# Donor 4725

# Genetic Testing Summary

Fairfax Cryobank recommends reviewing this genetic testing summary with your healthcare provider to determine suitability.

Last Updated: 11/15/23

Donor Reported Ancestry: Venezuelan, Spanish, Italian  Jewish Ancestry: No

| Genetic Test* | Result | Comments/Donor's Residual Risk** |
|---|---|---|
| Chromosome analysis (karyotype) | Normal male karyotype | No evidence of clinically significant chromosome abnormalities |
| Hemoglobin evaluation | Normal hemoglobin fractionation and MCV/MCH results | Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies |
| Cystic Fibrosis (CF) carrier screening | Negative by genotyping of 99 mutations in the CFTR gene | 1/270 |
| Spinal Muscular Atrophy (SMA) carrier screening | Negative for deletions of exon 7 in the SMN1 gene | 1/1000 |
| Hb Beta Chain-Related Hemoglobinopathy (including Beta Thalassemia and Sickle Cell Disease) by genotyping | Negative for 28 mutations tested in the HBB gene | 1/160 |
| **Special Testing** | | |
| Gene: SERPINA1 | Carrier: Alpha-1 Antitrypsin Deficiency (SERPINA1) Z variant. | Partner testing is indicated before using this donor. All children have a 50%r risk of inheriting this variant and being healthy carriers. |

*No single test can screen for all genetic disorders. A negative screening result significantly reduces, but cannot eliminate, the risk for these conditions in a pregnancy.

**Donor residual risk is the chance the donor is still a carrier after testing negative.

4399 Santa Anita Ave.
El Monte, CA, 91731
(p) 626-350-0537 (f) 626-454-1667
info@fulgentgenetics.com
www.fulgentgenetics.com

fulgent

[redacted]

Patient Information:
**4725, Donor**
**DOB:** [redacted]
Sex: M
MR#: 4725
Patient#: [redacted]

Accession:
[redacted]
Test#: [redacted]3
Order# [redacted]
Ext Test#: [redacted]
Ext Order#: [redacted]
Specimen Type: DNA
Collected: Not provided
Received Date: Oct 31,2023
Authorized Date: Nov 06,2023

Physician:
**Seitz, Suzanne**
ATTN: Seitz, Suzanne
Fairfax Cryobank
3015 Williams Drive
Fairfax, VA 22031
Phone:
Fax:

Laboratory:
**Fulgent Genetics**
CAP#: 8042697
CLIA#: 05D2043189
Laboratory Director:
Dr. Hanlin (Harry) Gao
Report Date: **Nov 12,2023**

Final Report

## TEST PERFORMED

**Alpha-1 Antitrypsin Deficiency - Gene**
(1 Gene Panel; gene sequencing with deletion and duplication analysis)

## RESULTS:

No clinically significant sequence or copy-number variants were identified which are sufficient for a molecular diagnosis.
However, one variant of potential clinical relevance is reported.

*Clinically significant Variants*
*None*

*Additional Variants of Potential Clinical Relevance*

| Gene Info | | Variant Info | | |
|---|---|---|---|---|
| GENE | INHERITANCE | VARIANT | ZYGOSITY | CLASSIFICATION |
| *SERPINA1* NM_000295.5 | Autosomal Recessive | c.1096G>A p.Glu366Lys | Heterozygous (Pi*Z) | **Pathogenic (carrier)** |

## INTERPRETATION:

**Notes and Recommendations:**

- As requested, this report only includes variants classified as Pathogenic, Likely Pathogenic, or Risk Allele at the time of analysis. If detected, this report does not include variants classified as of uncertain significance.
- Gene specific notes and limitations may be present. See below.
- These results should be interpreted in the context of this individual's clinical findings, biochemical profile, and family history.
- Genetic counseling is recommended. Available genetic counselors and additional resources can be found at the National Society of Genetic Counselors (NSGC; https://www.nsgc.org)
- Guide to Interpreting Genomic Reports: A Genomics Toolkit (CSER Consortium; February 2017) (https://www.genome.gov/For-Health-Professionals/Provider-Genomics-Education-Resources#hep)

# About *SERPINA1*

Biallelic mutations in SERPINA1 have been associated with emphysema due to alpha-1 antitrypsin (A1AT) deficiency, emphysema-cirrhosis due to A1AT deficiency, and hemorrhagic diathesis (OMIM: 107400). Patients with A1AT deficiency may have

4399 Santa Anita Ave.
El Monte, CA, 91731
(p) 626-350-0537 (f) 626-454-1667
info@fulgentgenetics.com
www.fulgentgenetics.com

variable risk for emphysema and liver disease, depending on the combination of inherited mutant alleles (e.g. PI*Z, PI*S, PI*F, PI*I, PI*QO) (PubMed: 20301692, 32268028; OMIM: 107400).

See OMIM gene entry for *SERPINA1* (OMIM: 107400) for further information.

100% of the coding sequence of the NM_000295.5 transcript of *SERPINA1* gene was sequenced to a minimum depth of 20x in the submitted specimen. A second sequencing mutation was not detected in this gene, nor were copy number variants observed, however, the presence of mutations in the deep intronic or regulatory regions cannot be ruled out. As the clinical condition(s) associated with mutations in the *SERPINA1* gene are recessive and only a single heterozygous variant has been detected, this result is interpreted as carrier status only. Further clinical evaluation may be warranted to clarify these findings.

## *SERPINA1* NM_000295.5:c.1096G>A (p.Glu366Lys)

Classification: **Pathogenic**

| | |
|---|---|
| Zygosity and Inheritance | • This heterozygous Pathogenic variant is consistent with this individual being a carrier for an autosomal recessive SERPINA1-related condition. |
| Variant Type | • Genomic change: Chr14(GRCh37):g.94844947C>T.<br>• This variant is in the dbSNP database: rs28929474<br>• This variant is predicted to result in a single amino acid substitution (missense) of **Glu** to **Lys** at codon 366 in exon 5 of the *SERPINA1* gene. |
| Variant in Cases | • This variant, also reported as p.Glu342Lys or PiZ (Z allele), is the most common disease allele associated with A1AT deficiency (PubMed: 6306478, 20981092, 19738092, 23858502). Heterozygous carriers of the p.Glu366Lys/p.Glu342Lys/PiZ allele are reported to have decreased serum A1AT concentrations that are ~61% of those in noncarriers (PubMed: 19083091, 23632999). In a newborn screening study of 200,000 infants, 122 newborns screened positive for PI*ZZ and 14 of these 122 individuals developed prolonged obstructive jaundice (PubMed: 1083485). Notably, this original study has significant limitations in that it did not rule-out other forms of genetic and non-genetic liver disease.<br>• Current evidence suggests that the overall risk for an individual with the PI*ZZ genotype to develop severe liver disease in childhood is generally low (~2%) (PubMed: 20301692). A1AT deficiency is a mild condition, and many heterozygous and homozygous individuals are asymptomatic.<br>• This variant is classified as a "Disease Mutation" (DM) in the Human Gene Mutation Database (HGMD).<br>• This variant has one or more entries in ClinVar: RCV000762931.1, RCV000019567.3, RCV000019595.2, RCV000019594.2, RCV000768543.1, RCV001195107.1, RCV000148877.22, RCV000623762.1, RCV000194811.1, RCV000255454.5 |
| Variant in Controls | • This variant has been observed at a frequency of 1.12% (3176/282742 alleles).<br>• The highest allele frequency that this variant has been observed at in any sub-population with available data is 1.84% in the European (Non-Finnish) population.<br>• There are 26 homozygous control individuals for this variant.<br>• The Broad Institute gnomAD database (>120,000 Individuals with no known severe, pediatric onset disease) was used for this analysis. |
| Other Variant Information | • This alternate amino acid observed in this individual (Lys) is the wild type amino acid in 1 out of 82 vertebrate species, 1 of which are mammals. This may indicate that this amino acid alteration retains some or all of the function of the gene.<br>• Amino acid conservation data:<br>  ◦ Primates: 12 out of 12 match the wild type.<br>  ◦ Mammals: 56 out of 58 match the wild type and 1 match the alternate.<br>  ◦ Vertebrates: 80 out of 82 match the wild type and 1 match the alternate.<br>• The physiochemical difference between Glu and Lys as measured by Grantham's Distance is 56. This score is considered a "moderate" change. (PubMed: 4843792, 6442359).<br>• Computational predictions for p.Glu366Lys (0P/2B /AGVGD, SIFT) (REVEL = 0.69) (gnomAD: Z = -0.37 [Exp: 226.2, Obs: 242]) (granthamDist = 56). |

4399 Santa Anita Ave.
El Monte, CA, 91731
(p) 626-350-0537 (f) 626-454-1667
info@fulgentgenetics.com
www.fulgentgenetics.com

## GENES TESTED:

**Alpha-1 Antitrypsin Deficiency - Gene**
1 genes tested (100.00% at >20x).

*SERPINA1*

**Gene Specific Notes and Limitations**

No gene specific limitations apply to the genes on the tested panel.

## METHODS:

Genomic DNA was isolated from the submitted specimen indicated above (if cellular material was submitted). DNA was barcoded, and enriched for the coding exons of targeted genes using hybrid capture technology. Prepared DNA libraries were then sequenced using a Next Generation Sequencing technology. Following alignment to the human genome reference sequence (assembly GRCh37), variants were detected in regions of at least 10x coverage. For this specimen, 100.00% and 100.00% of coding regions and splicing junctions of genes listed had been sequenced with coverage of at least 10x and 20x, respectively, by NGS or by Sanger sequencing. The remaining regions did not have 10x coverage, and were not evaluated. Variants were interpreted manually using locus specific databases, literature searches, and other molecular biological principles. To minimize false positive results, any variants that do not meet internal quality standards are confirmed by Sanger sequencing. Variants classified as pathogenic, likely pathogenic, or risk allele which are located in the coding regions and nearby intronic regions (+/- 20bp) of the genes listed above are reported. Variants outside these intervals may be reported but are typically not guaranteed. When a single pathogenic or likely pathogenic variant is identified in a clinically relevant gene with autosomal recessive inheritance, the laboratory will attempt to ensure 100% coverage of coding sequences either through NGS or Sanger sequencing technologies ("fill-in"). All genes listed were evaluated for large deletions and/or duplications. However, single exon deletions or duplications will not be detected in this assay, nor will copy number alterations in regions of genes with significant pseudogenes. Putative deletions or duplications identified by NGS are confirmed by an orthogonal method (qPCR or MLPA), unless exceeding an internally specified and validated quality score, beyond which deletions and duplications are considered real without further confirmation. New York patients: diagnostic findings are confirmed by Sanger, MLPA, or qPCR; exception SNV variants in genes for which confirmation of NGS results has been performed >=10 times may not be confirmed if identified with high quality by NGS. Bioinformatics: The Fulgent Germline v2019.2 pipeline was used to analyze this specimen.

## LIMITATIONS:

These test results and variant interpretation are based on the proper identification of the submitted specimen, accuracy of any stated familial relationships, and use of the correct human reference sequences at the queried loci. In very rare instances, errors may result due to mix-up or co-mingling of specimens. Positive results do not imply that there are no other contributors, genetic or otherwise, to this individual's phenotype, and negative results do not rule out a genetic cause for the indication for testing. Official gene names change over time. Fulgent uses the most up to date gene names based on HUGO Gene Nomenclature Committee (https://www.genenames.org) recommendations. If the gene name on report does not match that of ordered gene, please contact the laboratory and details can be provided. Result interpretation is based on the available clinical and family history information for this individual, collected published information, and Alamut annotation available at the time of reporting. This assay is designed and validated for detection of germline variants only. It is not designed or validated for the detection of low-level mosaicism or somatic mutations. This assay will not detect certain types of genomic aberrations such as translocations, inversions, or repeat expansions (eg. trinucleotide or hexanucleotide repeat expansion). DNA alterations in regulatory regions or deep intronic regions (greater than 20bp from an exon) may not be detected by this test. Unless otherwise indicated, no additional assays have been performed to evaluate genetic changes in this specimen. There are technical limitations on the ability of DNA sequencing to detect small insertions and deletions. Our laboratory uses a sensitive detection algorithm, however these types of alterations are not detected as reliably as single nucleotide variants. Rarely, due to systematic chemical, computational, or human error, DNA variants may be missed. Although next generation sequencing technologies and our bioinformatics analysis significantly reduce the confounding contribution of pseudogene sequences or other highly-homologous sequences, sometimes these may still interfere with the technical ability of the assay to identify pathogenic alterations in both sequencing and deletion/duplication analyses. Deletion/duplication analysis can identify alterations of genomic regions which are two or more contiguous exons in size; single exon deletions or duplications may occasionally be identified, but are not routinely detected by this test. When novel DNA duplications are identified, it is not possible to discern the genomic location or orientation of the duplicated segment, hence the

4399 Santa Anita Ave.
El Monte, CA, 91731
(p) 626-350-0537 (f) 626-454-1667
info@fulgentgenetics.com
www.fulgentgenetics.com

[redacted]

effect of the duplication cannot be predicted. Where deletions are detected, it is not always possible to determine whether the predicted product will remain in-frame or not. Unless otherwise indicated, deletion/duplication analysis has not been performed in regions that have been sequenced by Sanger.

## SIGNATURE:

**Dr. Harry Gao, DABMG, FACMG** on **11/12/2023 08:58 AM PST**
Electronically signed

## DISCLAIMER:

This test was developed and its performance characteristics determined by**Fulgent Genetics**. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. Since genetic variation, as well as systematic and technical factors, can affect the accuracy of testing, the results of testing should always be interpreted in the context of clinical and familial data. For assistance with interpretation of these results, healthcare professionals may contact us directly at **(626) 350-0537** or **info@fulgentgenetics.com**. It is recommended that patients receive appropriate genetic counseling to explain the implications of the test result, including its residual risks, uncertainties and reproductive or medical options.

Counsyl

**Results Reci t**

Fairfax Cryobank - [redacted]

[redacted]

Report Date: 12/09/2013

**Male**

Name: DONOR 4725
DOB: [redacted]
Ethnicity: Hispanic
Sample Type: OG-510 Saliva
Date of Collection: 12/03/2013
Date Received: 12/05/2013
Barcode: [redacted]
Indication: Egg or Sperm Donor
Test Type: The Counsyl Test

**Female**

Not tested

## Counsyl Test Results Summary (Egg or Sperm Donor)

The Counsyl test (**Fairfax Cryobank Fundamental Panel**) uses targeted genotyping and copy number analysis as described in the methods section on page 2 to determine carrier status associated with **3 diseases**. Please refer to page 3 for a complete list of diseases and genes included in this panel.

### *DONOR 4725*

DONOR 4725's DNA test shows that he is not a carrier of any disease-causing mutation tested.

### *Partner*

The reproductive risk presented is based on a hypothetical pairing with a partner of the same ethnic group.

## *Reproductive Risk Summary*

No increased reproductive risks to highlight. Please refer to the following pages for detailed information about the results.

### Clinical Notes

- If necessary, patients can discuss residual risks with their physician or a genetic counselor. To schedule a complimentary appointment to speak with a genetic counselor about these results, please visit counsyl.com/counseling/.

ENTERED
1-17-14
km

## Methods and Limitations

**DONOR 4725: The Counsyl Test - targeted genotyping and copy number analysis.**

**Targeted genotyping:** Targeted DNA mutation analysis is used to simultaneously determine the genotype of 127 variants associated with 2 diseases. The test is not validated for detection of homozygous mutations, and although rare, asymptomatic individuals affected by the disease may not be genotyped accurately.

**Copy number analysis:** Targeted copy number analysis is used to determine the copy number of exon 7 of the SMN1 gene relative to other genes. Other mutations may interfere with this analysis. Some individuals with two copies of SMN1 are carriers with two SMN1 genes on one chromosome and a SMN1 deletion on the other chromosome. In addition, a small percentage of SMA cases are caused by nondeletion mutations in the SMN1 gene. Thus, a test result of two SMN1 copies significantly reduces the risk of being a carrier; however, there is still a residual risk of being a carrier and subsequently a small risk of future affected offspring for individuals with two or more SMN1 gene copies. Some SMA cases arise as the result of de novo mutation events which will not be detected by carrier testing.

**Limitations:** In an unknown number of cases, nearby genetic variants may interfere with mutation detection. Other possible sources of diagnostic error include sample mix-up, trace contamination, bone marrow transplantation, blood transfusions and technical errors. The Counsyl test does not fully address all inherited forms of intellectual disability, birth defects and genetic disease. A family history of any of these conditions may warrant additional evaluation. Furthermore, not all mutations will be identified in the genes analyzed and additional testing may be beneficial for some patients. For example, individuals of African, Southeast Asian, and Mediterranean ancestry are at increased risk for being carriers for hemoglobinopathies, which can be identified by CBC and hemoglobin electrophoresis or HPLC (*ACOG Practice Bulletin No. 78. Obstet. Gynecol. 2007;109:229-37*).

This test was developed and its performance characteristics determined by Counsyl, Inc. It has not been cleared or approved by the US Food and Drug Administration (FDA). The FDA does not require this test to go through premarket review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. These results are adjunctive to the ordering physician's workup. CLIA Number: **#05D1102604.**


Lab Directors:

Hyunseok Kang

H. Peter Kang, MD, MS, FCAP

Jelena Brezo

Jelena Brezo, PhD, FACMG

Counsyl

Male

Name: DONOR 4725
DOB: [redacted]

Femal

Not tested

## Diseases Tested

**Cystic Fibrosis - Gene:** CFTR. **Variants (99):** G85E, R117H, R334W, R347P, A455E, G542X, G551D, R553X, R560T, R1162X, W1282X, N1303K, F508del, I507del, 2184delA, 3659delC, 621+1G>T, 711+1G>T, 1717-1G>A, 1898+1G>A, 2789+5G>A, 3120+1G>A, 3849+10kbC>T, E60X, R75X, E92X, Y122X, G178R, R347H, Q493X, V520F, S549N, P574H, M1101K, D1152H, 2143delT, 394delTT, 444delA, 1078delT, 3876delA, 3905insT, 1812-1G>A, 3272-26A>G, 2183AA>G, S549R(A>C), R117C, L206W, G330X, T338I, R352Q, S364P, G480C, C524X, S549R(T>G), Q552X, A559T, G622D, R709X, K710X, R764X, Q890X, R1066C, W1089X, Y1092X, R1158X, S1196X, W1204X(c.3611G>A), Q1238X, S1251N, S1255X, 3199del6, 574delA, 663delT, 935delA, 936delTA, 1677delTA, 1949del84, 2043delG, 2055del9>A, 2108delA, 3171delC, 3667del4, 3791delC, 1288insTA, 2184insA, 2307insA, 2869insG, 296+12T>C, 405+1G>A, 405+3A>C, 406-1G>A, 711+5G>A, 712-1G>T, 1898+1G>T, 1898+5G>T, 3120G>A, 457TAT>G, 3849+4A>G, Q359K/T360K. **Detection rate:** Hispanic 83%.

**Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease) - Gene:** HBB. **Variants (28):** Hb S, K17X, Q39X, Phe41fs, Ser9fs, IVS-II-654, IVS-II-745, IVS-II-850, IVS-I-6, IVS-I-110, IVS-I-5, IVS-I-1(G>A), -88C>T, -28A>G, -29A>G, Lys8fs, Phe71fs, IVS-II-849(A>C), IVS-II-849(A>G), Gly24 T>A, -87C>G, Hb C, W15X, Gly16fs, Glu6fs, Hb E, Hb D-Punjab, Hb O-Arab. **Detection rate:** Hispanic <10%.

**Spinal Muscular Atrophy (copy number analysis only) - Gene:** SMN1. **Variant (1):** SMN1 copy number. **Detection rate:** Hispanic 90%.

ENTERED
1-17-14

Counsyl

Male

Name: DONOR 4725
DOB: [redacted]

Femal

Not tested

## Risk Calculations

Below are the risk calculations for all diseases tested. Since negative results do not completely rule out the possibility of being a carrier, the **residual risk** represents the patient's post-test likelihood of being a carrier and the **reproductive risk** represents the likelihood the patient's future children could inherit each disease. These risks are inherent to all carrier screening tests, may vary by ethnicity, are predicated on a negative family history and are present even after a negative test result. Inaccurate reporting of ethnicity may cause errors in risk calculation.

| Disease | DONOR 4725<br>Residual Risk | Reproductive Risk |
|---|---|---|
| Cystic Fibrosis | 1 in 270 | 1 in 48,000 |
| Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease) | 1 in 160 | 1 in 100,000 |
| Spinal Muscular Atrophy | SMN1: 2 copies<br>1 in 1,000 | 1 in 490,000 |

GENETICS & IVF
*Institute*

# Cytogenetic Report

Client Fairfax Cryobank - [redacted]

Address [redacted]

Reporting Phone # [redacted] Fax # [redacted] Email [redacted]

Patient name/Donor Alias Donor # 4725 Patient DOB N/A

Donor # 4725-[redacted] Specimen type Peripheral Blood

Collection Date 12/03/2013 Accession # [redacted]

Date Received 12/04/2013

## RESULTS

### CYTOGENETIC ANALYSIS

| | | | |
|---|---|---|---|
| Cells counted | 20 | Type of banding | GTG |
| Cells analyzed | 5 | Band resolution | 550 |
| Cells karyotyped | 2 | | |
| Modal chromosome # | 46 | | |

KARYOTYPE 46,XY

### FISH

Probe(s) N/A

Nuclei scored N/A

INTERPRETATION

Normal male karyotype
No clonal numerical or structural abnormalities were identified. This normal cytogenetic result does not exclude the possibility of the presence of subtle rearrangements beyond the technical limits of detection with this test.

Comments

Wayne S. Stanley, Ph.D., FACMG
Clinical Cytogeneticist

12/14/13
Date

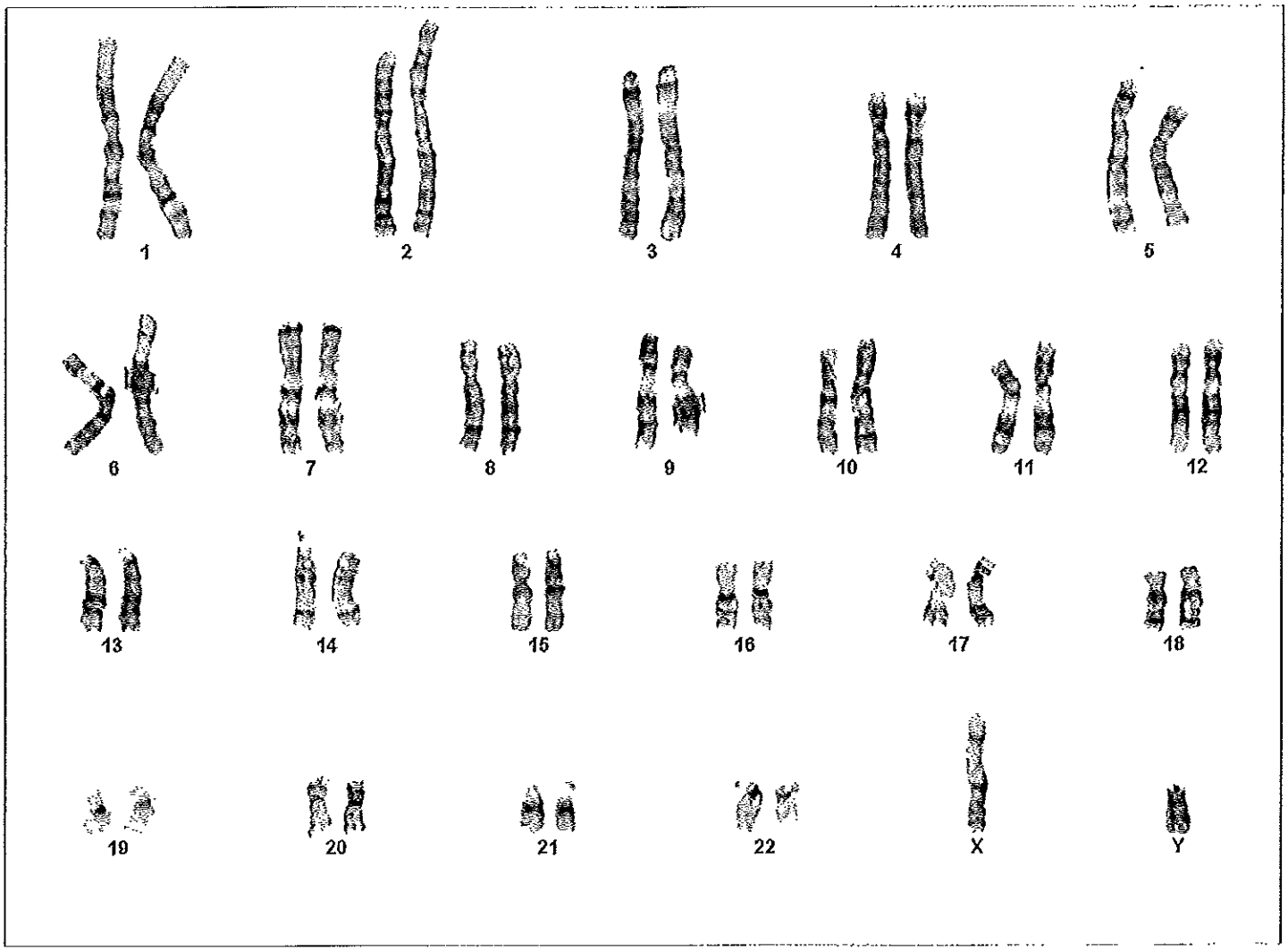
ENTERED
1.17.14

Genetics a' ' IVF Preimplantation Genetics La' 'ratory

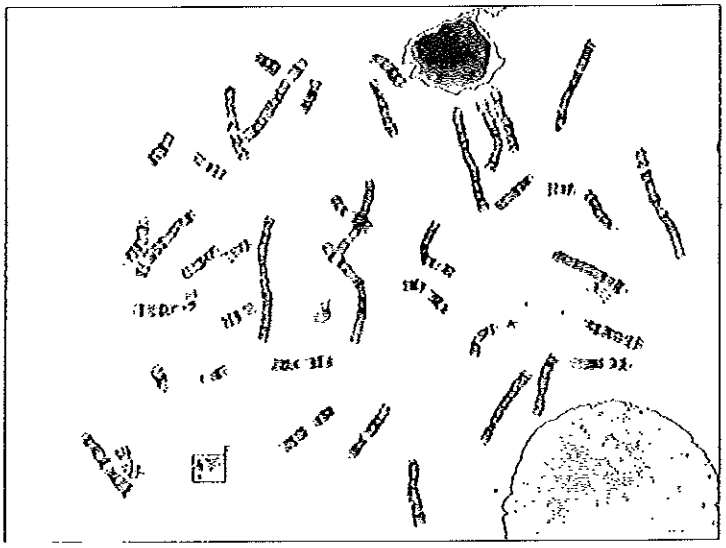
Patient name: DONOR # 4725

Case name: [redacted]

46,XY




Case: 13-183CG Slide: A1 Cell: 4



Quest Diagnostics

**Report Status: Final**

**ID4725, NG**

| Patient Information | Specimen Information | Client Information |
|---|---|---|
| **ID4725, NG**<br>**DOB:** [redacted] **AGE:** [redacted]<br>Gender: M Fasting: U<br>Phone: NG<br>Patient ID: 4725[redacted] | Specimen: [redacted]<br>Requisition: [redacted]<br>Collected: 12/03/2013 / 11:30 CST<br>Received: 12/04/2013 / 04:51 CST<br>Reported: 12/05/2013 / 08:12 CST | Client #: 41550 AUS0000<br>[redacted]<br>FAIRFAX CRYOBANK<br>[redacted] |

| Test Name | In Range | Out Of Range | Reference Range | Lab |
|---|---|---|---|---|
| HEMOGLOBINOPATHY EVALUATION | | | | |
| RED BLOOD CELL COUNT | 5.24 | | 4.20-5.80 Million/uL | IG |
| HEMOGLOBIN | 15.6 | | 13.2-17.1 g/dL | |
| HEMATOCRIT | 48.0 | | 38.5-50.0 % | |
| MCV | 91.6 | | 80.0-100.0 fL | |
| MCH | 29.7 | | 27.0-33.0 pg | |
| RDW | 13.4 | | 11.0-15.0 % | |
| HEMOGLOBIN A | 97.3 | | >96.0 % | IG |
| HEMOGLOBIN F | <1.0 | | <2.0 % | |
| HEMOGLOBIN A2 (QUANT) | 2.7 | | 1.8-3.5 % | |
| INTERPRETATION | | | | |
| Normal phenotype. | | | | |

**PERFORMING SITE:**

IG QUEST DIAGNOSTICS-IRVING, 4770 REGENT BLVD., IRVING, TX 75063 Laboratory Director: ELISABETH S BROCKIE, DO, CLIA: 45D0697943

ENTERED
1.19.14
MM

CLIENT SERVICES: 866.697.8378 SPECIMEN: [redacted] PAGE 1 OF 1