

Supplementary Material

In Silico Structural Analysis Predicting the Pathogenicity of PLP1 Mutations in Multiple Sclerosis

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Table S1. Prediction of pathogenicity of amino acid substitutions and their molecular mechanisms of *PLP1* variants provided by MutPred2

Variant	MutPred2 Score	Molecular mechanism disrupted	Probability	P-value
L31P	0.973	Altered Transmembrane protein	0.33	6.8e-05
L31V	0.854	Altered Transmembrane protein	0.26	1.2e-03
L31R	0.972	Altered Transmembrane protein	0.33	4.9e-05
R137W	0.684	Loss of Helix	0.31	3.1e-03
H140Y	0.556	Altered Ordered interface	0.31	2.3e-03,
		Altered Transmembrane protein	0.11	0.04

Table S2. Analysis of missense mutations on protein stability, performed by SDM and DynaMut. DynaMut data (Table 3) are included for comparison.

DynaMut					SDM ¹	
Variant	$\Delta\Delta G$ (kcal/mol)	Outcome	$\Delta\Delta S_{VibENC_{CoM}}$ (kcal.mol ⁻¹ .K ⁻¹)	Outcome	$\Delta\Delta G$ (kcal/mol)	Outcome
L31V	-0.133	destabilizing	0.083	increase	-0.67	destabilizing
L31P	-1.011	destabilizing	0.413	increase	-2. 23	destabilizing
L31R	-0.256	destabilizing	0.231	increase	-0.29	destabilizing
R137W	-0.400	destabilizing	0.111	increase	0.25	stabilizing
H140Y	0.519	stabilizing	-0.063	decrease	0.65	stabilizing

¹Site Directed Mutator

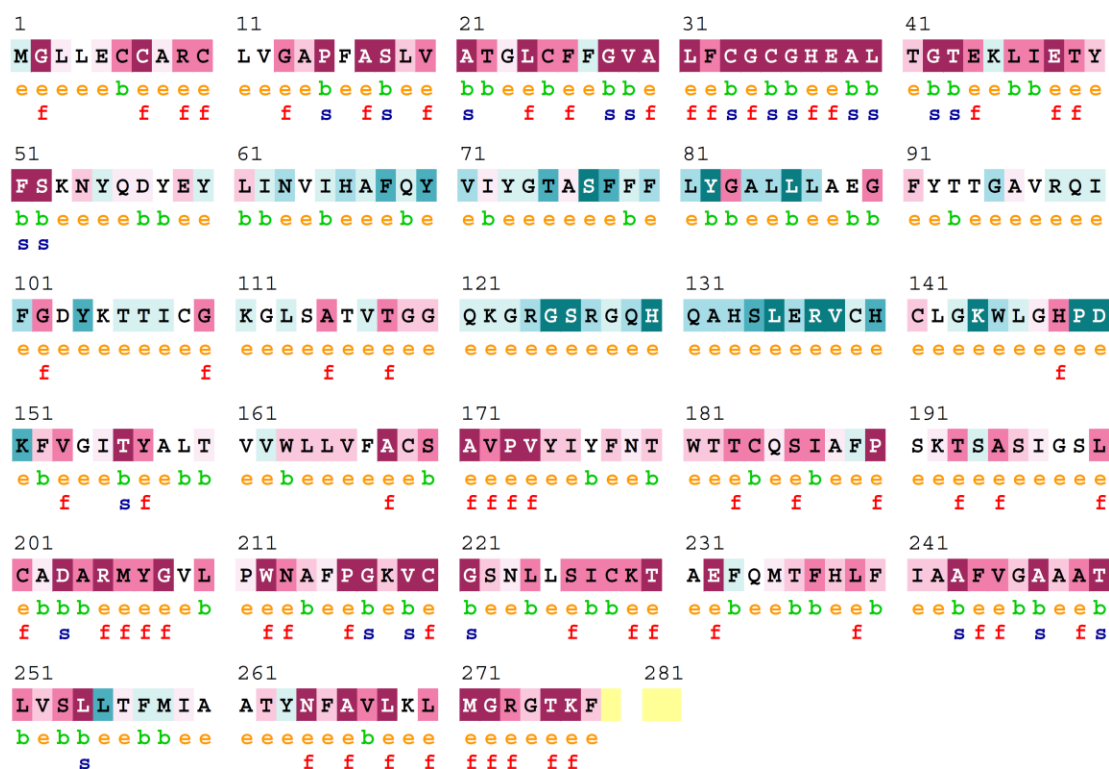


Figure S1. Prediction of evolutionary conserved amino acid residues of PLP1, performed by ConSurf server. Conservation score is represented as color coding bars.

e: an exposed residue according to the NACSES algorithm; b: a buried residue according to the NACSES algorithm; f: a predicted functional residue (highly conserved and exposed); s: a predicted structural residue (highly conserved and buried).

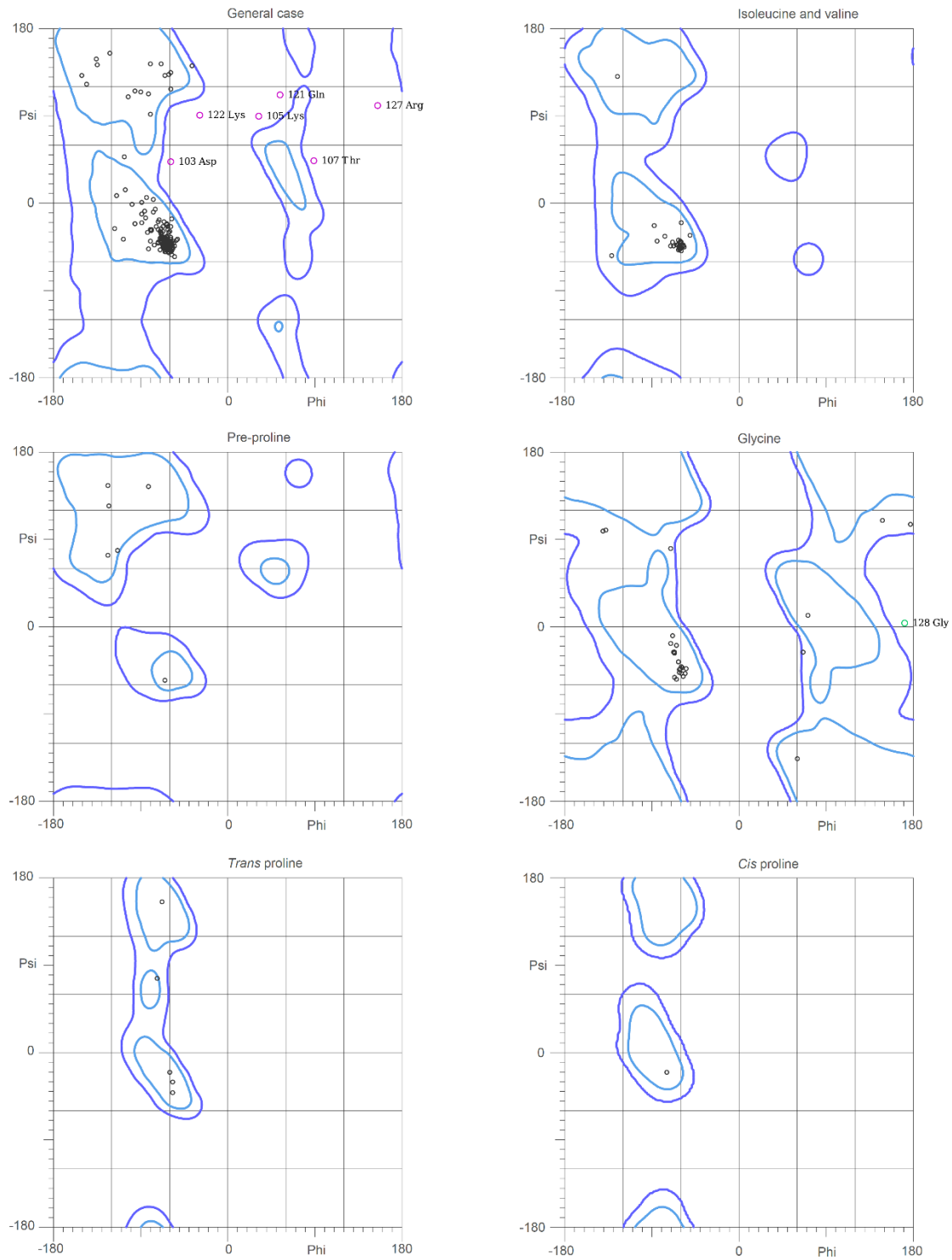


Figure S3. Ramachandran plots of PLP1 in the AlphaFold model.

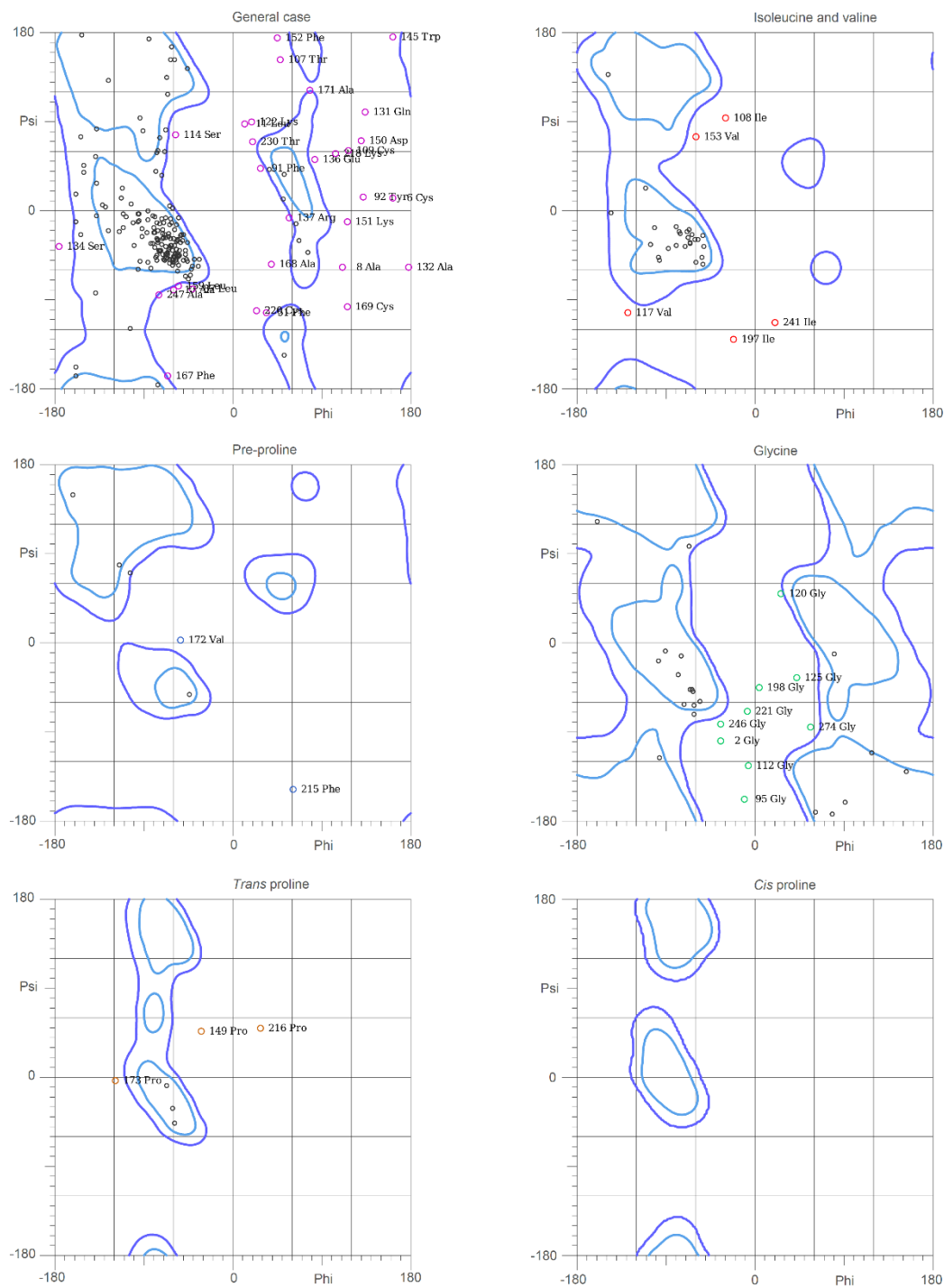


Figure S4. Ramachandran plots of PLP1 in the I-Tasser model.