Information about the subject

Name: ***

Gender: male

date of birth:***

nation:-

sample information

Sample type: peripheral blood

Sampling date: 2023-12-01

Test date: 2023-12-04

Family number: GPD-B2307586JX

Inspection information

Inspection item: enhanced whole-exome family test package

WES-trio -plus
submitting physician:--

Sampling unit: - -

Clinical information

Easy fatigue for more than 8 months, unstable instability for 3 days, CK: 9763u / l, LDH: 2263u / l, HCT: 7.35mol / l, ACT2:2.09nmol/l, electromyography: visible in both legs Signs of myogenic damage, the child sister 1 + years early, the cause of death "myocarditis".

Core phenotypes

Vertical head instability; abnormal electromyogram; increased serum creatine phosphokinase; increased lactate dehydrogenase activity; increased muscle fatigue

Test conclusion

Suspected pathogenic variants and significant unknown variants possibly associated with the proband's phenotype were detected on the NAXD gene.

detection result

Variant classification	number	Report location
1. nuclear genome – variants highly fit to the proband phenotype and the inheritance pattern	2	Report on 2 pages
2. nuclear genome – variants only partially associated with the proband phenotype / highly consistent but not by the inheritance pattern	1	Report on 3 pages
3. nuclear genome-secondary (unexpected) discovery of sites of variation on the gene	0	-
4. candidate variant loci in the mitochondrial loop genome	0	-

Results: Based on the phenotypes such as erector instability and EMG abnormality, the sequencing data of proband families were analyzed with copy number prediction in the NAXD gene. Two variant loci highly consistent with the proband's phenotype and the inheritance pattern were detected above: c.43C>T（p.Arg15Ter）、c.781G>T（p. Gly261Cys). Higher phenotype agreement with the proband and a higher inheritance pattern, Although, c.781G>T（p. Gly261Cys), Insufficient evidence of pathogenicity, but it is recommended to focus on this base at the same time, one variant locus partially consistent with the proband was detected, which could not fully explain the proband phenotype, so we made a detailed knot on these loci interpretation, you can see the report on follow pages.

This simultaneous analysis of the mitochondrial loop genome data revealed no suspicious candidate loci.

propose

It is recommended that doctors refer to the test results, combined with the comprehensive analysis of specific clinical and other test results, and focus on the NAXD gene.

Results interpretation

1. nuclear genome-variants highly consistent to the proband phenotype and inheritance pattern: 2

gen	chromosome Location (hg38)	The reference transcript exon	Nucleotide alterations Amino acid changes	function change	Variants in the zygotic form of the family members			crowd frequency	Pathogenic grading
					proband	father	mother		
NAXD	chr13:110615644	NM_001242882.2 exon1	c.43C>T p.Arg15Ter	Nonsense-heteromorphosis	Heterozygous (54/130)	wild type (0/39)	Heterozygous (46/106)	uncollected record	Suspected disease
NAXD	chr13:110637191	NM_001242882.2 exon9	c.781G>T p.Gly261Cys	Missense-heteromorphosis	Heterozygous (96/206)	Heterozygous (91/202)	wild type (0/38)	uncollected record	The meaning is not clear
Related diseases		Early-onset progressive encephalopathy with cerebral oedema and / or leukoencephalopathy type 2 (618321, AR)							

Variation description:

c.43C>T （p. Arg15Ter): 1) None of this variant was included in the general population database (GnomAD), suggesting that this variant is rare in the general population (PM2_Support In); 2) No clinical and functional reports of this variant; 3) this variant is expected to cause degradation of the encoded transcript (NMD) and the gene associated disease is known to be functional Loss (loss of function, LOF) variant pathogenic (PVS 1); 4) sequencing showed that the proband inherited the variant from the mother; according to the ACMG guidelines The mutation was found to be suspected of being pathogenic.

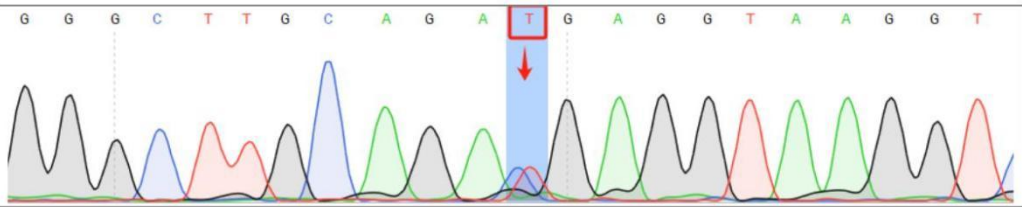
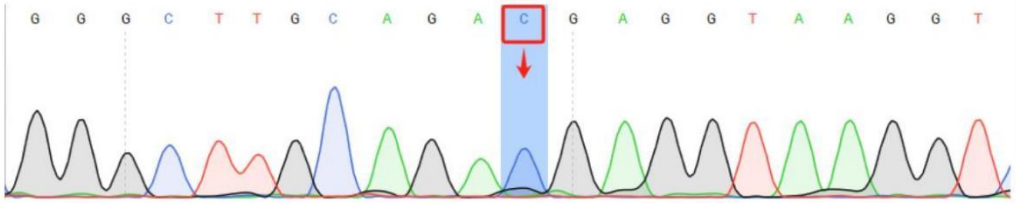
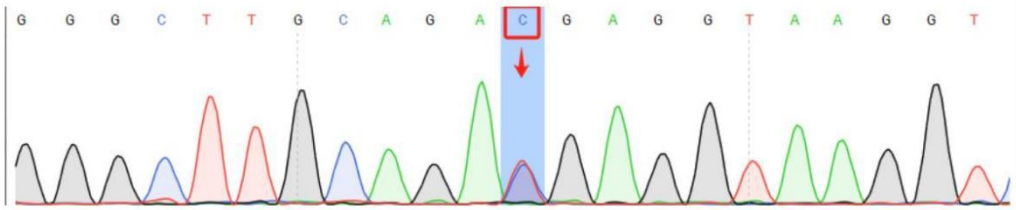
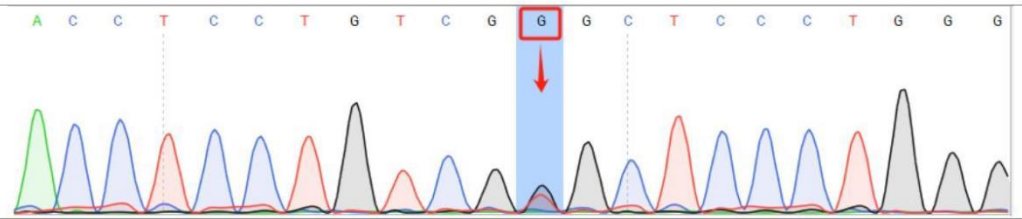
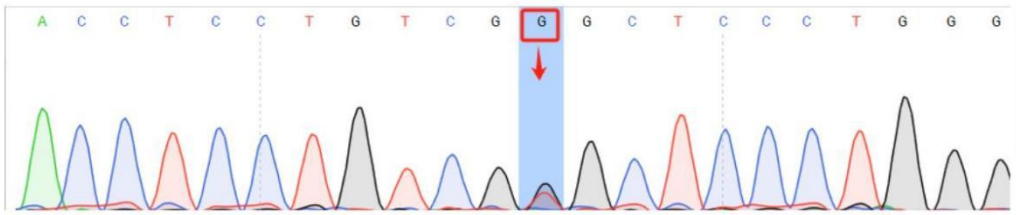
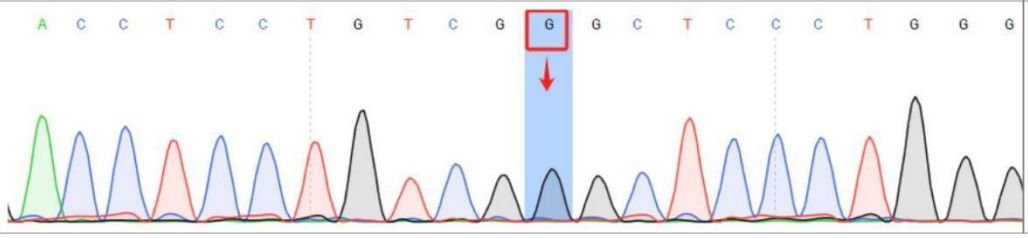
c.781G>T （p. Gly261Cys): 1) None of the variant was included in the general population database (GnomAD), suggesting that this variant is rare in the general population (PM 2 _ Supporting); 2) No clinical and functional reports of this variant; 3) The REVEL value of bioinformation prediction software is 0.857, suggesting that the variant is deleterious (PP3_Moderat E e; 4) This variant and the suspected pathogenic variant c.43C>T （p. Arg15Ter) Composition compound heterozygous form (PM3) (validation results see page 9 of the report); according to ACMG Guidelines, temporarily determine the significance of this variant detected is not clear.

Genes and diseases:

The NAXD gene is involved in the repair of metabolites, enabling ATP and depends on NAD (P) H-hydrate dehydratase activity.

In conclusion, the above two variant loci were detected in the NAXD gene this time, and the related diseases agreed with the proband and the genetic pattern, although c.781G>T （p.Gly261 Cys) currently has insufficient evidence of pathogenicity, but it is still recommended to focus on this gene and to combine specific clinical comprehensive analysis.

The first-generation sequencing results

Verify the site 1	NAXD :chr13:110615644:NM_001242882.2:exon1:c.43C>T:p.Arg15Ter	
Sample (number)	**Map of the Sanger sequencing peaks**	bear fruit
proband **（GPD -B2307586）**		Heterozygo-sis
The proband father **（GPD -B2307587）**		wild type
The proband's mother **（GPD -B2307588）**		Heterozygo-sis
Verify the site 2	NAXD :chr13:110637191:NM_001242882.2:exon9:c.781G>T:p.Gly261Cys	
Sample (number)	**Map of the Sanger sequencing peaks**	bear fruit
proband **（GPD -B2307586）**		Heterozygo -sis
The proband father **（GPD -B2307587）**		Heterozygo-sis
The proband's mother **（GPD -B2307588）**		wild type