# Whole Exome Sequencing Analysis

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|---|---|---|---|---|---|
| **Patient name** | : | **Baby. XY** | **PIN** | : | **XXX** |
| **Gender/ Age** | : | **Male/ 8 Months** | **Sample number** | : | **XXX** |
| **Hospital/ Clinic** | : | **XXXX** | **Sample collection date** | : | **01-02-2025** |
| **Hospital/ Clinic** | : | **XXXX** | **Sample received date** | : | **01-02-2025** |
| **Specimen** | : | **Peripheral Blood** | **Report date** | : | **06-05-2025** |

## Clinical history

Proband, Baby. XY is presented with chief complaints of jerky movements since 8 months of age and infantile spasms. His EEG indicative of frequent bilateral generalized spikes and waves. His MRI indicative of gliosis with blooming artifact involving the right frontotemporal region, with ex vacuo dilatation of the right lateral ventricle and gliosis in the left periventricular white matter region. Proband, Baby. XY is suspected to be affected with inborn errors of metabolism and has been evaluated for pathogenic variations.

## Results

**No pathogenic or likely pathogenic variant causative of the reported phenotype was detected**

**List of uncertain significant variant identified:**

| Gene | Region | Variant* | Allele Status | Disease | Classification* | Inheritance pattern |
|---|---|---|---|---|---|---|
| *SERPINI1* (+) | Exon 4 | c.529T>C **(p.Tyr177His)** | Heterozygous | Encephalopathy, familial, with neuroserpin inclusion bodies **(OMIM#604218)** | **Uncertain Significance (PM2)** | Autosomal Dominant |

*Genetic test results are based on the recommendation of American college of Medical Genetics [1].
No other variant that warrants to be reported for the given clinical indication was identified.

# Whole Mitochondrial Genome Sequencing

**No pathogenic or likely pathogenic variant causative of the reported phenotype was detected**

## CNV Findings

No significant Copy Number Variations (CNV) related to phenotype was detected.

## Interpretation

***SERPINI1*: c.529T>C**

**Variant summary:** A heterozygous missense variation in exon 4 of the *SERPINI1* gene (chr3:g.167792637T>C, NM_001122752.2, Depth: 172x) that results in the amino acid substitution of Histidine for Tyrosine at codon 177 (p.Tyr177His) was detected.

**Population frequency:** This variant has not been reported in gnomAD database and 1000 genomes database.

**Clinical evidence:** A missense variant in the same amino acid position (c.530A>C; p.Tyr177Ser) has been classified as uncertain significance in ClinVar database [3].

**OMIM phenotype:** Encephalopathy, familial, with neuroserpin inclusion bodies (OMIM#604218) is caused by heterozygous mutation in the *SERPINI1* gene (OMIM*602445). Familial encephalopathy with neuroserpin inclusion bodies (FENIB) is an autosomal dominant disorder characterized by progressive epilepsy and dementia. Onset of symptoms ranges from the second to fifth decades of life. Severity is variable. This disease follows autosomal dominant pattern of inheritance [2].

**Variant classification:** Based on the evidence, this variant is classified as a variant of uncertain significance.
**In this view, clinical correlation and familial segregation analysis are strongly recommended to establish**

**the significance of the finding. If the results do not correlate, additional testing may be considered based on the phenotype observed.**

## Recommendations

- Sequencing the variant(s) in the parents and the other affected and unaffected members of the family is recommended to confirm the significance.
- Alternative test is strongly recommended to rule out the deletion/duplication.
- Genetic counselling is advised.

## Methodology

DNA extracted from the blood was used to perform whole exome using whole exome capture kit. The targeted libraries were sequenced to a targeted depth of 80 to 100X using Genolab M sequencing platform. This kit has deep exonic coverage of all the coding regions including the difficult to cover regions. The sequences obtained are aligned to human reference genome (GRCh38.p13) using Sentieon aligner and analyzed using Sentieon for removing duplicates, recalibration and re-alignment of indels. Sentieon DNAscope has been used to call the variants. Detected variants were annotated and filtered using the VarSeq software with the workflow implementing the ACMG guidelines for variant classification. The variants were annotated using 1000 genomes (V2), gnomAD (v3.1,2.1.1), ClinVar, OMIM, dbSNP, NCBI RefSeq Genes. *In-silico* predictions of the variant was carried out using VS-SIFT, VS-PolyPhen2, PhyloP, GERP++, GeneSplicer, MaxEntScan, NNSplice, PWM Splice Predictor. Only non-synonymous and splice site variants found in the coding regions were used for clinical interpretation. Silent variations that do not result in any change in amino acid in the coding region are not reported.

## Sequence data attributes

| | |
|---|---|
| Total reads generated | 10.34 Gb |
| Data ≥ Q30 | 95.62% |

Genetic test results are reported based on the recommendations of American College of Medical Genetics [1], as described below:

| Classification | Interpretation |
|---|---|
| Pathogenic | A disease-causing variation in a gene which can explain the patients' symptoms has been detected. This usually means that a suspected disorder for which testing had been requested has been confirmed |
| Likely Pathogenic | A variant which is very likely to contribute to the development of disease however, the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm this assertion of pathogenicity. |
| Variant of Uncertain Significance | A variant has been detected, but it is difficult to classify it as either pathogenic (disease causing) or benign (non- disease causing) based on current available scientific evidence. Further testing of the patient or family members as recommended by your clinician may be needed. It is probable that their significance can be assessed only with time, subject to availability of scientific evidence. |

## Disclaimer

- The classification of variants of unknown significance can change over time. Anderson Diagnostics and Labs cannot be held responsible for it.
- Intronic variants, UTR, Promoter region variants are not assessed using this assay.
- This assay has a sensitivity of 70-75% in detecting large deletions/duplications of more than 10 base pairs or copy number variations (CNV). However, it is important to note that any CNVs detected must be confirmed using an alternate method.
- Certain genes may not be covered completely, and few mutations could be missed. Variants not detected by this assay may impact the phenotype.
- The variations have not been validated by Sanger sequencing.
- The above findings and result interpretation was done based on the clinical indication provided at the time of reporting.
- It is also possible that a pathogenic variant is present in a gene that was not selected for analysis and/or interpretation in cases where insufficient phenotypic information is available.
- Genes with pseudogenes, paralog genes and genes with low complexity may have decreased sensitivity and specificity of variant detection and interpretation due to inability of the data and analysis tools to unambiguously determine the origin of the sequence data in such regions.

- Incidental or secondary findings that meet the ACMG guidelines can be given upon request [4].

## References

1. Richards, S, et al. Standards and Guidelines for the Interpretation of Sequence Variants: A Joint Consensus Recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genetics in medicine: official journal of the American College of Medical Genetics. 17.5 (2015): 405-424.
2. Amberger J, Bocchini CA, Scott AF, Hamosh A. McKusick's Online Mendelian Inheritance in Man (OMIM). Nucleic Acids Res. 2009 Jan;37(Database issue):D793-6. doi: 10.1093/nar/gkn665. Epub 2008 Oct 8.
3. https://www.ncbi.nlm.nih.gov/clinvar/variation/VCV002009830.2
4. Miller, David T., et al. "ACMG SF v3. 1 list for reporting of secondary findings in clinical exome and genome sequencing: A policy statement of the American College of Medical Genetics and Genomics (ACMG)." Genetics in Medicine 24.7 (2022): 1407-1414.

## This report has been reviewed and approved by:

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|---|---|---|---|
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# Appendix 1: Gene Coverage

## Indication Based Analysis:

| Gene_Name | Percentage of coding region covered | Gene_Name | Percentage of coding region covered | Gene_Name | Percentage of coding region covered | Gene_Name | Percentage of coding region covered |
|---|---|---|---|---|---|---|---|
| *AAAS* | 100.0 | *AARS1* | 100.0 | *AARS2* | 100.0 | *AASS* | 100.0 |
| *ABCA1* | 100.0 | *ABCA2* | 100.0 | *ABCA7* | 100.0 | *ABCB7* | 100.0 |
| *ABCC8* | 100.0 | *ABCD1* | 100.0 | *ABHD12* | 100.0 | *ABHD5* | 100.0 |
| *ACAD8* | 100.0 | *ACADM* | 100.0 | *ACADS* | 100.0 | *ACADSB* | 100.0 |
| *ACADVL* | 100.0 | *ACAT1* | 100.0 | *ACAT2* | 100.0 | *ACBD5* | 100.0 |
| *ACO2* | 100.0 | *ACOX1* | 100.0 | *ACOX2* | 100.0 | *ACP5* | 100.0 |
| *ACTB* | 100.0 | *ACTL6B* | 100.0 | *ADA2* | 100.0 | *ADAM22* | 100.0 |
| *ADAMTS13* | 100.0 | *ADAR* | 100.0 | *ADCY5* | 99.93 | *ADCY6* | 100.0 |
| *ADD3* | 100.0 | *ADGRG1* | 100.0 | *ADGRV1* | 100.0 | *ADH1C* | 100.0 |
| *ADNP-AS1* | 100.0 | *ADPRS* | 100.0 | *ADSL* | 100.0 | *AFG3L2* | 100.0 |
| *AGA* | 100.0 | *AGTPBP1* | 100.0 | *AHCY* | 100.0 | *AHI1* | 100.0 |
| *AIFM1* | 100.0 | *AIMP1* | 100.0 | *ALAD* | 100.0 | *ALDH18A1* | 100.0 |
| *ALDH3A2* | 100.0 | *ALDH5A1* | 100.0 | *ALDH6A1* | 100.0 | *ALDH7A1* | 100.0 |
| *ALG13* | 100.0 | *ALG6* | 100.0 | *ALS2* | 100.0 | *AMACR* | 100.0 |
| *AMPD2* | 100.0 | *ANG* | 100.0 | *ANK3* | 100.0 | *ANKLE2* | 100.0 |
| *ANO10* | 100.0 | *ANO3* | 100.0 | *ANOS1* | 100.0 | *AP1S2* | 99.52 |
| *AP3B2* | 100.0 | *AP3D1* | 100.0 | *AP4B1* | 100.0 | *AP4E1* | 100.0 |
| *AP4M1* | 100.0 | *AP4S1* | 100.0 | *AP5Z1* | 100.0 | *APOB* | 100.0 |
| *APP* | 100.0 | *APTX* | 100.0 | *ARCN1* | 100.0 | *ARFGEF1* | 100.0 |
| *ARFGEF2* | 100.0 | *ARG1* | 100.0 | *ARHGEF15* | 100.0 | *ARHGEF9* | 100.0 |
| *ARL13B* | 100.0 | *ARL6* | 100.0 | *ARL6IP1* | 100.0 | *ARMC9* | 100.0 |
| *ARNT2* | 100.0 | *ARSA* | 100.0 | *ARV1* | 100.0 | *ARX* | 99.16 |
| *ASAH1* | 100.0 | *ASL* | 100.0 | *ASNS* | 100.0 | *ASS1* | 100.0 |
| *ATCAY* | 100.0 | *ATG5* | 100.0 | *ATL1* | 100.0 | *ATM* | 100.0 |
| *ATP13A2* | 100.0 | *ATP1A2* | 100.0 | *ATP1A3* | 100.0 | *ATP2B3* | 100.0 |
| *ATP2B4* | 100.0 | *ATP5F1E* | 100.0 | *ATP6AP2* | 100.0 | *ATP7A* | 100.0 |
| *ATP7B* | 100.0 | *ATP8A2* | 100.0 | *ATPAF2* | 100.0 | *ATRX* | 100.0 |
| *ATXN7* | 100.0 | *AUH* | 100.0 | *B3GALT6* | 92.53 | *B4GALNT1* | 100.0 |
| *B4GAT1* | 100.0 | *B9D1* | 100.0 | *BBS1* | 100.0 | *BBS10* | 100.0 |
| *BBS12* | 100.0 | *BBS2* | 100.0 | *BBS4* | 100.0 | *BBS5* | 100.0 |
| *BBS7* | 100.0 | *BBS9* | 100.0 | *BCAP31* | 100.0 | *BCKDHA* | 100.0 |
| *BCKDHB* | 100.0 | *BCL11B* | 100.0 | *BCOR* | 100.0 | *BCS1L* | 100.0 |
| *BICD2* | 100.0 | *BOLA3* | 100.0 | *BRAT1* | 100.0 | *BSCL2* | 100.0 |
| *BTD* | 100.0 | *C12orf4* | 100.0 | *C19orf12* | 100.0 | *C6orf223* | 100.0 |
| *CA8* | 100.0 | *CACNA1A* | 100.0 | *CACNA1B* | 99.96 | *CACNA1D* | 100.0 |
| *CACNA1G* | 100.0 | *CACNA1H* | 100.0 | *CACNA2D2* | 100.0 | *CACNB4* | 100.0 |
| *CAD* | 100.0 | *CAMTA1* | 100.0 | *CAPN1* | 100.0 | *CARS2* | 100.0 |
| *CASK* | 100.0 | *CASR* | 100.0 | *CATIP-AS2* | 100.0 | *CAV1* | 100.0 |
| *CBS* | 17.7 | *CC2D2A* | 100.0 | *CCDC28B* | 100.0 | *CCDC88C* | 100.0 |
| *CCT5* | 100.0 | *CDKL5* | 100.0 | *CEP104* | 100.0 | *CEP120* | 100.0 |
| *CEP152* | 100.0 | *CEP290* | 100.0 | *CEP41* | 100.0 | *CERS1* | 99.38 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *CFH* | 100.0 | *CHAMP1* | 100.0 | *CHCHD10* | 100.0 | *CHD2* | 100.0 |
| *CHMP1A* | 99.69 | *CHMP2B* | 100.0 | *CHP1* | 100.0 | *CHRNA2* | 100.0 |
| *CHRNA4* | 100.0 | *CHRNA7* | 84.72 | *CHRNB2* | 100.0 | *CHROMR* | 100.0 |
| *CIT* | 100.0 | *CIZ1* | 100.0 | *CKAP2L* | 100.0 | *CLCN2* | 100.0 |
| *CLCN4* | 100.0 | *CLIC2* | 100.0 | *CLN3* | 100.0 | *CLN5* | 100.0 |
| *CLN6* | 100.0 | *CLN8* | 100.0 | *CLP1* | 100.0 | *CLPB* | 100.0 |
| *CLPP* | 100.0 | *CLTC* | 100.0 | *CNPY3* | 100.0 | *CNTN2* | 100.0 |
| *CNTNAP1* | 100.0 | *CNTNAP2* | 100.0 | *COA3* | 100.0 | *COA7* | 100.0 |
| *COA8* | 100.0 | *COASY* | 100.0 | *COG2* | 100.0 | *COG4* | 100.0 |
| *COG5* | 100.0 | *COL18A1* | 100.0 | *COL4A1* | 100.0 | *COL4A2* | 100.0 |
| *COL6A3* | 100.0 | *COQ2* | 100.0 | *COQ4* | 100.0 | *COQ5* | 100.0 |
| *COQ6* | 100.0 | *COQ7* | 100.0 | *COQ8A* | 100.0 | *COQ9* | 100.0 |
| *COX10* | 100.0 | *COX14* | 100.0 | *COX15* | 100.0 | *COX20* | 100.0 |
| *COX6B1* | 100.0 | *COX8A* | 100.0 | *CP* | 100.0 | *CPLANE1* | 100.0 |
| *CPLX1* | 100.0 | *CPS1* | 100.0 | *CPT1A* | 100.0 | *CPT1C* | 100.0 |
| *CPT2* | 100.0 | *CREBBP* | 100.0 | *CRLF1* | 100.0 | *CRPPA* | 88.62 |
| *CSF1R* | 100.0 | *CSPP1* | 100.0 | *CSTB* | 100.0 | *CTBP1* | 100.0 |
| *CTC1* | 100.0 | *CTDP1* | 100.0 | *CTNNB1* | 100.0 | *CTSD* | 100.0 |
| *CTSF* | 100.0 | *CUL4B* | 100.0 | *CUX2* | 100.0 | *CWF19L1* | 100.0 |
| *CYB5R3* | 100.0 | *CYC1* | 100.0 | *CYFIP2* | 100.0 | *CYP27A1* | 100.0 |
| *CYP2U1* | 100.0 | *CYP7B1* | 100.0 | *DAB1* | 100.0 | *DARS1* | 100.0 |
| *DARS2* | 100.0 | *DBT* | 100.0 | *DCAF17* | 100.0 | *DCC* | 100.0 |
| *DCPS* | 100.0 | *DCTN1* | 100.0 | *DCX* | 100.0 | *DDC* | 100.0 |
| *DDHD1* | 100.0 | *DDHD2* | 100.0 | *DDX3X* | 100.0 | *DEAF1* | 100.0 |
| *DECR1* | 100.0 | *DENND5A* | 100.0 | *DEPDC5* | 100.0 | *DHCR24* | 100.0 |
| *DHCR7* | 100.0 | *DHFR* | 100.0 | *DHPS* | 100.0 | *DKC1* | 100.0 |
| *DLAT* | 100.0 | *DLD* | 100.0 | *DLG3* | 100.0 | *DMXL2* | 100.0 |
| *DNA2* | 100.0 | *DNAJB2* | 100.0 | *DNAJC12* | 100.0 | *DNAJC13* | 100.0 |
| *DNAJC19* | 100.0 | *DNAJC3* | 100.0 | *DNAJC5* | 98.91 | *DNAJC6* | 100.0 |
| *DNM1* | 100.0 | *DNM1L* | 100.0 | *DNM2* | 100.0 | *DNMT1* | 100.0 |
| *DOCK3* | 100.0 | *DOCK7* | 100.0 | *DOCK8* | 100.0 | *DPM1* | 100.0 |
| *DPYD* | 100.0 | *DPYS* | 100.0 | *DRD3* | 100.0 | *DRD5* | 100.0 |
| *DYNC1H1* | 100.0 | *DYRK1A* | 100.0 | *EARS2* | 100.0 | *EBF3* | 100.0 |
| *ECHS1* | 100.0 | *EEF1A2* | 100.0 | *EEF2* | 100.0 | *EFHC1* | 97.5 |
| *EGR2* | 100.0 | *EIF2B1* | 100.0 | *EIF2B2* | 100.0 | *EIF2B3* | 100.0 |
| *EIF2B4* | 100.0 | *EIF2B5* | 100.0 | *EIF4G1* | 100.0 | *ELOVL1* | 100.0 |
| *ELOVL4* | 100.0 | *ELOVL5* | 100.0 | *ELP2* | 100.0 | *EMC1* | 100.0 |
| *EML1* | 100.0 | *ENSG00000284762* | 100.0 | *ENTPD1* | 100.0 | *EPM2A* | 100.0 |
| *ERAL1* | 100.0 | *ERBB4* | 100.0 | *ERCC1* | 100.0 | *ERCC2* | 100.0 |
| *ERCC3* | 100.0 | *ERCC4* | 100.0 | *ERCC5* | 100.0 | *ERCC6* | 100.0 |
| *ERCC8* | 100.0 | *ERLIN1* | 100.0 | *ERLIN2* | 100.0 | *ETFA* | 100.0 |
| *ETFB* | 100.0 | *ETFDH* | 100.0 | *ETHE1* | 100.0 | *EXOSC3* | 100.0 |
| *EXOSC8* | 100.0 | *EXOSC9* | 100.0 | *EXT2* | 100.0 | *EZH2* | 100.0 |
| *FA2H* | 100.0 | *FAH* | 100.0 | *FAR1* | 100.0 | *FARS2* | 100.0 |
| *FASTKD2* | 100.0 | *FAT2* | 100.0 | *FBXL4* | 100.0 | *FBXO7* | 100.0 |
| *FGD4* | 100.0 | *FGF12* | 100.0 | *FGF14* | 100.0 | *FGFR1* | 100.0 |
| *FIG4* | 100.0 | *FITM2* | 100.0 | *FKRP* | 100.0 | *FKTN* | 100.0 |
| *FLNA* | 100.0 | *FLNC* | 100.0 | *FLVCR1* | 100.0 | *FOLR1* | 100.0 |
| *FOXG1* | 98.87 | *FOXRED1* | 100.0 | *FRMD4A* | 100.0 | *FRRS1L* | 100.0 |
| *FTL* | 100.0 | *FUCA1* | 100.0 | *FUS* | 100.0 | *FXN* | 100.0 |
| *GABBR2* | 99.6 | *GABRA1* | 100.0 | *GABRA2* | 100.0 | *GABRB1* | 100.0 |
| *GABRB2* | 100.0 | *GABRB3* | 100.0 | *GABRD* | 100.0 | *GABRG2* | 100.0 |

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|---|---|---|---|---|---|---|---|
| *GAD1* | 100.0 | *GALC* | 100.0 | *GALE* | 100.0 | *GALK1* | 100.0 |
| *GALT* | 100.0 | *GAMT* | 100.0 | *GAN* | 100.0 | *GATAD2B* | 100.0 |
| *GATM* | 100.0 | *GBA* | 98.29 | *GBA2* | 100.0 | *GBE1* | 100.0 |
| *GCDH* | 100.0 | *GCH1* | 100.0 | *GCLC* | 100.0 | *GDAP2* | 100.0 |
| *GEMIN4* | 100.0 | *GFAP* | 100.0 | *GFM1* | 100.0 | *GFM2* | 100.0 |
| *GIGYF2* | 100.0 | *GJA1* | 100.0 | *GJB1* | 100.0 | *GJC2* | 100.0 |
| *GLB1* | 100.0 | *GLRA1* | 100.0 | *GLRX5* | 100.0 | *GLS* | 100.0 |
| *GLUD2* | 100.0 | *GLYCTK* | 100.0 | *GM2A* | 100.0 | *GMPPA* | 100.0 |
| *GMPPB* | 100.0 | *GNAL* | 100.0 | *GNAO1* | 100.0 | *GNMT* | 100.0 |
| *GOSR2* | 100.0 | *GPAA1* | 100.0 | *GPR88* | 100.0 | *GRIA3* | 100.0 |
| *GRID2* | 100.0 | *GRIK2* | 100.0 | *GRIN1* | 100.0 | *GRIN2A* | 100.0 |
| *GRIN2B* | 100.0 | *GRIN2D* | 98.52 | *GRM1* | 100.0 | *GRN* | 100.0 |
| *GSS* | 100.0 | *GUF1* | 100.0 | *HACE1* | 100.0 | *HADH* | 100.0 |
| *HADHA* | 100.0 | *HADHB* | 100.0 | *HARS1* | 100.0 | *HARS2* | 100.0 |
| *HCFC1* | 100.0 | *HCN1* | 100.0 | *HDAC4* | 100.0 | *HEPACAM* | 100.0 |
| *HEPN1* | 100.0 | *HERC1* | 100.0 | *HEXA* | 100.0 | *HEXB* | 100.0 |
| *HIBCH* | 100.0 | *HIKESHI* | 100.0 | *HK1* | 100.0 | *HLCS* | 100.0 |
| *HMBS* | 100.0 | *HMGCL* | 100.0 | *HNRNPA1* | 100.0 | *HNRNPA2B1* | 100.0 |
| *HNRNPH2* | 100.0 | *HNRNPU* | 100.0 | *HPCA* | 100.0 | *HPD* | 100.0 |
| *HPDL* | 100.0 | *HPRT1* | 100.0 | *HSD17B10* | 100.0 | *HSD17B4* | 100.0 |
| *HSPD1* | 100.0 | *HSPG2* | 99.98 | *HTRA1* | 99.66 | *HTRA2* | 100.0 |
| *IBA57* | 100.0 | *IFIH1* | 100.0 | *IFRD1* | 100.0 | *IFT140* | 100.0 |
| *IFT172* | 100.0 | *IFT27* | 100.0 | *INPP5E* | 100.0 | *INTS8* | 100.0 |
| *IQSEC2* | 100.0 | *IRF2BPL* | 100.0 | *ISCA2* | 100.0 | *ITM2B* | 100.0 |
| *ITPA* | 100.0 | *ITPR1* | 100.0 | *IVD* | 100.0 | *ABCA1* | 100.0 |
| *ARHGEF9* | 100.0 | *ARMC9* | 100.0 | *ASS1* | 100.0 | *ATP8A2* | 100.0 |
| *BCOR* | 100.0 | *CACNA1B* | 99.96 | *CIZ1* | 100.0 | *COQ2* | 100.0 |
| *CRLF1* | 100.0 | *CRPPA* | 88.62 | *CSF1R* | 100.0 | *CTDP1* | 100.0 |
| *DMXL2* | 100.0 | *DNAJC3* | 100.0 | *ENSG00000272442* | 100.0 | *FAT2* | 100.0 |
| *FRMD4A* | 100.0 | *GATM* | 100.0 | *GFM2* | 100.0 | *GLB1* | 100.0 |
| *HERC1* | 100.0 | *KCNMA1* | 100.0 | *KLC2* | 100.0 | *LAMA2* | 100.0 |
| *LRRK2* | 100.0 | *LYST* | 100.0 | *MME* | 100.0 | *NDUFAF5* | 100.0 |
| *NDUFS4* | 100.0 | *NOS3* | 100.0 | *NRXN1* | 100.0 | *NT5C2* | 100.0 |
| *OFD1* | 100.0 | *PEX2* | 100.0 | *PIEZO2* | 100.0 | *PLCB1* | 100.0 |
| *PNKD* | 100.0 | *PPP3CA* | 100.0 | *PRICKLE2* | 100.0 | *PRKN* | 100.0 |
| *PROK2* | 100.0 | *RORA* | 100.0 | *SLC20A2* | 100.0 | *SYNE1* | 100.0 |
| *SZT2* | 100.0 | *TPK1* | 100.0 | *TRAPPC11* | 100.0 | *TTBK2* | 100.0 |
| *TTR* | 100.0 | *UNC80* | 100.0 | *WWOX* | 100.0 | *JAM3* | 100.0 |
| *KANK1* | 100.0 | *KANSL1* | 100.0 | *KARS1* | 100.0 | *KATNIP* | 100.0 |
| *KCNA1* | 100.0 | *KCNA2* | 100.0 | *KCNA4* | 100.0 | *KCNB1* | 100.0 |
| *KCNC1* | 100.0 | *KCNC3* | 98.74 | *KCND3* | 100.0 | *KCNH5* | 100.0 |
| *KCNJ10* | 100.0 | *KCNJ11* | 100.0 | *KCNJ6* | 100.0 | *KCNMA1* | 100.0 |
| *KCNQ2* | 100.0 | *KCNQ3* | 100.0 | *KCNT1* | 99.72 | *KCNT2* | 100.0 |
| *KCTD17* | 100.0 | *KCTD7* | 100.0 | *KDM5C* | 100.0 | *KIAA0586* | 100.0 |
| *KIDINS220* | 100.0 | *KIF1A* | 100.0 | *KIF1B* | 100.0 | *KIF1C* | 100.0 |
| *KIF2A* | 100.0 | *KIF5A* | 100.0 | *KIF5C* | 100.0 | *KIF7* | 99.97 |
| *KLC2* | 100.0 | *KMT2B* | 99.43 | *KY* | 100.0 | *L1CAM* | 100.0 |
| *L2HGDH* | 100.0 | *LAGE3* | 100.0 | *LAMA2* | 100.0 | *LAMB2* | 100.0 |
| *LARGE1* | 100.0 | *LGI1* | 100.0 | *LIAS* | 100.0 | *LIPT1* | 100.0 |
| *LIPT2* | 100.0 | *LMBRD1* | 100.0 | *LMNB1* | 100.0 | *LMNB2* | 98.42 |
| *LOC124901323* | 100.0 | *LRP4* | 100.0 | *LRPPRC* | 100.0 | *LRRK2* | 100.0 |
| *LRSAM1* | 100.0 | *LYRM7* | 100.0 | *LYST* | 100.0 | *MAG* | 100.0 |

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|---|---|---|---|---|---|---|---|
| *MAGI2* | 99.07 | *MAN2B1* | 100.0 | *MAPT* | 100.0 | *MARS1* | 100.0 |
| *MARS2* | 100.0 | *MAT1A* | 100.0 | *MATR3* | 100.0 | *MBD5* | 100.0 |
| *MCCC1* | 100.0 | *MCCC2* | 100.0 | *MCOLN1* | 100.0 | *MDH2* | 100.0 |
| *MECP2* | 100.0 | *MECR* | 100.0 | *MED13L* | 100.0 | *MED17* | 100.0 |
| *MED25* | 100.0 | *MEF2C* | 100.0 | *MFF* | 100.0 | *MFN2* | 100.0 |
| *MFSD2A* | 100.0 | *MFSD8* | 100.0 | *MGME1* | 100.0 | *MICU1* | 100.0 |
| *MIPEP* | 100.0 | *MIR3936HG* | 100.0 | *MKS1* | 100.0 | *MLC1* | 100.0 |
| *MLYCD* | 100.0 | *MMAA* | 100.0 | *MMAB* | 100.0 | *MMACHC* | 100.0 |
| *MMADHC* | 100.0 | *MME* | 100.0 | *MMUT* | 100.0 | *MOCS1* | 100.0 |
| *MOCS2* | 100.0 | *MORC2* | 100.0 | *MPDU1* | 100.0 | *MPV17* | 100.0 |
| *MPZ* | 100.0 | *MRE11* | 100.0 | *MRPS22* | 100.0 | *MRPS34* | 100.0 |
| *MTHFR* | 100.0 | *MTO1* | 100.0 | *MTPAP* | 100.0 | *MTR* | 100.0 |
| *MTRR* | 100.0 | *MTTP* | 100.0 | *MVK* | 100.0 | *MYBPC1* | 100.0 |
| *MYH14* | 100.0 | *MYO1C* | 100.0 | *MYO7A* | 100.0 | *NADK2* | 99.44 |
| *NAGA* | 100.0 | *NAGLU* | 100.0 | *NALCN* | 100.0 | *NANS* | 100.0 |
| *NAT8L* | 97.96 | *NAXE* | 100.0 | *NDE1* | 100.0 | *NDRG1* | 100.0 |
| *NDUFA1* | 100.0 | *NDUFA10* | 100.0 | *NDUFA11* | 100.0 | *NDUFA12* | 100.0 |
| *NDUFA13* | 100.0 | *NDUFA2* | 100.0 | *NDUFA4* | 100.0 | *NDUFA9* | 100.0 |
| *NDUFAF1* | 100.0 | *NDUFAF2* | 100.0 | *NDUFAF3* | 100.0 | *NDUFAF4* | 100.0 |
| *NDUFAF5* | 100.0 | *NDUFAF6* | 100.0 | *NDUFB3* | 100.0 | *NDUFB9* | 100.0 |
| *NDUFS1* | 100.0 | *NDUFS2* | 100.0 | *NDUFS3* | 100.0 | *NDUFS4* | 100.0 |
| *NDUFS6* | 100.0 | *NDUFS7* | 100.0 | *NDUFS8* | 100.0 | *NDUFV1* | 100.0 |
| *NDUFV2* | 100.0 | *NECAP1* | 100.0 | *NEFH* | 100.0 | *NEFL* | 100.0 |
| *NEU1* | 100.0 | *NEXMIF* | 100.0 | *NF1* | 100.0 | *NF2* | 100.0 |
| *NFASC* | 100.0 | *NGLY1* | 100.0 | *NHLRC1* | 100.0 | *NIPA1* | 100.0 |
| *NMNAT1* | 100.0 | *NOL3* | 100.0 | *NOS3* | 100.0 | *NOTCH3* | 95.68 |
| *NPC1* | 100.0 | *NPC2* | 100.0 | *NPHP1* | 100.0 | *NPHP3-ACAD11* | 100.0 |
| *NR2F1* | 100.0 | *NR4A2* | 100.0 | *NRXN1* | 100.0 | *NSUN2* | 100.0 |
| *NT5C2* | 100.0 | *NTRK2* | 100.0 | *NUBPL* | 100.0 | *NUP62* | 100.0 |
| *OCLN* | 90.0 | *ODF3B* | 100.0 | *OFD1* | 100.0 | *OPA1* | 100.0 |
| *OPA3* | 100.0 | *OPHN1* | 100.0 | *OPTN* | 100.0 | *OSGEP* | 100.0 |
| *OTC* | 100.0 | *PACS2* | 100.0 | *PAFAH1B1* | 100.0 | *PAH* | 100.0 |
| *PANK2* | 100.0 | *PANO1* | 100.0 | *PARK7* | 100.0 | *PARN* | 100.0 |
| *PARS2* | 100.0 | *PC* | 100.0 | *PCBD1* | 100.0 | *PCCA* | 100.0 |
| *PCCB* | 100.0 | *PCDH12* | 100.0 | *PCDH19* | 100.0 | *PCLO* | 100.0 |
| *PCNA* | 100.0 | *PDE10A* | 99.54 | *PDE6D* | 100.0 | *PDE8B* | 100.0 |
| *PDGFB* | 100.0 | *PDGFRB* | 100.0 | *PDHA1* | 100.0 | *PDHB* | 100.0 |
| *PDHX* | 100.0 | *PDP1* | 100.0 | *PDSS1* | 100.0 | *PDSS2* | 100.0 |
| *PDYN* | 100.0 | *PET100* | 100.0 | *PEX1* | 100.0 | *PEX10* | 100.0 |
| *PEX11B* | 100.0 | *PEX12* | 100.0 | *PEX13* | 100.0 | *PEX14* | 100.0 |
| *PEX16* | 100.0 | *PEX19* | 100.0 | *PEX2* | 100.0 | *PEX26* | 100.0 |
| *PEX3* | 100.0 | *PEX5* | 100.0 | *PEX6* | 100.0 | *PEX7* | 100.0 |
| *PFN1* | 100.0 | *PGAP1* | 100.0 | *PGK1* | 100.0 | *PGM3* | 100.0 |
| *PHGDH* | 100.0 | *PHKA1* | 100.0 | *PHYH* | 100.0 | *PIBF1* | 100.0 |
| *PIEZO2* | 100.0 | *PIGA* | 100.0 | *PIGG* | 100.0 | *PIGN* | 100.0 |
| *PIGO* | 100.0 | *PIGP* | 100.0 | *PIGQ* | 100.0 | *PIGS* | 100.0 |
| *PIGV* | 100.0 | *PIK3R5* | 100.0 | *PINK1* | 99.91 | *PITRM1* | 100.0 |
| *PLA2G6* | 100.0 | *PLAA* | 100.0 | *PLCB1* | 100.0 | *PLD3* | 100.0 |
| *PLEKHG2* | 100.0 | *PLEKHG4* | 100.0 | *PLP1* | 100.0 | *PLXND1* | 99.93 |
| *PMM2* | 100.0 | *PMP22* | 100.0 | *PMPCA* | 100.0 | *PNKD* | 100.0 |
| *PNKP* | 100.0 | *PNP* | 100.0 | *PNPLA6* | 100.0 | *PNPLA8* | 100.0 |

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|---|---|---|---|---|---|---|---|
| *PNPO* | 100.0 | *PNPT1* | 100.0 | *PODXL* | 100.0 | *POLG* | 100.0 |
| *POLG2* | 100.0 | *POLR1C* | 100.0 | *POLR3A* | 100.0 | *POLR3B* | 100.0 |
| *POMGNT1* | 100.0 | *POMGNT2* | 100.0 | *POMK* | 100.0 | *POMT1* | 100.0 |
| *POMT2* | 100.0 | *PON1* | 100.0 | *PPP1R15B* | 100.0 | *PPP3CA* | 100.0 |
| *PPT1* | 100.0 | *PQBP1* | 100.0 | *PRDM8* | 100.0 | *PRF1* | 100.0 |
| *PRICKLE1* | 100.0 | *PRICKLE2* | 100.0 | *PRKCG* | 100.0 | *PRKN* | 100.0 |
| *PRKRA* | 100.0 | *PROK2* | 100.0 | *PROKR2* | 100.0 | *PRPH* | 100.0 |
| *PRPS1* | 100.0 | *PRRT2* | 100.0 | *PRX* | 100.0 | *PSAP* | 100.0 |
| *PSAT1* | 100.0 | *PSEN1* | 100.0 | *PSEN2* | 100.0 | *PSMB8* | 100.0 |
| *PTEN* | 100.0 | *PTF1A* | 100.0 | *PTPN23* | 100.0 | *PTRH1* | 100.0 |
| *PTRH2* | 100.0 | *PTRHD1* | 100.0 | *PTS* | 100.0 | *PUM1* | 100.0 |
| *PURA* | 100.0 | *PYCR2* | 100.0 | *PYROXD1* | 100.0 | *QARS1* | 100.0 |
| *QDPR* | 98.15 | *RAB18* | 100.0 | *RAB27A* | 100.0 | *RAB39B* | 100.0 |
| *RAB3GAP1* | 100.0 | *RAD50* | 100.0 | *RARS1* | 100.0 | *RARS2* | 100.0 |
| *REEP1* | 100.0 | *REEP2* | 100.0 | *RELN* | 100.0 | *RETREG1* | 100.0 |
| *RFT1* | 100.0 | *RHOBTB2* | 100.0 | *RLIM* | 100.0 | *RNASEH1* | 100.0 |
| *RNASEH2A* | 100.0 | *RNASEH2B* | 100.0 | *RNASEH2B-AS1* | 100.0 | *RNASEH2C* | 100.0 |
| *RNASET2* | 100.0 | *RNF113A* | 100.0 | *RNF125* | 100.0 | *RNF168* | 100.0 |
| *RNF170* | 100.0 | *RNF216* | 100.0 | *ROGDI* | 97.38 | *RORA* | 100.0 |
| *RPGRIP1L* | 100.0 | *RPIA* | 100.0 | *RPL10* | 95.0 | *RRM2B* | 100.0 |
| *RTN2* | 100.0 | *RTN4IP1* | 100.0 | *RTTN* | 100.0 | *RUBCN* | 100.0 |
| *SACS* | 100.0 | *SAMD9L* | 100.0 | *SAMHD1* | 100.0 | *SARS1* | 100.0 |
| *SCARB2* | 100.0 | *SCN1A* | 100.0 | *SCN1A-AS1* | 100.0 | *SCN1B* | 100.0 |
| *SCN2A* | 100.0 | *SCN3A* | 100.0 | *SCN8A* | 100.0 | *SCN9A* | 100.0 |
| *SCO1* | 100.0 | *SCO2* | 100.0 | *SCP2* | 100.0 | *SCYL1* | 100.0 |
| *SDHA* | 100.0 | *SDHAF1* | 100.0 | *SDHB* | 100.0 | *SDHD* | 100.0 |
| *SELENOI* | 100.0 | *SEPSECS* | 100.0 | *SERAC1* | 100.0 | *SETX* | 100.0 |
| *SFXN4* | 100.0 | *SGCE* | 100.0 | *SGPL1* | 100.0 | *SH3TC2* | 100.0 |
| *SHMT2* | 100.0 | *SIGMAR1* | 100.0 | *SIK1* | 24.29 | *SIL1* | 100.0 |
| *SLC12A5* | 100.0 | *SLC12A6* | 100.0 | *SLC13A5* | 100.0 | *SLC16A2* | 100.0 |
| *SLC17A5* | 100.0 | *SLC18A2* | 100.0 | *SLC19A2* | 94.44 | *SLC19A3* | 100.0 |
| *SLC1A2* | 100.0 | *SLC1A3* | 100.0 | *SLC1A4* | 100.0 | *SLC20A2* | 100.0 |
| *SLC22A5* | 100.0 | *SLC25A12* | 100.0 | *SLC25A13* | 100.0 | *SLC25A15* | 100.0 |
| *SLC25A20* | 100.0 | *SLC25A22* | 100.0 | *SLC25A4* | 100.0 | *SLC25A46* | 100.0 |
| *SLC2A1* | 100.0 | *SLC30A10* | 100.0 | *SLC30A9* | 100.0 | *SLC33A1* | 100.0 |
| *SLC35A2* | 100.0 | *SLC39A14* | 100.0 | *SLC39A4* | 100.0 | *SLC44A1* | 100.0 |
| *SLC46A1* | 100.0 | *SLC52A2* | 100.0 | *SLC52A3* | 100.0 | *SLC6A1* | 100.0 |
| *SLC6A17* | 100.0 | *SLC6A19* | 100.0 | *SLC6A3* | 100.0 | *SLC6A8* | 100.0 |
| *SLC9A1* | 100.0 | *SLC9A6* | 100.0 | *SMAD4* | 100.0 | *SMC1A* | 100.0 |
| *SMG9* | 100.0 | *SMPD1* | 100.0 | *SMS* | 98.95 | *SNAP25* | 100.0 |
| *SNCA* | 100.0 | *SNHG14* | 100.0 | *SNX14* | 100.0 | *SOD1* | 100.0 |
| *SOX2* | 100.0 | *SOX6* | 100.0 | *SPART* | 100.0 | *SPAST* | 100.0 |
| *SPG11* | 100.0 | *SPG21* | 100.0 | *SPG7* | 100.0 | *SPR* | 100.0 |
| *SPTAN1* | 100.0 | *SPTBN2* | 100.0 | *SPTBN4* | 100.0 | *SPTLC2* | 100.0 |
| *SQSTM1* | 100.0 | *SRPX2* | 100.0 | *SRY* | 100.0 | *ST3GAL3* | 100.0 |
| *STAMBP* | 100.0 | *STN1* | 100.0 | *STUB1* | 100.0 | *STXBP1* | 100.0 |
| *SUCLA2* | 100.0 | *SUFU* | 100.0 | *SUMF1* | 100.0 | *SUOX* | 100.0 |
| *SURF1* | 100.0 | *SVBP* | 100.0 | *SYN1* | 100.0 | *SYNE1* | 100.0 |
| *SYNGAP1* | 100.0 | *SYNJ1* | 100.0 | *SYT14* | 100.0 | *SYT2* | 100.0 |
| *SZT2* | 100.0 | *TACO1* | 100.0 | *TAF1* | 100.0 | *TAF2* | 100.0 |
| *TANGO2* | 100.0 | *TARDBP* | 100.0 | *TAT* | 100.0 | *TBC1D20* | 100.0 |
| *TBC1D23* | 100.0 | *TBC1D24* | 100.0 | *TBCD* | 100.0 | *TBCE* | 100.0 |

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|---|---|---|---|---|---|---|---|
| *TBK1* | 100.0 | *TCF4* | 100.0 | *TCN2* | 100.0 | *TCTN1* | 100.0 |
| *TCTN2* | 100.0 | *TCTN3* | 100.0 | *TDP1* | 100.0 | *TDP2* | 100.0 |
| *TECPR2* | 100.0 | *TELO2* | 100.0 | *TENM4* | 100.0 | *TFG* | 100.0 |
| *TGM6* | 100.0 | *TH* | 100.0 | *THAP1* | 100.0 | *THG1L* | 100.0 |
| *THOC2* | 100.0 | *TIMM8A* | 100.0 | *TIMMDC1* | 100.0 | *TINF2* | 100.0 |
| *TMEM107* | 100.0 | *TMEM138* | 100.0 | *TMEM216* | 100.0 | *TMEM231* | 100.0 |
| *TMEM237* | 100.0 | *TMEM240* | 100.0 | *TMEM67* | 100.0 | *TMEM70* | 100.0 |
| *TMX2* | 100.0 | *TOR1A* | 100.0 | *TP53RK* | 100.0 | *TPI1* | 100.0 |
| *TPK1* | 100.0 | *TPM2* | 100.0 | *TPP1* | 100.0 | *TRAPPC11* | 100.0 |
| *TRAPPC12* | 100.0 | *TRAPPC4* | 100.0 | *TREM2* | 100.0 | *TREX1* | 100.0 |
| *TRNT1* | 100.0 | *TRPC3* | 100.0 | *TRPM7* | 100.0 | *TSC1* | 100.0 |
| *TSC2* | 100.0 | *TSEN15* | 100.0 | *TSEN2* | 100.0 | *TSEN54* | 99.07 |
| *TSFM* | 100.0 | *TTBK2* | 100.0 | *TTC19* | 100.0 | *TTC21B* | 100.0 |
| *TTPA* | 100.0 | *TTR* | 100.0 | *TUBA1A* | 100.0 | *TUBA4A* | 100.0 |
| *TUBB* | 100.0 | *TUBB3* | 100.0 | *TUBB4A* | 100.0 | *TUBG1* | 100.0 |
| *TWNK* | 100.0 | *TXN2* | 100.0 | *TYMP* | 100.0 | *TYROBP* | 100.0 |
| *UBA5* | 100.0 | *UBE2A* | 100.0 | *UBE3A* | 100.0 | *UBQLN2* | 100.0 |
| *UBR4* | 100.0 | *UBTF* | 100.0 | *UCHL1* | 100.0 | *UFC1* | 100.0 |
| *UNC80* | 100.0 | *UPB1* | 100.0 | *UQCC2* | 100.0 | *UQCC3* | 100.0 |
| *UQCRB* | 100.0 | *UQCRC2* | 100.0 | *UQCRFS1* | 100.0 | *UQCRQ* | 100.0 |
| *UROC1* | 100.0 | *USP18* | 90.0 | *VAC14* | 100.0 | *VAMP1* | 100.0 |
| *VAPB* | 100.0 | *VARS2* | 100.0 | *VCP* | 100.0 | *VLDLR* | 100.0 |
| *VPS11* | 100.0 | *VPS13A* | 100.0 | *VPS13C* | 100.0 | *VPS13D* | 100.0 |
| *VPS16* | 100.0 | *VPS35* | 100.0 | *VPS37A* | 100.0 | *VPS51* | 100.0 |
| *VPS53* | 100.0 | *VRK1* | 100.0 | *VWA3B* | 100.0 | *WARS2* | 100.0 |
| *WASHC5* | 100.0 | *WDR26* | 100.0 | *WDR45* | 100.0 | *WDR62* | 100.0 |
| *WDR73* | 100.0 | *WDR81* | 100.0 | *WFS1* | 100.0 | *WNK1* | 100.0 |
| *WWOX* | 100.0 | *XK* | 100.0 | *XPA* | 100.0 | *XPNPEP3* | 100.0 |
| *XPR1* | 100.0 | *XRCC1* | 100.0 | *XRCC4* | 100.0 | *YME1L1* | 100.0 |
| *YWHAG* | 100.0 | *ZC4H2* | 100.0 | *ZEB2* | 100.0 | *ZFYVE26* | 100.0 |
| *ZFYVE27* | 100.0 | *ZNF142* | 100.0 | *ZNF335* | 100.0 | *ZNF423* | 100.0 |
| *ZNHIT3* | 100.0 | *SERPINI1* | 100.0 | | | | |