Hello parents of

# Sarah Smith

Welcome to your personalized health & insights report, the next step to living your healthiest life.

**What's Inside:** Test Results × Next Steps × FAQ × Test Methodology & Limitations

Provided by

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Child Test

# Sarah,

## During our Whole Exome Sequencing, we looked at approximately 20,000 genes associated with hundreds of health conditions, and tested for 7 groups of conditions.

## Your results came back negative, with no mutations detected.

Negative (normal) test results mean that no genetic changes (mutations) with medical implications were found in the genes analyzed by this test. Having a negative test result significantly reduces, but does not eliminate, the chance that there is a mutation in one of these genes.

Negative results are generally reassuring, but don't mean that a medical condition won't develop due to other non-genetic causes. In addition, if your personal or family history changes in the future, additional genetic testing may be beneficial.

*Continue to learn more* →

**FULL NAME** Sarah Jane Smith • **DATE OF BIRTH** July 28, 1990 • **ANCESTRY** N/A • **SAMPLE ID** #00000
**SAMPLE COLLECTION DATE** November 22, 2017 • **REPORT DATE** November 27, 2017

# Sarah,

## even though no mutation was identified, we encourage you to share your results with your healthcare provider.

While genes play a role in increasing the chances for different health conditions, non-genetic factors such as lifestyle or environmental factors, as well as family history, have a significant contribution as well. Your healthcare provider may use these results along with other information to establish a personalized plan for you.

## What is the implication of your results for your relatives?

Having negative results means that you are passing presumably normal copies of these genes to any current or future children. However, your results do not mean that other family members (siblings, parents, and others) can't have a mutation. Sharing results with your family may be informative. If your family members have questions about their personal genetics, it is best for them to have their own testing.

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Listed below are genes that were evaluated as part of your test. The genes are categorized by condition.

## Hereditary Cardiac Conditions

**5** DISEASES TESTED FOR — **23** GENES TESTED TOTAL

| | | |
|---|---|---|
| 1 | Arrhythmogenic right ventricular cardiomyopathy | DSC2 DSG2 DSP PKP2 TMEM43 |
| 2 | Catecholaminergic polymorphic ventricular tachycardia | RYR2 |
| 3 | Familial Hypercholesterolemia | APOB LDLR PCSK9 |
| 4 | Hypertrophic / Dilated Cardiomyopathy | ACTC1 LMNA MYH7 MYL3 TNNI3 GLA MYBPC3 MYL2 PRKAG2 TNNT2 TPM1 |
| 5 | Romano-Ward long-QT syndrome types 1, 2 and 3, Brugada syndrome | KCNH2 KCNQ1 SCN5A |

## Anesthesia Complications

**1** DISEASE TESTED FOR — **2** GENES TESTED TOTAL

| | | |
|---|---|---|
| 1 | Malignant Hyperthermia susceptibility | CACNA1S RYR1 |

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## Hereditary Predisposition to Seizures

**63** DISEASES TESTED TOTAL — **77** GENES TESTED TOTAL

| CATEGORIES OF SEIZURE DISORDERS TESTED FOR | GENES IN EACH CATEGORY | DISEASES TOTAL PER CATEGORY | GENES TOTAL PER CATEGORY |
|---|---|---|---|
| Isolated Seizures | CSTB, KCNQ2, KCNQ3, MEF2C, SCN1A, SPTAN1, STXBP1, TAZ, ARX, SCN8A, GABRB3, ATP1A2, KCNAB1, PRRT2, RELN | 14 | 15 |
| Seizures Associated with Intellectual and Developmental Disability | PCDH19, IQSEC2, DYRK1A, CASK, GRIN2A, GRIN2B, SHANK3, SYNGAP1, UPF3B, ZEB2 | 8 | 10 |
| Seizures Associated with Neurologic Disease | EPM2A, FOXRED1, GPHN, LRPPRC, NDUFA2, NDUFA9, NDUFAF5, NDUFS2, NDUFS4, NDUFV2, NFU1, NHLRC1, PDHA1, PDHB, PNPT1, POLG, SDHAF1, SUCLA2, SUCLG1, TIMM8, TRMU, UBE3A, UQCRC2, WFS1, AFF2 (FMR2) | 18 | 25 |
| Seizures Associated with Metabolic Disease | ALDH7A1, CASR, CDKL5, EIF2AK3, ETFA, ETFB, ETFDH, ETHE1, FOXG1, GAMT, GLDC, HADH, HEXA, HEXB, MECP2, NEU1, NPC1, NPC2, PC, PDHX, PDP1, PHGDH, PNPO, SERAC1, SLC25A19, SLC25A20, SLC2A1 | 23 | 27 |

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## Hereditary Hearing Loss

**78** DISEASES TESTED TOTAL

**61** GENES TESTED TOTAL

| CATEGORIES OF HEARING LOSS CONDITIONS TESTED FOR | GENES IN EACH CATEGORY | DISEASES TOTAL PER CATEGORY | GENES TOTAL PER CATEGORY (SOME GENES BELONG TO BOTH CATEGORIES) |
|---|---|---|---|
| Syndromic: Hearing Loss Associated with a Systemic Condition | BSND, CDH23, CLRN1, COL11A2, DIAPH1, DSPP, EYA1, GJB2, GJB3, GJB6, GPR98 (ADGRV1), GPSM2, GRHL2, KCNE1, KCNQ1, MYH14, MYH9, MYO7A, PCDH15, PRPS1, SLC26A4, TIMM8A, TJP2, USH1C, USH2A, WFS1, DFNB31 | 28 | 27 |
| Non-syndromic: Isolated Occurrence | BSND, CCDC50, CDH23, CLDN14, COCH, COL11A2, CRYM, DFNA5, DIAPH1, DSPP, ESRRB, EYA4, GIPC3, GJB2, GJB3, GJB6, GRHL2, GRXCR1, HGF, ILDR1, KCNQ4, LHGPL5, LOXHD1, LRTOMT, MARVELD2, MYH14, MYH9, MYO15A, MYO1A, MYO3A, MYO6, MYO7A, OTOF, PCDH15, POU3F4, POU4F3, PRPS1, PTPRQ, SERPINB6, SLC17A8, SLC26A4, SLC26A5, TECTA, TMC1, TMIE, TMPRSS3, TPRN, TRIOBP, USH1C, WFS1, DFNB31, DFNB59 | 50 | 52 |

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## Hereditary Metabolic Conditions

**107** DISEASES TESTED TOTAL — **136** GENES TESTED TOTAL

| CATEGORIES OF HEREDITARY METABOLIC CONDITIONS TESTED FOR | GENES IN EACH CATEGORY | DISEASES TOTAL PER CATEGORY | GENES TOTAL PER CATEGORY (SOME GENES BELONG TO BOTH CATEGORIES) |
|---|---|---|---|
| Amino Acid and Organic Acid Metabolic Disorders | AASS, ACAD8, ACADSB, ACAT1, AGXT2L2, ALDH4A1, ALDH6A1, ARG1, ASL, ASS1, AUH, BCAT1, BCAT2, BCKDHA, BCKDHB, BTD, CBS, CPS1, CTH, D2HGDH, DBT, DHTKD1, DLD, DYNC2H1, ETFA, ETFB, ETFDH, FAH, FH, GCDH, GCH1, GK, HAL, HGD, HIBCH, HLCS, HMGCL, HPD, HSD17B10, IDH2, IFT80, IVD, KYNU, L2HGDH, MAT1A, MCCC1, MCCC2, MLYCD, MMAA, MMAB, MMACHE, MMADHC, MUT, MVK, NAGS, OTC, PAH, PCBD1, PCCA, PCCB, PRODH, PTS, QDPR, SLC25A13, SLC25A15, SLC6A19, SLC6A20, SLC7A7, TAT, TAZ | 59 | 70 |
| Sugar Metabolic Disorders | FBP1, GALE, GALK1, GALT, GLUT1, GLYCTK, LCT, MCM6 | 8 | 8 |
| Fatty Acid Metabolic Disorder | ACADM, ACADL, ACADS, ETHE1, HADH, HADHA, SLC1A1 | 7 | 7 |
| Peroxisomal Disorders | AGTX, GRHPR, HOGA1, PEX1, PEX2, PEX5, PEX6, PEX7, PEX10, PEX13, PEX26, PHYH | 5 | 12 |
| Purine and Pyrimidine Metabolic Disorders | ADA, APRT, DPYD, DPYS, HDH, HPRT1, MOCOS, UMPS, UPB1 | 9 | 9 |

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|---|---|---|---|
| Lactic Acid, Hyperpyruvic Acid Metabolic Disorders | COA5, COX6B1, COX10, COX14, COX15, EHHADH, FASTKD2, LRPPRC, PC, PDHA1, PDHB, PDP1, SCO1, SCO2, SURF1, TACO1 | 7 | 16 |
| Sugar Metabolic Disorders | AASDHPPT, AGXT2, ALDH5A1, ASPA, CNDP1, FTCD, GGT1, GSS, PHYH, SARDH, SLC24A13, SLC36A2, SLC6A19, SLC6A20 | 12 | 14 |

## Hereditary Connective Tissue Conditions

**4** DISEASE TESTED FOR — **7** GENES TESTED TOTAL

| | | |
|---|---|---|
| 1 | Loeys-Dietz syndrome | TGFBR1 TGFBR2 |
| 2 | Vascular Ehlers-Danlos syndrome | COL3A1 |
| 3 | Marfan syndrome | FBN1 |
| 4 | Familial Thoracic Aortic Aneurysms / Dissections | ACTA2 MYH11 SMAD3 TGFBR1 TGFBR2 |

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## Hereditary Predisposition to Cancer

**13** DISEASE TESTED FOR — **18** GENES TESTED TOTAL

| | | |
|---|---|---|
| 1 | Familial Adenomatous Polyposis | APC |
| 2 | Hereditary Paraganglioma-Pheochromocytoma | SDHAF2 SDHB SDHC SDHD |
| 3 | Juvenile Polyposis | BMPR1A SMAD4 |
| 4 | Li-Fraumeni | TP53 |
| 5 | Multiple Endocrine Neoplasia, Type 1 | MEN1 |
| 6 | Multiple Endocrine Neoplasia, Type 2 | RET |
| 7 | Neurofibromatosis, Type 2 | NF2 |
| 8 | Peutz-Jeghers | STK11 |
| 9 | PTEN Hamartoma Tumor | PTEN |
| 10 | Retinoblastoma | RB1 |
| 11 | Tuberous Sclerosis Complex | TSC1 TSC2 |
| 12 | Von-Hippel Lindau | VHL |
| 13 | WT1-related Wilms tumor | WT1 |

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Questions? Contact support@plumcarehealth.com

Lab Director Date

# Frequently Asked Questions

## What is Whole Exome Sequencing (WES)?

Your DNA is the genetic material that makes up what is called your genome. You have over 20,000 genes in each cell of your body. These genes come in pairs, one from your mother and one from your father. Each gene is divided into smaller units. The units called exons (or the exome) make up only 1–2% of your entire genome, but are the part of your genome that tells your body how to to grow and develop.

Whole Exome Sequencing is the process of testing the DNA sequence of your exome, where nearly 85% of disease-causing DNA variations (mutations) are found. WES provides you a cost effective way of collecting a large amount of actionable genomic information for your use.

## What are genetic changes? Are they always harmful?

A genetic change in our genes refers to a difference in our genetic makeup compared to a reference sequence. The majority of genetic changes make us unique from one another and have no implications on our health. We refer to these changes as benign (harmless) or likely benign polymorphisms. Some genetic changes, however, increase the risk for certain health conditions. These genetic changes are called likely pathogenic or pathogenic mutations. A mutation means that the gene does not function the way that it typically does.

There are many genetic changes that are found where we don't yet know whether they have any implications on our health. These genetic changes are called Variants of Uncertain Significance (VUS). VUSs are a common finding, particularly when many genes are analyzed. Health screenings and management are not affected by finding a VUS, and therefore, PlumCare will not report these as part of your results. PlumCare will continue to follow scientific advances for any reclassification of variants, and those with a subscription will be recontacted with any new and relevant information.

## Why is testing me and two other family members important?

By comparing your genetic information to that of your close family members, we can better understand whether genetic changes that are shared in your family have any significance for your family's health.

## How can I speak with a genetic counselor?

PlumCare offers complimentary genetic counseling services. To schedule an appointment with one of our genetic counselors, please contact support@plumcarehealth.com.

# Test methodology & limitations

Using genomic DNA from the submitted specimen(s), the SeqCap EZ Exome v2 was used to target the exon regions of the genome(s). These targeted regions were sequenced using the Illumina HiSeq 4000 sequencing system. The DNA sequence was mapped to and analyzed in comparison with the published human genome build UCSC hg19 reference sequence. The targeted coding exons and splice junctions of the known protein-coding RefSeq genes were assessed for the average depth of coverage and data quality threshold values.

The sequencing technology used generally allows for the identification of mutations across at least 93% of the bases targeted in the exome. Variations in DNA capture performance, as well technological limitations with sequencing, may not allow the calling of variants across all DNA bases in the exome. Actual performance is variable. Some types of genomic changes will not be detected in this test, including copy number variants, mosaicism, and large scale structural variants such as translocations.

Accuracy of insertion and deletion calling is generally lower than single base variant calling. Variant interpretation is valid for the date of the report, and may change given updated information or published literature. This report is not diagnostic; genetic counseling and other medical follow-up is recommended to assess the risk to develop health conditions. Conditions studied in the panels may have other causes in addition to genetics. Depending on the source of client DNA, we may have sequenced non-germline DNA. PlumCare guarantees correct sample handling from point of receipt of customer DNA only.