A Novel Hemizygous Frameshift OPHN1 Gene Mutation Associated with Mental Retardation, X-Linked, with Cerebellar Hypoplasia and Distinctive Facial Appearance

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INTRODUCTION

The oligophrenin-1 (OPHN1) gene encodes a Rho-GTPase-activating protein that promotes GTP hydrolysis of Rho sub-family members. Rho proteins are important mediators of intracellular signal transduction affecting cell migration and cell morphogenesis.

Mutation in the OPHN1 on chromosome Xq12 causes Mental retardation, X-linked, with cerebellar hypoplasia characterized by moderate to severe intellectual deficit and cerebellar abnormalities and distinctive facial appearance.

We planned WES from a 2-year-old male case who presented with the finding of delay in psychomotor development. The age of onset of clinical findings was 8 months. He also had speech delay, hypotonia, strabismus, constipation and neutropenia. There was cerebellar hypoplasia in his cranial MRI.

METHODS

DNA extraction

Library preparation with Illumina Nextera Exome kit

Sequencing with illumina Nextseq500 platform

Analyze data and annote variants

Sanger Sequencing for Confirmation

RESULTS

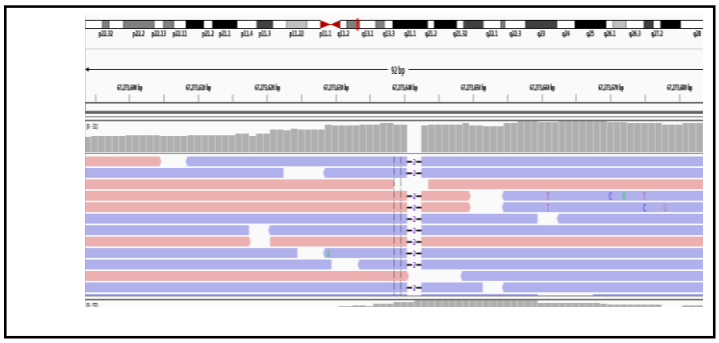

Figure 1: IGV Images of the patient

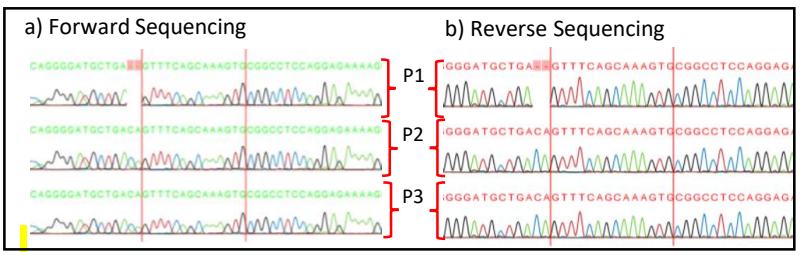

Figure 2: Sanger Images (P1: Patient, P2: The patient's mother, P3: The patient's father)

Table 1: Variant Classification

Gene	Variant	HGMD	ClinVar	ACMG Classification	GERP RS
OPHN1 (NM_002547.3)	c.2169_2170delCA	Not reported	Not reported	Pathogenic (PVS1, PM2, PP3)	1,9059

DISCUSSION & CONCLUSION

We identified a novel hemizygous deletion at OPHN1 (NM_002547.4) gene with a position c.2169_2170del following variant which is also de novo, because it was not detected in the mother. With this mutation, we added a new one to the variants detected in the OPHN1 gene. Functional studies are needed to contribute to the determination of the pathogenicity of this variant.

REFERENCES

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