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Neurazon INC.

Precision Health Analysis Department - Children with Autism and Developmental DisordersÁ

Quebec, Canada

Case no: 5221163497 First Name: Sultan Last Name: Alrawili DOB: 15.01.2020

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: NEGATIVE

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:** NEGATIVE

Potential Uncontrolled Electrical Activity: NEGATIVE

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 Al 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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Reports without signature are invalid. Results are valid only for the sample analyzed.



> Contact Details

Tel.: +1 438-497 4440





Recommended Homeopathy Plan

Step: 1st

step Name: Sultan Alrawili

DOB: 15.01.2020

	Item name	Ingredient	Purpose	Quantity	Duration	Details
1	Centovita: PEACEFUL MINDS: CALM & FOCUS MAGNESIUM HERBAL FORMULA FOR CHILDREN	Multiple	Variant found	1.5 ml in the morning 1.5 ml at night	4 months	www.centovita.com or amazon
2	Centovita: EASYSPEAK BRAIN BOOST: BRAIN AND SPEECH SUPPORT FOR CHILDREN	Multiple	Variant found	3 ml in the morning	4 months	www.centovita.com or amazon
3	B-METHYLATION BOOST: LIQUID B COMPLEX AND METHYLATION SUPPORT FOR CHILDREN	Multiple	Variant found	3 ml in the morning	4 months	www.centovita.com or amazon

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 Al 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 Al 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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From:

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Case no: 5221163497 First Name: SULTAN Last Name: ALRAWILI DOB: 15.01.2020

Sex: Male

Order no: 5221163497 Report Type: Final report



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:									
Class 3 variant; c.1042A>G / p.lle348Val in the ZEB2 gene was identified.									
Gene (Transcript)	Nucleotide Location (protein) dbSNP		Zygosity	Variant Classification	Disease (OMIM#, Inheritance)				
ZEB2 NM_014795.4	Exon 8	c.1042A>G p.lle348Val	Heterozygous	Class 3	OMIM: 235730 Autosomal Dominant				

Details About Gene and Variants:

ZEB2: The protein encoded by this gene is a member of the Zfh1 family of 2-handed zinc finger/homeodomain proteins. It is located in the nucleus and functions as a DNA-binding transcriptional repressor that interacts with activated SMADs. Mutations in this gene are associated with Hirschsprung disease/Mowat-Wilson syndrome. Alternatively spliced transcript variants have been found for this gene.[provided by RefSeq, Jan 2010]

The ZEB2 variant c.1042A>G / p.lle348Val was detected in heterozygous state. It is classified as Variant of Unknown Significance (VUS/class 3) according to the recommendations of ACMG. This variant is associated with autosomal dominant Mowat-Wilson Syndrome (OMIM: 235730).

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):

According to the ACMG guidelines (Genetics in Medicine, 2023; PMID: PMID: 37347242), Class 1 or 2 incidental changes 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.



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Carriership Findings:

Class 1 and class 2 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.

Method:

Whole Exome Sequencing is performed by DiagnoSeq 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 Human Core Exome Plus kit. The generated library is sequenced on the Illumina Novaseq 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 and VCF formats. Whole Exome Sequencing analysis is performed on FASTQ data 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 and are classified in Class 1 - 5 scoring **. 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:

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Average Depth (RefSeq Exome)	128
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 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,

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additional testing should be considered.

**Variant Classification (According to American College of Medical Genetics ACMG)

Class 1 - Pathogenic

Class 2 – Likely pathogenic

Class 3 - Variant of Unknown Significance - VUS

Class 4 – Likely benign

Class 5 - Benign

This test was analyzed by Neurazon, Canada.

Digitally Approved by:

Dr. Carmel Katz

Lead Scientist and Geneticist

Lead Bioinformatics Specialist

At Neurazon



