North West Genomic Laboratory Hub (Manchester Site)
Manchester Centre for Genomic Medicine
6th Floor, St Mary's Hospital, Manchester, M13 9WL
Scientific Operational Director: Dr E. Howard
https://mft.nhs.uk/nwglh/ mft.genomics@nhs.net Tel +44(0) 161 276 6122

NHS North West
NHS Genomic Laboratory Hub

Forename:	**Geneticsthree**	Report No:	**R24-00BX-1**
Surname:	**BEAKER**	Hospital No:	**Not provided**
Sex:	**Male**	Other No:	**Not provided**
DoB:	**01/01/1970**	Sample:	**DNA (External)**
NHS No:			
Hive Order ID:	**1000104558**		

Collected:	**Not provided**	Received:	**03/06/2024 12:12**	Activated:	**03/06/2024**
				Reported:	**04/06/2025**

Referred by: McTest Test, Wythenshawe Hospital, Manchester, M23 9LT, (test@test.com)

Genomics Laboratory Report

Reason for Testing

To investigate the cause of this individual's phenotype (see Appendix I overleaf).
Clinical Indication: Hypotonic infant (R69.5). The details of any additional panels applied can be found in Appendix I overleaf.

RESULT SUMMARY:

Likely pathogenic variant detected.
Likely genetic diagnosis of autosomal dominant CSNK2B-related disease.

Result and Interpretation

This individual is heterozygous for a likely pathogenic CSNK2B variant, c.256C>T p.(Arg86Cys) (details in Appendix II overleaf). Monoallelic pathogenic CSNK2B variants cause autosomal dominant Poirier-Bienvenu neurodevelopmental syndrome (OMIM# 618732).

This result is likely to be the genetic cause of this individual's clinical symptoms, and would be consistent with an autosomal dominant mode of inheritance.

This result has implications for other family members. Testing for CSNK2B c.256C>T p.(Arg86Cys) is available to other relatives of this individual, as appropriate (via referral to a clinical genetics service).

Reported By:
Jonathan Edgerley
Clinical Scientist

Authorised By:

Jonathan Edgerley
Clinical Scientist

APPENDIX I - Test Methodology:

Clinical indication: *Hypotonic infant (R69.5)*

Affiliated panel(s): *Copy panels here with version numbers*

Whole genome sequencing (Illumina) and analysis of variants prioritised by the Genomics England bioinformatics pipeline for the Genomic Medicine Service gene panel(s) listed above. Please note that the sensitivity of this test is limited by the types of detectable variants, regions of low read depth coverage and incomplete ascertainment of disease-gene associations. Variants are evaluated in accordance with ACMG/ACGS guidance; only pathogenic, likely pathogenic and variants of uncertain significance considered to be clinically actionable are reported.

Penetrance: *Complete OR Incomplete*
Patient phenotype: *HPO term 1; HPO term 2 (copy from Congenica HPO terms tab) OR Unaffected parent*

APPENDIX II - Variant Details and Classification Evidence:

HGVS description: *NM_001320.6(CSNK2B):c.256C>T p.(Arg86Cys)*	***Classification:*** *Likely pathogenic*	
Genomic coordinates: *Chr6(GRCh38):g.31668619C>T*	***Zygosity:*** *Heterozygous*	***Inheritance:*** *de novo*

Evidence for variant classification using ACGS best practice guidelines 2020 (https://www.acgs.uk.com/quality/best-practice-guidelines/).
Key: Evidence code_Level

PM2_Moderate
Absent in control individuals from the gnomAD dataset (The Genome Aggregation Database, gnomAD v2.1.1 and v3.1.2, Cambridge, MA (http://gnomad.broadinstitute.org/)).

PP2_Supporting
CSKN2B has a low rate of benign missense variation, and missense variants in CSKN2B are a common mechanism of CSNK2B-related disease (The Genome Aggregation Database, gnomAD v2.1.1 and v3.1.2, Cambridge, MA (http://gnomad.broadinstitute.org/)).

PP3_Supporting
Multiple lines of computational evidence predict a deleterious effect on the gene or gene product.
Computational missense predictions were performed using REVEL (Ioannidis 2016 PMID: 27666373).

PS4_Moderate
The prevalence of this variant in cases is significantly increased compared with its prevalence in controls (ClinVar: https://www.ncbi.nlm.nih.gov/clinvar/), (Ernst, 2021 PMID: 34041744).

PS2_Moderate
Confirmed to have arisen de novo in multiple patient(s) with CSNK2B-related disease (ClinVar: https://www.ncbi.nlm.nih.gov/clinvar/).