BAYLOR GENETICS

BAYLOR GENETICS
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PATIENT CASE

Whole Exome Sequencing (WES)

Whole Exome Sequencing identifies two intronic variants to help explain a neurodevelopmental disorder case.

Initial Presentation:

- 3-year-old patient with delayed speech, language development, motor delay, developmental regression, features of autism, impaired upward gaze, and unsteady gait
- Brain imaging including MRI was unremarkable

Genetic Tests Performed:

- Proband WES

WES Test Findings:

- Two atypical splice variants — one variant of uncertain significance (VUS) and one likely pathogenic variant in the *NPC1* gene were identified which may be consistent with a diagnosis of Neimann Pick Disease Type C1/D
- Baylor Genetics routinely evaluates suspicious intronic variants past the typical intronic cutoff of 20bp, which allowed the second variant to be identified

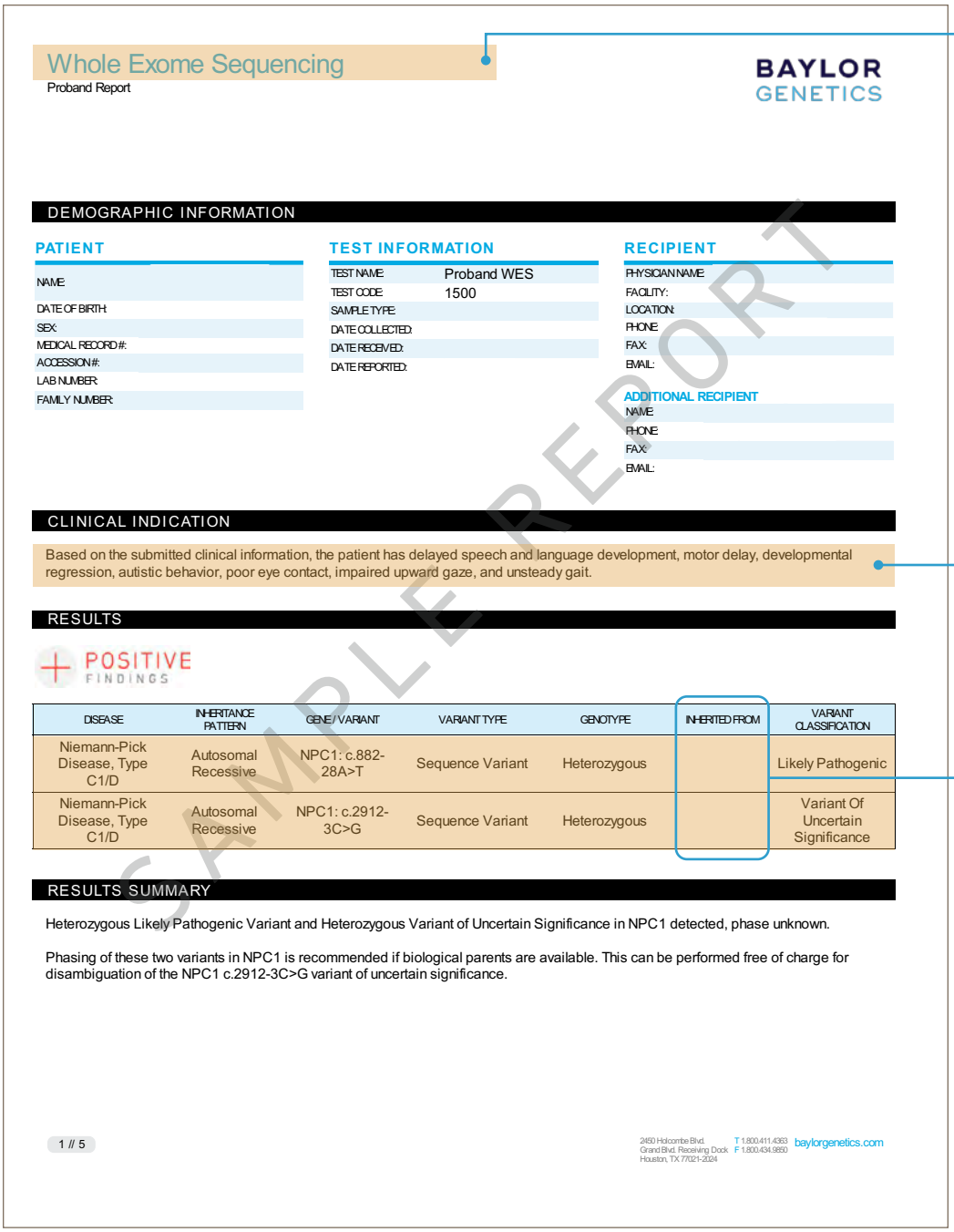
Impact on Medical Management:

- Additional parental testing was offered to determine if the *NPC1* variants are in cis or trans to better understand if these findings constitute a diagnosis of Neimann Pick Disease

The WES technology at Baylor Genetics enabled the identification of the VUS and likely pathogenic intronic variants.

A diagnosis of Neimann Pick Disease, which is consistent with this patient's symptoms, can now be considered, and further studies initiated.

Parental testing was recommended to help clarify phasing of the *NPC1* variants as proband only WES cannot determine if the variants are in cis or trans.



Whole Exome Sequencing

Proband Report

BAYLOR GENETICS

DEMOGRAPHIC INFORMATION

PATIENT

NAME:	
DATE OF BIRTH:	
SEX:	
MEDICAL RECORD #:	
ACCESSION #:	
LAB NUMBER:	
FAMILY NUMBER:	

TEST INFORMATION

TEST NAME:	Proband WES
TEST CODE:	1500
SAMPLE TYPE:	
DATE COLLECTED:	
DATE RECEIVED:	
DATE REPORTED:	

RECIPIENT

PHYSICIAN NAME:	
FACILITY:	
LOCATION:	
PHONE:	
FAX:	
EMAIL:	

ADDITIONAL RECIPIENT

NAME:	
PHONE:	
FAX:	
EMAIL:	

CLINICAL INDICATION

Based on the submitted clinical information, the patient has delayed speech and language development, motor delay, developmental regression, autistic behavior, poor eye contact, impaired upward gaze, and unsteady gait.

RESULTS

POSITIVE FINDINGS

DISEASE	INHERITANCE PATTERN	GENE/VARIANT	VARIANT TYPE	GENOTYPE	INHERITED FROM	VARIANT CLASSIFICATION
Niemann-Pick Disease, Type C1/D	Autosomal Recessive	NPC1: c.882-28A>T	Sequence Variant	Heterozygous		Likely Pathogenic
Niemann-Pick Disease, Type C1/D	Autosomal Recessive	NPC1: c.2912-3C>G	Sequence Variant	Heterozygous		Variant Of Uncertain Significance

RESULTS SUMMARY

Heterozygous Likely Pathogenic Variant and Heterozygous Variant of Uncertain Significance in NPC1 detected, phase unknown.

Phasing of these two variants in NPC1 is recommended if biological parents are available. This can be performed free of charge for disambiguation of the NPC1 c.2912-3C>G variant of uncertain significance.

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SAMPLE REPORT

Test Name

The clinical indication for testing was broad and the provider felt that comprehensive testing was indicated.

Key findings summary with disease and variant information. Two pathogenic variants were identified but because parental samples were not received it is unclear if the variants were inherited or *de novo*.