BAYLOR GENETICS

BAYLOR GENETICS
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PATIENT CASE

Whole Genome Sequencing (WGS)

Whole Genome Sequencing provides a diagnosis and clarifies previous testing from another laboratory.

Initial Presentation:

- 11-year-old female with juvenile myoclonic seizure and ataxia

Genetic Tests Performed:

- Trio WGS
- The patient previously had a targeted epilepsy panel from another laboratory ordered with non-diagnostic results; (3 variants of uncertain significance (VUS) reported)

Trio WGS Test Findings:

- A homozygous pathogenic CCCCGCCCCGCG repeat expansion with repeat number >50 in the *CSTB* gene was detected, consistent with a diagnosis of progressive myoclonic epilepsy 1A in this individual
- The patient's parents were heterozygous for repeat number >40 in this gene. This gene has autosomal recessive inheritance

Impact on Medical Management:

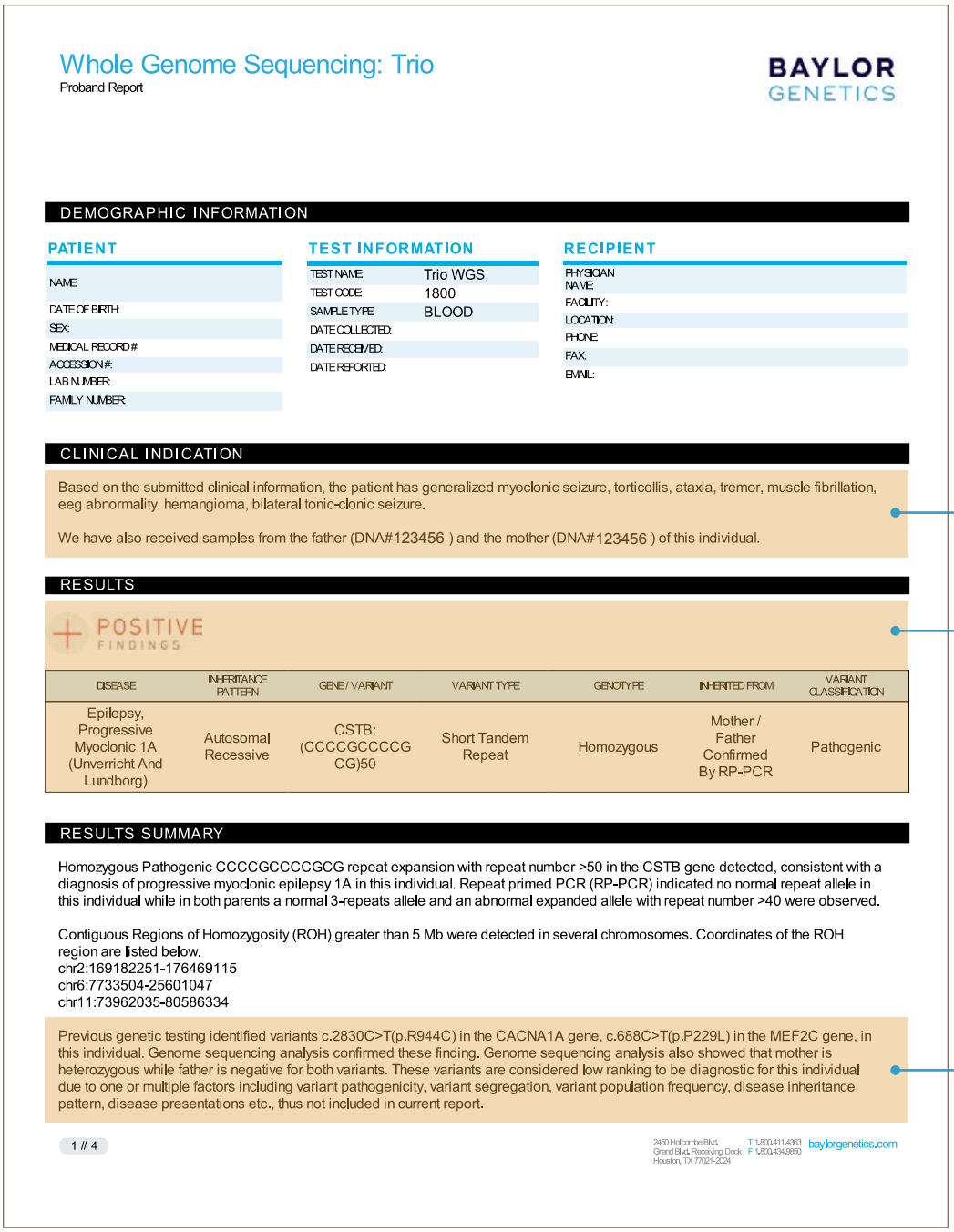
- Testing by Baylor Genetics' WGS enabled a final diagnosis after previous genetic testing results identified other variants unlikely to explain the patient's symptoms
- Knowing the specific cause of the patient's epilepsy allowed the provider to establish a more personalized treatment plan
  - > Certain medications are effective for some types of epilepsy, but for others, they may have no benefit or cause adverse effects
- Since the parents' carrier status is known, the reproductive risk can be better ascertained for future pregnancies

Many epilepsy-specific and NGS-based panels do not include trinucleotide repeat assessment. Baylor Genetics' WGS offers concurrent testing of many trinucleotide repeat conditions such as the *CSTB* gene while also being comprehensive for sequencing variants.

After undergoing several tests with another laboratory, WGS at Baylor Genetics was able to result a clear diagnosis for this patient, and previous test results were able to be properly contextualized.

If a comprehensive test like WGS was the first test performed, this patient would have received a unifying diagnosis earlier, avoiding unnecessary testing and related expenses.

WGS being performed in a trio setting provided inheritance information. A rapid result also allowed for expedited actionable results that could directly impact the patients management.



Whole Genome Sequencing: Trio

Proband Report

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DEMOGRAPHIC INFORMATION

PATIENT

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

TEST INFORMATION

TEST NAME:	Trio WGS
TEST CODE:	1800
SAMPLE TYPE:	BLOOD
DATE COLLECTED:	
DATE RECEIVED:	
DATE REPORTED:	

RECIPIENT

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

CLINICAL INDICATION

Based on the submitted clinical information, the patient has generalized myoclonic seizure, torticollis, ataxia, tremor, muscle fibrillation, eeg abnormality, hemangioma, bilateral tonic-clonic seizure.

We have also received samples from the father (DNA#123456) and the mother (DNA#123456) of this individual.

RESULTS

POSITIVE FINDINGS

DISEASE	INHERITANCE PATTERN	GENE / VARIANT	VARIANT TYPE	GENOTYPE	INHERITED FROM	VARIANT CLASSIFICATION
Epilepsy, Progressive Myoclonic 1A (Unverricht And Lundborg)	Autosomal Recessive	CSTB: (CCCCGCCCCG CG)50	Short Tandem Repeat	Homozygous	Mother / Father Confirmed By RP-PCR	Pathogenic

RESULTS SUMMARY

Homozygous Pathogenic CCCCGCCCCGCG repeat expansion with repeat number >50 in the CSTB gene detected, consistent with a diagnosis of progressive myoclonic epilepsy 1A in this individual. Repeat primed PCR (RP-PCR) indicated no normal repeat allele in this individual while in both parents a normal 3-repeats allele and an abnormal expanded allele with repeat number >40 were observed.

Contiguous Regions of Homozygosity (ROH) greater than 5 Mb were detected in several chromosomes. Coordinates of the ROH region are listed below.
chr2:169182251-176469115
chr6:7733504-25601047
chr11:73962035-80586334

Previous genetic testing identified variants c.2830C>T(p.R944C) in the CACNA1A gene, c.688C>T(p.P229L) in the MEF2C gene, in this individual. Genome sequencing analysis confirmed these finding. Genome sequencing analysis also showed that mother is heterozygous while father is negative for both variants. These variants are considered low ranking to be diagnostic for this individual due to one or multiple factors including variant pathogenicity, variant segregation, variant population frequency, disease inheritance pattern, disease presentations etc., thus not included in current report.

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

A homozygous pathogenic repeat number was identified in the CSTB gene. Both of the patient's parents are heterozygous for a pathogenic repeat number, which given this condition has autosomal recessive inheritance indicates their carrier status.

Results summary with disease and variant information. One likely pathogenic and one pathogenic variant were identified. Previous testing results were considered unlikely to explain the patient's phenotype.