



Supplementary Material

Structural predictive model of Presenilin-2 protein and analysis of structural effects of familial Alzheimer's disease mutations

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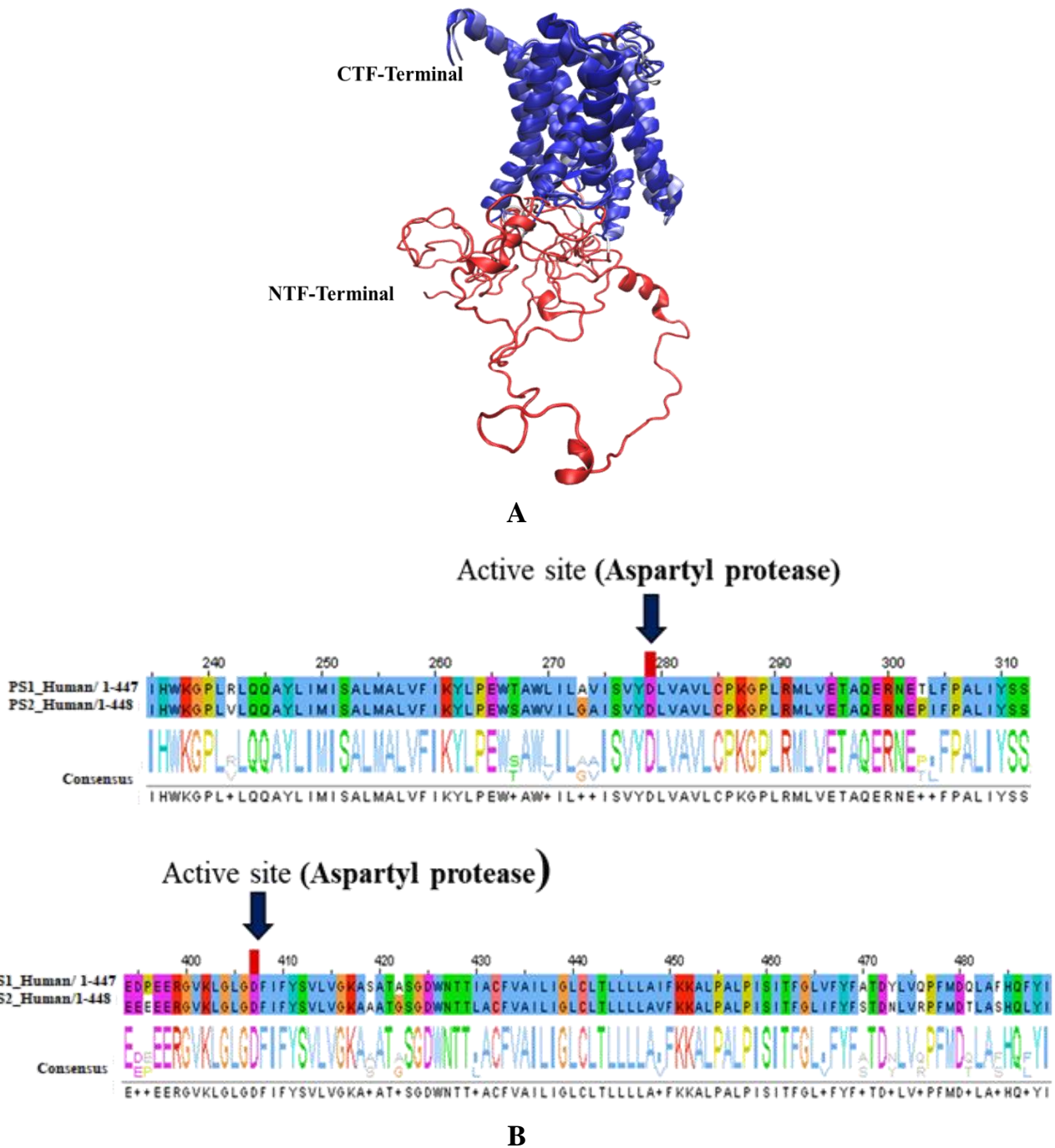
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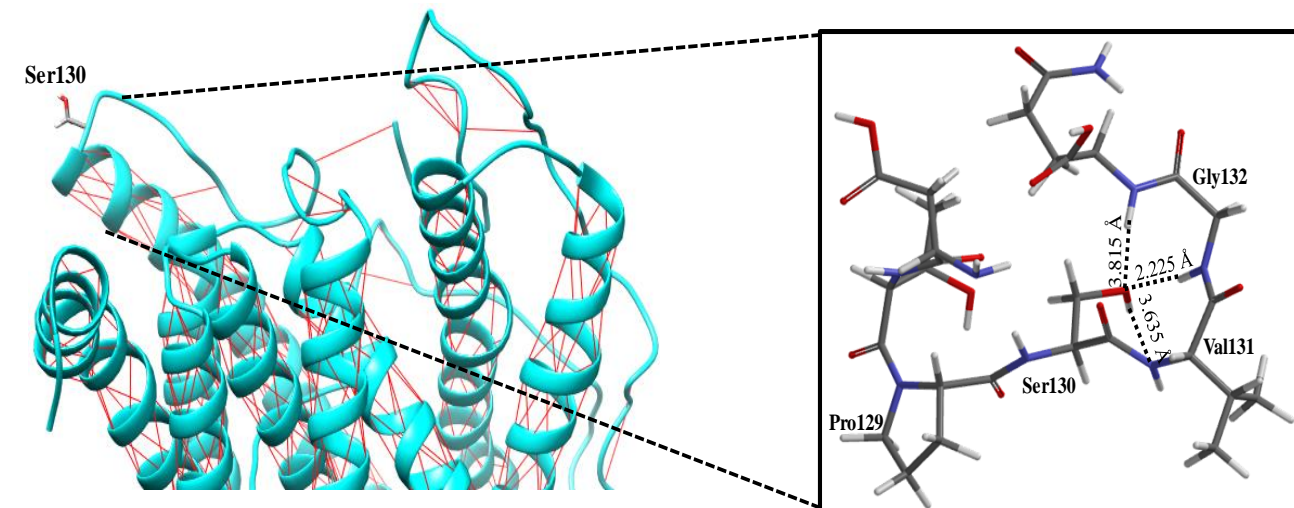
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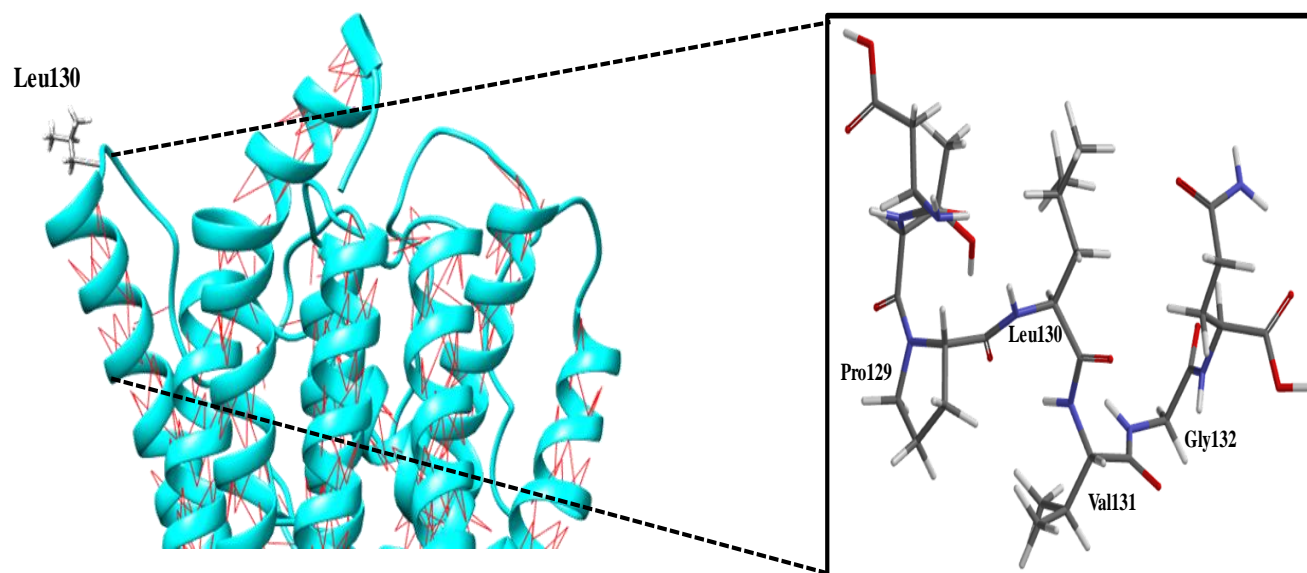


Sup. Figure 1. Alignment of PS1 protein with PS2: A) Quantitative multi-alignment of proteins at 3D level using color coding: values are considered in the alignment in (Red) with high standard deviation (RMSD), standard deviation in the range of [2.0-2.5] Å (White), highly conserved and low standard deviation regions (Blue); B) Active site alignment of the primary amino acid sequence of PS1 with PS2.

— Hydrogen bonds with constraints 2.7Å and 45°

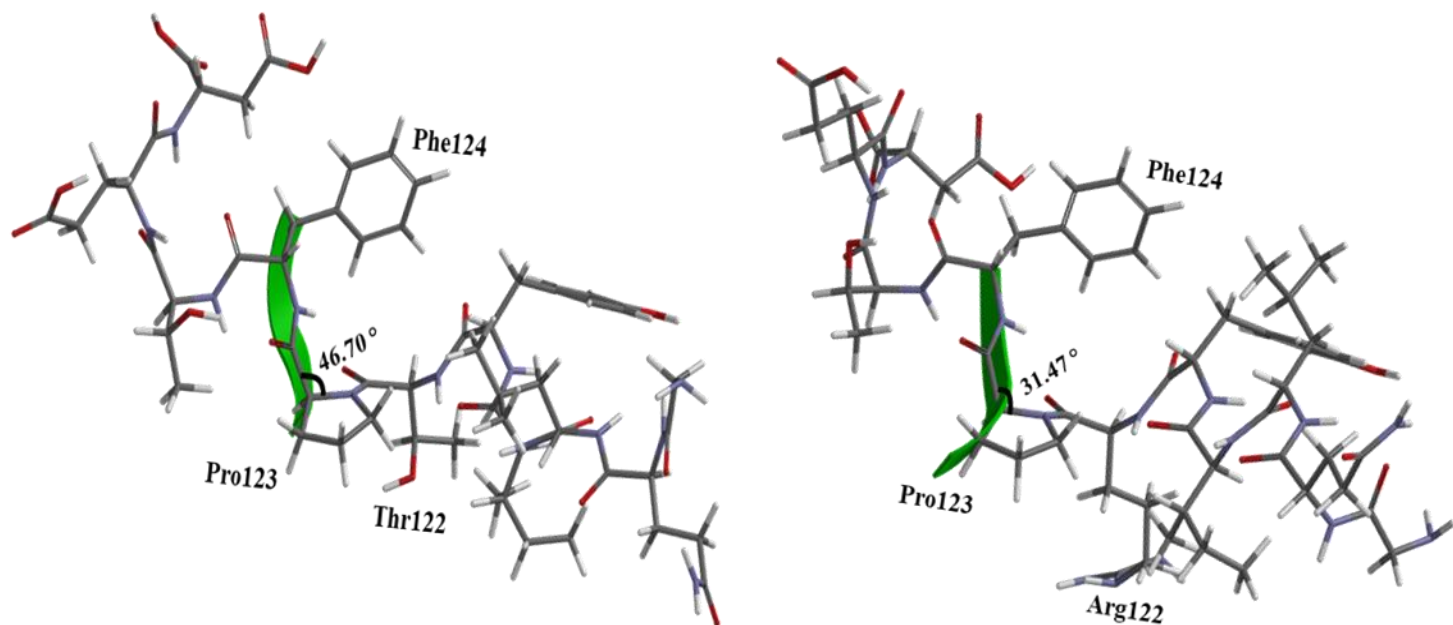


A



B

Sup. Figure 2. Topological and electronic structure change of the Ser130Leu mutation: A) Hydrogen bonds calculation (red) in ribbon representation of the wild-type PS2 protein; B) Hydrogen bonds calculation (red) in ribbon representation of the Ser130Leu PS2 protein mutation.



Sup. Figure 3. Angle change for PS2 wild type protein (Left) and Thr122Arg mutation (Right).

Table Sup.1

Canonical function TM2-TM3-TM5						
Protein PS2 (239)	Energy total (kJ/mol)	Amount of A β 40	Amount A β 42	Delta40	Delta42	Hidropathicity (239)
Wild type 1	328534,4815	1,00	1,00	0,00	0,00	2,644
M239I	331629,757	0,44	3,14	-0,56	2,14	2,933
M239V	330776,1052	0,31	3,30	-0,69	2,30	2,900

A

Moonlighting function TM1-TM2							
Protein PS2 (130)	Energy total (kJ/mol)	Amount of A β 40	Amount A β 42	Delta40	Delta42	Phosphorylation (130)	Hidropathicity (130)
Wild type 2	334625,8934	1,00	1,00	0,00	0,00	0,627	-1,589
S130L	335897,732	0,86	1,22	-0,14	0,22	0	-1,078

B

Moonlighting function TM1-TM2						
Protein PS2	Energy total (kJ/mol)	Amount of A β 40	Amount A β 42	Phosphorylation (122)	Phosphorylation (125)	Hidropathicity (122)
Wild type	333370,1626	N/D	N/D	0,513	0,431	-0,022
T122R	318579,7143	N/D	N/D	0	0,712	-0,444

C

Table Sup.1 Energetic values calculated in the system with PS2 in the γ -secretase enzyme: A) Energy average of canonical PS2 function and M239I, M239V mutations; B) Energy average and characterization for the wild type and mutated moonlighting function Ser130Leu; C) Energy average and characterization for the moonlighting wild type and mutated Thr122Arg function.