







Article

Structural Protein Effects Underpinning Cognitive Developmental Delay of the *PURA* p.Phe233del Mutation Modelled by Artificial Intelligence and the Hybrid Quantum Mechanics–Molecular Mechanics Framework

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Supplementary Figures

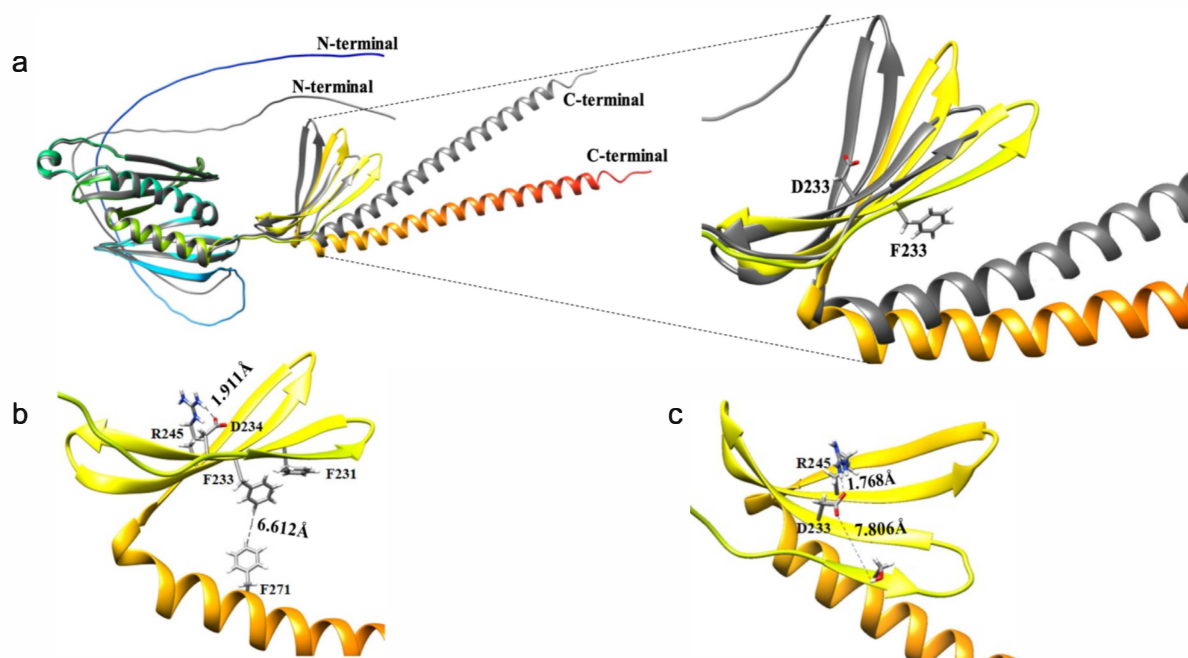


Figure S1. 3D analysis of PURAwt and PURA-Phe233del. **(a)** Needleman Wunsch global alignment for PURAwt (Rainbow) and PURA-Phe233del (Gray); **(b)** PURA wt protein region at 233; **(c)** PURA Phe233del protein region.

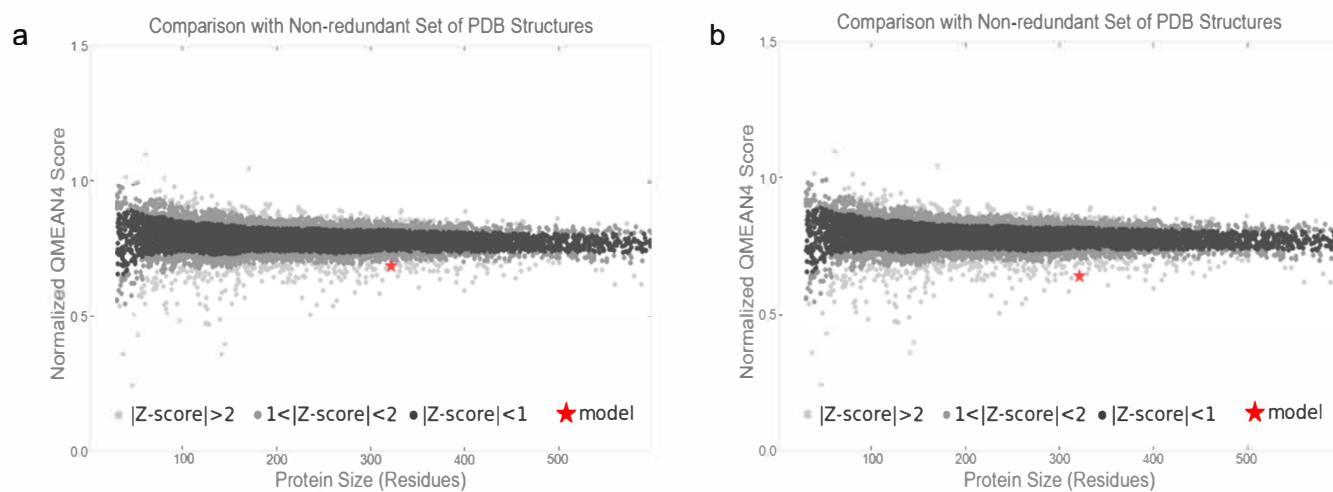


Figure S2. Z-score comparison diagram of experimentally solved structures for the (a) PURA wild type and (b) PURA Phe233del.

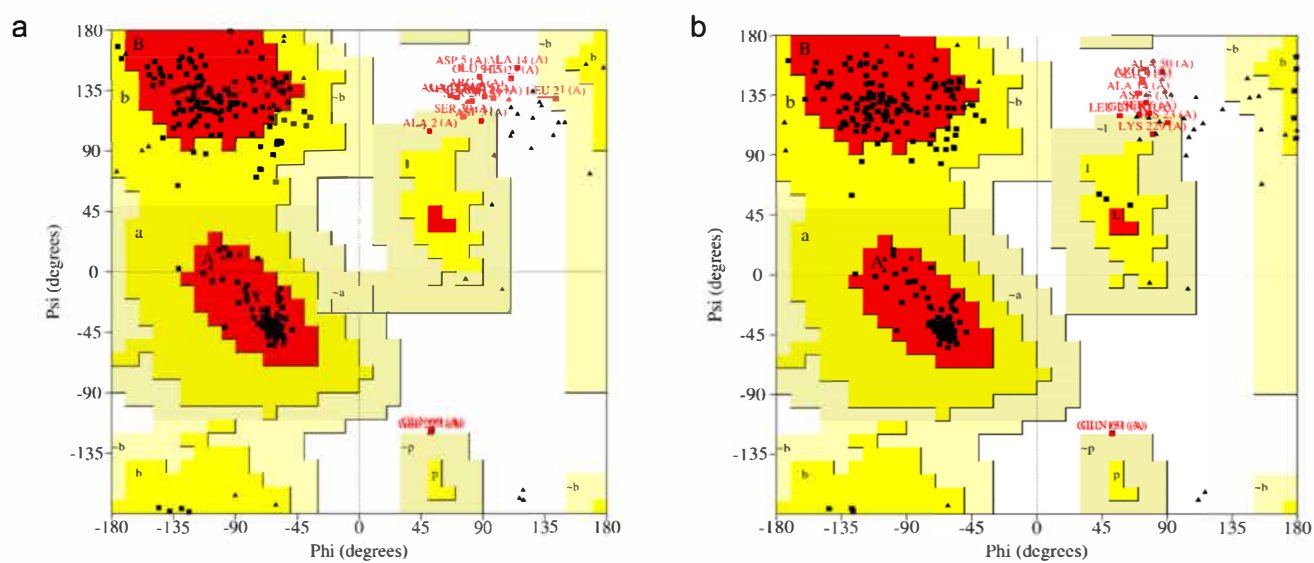


Figure S3. Ramachandran plots for the (a) PURAwt and (b) PURA-Phe233del using Procheck software.

Supplementary Tables

Table S1. NGS quality parameters.

Predictor DreamGenigs/ACMG Classification	Pathogenic
Gene	<i>PURA</i>
Chr	5
Coordinate	139494455
Ref	GCTT
Alt	G
c.Hgvs	c.697_699del
p.Hgvs	p.Phe233del
Protein Effect	INFRAME
Transcrito	NM_005859.5
Region	EXON
Zygosity/Father/Mother/Daughter	HOMZ_REF HOMZ_REF HETZ_ALT
Inheritance	AD
Coverage/Father/Mother/Daughter	165 145 162
Frequency/Alternate Allele/Father/Mother/Daughter	0 0 0.45679
Alt Count/Father/Mother/Daughter	0 0 74
ID dbSNP	rs786204835
Max Allele Freq	-
Max Allele Freq Origin	-
ACMG/Criteria	PS2+PM2+PP5
Phenotype OMIM/Additional, Information	Mental retardation, autosomal dominant 31 /
MIM Number	600473

HPO Terms	Delayed myelination / Absent speech / Feeding difficulties / Intellectual disability / Open mouth / Seizures / CNS hypomyelination / Autosomal dominant inheritance / Strabismus / Neonatal hypotonia / Myopathic facies / Respiratory insufficiency / Global developmental delay / Variable expressivity / Prominent forehead / Myoclonus / Broad-based gait / High palate / Telecanthus / Nystagmus
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Table S2. Energetic and stereochemical characterization of the models.

Model	Software	QMEAN6	Z-score	Errat	Ramachandran Plot
PURA wt	AlphaFold2	0.61	-2.41	93.89	Favoured region: 219 (84.6%)
					Allowed region: 23 (8.9%)
					Generously allowed region: 4 (1.5%)
					Disallowed region: 13 (5.0%)
PURA Phe293del	AlphaFold2	0.59	-3.60	89.66	Favoured region: 216 (83.7%)
					Allowed region: 30 (11.6%)
					Generously allowed region: 3 (1.2%)
					Disallowed region: 9 (3.5%)