes, if included, CFTR gene intronic variant/s; SMN1 gene exon 7-deletion; CYP21A2 gene frequent mutations; HBA1 and HBA2 genes frequent deletions; FXN gene GAA repeat sizing; FMR1 gene CGG repeat sizing (females only); DMD gene frequent deletions/duplications; F8 gene intron 22 inversion (females only). When requested, CNV analysis by MLPA is performed for CFTR, HBB and HBA1/HBA2. Based on our validations studies, reported samples will have analytical detection rate for SNV variants as per the control sample NA12878 (Control positive); PASS value: NA12878 Sensitivity SNV ≥ 0.97000 .

TEST LIMITATIONS

In the general population, there is a 3-5% risk for birth defects caused by genetic and/or non-genetic factors not detected by this type of test.

Analytically, the CGT test does not cover all known monogenic diseases nor all disease-causing variants for each tested gene. The test does not include the analysis of conditions associated with mitochondrial DNA nor multifactorial nor digenic inheritance. The test does not detect large rearrangements (inversions, deletions and duplications more than 15 nucleotides), variants located in regulatory regions or intronic regions outside the +/-3bp cut off (except if otherwise indicated), or in low sequence coverage areas (<7x). DNA changes caused by trinucleotide repeat expansions are not detected, except those indicated in the methodology section. For copy number variation analysis, when a normal result is obtained (2 copies detected), it is not possible to confirm that one copy is present in each of the two alleles (non-carrier) or if both copies are present in cis on the same allele, with no copies in the other allele (silent carrier). Clinical sensitivity varies among conditions. In particular, the sensitivity for SMN1 is approximately 96% because it is not possible to identify silent carriers among patients with 2 SMN1 copies detected and because point mutations or small indels are not analyzed. The CYP21A2 gene analysis presents unique challenges due to its high sequence homology (~98%) with the pseudogene CYP21A1P, which leads to frequent gene rearrangements and complex mutations. These challenges can cause difficulties in distinguishing CYP21A2 from CYP21A1P, increasing the risk of misdiagnosis. Different testing methods have specific limitations, requiring a combination of techniques such as long-range PCR, Sanger sequencing, next-generation sequencing (NGS), MLPA, and qPCR to achieve accurate results. These challenges and limitations may lead to false or inconclusive results. Therefore, genetic counselling is strongly recommended to evaluate the findings, discuss potential implications, and determine whether additional testing (such as MLPA) is necessary for an accurate diagnosis. In summary, sensitivity to detect pathogenic variants, if they result from complex gene conversion/gene rearrangements events, may be reduced. For the HEXB gene, the common 16 kb deletion that causes disease in 30% of affected patients is not included in CGT analysis. Furthermore, this test does not evaluate the HFE gene.

Then, a negative CGT result significantly reduces but does not completely exclude the possibility of being a carrier of a variant associated with single gene disorders (see residual risk table). The presence of pseudogenes and/or rare polymorphisms and/or homopolymers may lead to false negative or false positive results. In addition, a negative result for the CGT variants does not exclude the possibility of a de novo variant occurring in the offspring. Germline mosaicism or low-level somatic mosaicism cannot be detected. As with any laboratory test, there is a small chance that this result may be inaccurate for a procedural reason such as an error during sample collection, labelling, processing, data collection or interpretation. Please note that the clinical classification of variants can change over time. To check whether there have been any changes to the classification of reported variants, please contact IGENOMIX.

LEGAL/QUALITY

IGENOMIX ARGENTINA S.A will only release the report once a completed test requisition form is received. The clinic/clinician/certified health professional requesting the test is responsible for obtaining and taking custody of "Informed Consent" from the patient as depicted by national guidelines and/or legislation. This test was developed, and its performance characteristics determined by IGENOMIX SPAIN LAB, SLU. It has not been cleared or approved by the US Food and Drug Administration. The test is used as a laboratory developed test for clinical purposes.

Part of this test has been outsourced to a reference laboratory whose Quality Management System is based on high Quality Standards, periodically monitored by Igenomix SPAIN* and audited by independent external groups.

*IGENOMIX SPAIN holds CLIA Certificate of Compliance: #99D2146167.

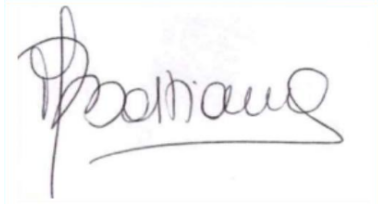
EXEMPTION CLAUSE OF DIAGNOSTIC LIABILITY

The genetic diagnosis services carried out by IGENOMIX ARGENTINA S.A are exclusively intended to be interpreted by qualified/certified health professionals.

The result obtained by this test and the information that could be derived from it, cannot be considered in any case as substitute of genetic counselling or medical treatment by a trained professional neither represent itself a medical enquiry. We recommend that you consult your physician for genetic testing & counselling upon reception of your results.

Any result should be interpreted in the context of all available clinical findings, within the general context of a medical investigation, which must be conducted by clinically trained professionals. IGENOMIX ARGENTINA S.A is not responsible for any decisions made or actions undertaken by the contracting party based on the results provided by IGENOMIX ARGENTINA S.A or otherwise., nor the harmful temporary consequences diverted by its use, making specific discretion of taking appropriate legal measures assuming an improper use of those mentioned studies and analysis.

SIGNED



Martina Di Bastiano

Laboratory Leader

COUNTERSIGNED



Arantxa Hervas PhD

3025-CV
Biotechnologist

This test or part of this test has been outsourced to a referral Laboratory. Lab CLIA No.: 99D2146167

LIST OF ANALYZED GENES

Gene mean coverage >100x GJB2, HBA1, HBA2, HBB, ATP7A, ATRX, DKC1, ARSL, IL1RAPL1, HSD17B10, UPF3B, BTK, CUL4B, DMD, EMD, CD40LG, WAS, THOC2, MTM1, OTC, PQBP1, CYBB, SH2D1A, PDHA1, OCRL, FGD1, BRWD3, PHF8, GLA, F9, RP2, GPR143, F8, COL4A5, G6PD, HPRT1, IL2RG, L1CAM, FMR1, PRPS1, RPGR, SYN1, KDM5C, ZNF711, CFTR, CYP21A2

Gene mean coverage 50x-100x HCFC1, SLC6A8, SLC16A2, OPHN1, DLG3, ABCD1, ARX, CHM, PLP1, NR0B1, FTSJ1, MID1, ZDHC9, NDP, RS1, GJB1, PGK1

Gene mean coverage < 50x MECP2, POU3F4, DCX, PAK3, EDA, AP1S2, IDS, AR, SMN1

GLOSSARY

TYPES OF INHERITANCE:

- **AR: Autosomal recessive**
Inherited conditions that require two pathogenic variants (one from each parent) in a given gene to display symptoms.
- **XR: X-linked recessive**
The gene is located on the X chromosome. Men with a pathogenic variant have the disease. Women with a pathogenic variant are carriers and generally asymptomatic or may mild symptoms.
- **Digenic inheritance**
In some diseases, the symptoms could be explained by the coexistence of pathogenic variants in two different genes related with the disease instead of two pathogenic variants in the same gene.

ALLELES:

Pathogenic variants present in the two copies of a gene.

- **Homozygous pathogenic variant (Hom.):**
Each copy of the gene has the same pathogenic variant. Generally, this is associated with clinical symptoms.
- **Compound heterozygous (Het.):**
Each copy of the gene has a different pathogenic variant. Generally, this is associated with clinical symptoms. This situation is referred as having variants "in trans".

Pathogenic variant present in one copy of a gene.

- **Heterozygous pathogenic variant (Het.):**
Only one copy of a gene has a pathogenic variant. There is another normal gene copy.

Note: Sometimes an individual has two pathogenic variants in the same gene copy. This situation is referred as having variants in cis and it is considered as a single pathogenic variant.

CNV:

Refers to copy number variation (deletion or duplication), i.e., the number of copies of a particular gene (or gene region) is different from the usual two copies.

LARGE GENE CONVERSION:

Refers to pathogenic variants caused by gene sequence exchange or replacement between a normal functional gene and a quasi-identical non-functional gene (pseudogene).

X-linked conditions

| Chrom | Gene | Disease/Condition | Carrier Rate | Residual Risk |
|-------|----------|---|----------------|-----------------|
| X | ABCD1 | Adrenoleukodystrophy | 1 in 3750 | 1 in 37500 |
| X | AP1S2 | Mental retardation, X-linked, syndromic, type 5 (Pettigrew syndrome) | < 1 in 100 000 | Reduced |
| X | AR | Androgen insensitivity syndrome | 1 in 6250 | 1 in 10417 |
| X | ARSL | Chondrodysplasia punctata, brachytelephalangic | < 1 in 100 000 | Reduced |
| X | ARX | Epileptic encephalopathy, early infantile, type 1; ARX-related developmental disorders | 1 in 25 000 | 1 in 100000 |
| X | ATP7A | Menkes disease; Occipital horn syndrome | 1 in 25000 | 1 in 100000 |
| X | ATRX | Mental retardation-hypotonic facies syndrome, X-linked; Alpha-thalassemia/mental retardation syndrome | < 1 in 100 000 | Reduced |
| X | BRWD3 | Mental retardation, X-linked, type 93 | 1 in 10000 | 1 in 50000 |
| X | BTK | Agammaglobulinemia X-linked, type 1 | 1 in 50,000 | 1 in 333333 |
| X | CD40LG | Hyper-IgM syndrome, type 1 (immunodeficiency, X-linked, with hyper-IgM, type 1) | < 1 in 100 000 | Reduced |
| X | CHM | Choroideremia | 1 in 18750 | 1 in 66964 |
| X | COL4A5 | Alport syndrome, X-linked | 1 in 10000 | 1 in 50000 |
| X | CUL4B | Mental retardation, X-linked, syndromic, type 15 (Cabezas type) | < 1 in 100 000 | Reduced |
| X | CYBB | Chronic granulomatous disease, X-linked | 1 in 300 | 1 in 1500 |
| X | DCX | Lissencephaly, X-linked, type 1 | 1 in 2500 | 1 in 50000 |
| X | DKC1 | Dyskeratosis congenita, X-linked | 1 in 62500 | 1 in 1250000 |
| X | DLG3 | Mental retardation, X-linked, type 90 | 1 in 45000 | 1 in 300000 |
| X | DMD | DMD-related conditions | 1 in 2625 | 1 in 131250 |
| X | EDA | Ectodermal dysplasia, type 1, hypohidrotic, X-linked | 1 in 2500 | 1 in 16667 |
| X | EMD | Emery-Dreifuss muscular dystrophy, type 1, X-linked | < 1 in 100 000 | Reduced |
| X | F8 | Hemophilia A | 1 in 3500 | 1 in 89285 |
| X | F9 | Hemophilia B | 1 in 6250 | 1 in 62500 |
| X | FGD1 | Aarskog-Scott syndrome; Mental retardation, X-linked syndromic, type 16 | 1 in 10000 | 1 in 125000 |
| X | FMR1 | FMR1-related conditions | 1 in 400 | 1 in 40000 |
| X | FTSJ1 | Mental retardation, X-linked 44 | 1 in 45000 | 1 in 300000 |
| X | G6PD | G6PD deficiency | 1 in 25 | 1 in 250 |
| X | GJB1 | Charcot-Marie-Tooth neuropathy, X-linked dominant, type 1 | 1 in 9803 | 1 in 196060 |
| X | GLA | Fabry disease | 1 in 18750 | 1 in 187500 |
| X | GPR143 | Ocular albinism, type 1 (Nettleship-Falls type) | 1 in 15000 | 1 in 18750 |
| X | HCFC1 | Mental retardation, X-linked 3 (methylmalonic acidemia and homocysteinemia, cbIX type) | < 1 in 100 000 | Reduced |
| X | HPRT1 | Lesch-Nyhan syndrome | 1 in 95000 | 1 in 380000 |
| X | HSD17B10 | HSD10 mitochondrial disease | < 1 in 100 000 | Reduced |
| X | IDS | Mucopolysaccharidosis, type 2 | 1 in 25000 | 1 in 125000 |
| X | IL1RAPL1 | Mental retardation, X-linked, type 21/34 | 1 in 25000 | 1 in 357143 |
| X | IL2RG | Severe combined immunodeficiency, X-linked | 1 in 25000 | 1 in 500000 |
| X | KDMS5C | Mental retardation, X-linked, syndromic, Claes-Jensen type | 1 in 4000 | 1 in 57143 |
| X | L1CAM | L1 Syndrome | 1 in 7500 | 1 in 150000 |
| X | MECP2 | Encephalopathy, neonatal severe; Rett syndrome | 1 in 37500 | 1 in 250000 |
| X | MID1 | Opitz GBBB syndrome, type 1 | 1 in 18750 | 1 in 125000 |
| X | MTM1 | Myotubular myopathy, X-linked | 1 in 12500 | 1 in 83333 |
| X | NDP | Norrie disease | 1 in 50,000 | <1 in 1,000,000 |
| X | NROB1 | Adrenal hypoplasia, congenital | 1 in 17500 | 1 in 58333 |
| X | OCRL | Lowe Syndrome; Dent disease type 2 | < 1 in 100 000 | Reduced |
| X | OPHN1 | Mental retardation, X-linked, with cerebellar hypoplasia and distinctive facial appearance | < 1 in 500 | Reduced |
| X | OTC | Ornithine transcarbamylase deficiency | 1 in 50000 | 1 in 166667 |
| X | PAK3 | Mental retardation, X-linked, type 30 | 1 in 40000 | 1 in 800000 |
| X | PDHA1 | Pyruvate dehydrogenase E1-alpha deficiency | < 1 in 100 000 | Reduced |
| X | PGK1 | Phosphoglycerate kinase 1 deficiency | < 1 in 100 000 | Reduced |
| X | PHF8 | Mental retardation syndrome, X-linked, Siderius type | < 1 in 100 000 | Reduced |
| X | PLP1 | Pelizaeus-Merzbacher disease | 1 in 353 | 1 in 441 |
| X | POU3F4 | Deafness, X-linked, type 2 | 1 in 556,112 | <1 in 1,000,000 |
| X | PQBP1 | Renpenning syndrome | < 1 in 100 000 | Reduced |
| X | PRPS1 | PRPS1-related disorders | < 1 in 100 000 | Reduced |
| X | RP2 | Retinitis pigmentosa, type 2, X-linked | 1 in 5000 | 1 in 62500 |
| X | RPGR | Retinitis pigmentosa, type 3, X-linked; Cone-rod dystrophy, X-linked, 1 | 1 in 20000 | 1 in 28571 |
| X | RS1 | Retinoschisis | 1 in 15000 | 1 in 100000 |
| X | SH2D1A | Lymphoproliferative syndrome, X-linked, type 1 | < 1 in 100 000 | Reduced |
| X | SLC16A2 | Allan-Hemdon-Dudley syndrome | < 1 in 100 000 | Reduced |
| X | SLC6A8 | Cerebral creatine deficiency syndrome, type 1 | < 1 in 100 000 | Reduced |
| X | SYN1 | Epilepsy, X-linked, with variable learning disabilities and behavior disorders | 1 in 30000 | 1 in 150000 |
| X | THOC2 | Mental retardation, X-linked 12 | < 1 in 100 000 | Reduced |
| X | UPF3B | Mental retardation, X-linked, syndromic, type 14 | 1 in 15000 | 1 in 75000 |
| X | WAS | Wiskott-Aldrich syndrome; Thrombocytopenia, X-linked | < 1 in 100 000 | Reduced |
| X | ZDHHC9 | Intellectual developmental disorder, X-linked syndromic, Raymond type | 1 in 45000 | 1 in 450000 |
| X | ZNF711 | Mental retardation, X-linked, type 97 | 1 in 45000 | 1 in 225000 |

Autosomal recessive conditions

| Chrom | Gene | Disease/ Condition | Carrier Rate | Residual Risk |
|-------|---------|--|--------------|---------------|
| 7 | CFTR | Cystic fibrosis | 1 in 25 | 1 in 833 |
| 6 | CYP21A2 | Congenital adrenal hyperplasia due to 21-hydroxylase deficiency | 1 in 62 | 1 in 1240 |
| 13 | GJB2 | Deafness, autosomal recessive, type 1A; Deafness, digenic, GJB2/GJB6 | 1 in 40 | 1 in 500 |
| 16 | HBA1 | Alpha thalassemia | 1 in 30 | 1 in 200 |
| 16 | HBA2 | Alpha thalassemia | 1 in 30 | 1 in 200 |
| 11 | HBB | HBB-related hemoglobinopathies | 1 in 67 | 1 in 6700 |
| 5 | SMN1 | Spinal muscular atrophy | 1 in 50 | 1 in 588 |

N/A: no data prevalence unknown