NEURAZON
WELLNESS STARTS WITH YOU

From:
Neurazon INC.
Precision Health Analysis Department - Children with Autism and Developmental Disorders
Quebec, Canada

Case no: 593114765
First Name: Shko
Last Name: Hussein
DOB: 26.09.2013
Sex: Male

Test requested: Precision Health Analysis®

Results:
True Autism Spectrum Disorder Variants: NEGATIVE
Acquired Autism Spectrum Disorder Variants: POSITIVE
Attention-Deficit/Hyperactivity Disorder Variants: NEGATIVE
Information Processing and Brain Development Variants: NEGATIVE
White Matter Delays Variants: POSITIVE
Methylation Variants: POSITIVE
Metabolic and Mitochondrial Function Variants: NEGATIVE
Neurotransmitters, Synaptic Health, and Behavior Variants: POSITIVE
Immune System Variants: NEGATIVE
Potential Digestive System Variants: NEGATIVE
Epigenetic Regulation Variants: POSITIVE
Potential Uncontrolled Electrical Activity: POSITIVE

Recommended Interpretation:

- Please note any clinically relevant variants detected that are associated with the described phenotype, if present.
- Review all variants listed in the attached report, if applicable.
- We recommend reevaluating the sequence dataset every 12 months or when there are changes in the phenotype.
- Reassessment by a multidisciplinary team is advised every 3 months to monitor any observed phenotypic changes using artificial intelligence.
- A tailored intervention plan should be developed and supervised by a multidisciplinary team.

ADDITIONAL INFORMATION

This assessment was developed and validated using the AI model of NEURAZON, based on the findings outlined in the attached report. The U.S. Food and Drug Administration (FDA) has determined that clearance or approval for this method is not required; therefore, neither has been sought. All test results are thoroughly reviewed, interpreted, and reported by our team of scientific and medical experts. For full details, please refer to the attached report.

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Recommended Homeopathy Plan

Step: 1st
step Name: Shko Hussein
DOB: 26.09.2013

Please refer to external report

ADDITIONAL INFORMATION

Recommendations: The provided guidance includes safe, non-drug, natural treatments intended to support the child's development. These recommendations are not a replacement for professional rehabilitation and training sessions and should always be followed under the supervision of a qualified specialist. Progress and improvement depend on the individual child, the underlying causes, and their response to the interventions, with recommendations adjusted based on regular evaluations every three months. If any signs of an allergic reaction occur, discontinue the treatment immediately and consult with a healthcare provider to modify the treatment plan accordingly.

Reevaluation: A reevaluation is necessary after the specified duration to reassess development using the AI model or as recommended by the professional team.

Next Steps: Begin the second phase of the protocol after the timeframe indicated in the treatment plan.

This assessment was developed and its performance validated using the AI model of NEURAZON, as detailed in the attached report. Based on the U.S. Food and Drug Administration (FDA) guidelines, this method does not require clearance or approval, and none has been pursued. This test is intended for clinical purposes. All results are thoroughly reviewed, interpreted, and reported by our team of scientific and medical experts. Please refer to the attached report for comprehensive details.

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Order no: 593114765
Report Type: Final report

Case no: 593114765
First Name: SHKO
Last Name: HUSSEIN
DOB: 26.09.2013
Sex: Male

Requested Test: WES (Whole Exome Sequencing)
Clinical Information/Indication: The analysis was performed according to the demand of referal center to identify variants in relevant genes associated with neurological disorders.
Result:

Main Findings:

A variant of unknown significance (VUS); c.3340C>T/p.Arg1114Trp in the SETD1B gene was identified.
A variant of unknown significance (VUS); c.537_543delinsA/p.Asn180_Gly181del in the SOX10 gene was identified.
A variant of unknown significance (VUS); c.3796C>T/p.Arg1266Cys in the MED12 gene was identified.
A variant of unknown significance (VUS); c.3293G>A/p.Arg1098His in the CYFIP2 gene was identified.

Gene (Transcript)	Location	Nucleotide (protein) dbSNP	Zygosity	Variant Classification	Disease (OMIM#, Inheritance)
SETD1B NM_001353345.2	Exon 10	c.3340C>T p.Arg1114Trp rs1355094091	Heterozygous	Variant of unknown significance (VUS)	Intellectual Developmental Disorder with Seizures and Language Delay OMIM:619000 Autosomal Dominant
SOX10 NM_006941.4	Exon 3	c.537_543delinsA p.Asn180_Gly181del	Heterozygous	Variant of unknown significance (VUS)	SOX10 Related Disorder OMIM: 602229 Autosomal Dominant
MED12 NM_005120.3	Exon 27	c.3796C>T p.Arg1266Cys rs1060502168	Hemizygous	Variant of unknown significance (VUS)	MED12 Related Disorder OMIM:300188 X-Linked Recessive/ X-Linked Dominant
CYFIP2 NM_001037333.3	Exon 29	c.3293G>A p.Arg1098His rs748704223	Heterozygous	Variant of unknown significance (VUS)	Developmental and Epileptic Encephalopathy 65 OMIM:618008 Autosomal Dominant

Details About Gene and Variants:
SETD1B: SET1B is a component of a histone methyltransferase complex that produces trimethylated histone H3 at Lys4. Diseases associated with SETD1B include Intellectual Developmental Disorder With Seizures And Language Delay and Autosomal Dominant Non-Syndromic Intellectual Disability. (Lee et al., 2007 [PubMed 17355966]).[supplied by OMIM, Mar 2008]

The SETD1B variant c.3340C>T/p.Arg1114Trp was detected in heterozygous state. It is classified as Variant of Unknown Significance (VUS) according to the recommendations of ACMG. This variant is associated with autosomal dominant Intellectual Developmental Disorder with Seizures and Language Delay (OMIM: 619000).

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SOX10: This gene encodes a member of the SOX (SRY-related HMG-box) family of transcription factors involved in the regulation of embryonic development and in the determination of the cell fate. The encoded protein may act as a transcriptional activator after forming a protein complex with other proteins. This protein acts as a nucleocytoplasmic shuttle protein and is important for neural crest and peripheral nervous system development. Mutations in this gene are associated with Waardenburg-Shah and Waardenburg-Hirschsprung disease. [provided by RefSeq, Jul 2008]

The SOX10 variant c.537_543delinsA/p.Asn180_Gly181del was detected in heterozygous state. It is classified as Variant of Unknown Significance (VUS) according to the recommendations of ACMG. This variant is associated with autosomal dominant SOX10 Related Disorder (OMIM: 602229).

MED12: The initiation of transcription is controlled in part by a large protein assembly known as the preinitiation complex. A component of this preinitiation complex is a 1.2 MDa protein aggregate called Mediator. This Mediator component binds with a CDK8 subcomplex which contains the protein encoded by this gene, mediator complex subunit 12 (MED12), along with MED13, CDK8 kinase, and cyclin C. The CDK8 subcomplex modulates Mediator-polymerase II interactions and thereby regulates transcription initiation and reinitation rates. The MED12 protein is essential for activating CDK8 kinase. Defects in this gene cause X-linked Opitz-Kaveggia syndrome, also known as FG syndrome, and Lujan-Fryns syndrome. [provided by RefSeq, Aug 2009]

The MED12 variant c.3796C>T/p.Arg1266Cys was detected in hemizygous state. It is classified as Variant of Unknown Significance (VUS) according to the recommendations of ACMG. This variant is associated with X-linked dominant and X-linked recessive MED12 Related Disorder (OMIM: 300188).

CYFIP2: Predicted to enable small GTPase binding activity. Involved in several processes, including cell-cell adhesion; positive regulation of proteolysis; and regulation of postsynapse assembly. Located in perinuclear region of cytoplasm and synapse. Part of SCAR complex. Implicated in developmental and epileptic encephalopathy 65. [provided by Alliance of Genome Resources, Jun 2025]

The CYFIP2 variant c.3293G>A/p.Arg1098His was detected in heterozygous state. It is classified as Variant of Unknown Significance (VUS) according to the recommendations of ACMG. This variant is associated with autosomal dominant Developmental and Epileptic Encephalopathy 65 (OMIM: 618008).

Recommendations:
- It is recommended to evaluate this patient's result together with clinical and laboratory findings.
- Genetic screening and clinical evaluation are recommended for family members.
- Genetic counseling is recommended.

Additional Findings:
The variants reported as additional findings refer to pathogenic changes that are not related to the referred phenotype but can cause additional phenotype thus require genetic counseling and further clinical evaluation.

ACMG Findings (ACMG 81 Genes):

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According to the ACMG guidelines (Genetics in Medicine, 2023; PMID: PMID: 37347242), pathogenic and likely pathogenic incidental variants in proposed diseases and genes are reported. Variants in the BRCA1/2, MLH1, MSH2, MSH6, PMS2, TMEM127, MAX and MUTYH genes associated with adult onset diseases in children (under 15 years of age) are not reported.

Carriership Findings:
Pathogenic and likely pathogenic variants in genes selected according to OMIM phenotypes associated with severe or early-onset diseases have been reported. The variants reported as carriership findings refer to pathogenic changes that are not related to the reported phenotype and require family screening in conjunction with genetic counseling due to potential carrier risk.

Gene (Transcript)	Location	Nucleotide (Protein) dbSNP	Zygosity	Variant Classification	Disease (OMIM#, Inheritance)
TACR3 NM_001059.3	Intron 2	c.737+1G>A rs760022956	Heterozygous	Pathogenic	Hypogonadotropic Hypogonadism 11 OMIM:614840 Autosomal Recessive

Method:
Whole Exome Sequencing is performed by using Twist Biosciences technology. First, approximately 36.5 Mb of Consensus Coding Sequences (CCS) (targeting> 98% of RefSeq and Gencode v28 regions derived from the human genome) are replicated from fragmented genomic DNA with the Twist Exome 2.0 kit. The generated library is sequenced on the MGI DNBSEQ-G400 NGS platform to achieve a minimum reading depth of 20x for>98% of the targeted bases. As a result of sequencing, raw data is obtained in FASTQ format. Whole Exome Sequencing analysis is performed using the Franklin by Genoox Analysis program. In addition to all disease-causing variants reported in the HGMD®, ClinVar, and CentoMD® databases as well as all variants with a Minor Allele Frequency (MAF) of less than 1% in the gnomAD database are considered. The research for related variables has focused on coding exons and surrounding +/- 20 intronic bases. All potential inheritance patterns are covered. In addition, the family history and clinical information provided are used to evaluate pathogenicity and variables defined by their cause of disease. Sequencing variants are classified into five classes according to the ACMG/AMP variant classification guidelines and ClinGen recommendations: pathogenic, likely pathogenic, Variant of unknown significance (VUS), likely benign, and benign[1]. All variables related to the patient's phenotype are reported, except for benign or possible benign variants. Low-quality single nucleotide variants and all related deletion/insertion variants are validated by Sanger sequencing.

Analysis Statistics:

Percent of target covered (depth>=20)	97.7%
Average Depth (targeted regions)	207
Variant Quality	99%

Method Limitations:
Polymorphisms in primary binding and regions, CNV duplications and somatic microsatellite variations, tissue mosaic, high GC nucleotide content can lead to false positive / negative results. False positive findings may occur due to large deletion / point

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mutation combined heterozygosity. Variants in transcripts other than canonical transcripts cannot be eliminated, and differences may occur between exon numbers and mutation positions depending on the transcript type sequenced. This method does not show heterozygous deletions and duplications in rare exons and nucleotide changes in other regions of the gene.

Variants with the allele fraction below 30% for regions with a sensitivity of this test of 50X read count are not reported. Additionally, due to technology limitations, some regions may be either not covered or poorly covered. Variables in these regions cannot be reliably detected. Areas with extremely low readings are considered artifacts as a result of validation studies, and they were not taken into account during the analysis. Copy number changes, inversions, translocations and repeat sequence increases cannot be detected by the NGS method.

The genetic results are interpreted in the context of the provided clinical findings, family history, and other laboratory data. Only variants in genes potentially related to the proband's medical condition are reported. Misinterpretation of results may occur if the provided information is inaccurate and/or incomplete. If the obtained genetic results do not concur with the clinical findings, additional testing should be considered.

Reference:
[1] Richards et al.Standarts and guidelines for the interpretation of sequence variants 17(5):405-424. doi:10.1038/gim.2015.30 GENETICS in MEDICINE,2015

This test was analyzed by Neurazon, Canada.

Digitally Approved by:

Dr. Carmel Katz

Lead Scientist and Geneticist

Lead Bioinformatics Specialist

At Neurazon