

Supplementary Materials

Intrinsic disorder in proteins with pathogenic repeat expansions

April L. Darling^{1,2,*} and Vladimir N. Uversky^{1,3,*}

¹*Department of Molecular Medicine and USF Health Byrd Alzheimer's Research Institute,
Morsani College of Medicine, University of South Florida, Tampa, FL 33612, USA*

²*James A. Haley Veteran's Hospital, Tampa, FL, 33612, USA*

³*Institute for Biological Instrumentation of the Russian Academy of Sciences, Pushchino,
Moscow region, 142290, Russia*

*Corresponding authors: A.L.D., Tel: 1-813-396-9249; E-mail: aldarlin@mail.usf.edu; V.N.U.,
Tel: 1-813-974-5816; E-mail: vuffersky@health.usf.edu

Figure S1. Intrinsic disorder propensity and some important disorder-related functional information generated for human proteins encoded by genes with nucleotide expansions by the D²P² database (<http://d2p2.pro/>) (Oates et al., 2013). Here, the outputs of several disorder predictors are shown by differently colored bars, whereas the blue-green-and-white bar in the middle of the plot shows the predicted disorder agreement between nine predictors, with blue and green parts corresponding to disordered regions by consensus. Yellow bar shows the location of the predicted disorder-based binding sites (molecular recognition features, MoRFs), whereas colored circles at the bottom of the plot show location of various PTMs.

References

Oates, M.E., Romero, P., Ishida, T., Ghalwash, M., Mizianty, M.J., Xue, B., Dosztanyi, Z., Uversky, V.N., Obradovic, Z., Kurgan, L., Dunker, A.K., Gough, J., 2013. D(2)P(2): database of disordered protein predictions. *Nucleic Acids Res* 41, D508-516.

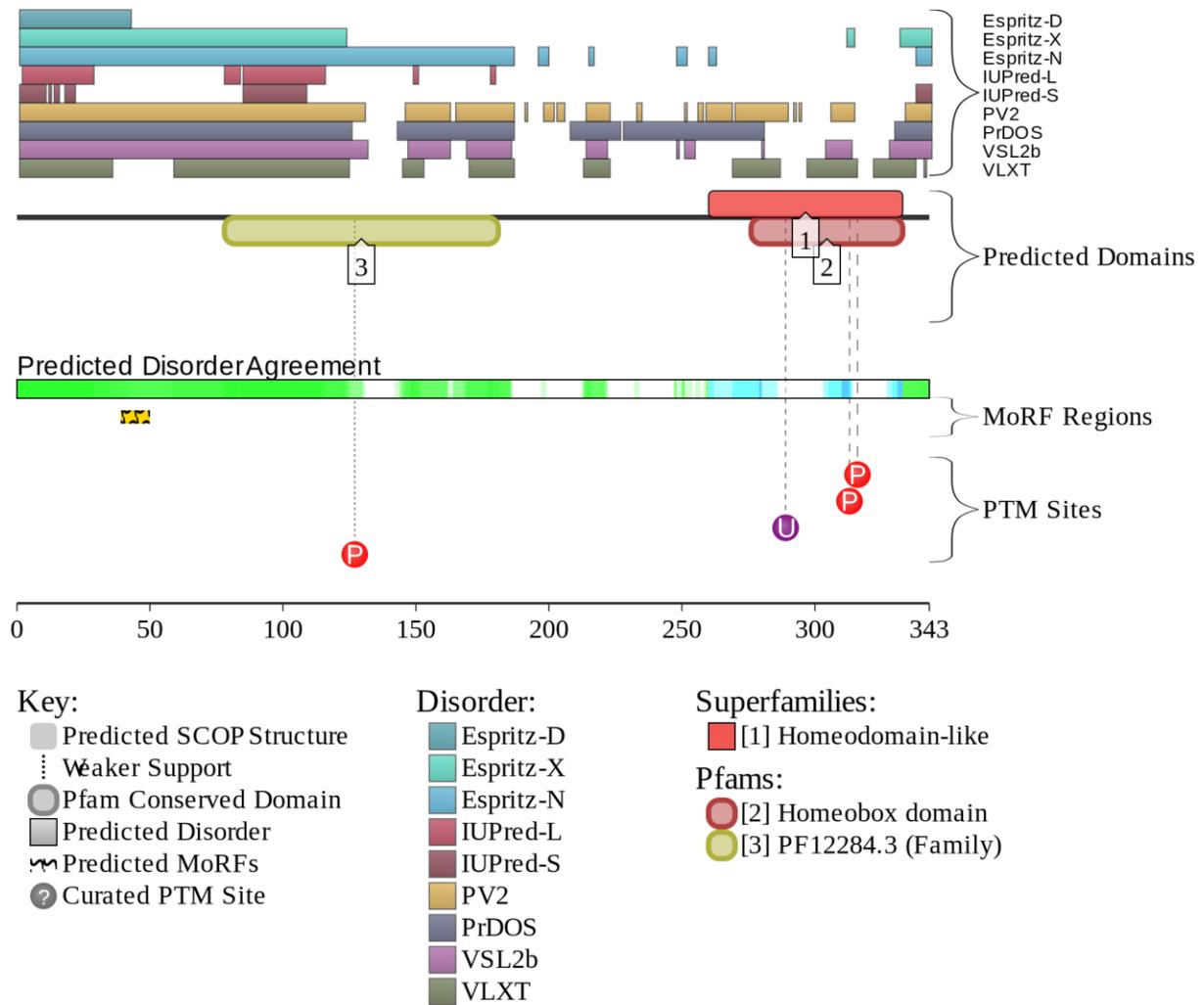


Figure S1A. D²P² output for homeobox protein HOXD13 (UniProt ID: P35453)

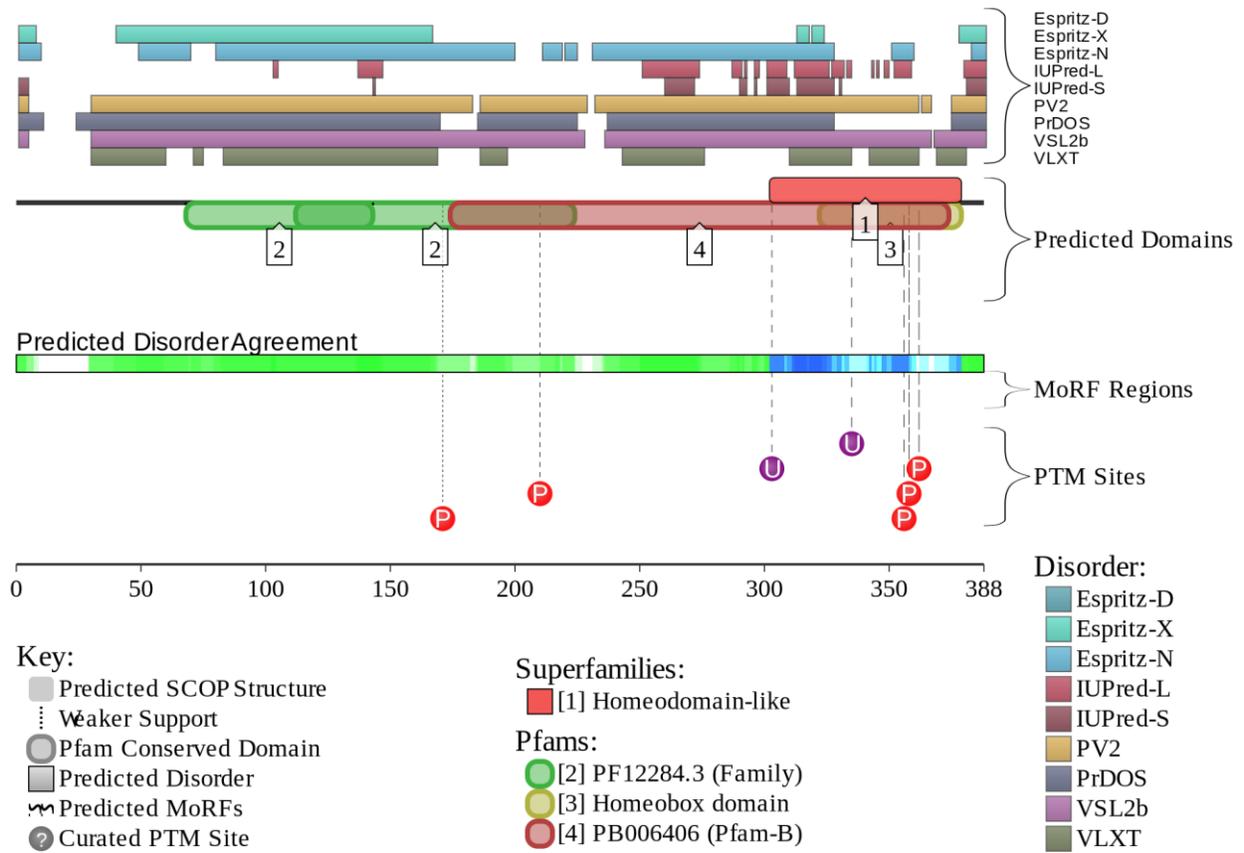


Figure S1B. D²P² output for the homeobox protein HOXA13 (UniProt ID: P31271)

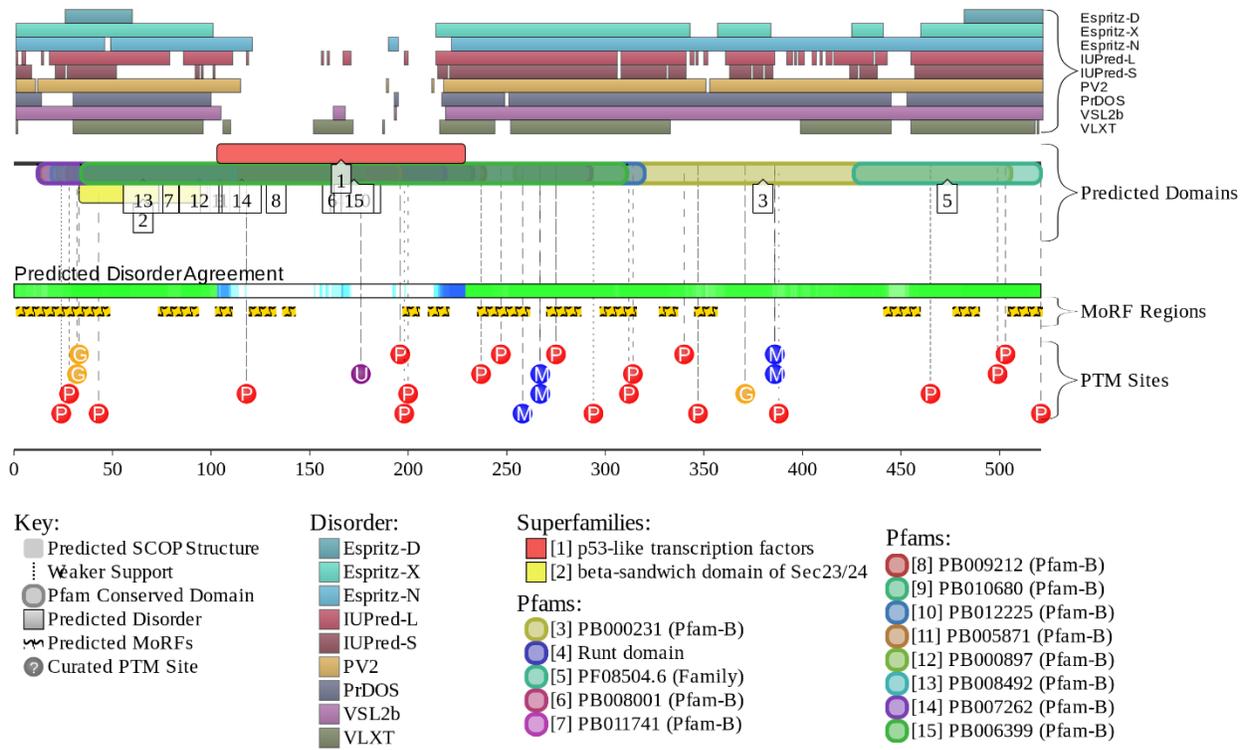


Figure S1C. D²P² output for runt-related transcription factor 2, RUNX2 (UniProt ID: Q13950)



Figure S1D. D²P² output for zinc finger protein ZIC2 (UniProt ID: O95409)

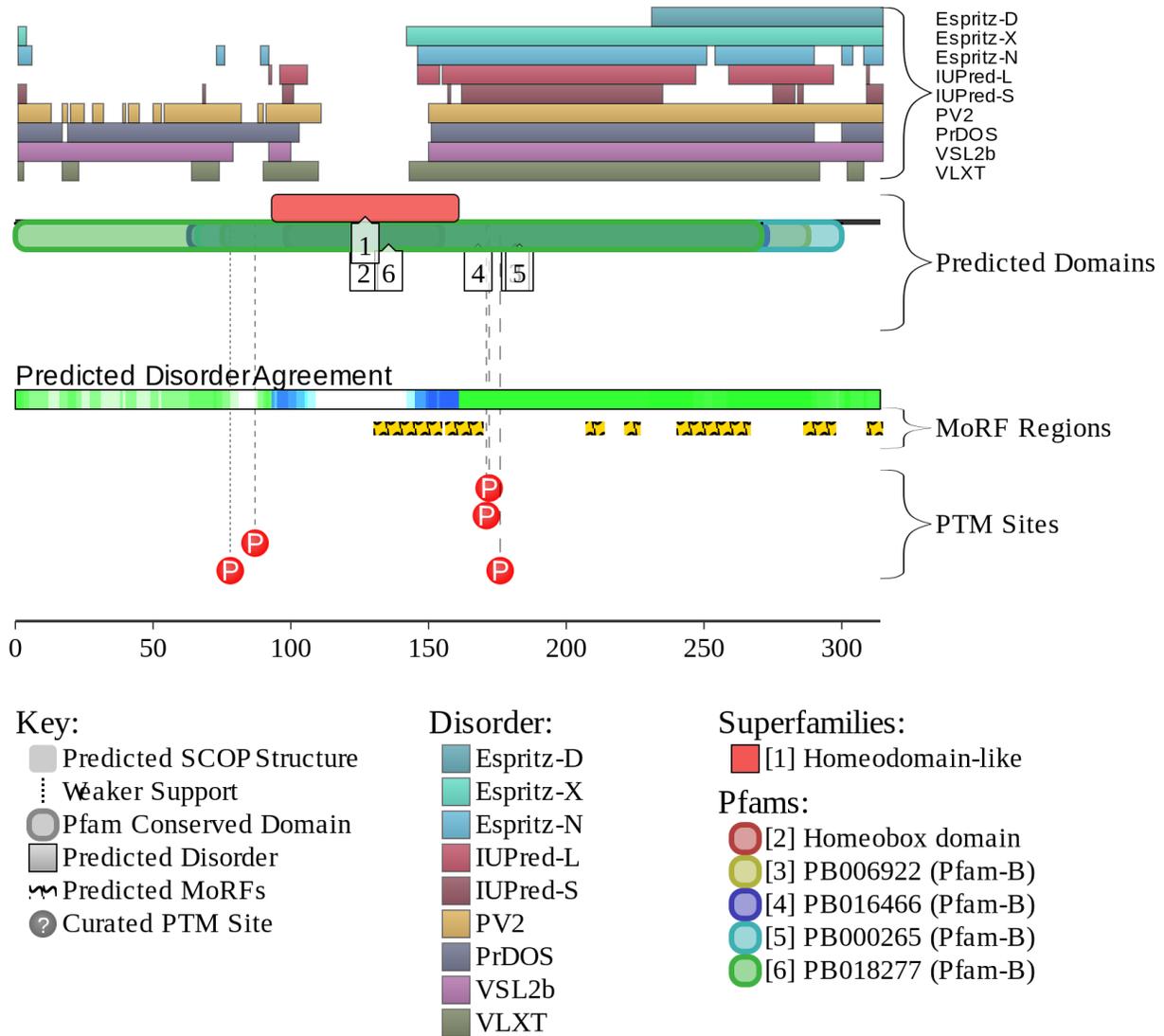


Figure S1E. D²P² output for paired mesoderm homeobox protein 2B (PHOX2B homeodomain protein, UniProt ID: Q99453)

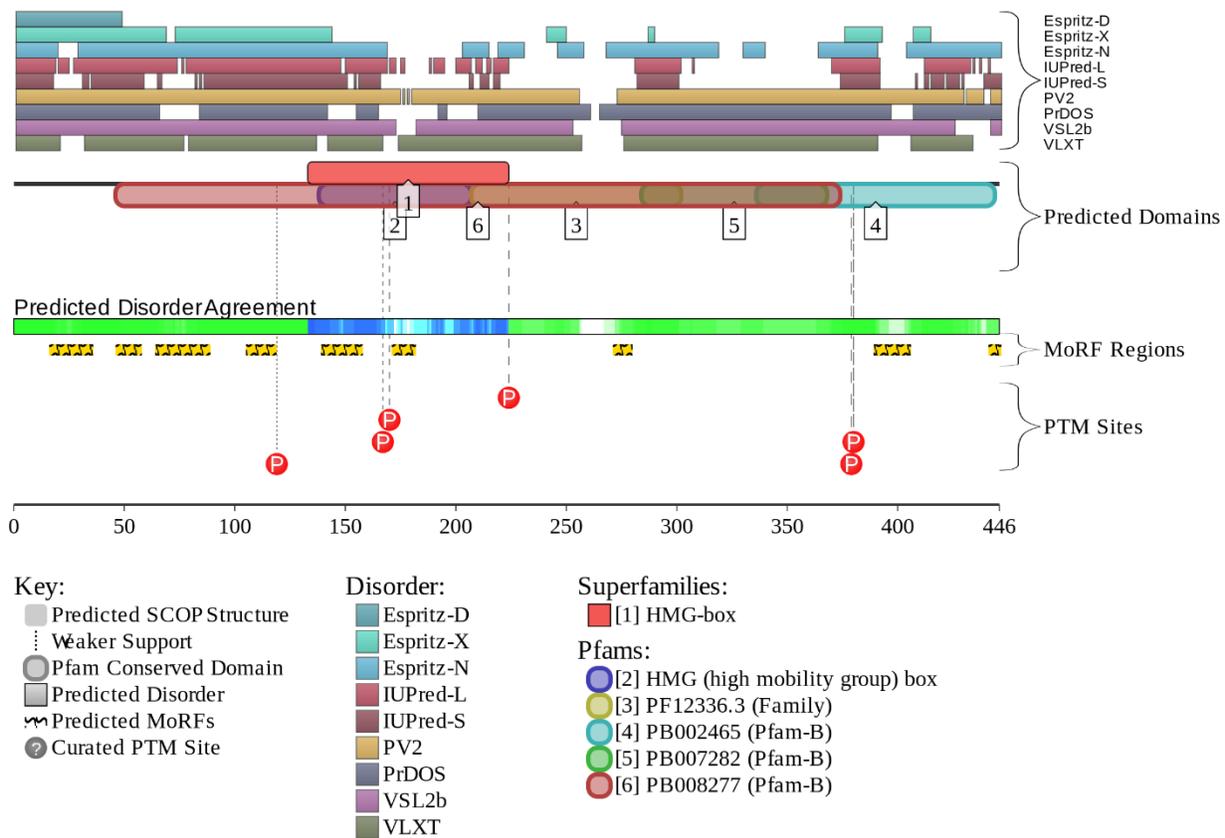


Figure S1F. D²P² output for transcription factor SOX3 (Sex-determining region Y-box3, UniProt ID: P41225)

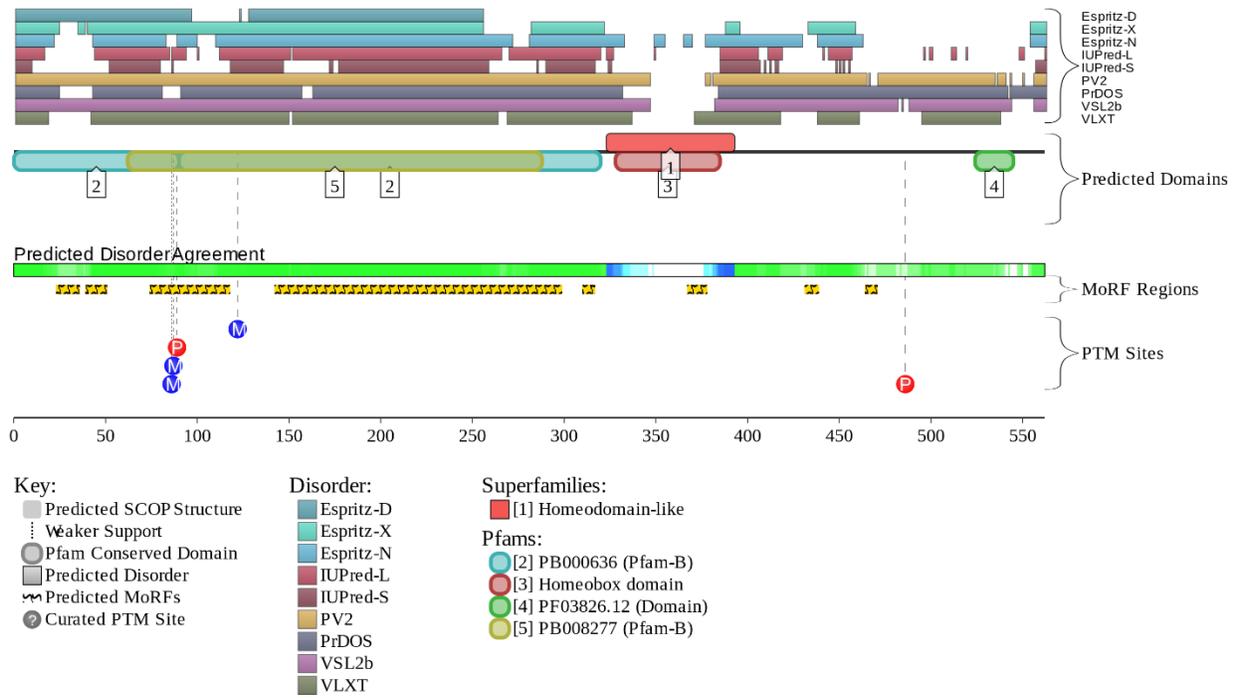


Figure S1G. D²P² output for homeobox protein ARX (Aristaless-related homeobox, UniProt ID: Q96QS3)

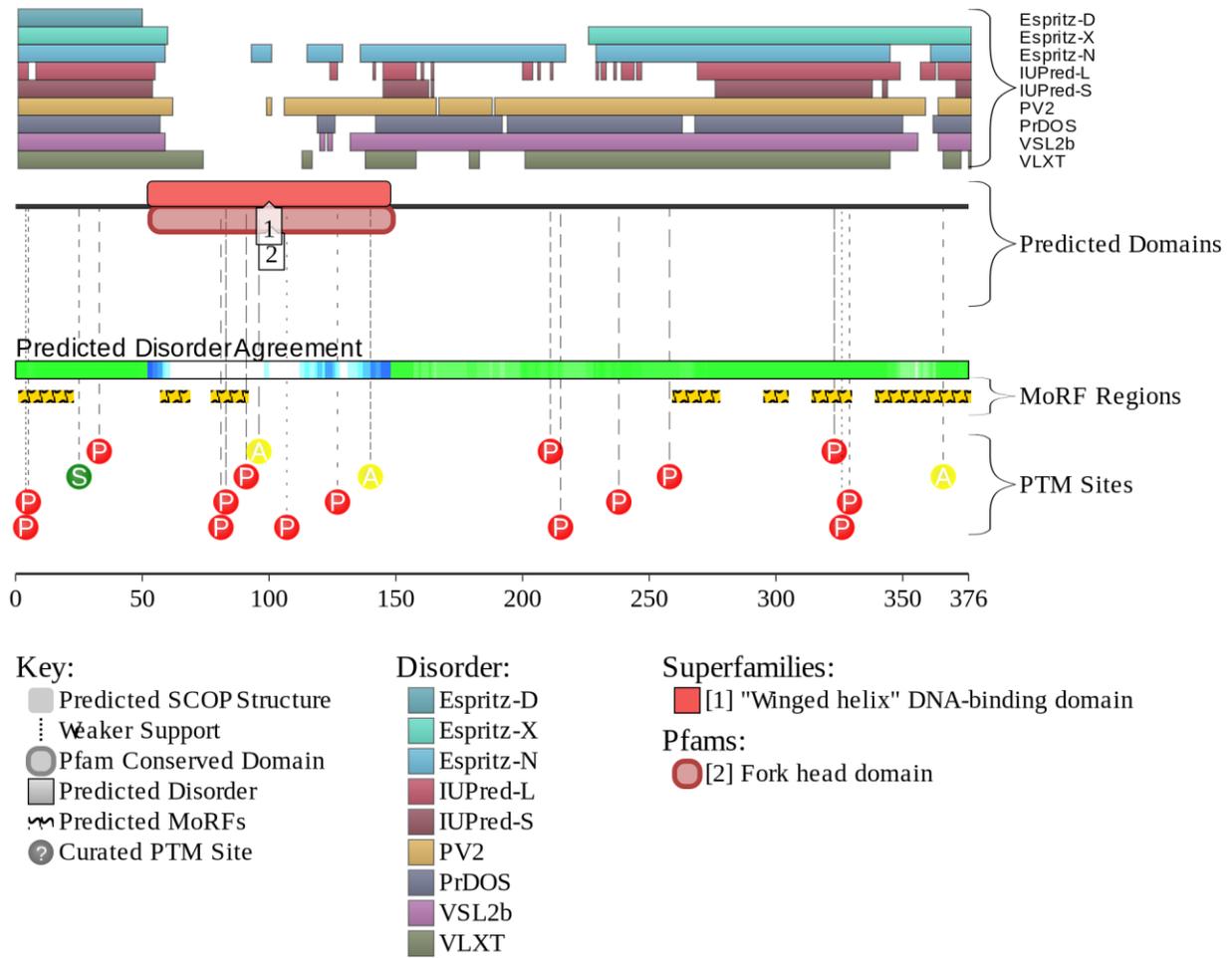


Figure S1H. D²P² output for human forkhead box protein L2 (FOXL2, UniProt ID: P58012)

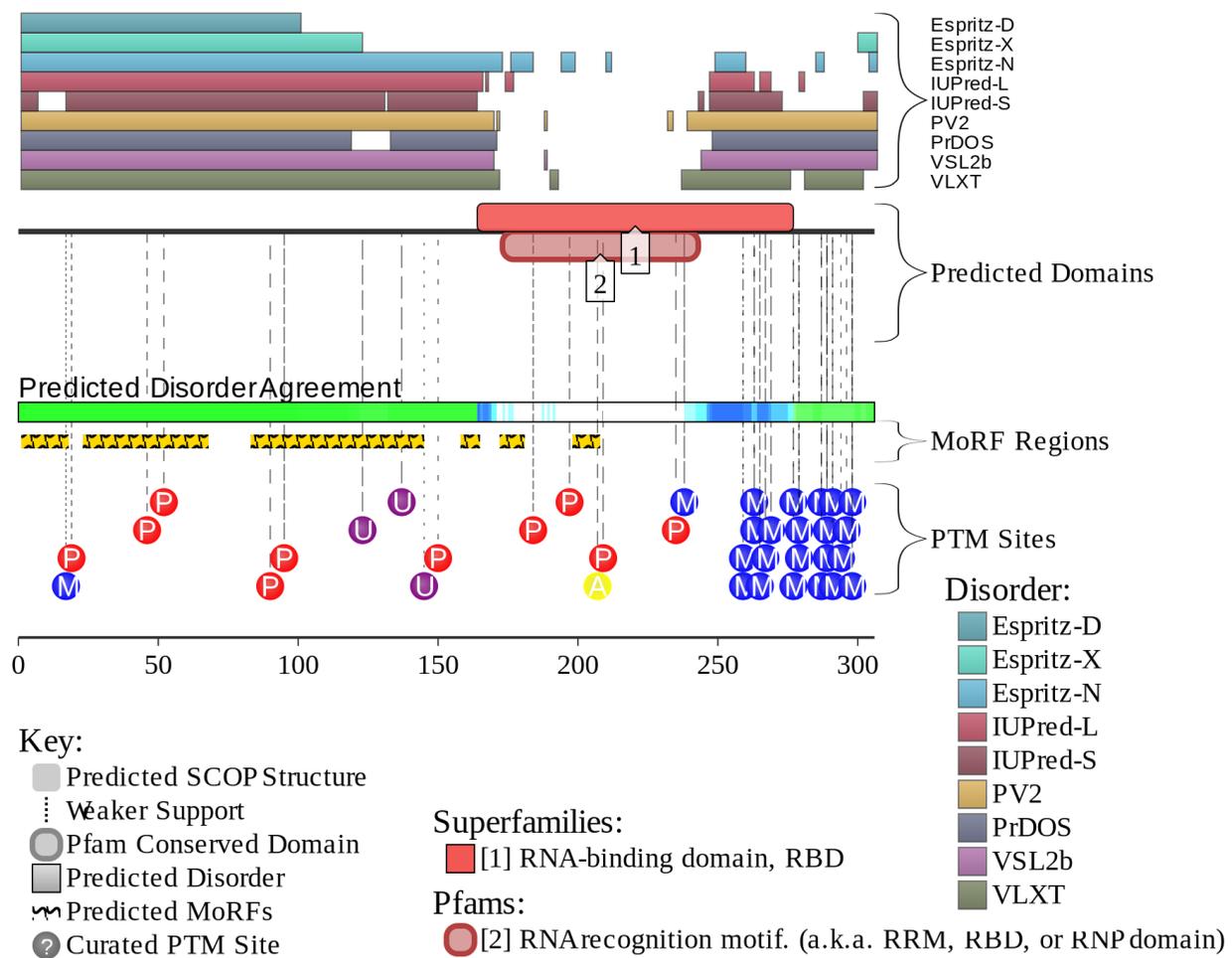


Figure S11. D²P² output for polyadenylate-binding protein 2/polyadenine-binding protein nuclear-1 (PABP2/PABPN1, UniProt ID: Q86U42)

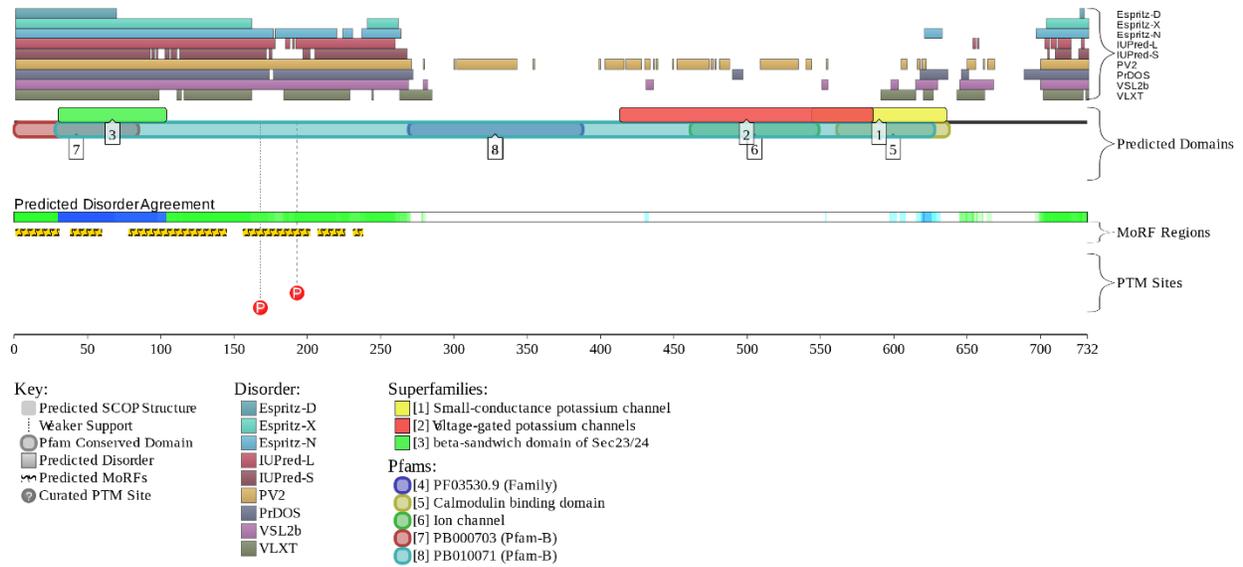


Figure S1J. D²P² output for human small conductance calcium-activated potassium channel protein 3 (SK3, UniProt ID: Q9UGI6) is not available. Presented is the D²P² output for mouse homologue (UniProt ID: P58391).

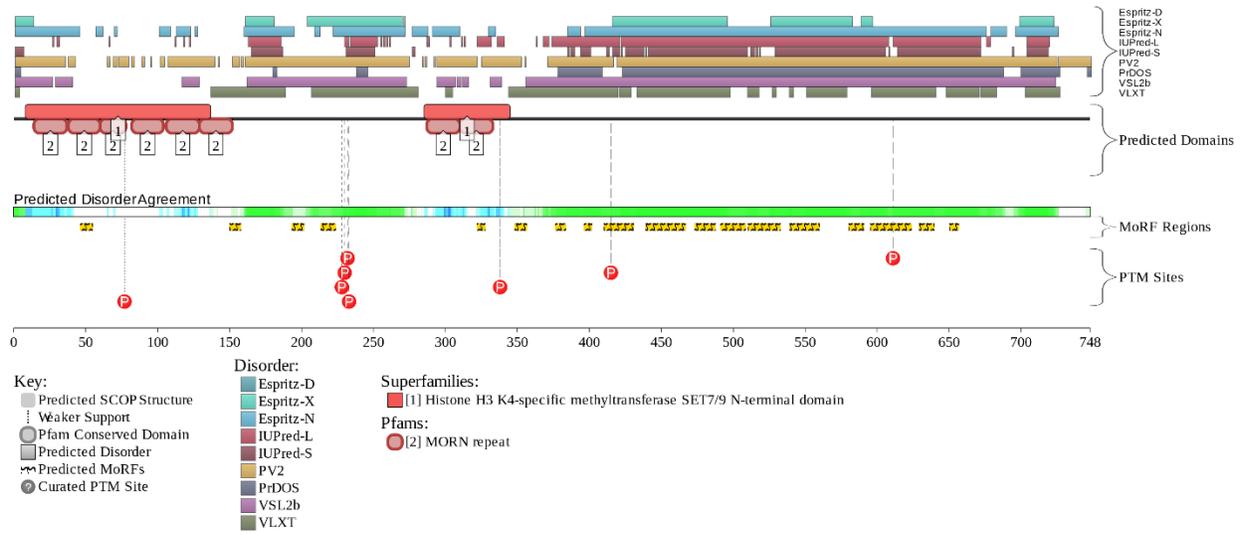


Figure S1K. D²P² output for human junctophilin-3 (JP-3, UniProt ID: Q8WXH2)



Figure S1L. D²P² output for human huntingtin (UniProt ID: P42858)

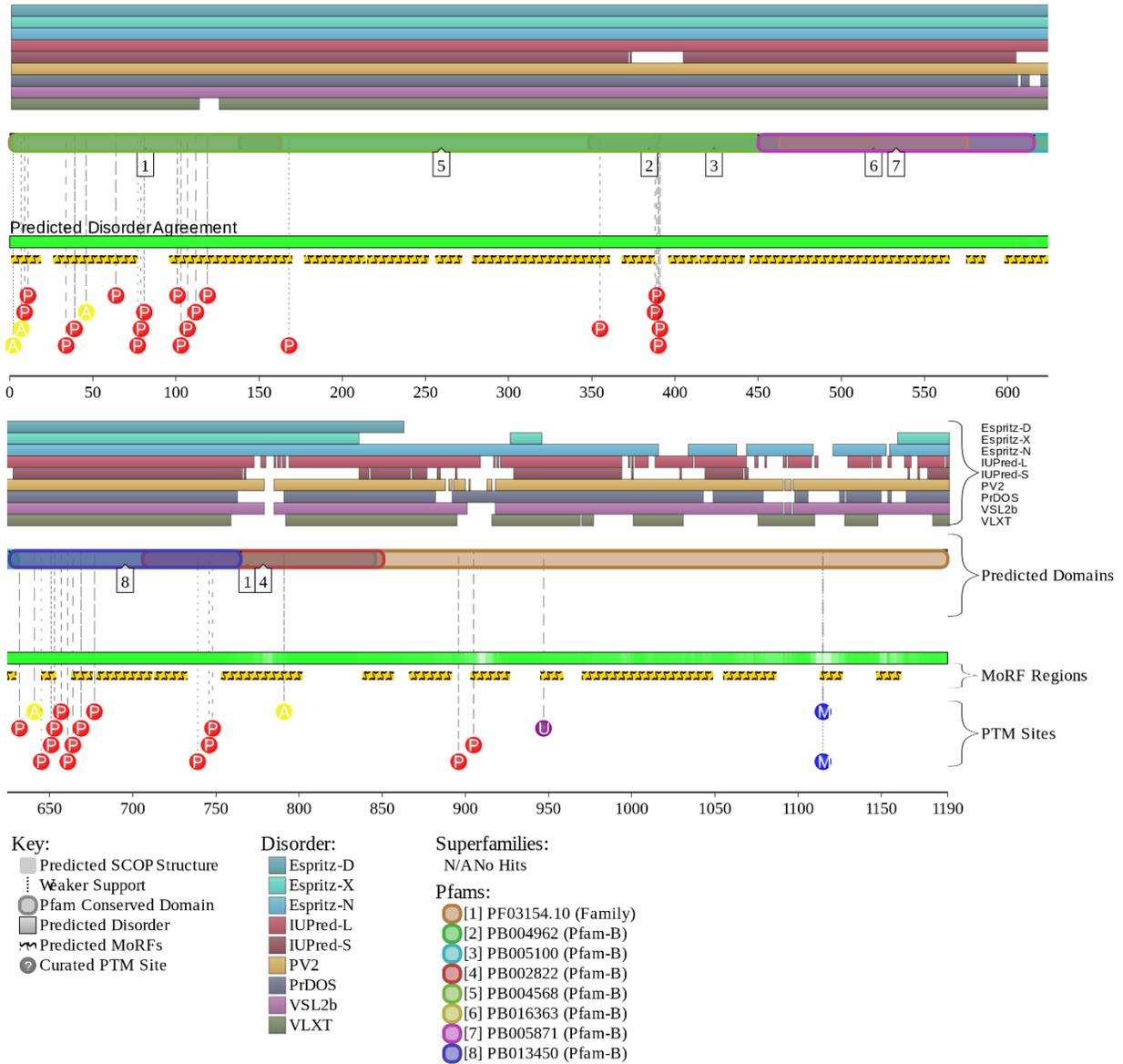
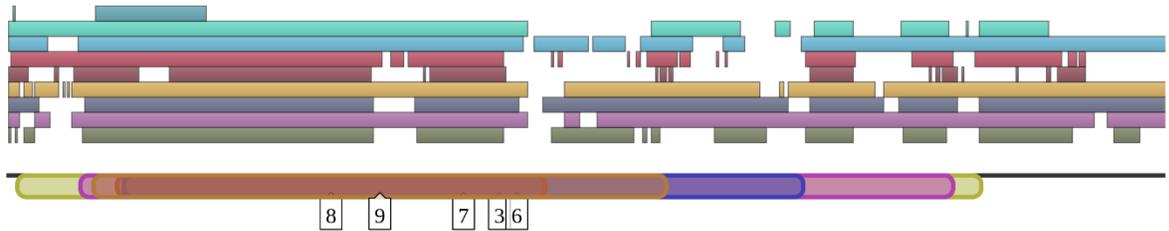
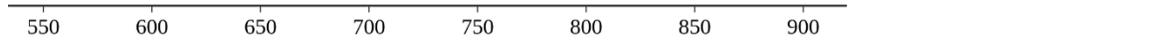
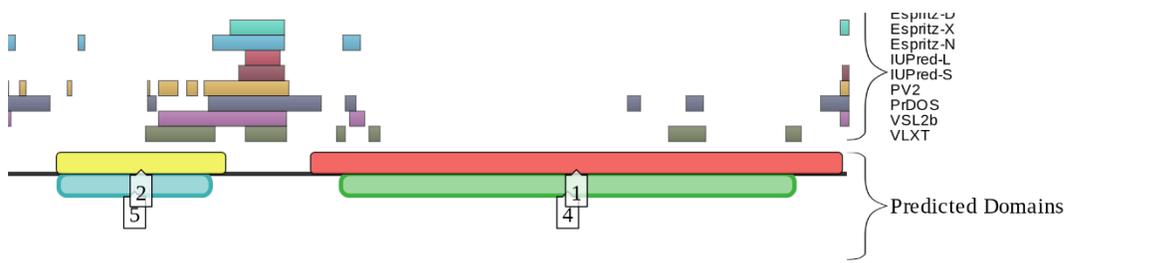


Figure S1M. D²P² output for atrophin-1 (UniProt ID: P54259)



Predicted Disorder Agreement



- | | | |
|---|--|--|
| <p>Key:</p> <ul style="list-style-type: none"> ■ Predicted SCOP Structure ⋮ Weaker Support ○ Pfam Conserved Domain ■ Predicted Disorder ⋈ Predicted MoRFs ⊙ Curated PTM Site | <p>Disorder:</p> <ul style="list-style-type: none"> ■ Espritz-D ■ Espritz-X ■ Espritz-N ■ IUPred-L ■ IUPred-S ■ PV2 ■ PrDOS ■ VSL2b ■ VLXT | <p>Superfamilies:</p> <ul style="list-style-type: none"> ■ [1] Nuclear receptor ligand-binding domain ■ [2] Glucocorticoid receptor-like (DNA-binding domain) <p>Pfams:</p> <ul style="list-style-type: none"> ○ [3] PF02166.11 (Family) ○ [4] Ligand-binding domain of nuclear hormone receptor ○ [5] Zinc finger, C4 type (two domains) ○ [6] PB010071 (Pfam-B) ○ [7] PB008983 (Pfam-B) ○ [8] PB008001 (Pfam-B) ○ [9] PB010624 (Pfam-B) |
|---|--|--|

Figure S1N. D²P² output for human androgen receptor (AR, UniProt ID: P10275)

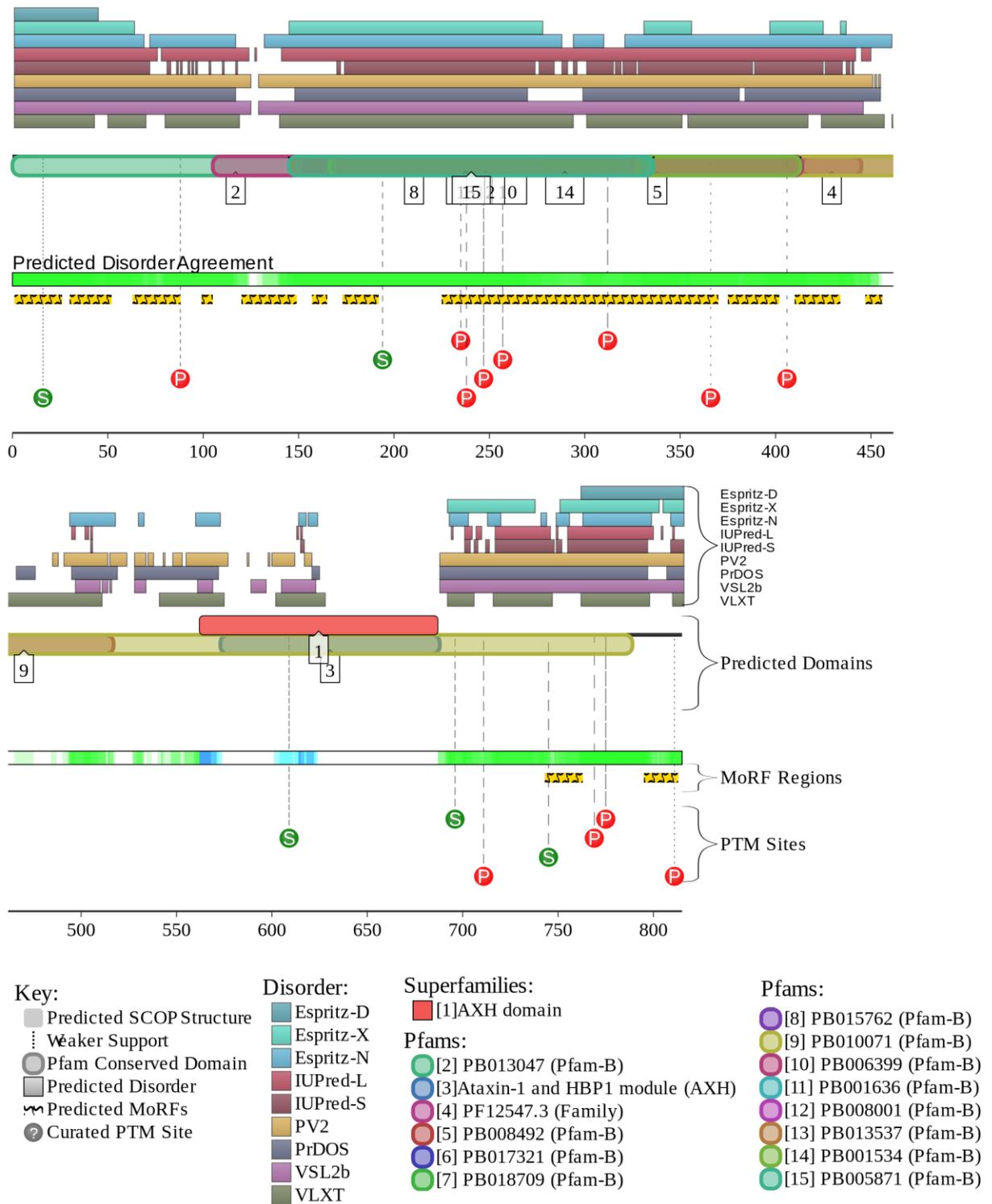


Figure S10. D²P² output for ataxin-1 (UniProt ID: P54253)

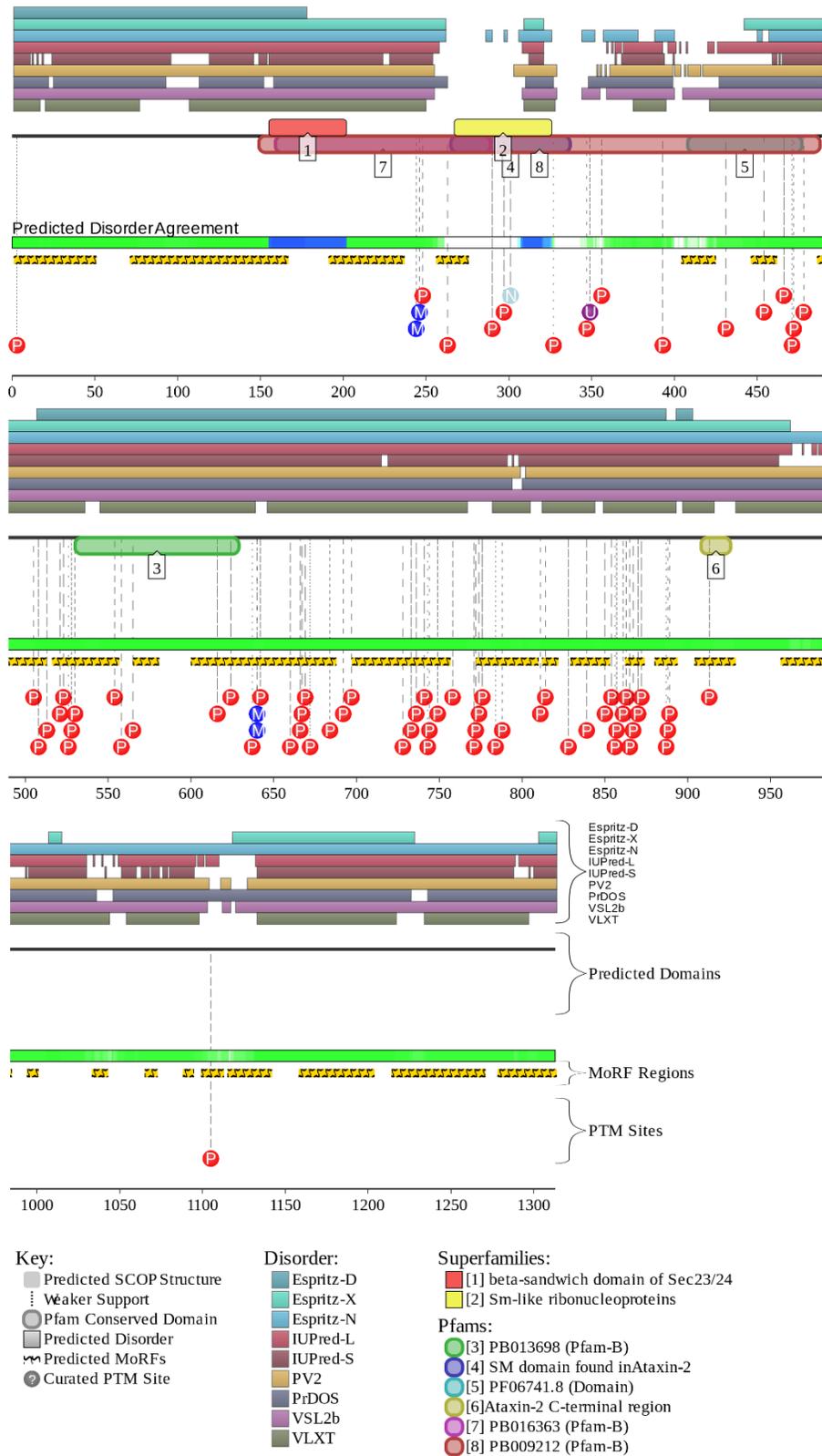


Figure S1P. D²P² output for human ataxin-2 (UniProt ID: Q99700)

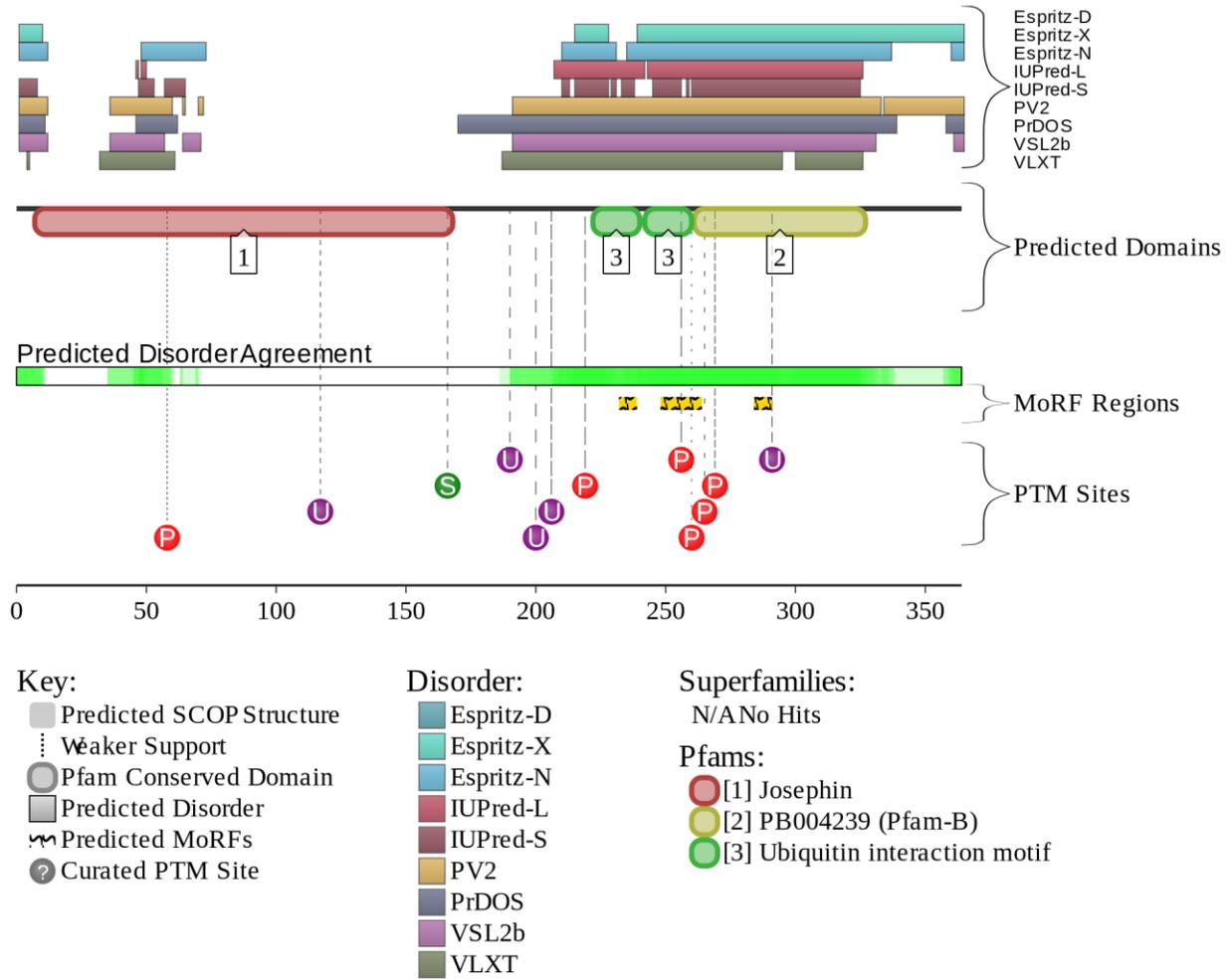


Figure S1Q. D²P² output for human ataxin-3 (UniProt ID: P54252)

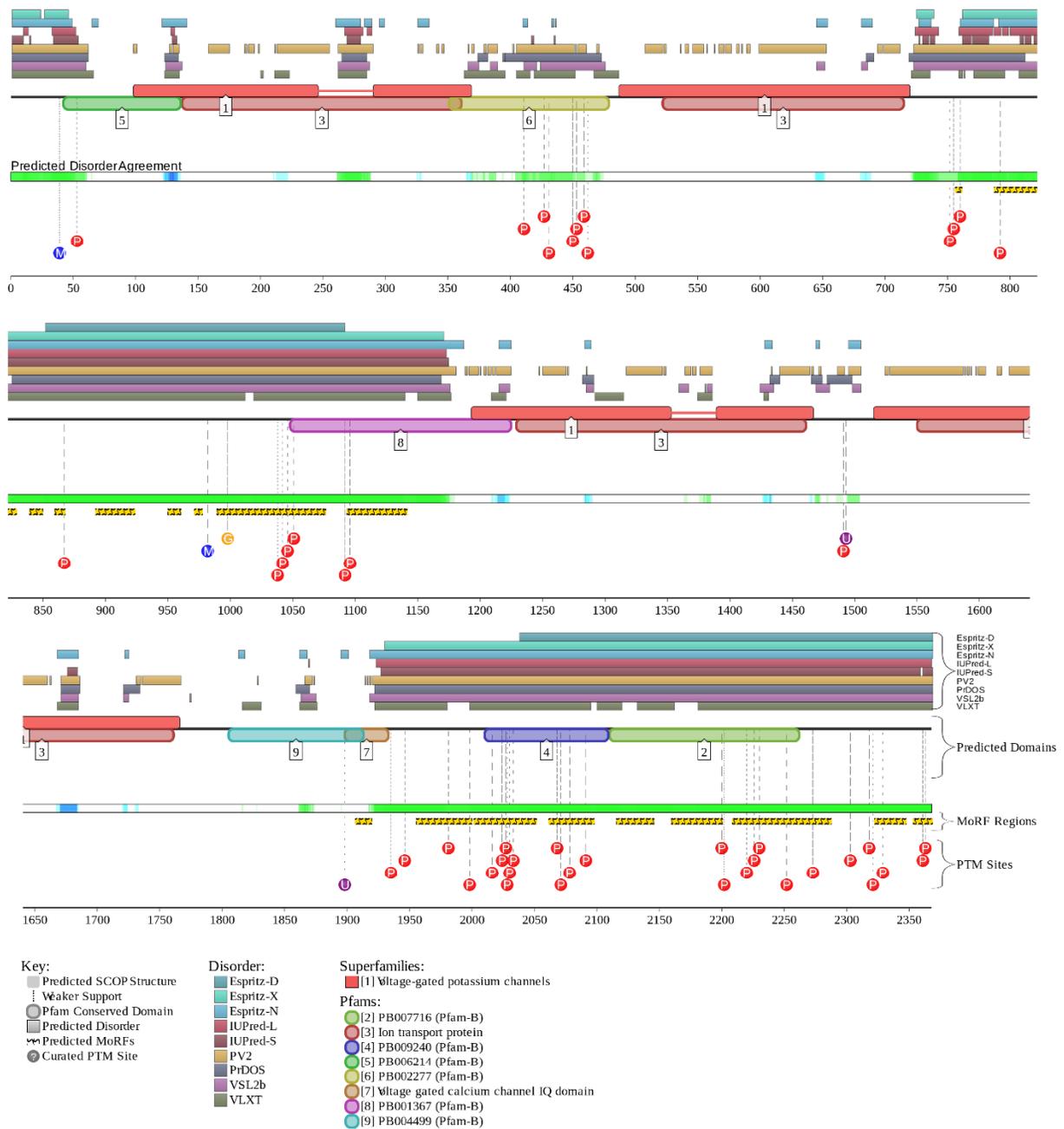


Figure S1R. D²P² output for voltage-dependent P/Q-type calcium channel subunit α 1A (CACNA1A, UniProt ID: O00555) is not available. Presented here is the D²P² output for mouse CACNA1A (UniProt ID: P97445).

ENSP00000420234, ENSP00000295900

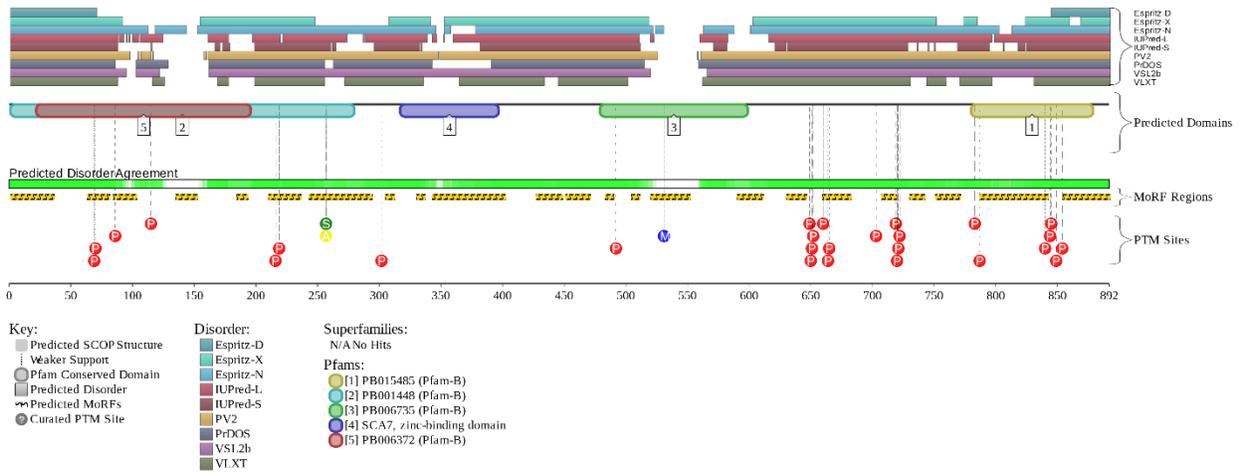


Figure S1S. D²P² output for ataxin-7 (UniProt ID: O15265)

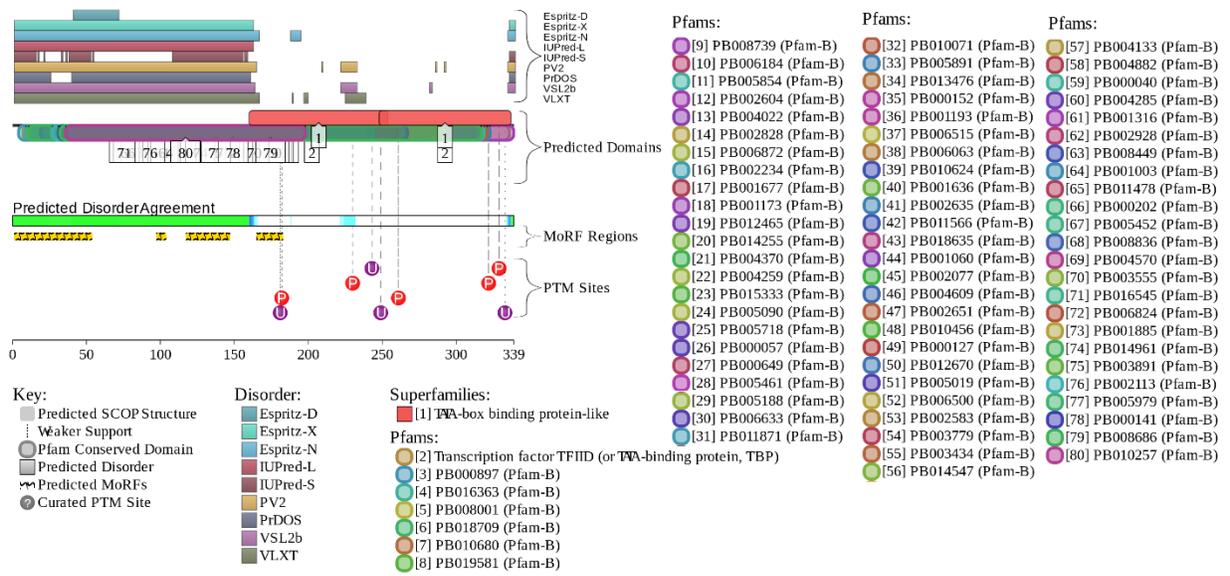


Figure S1T. D²P² output for TATA-box-binding protein (TBP, UniProt ID: P20226)

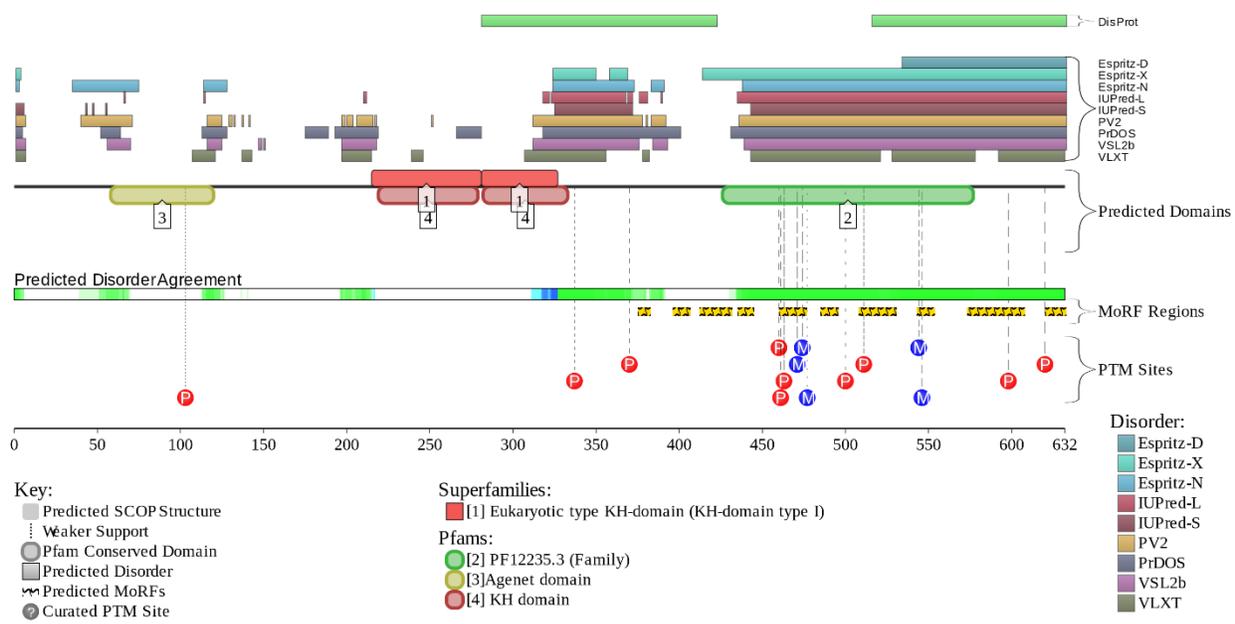


Figure S1U. D²P² output for synaptic functional regulator FMR1 (UniProt ID: Q06787)

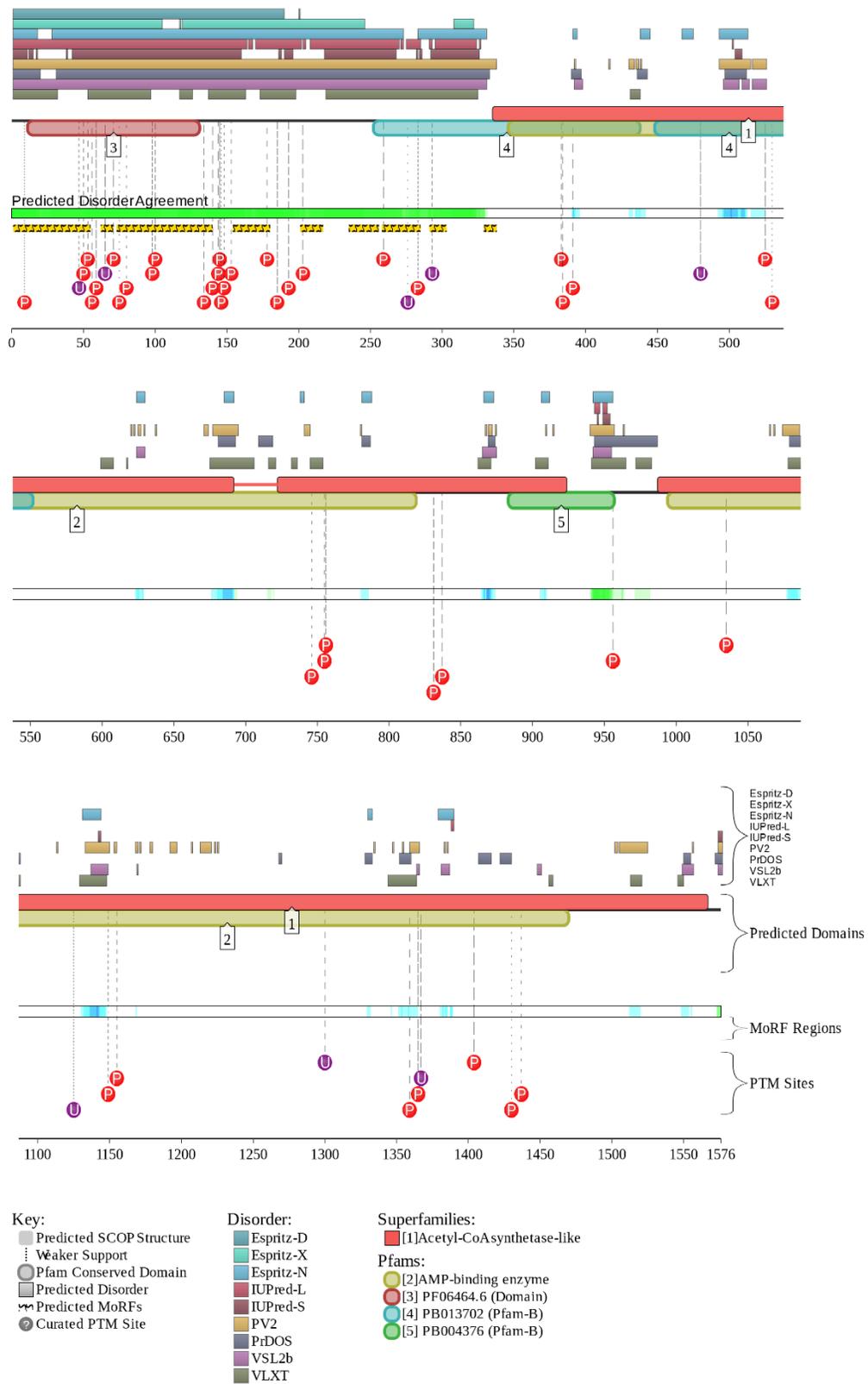


Figure S1V. D²P² output for disco-interacting protein 2 homolog B (UniProt ID: Q9P265)

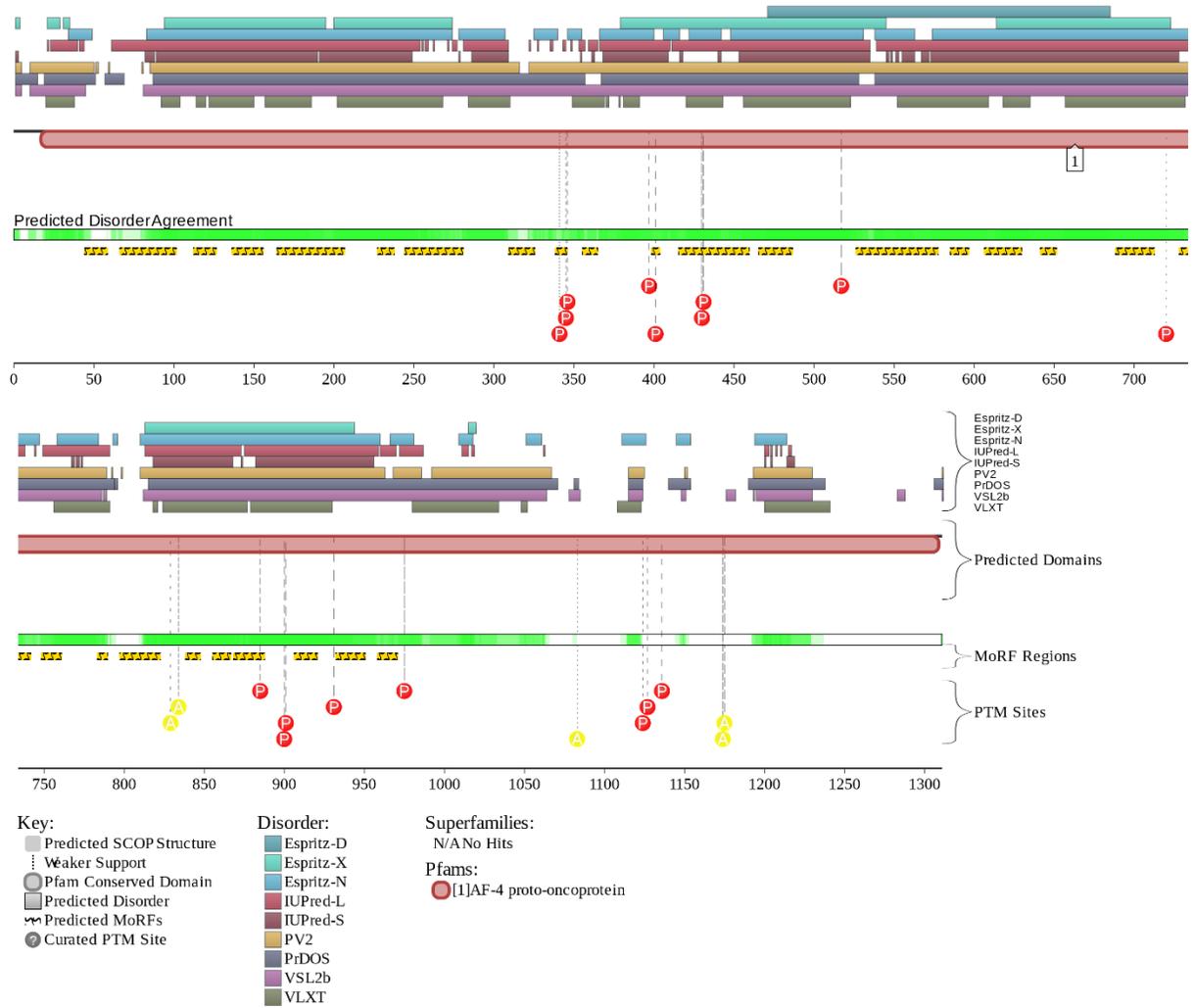


Figure S1W. D²P² output for AF4/FMR2 family member 2 (UniProt ID: P51816)

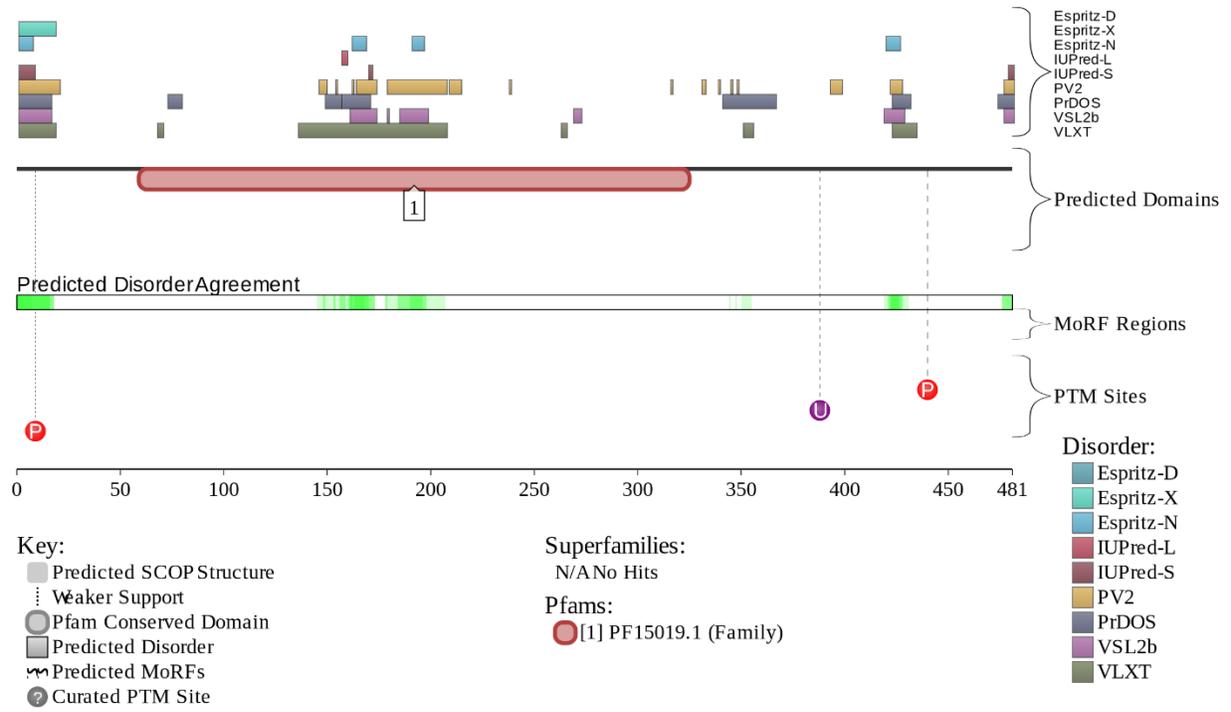
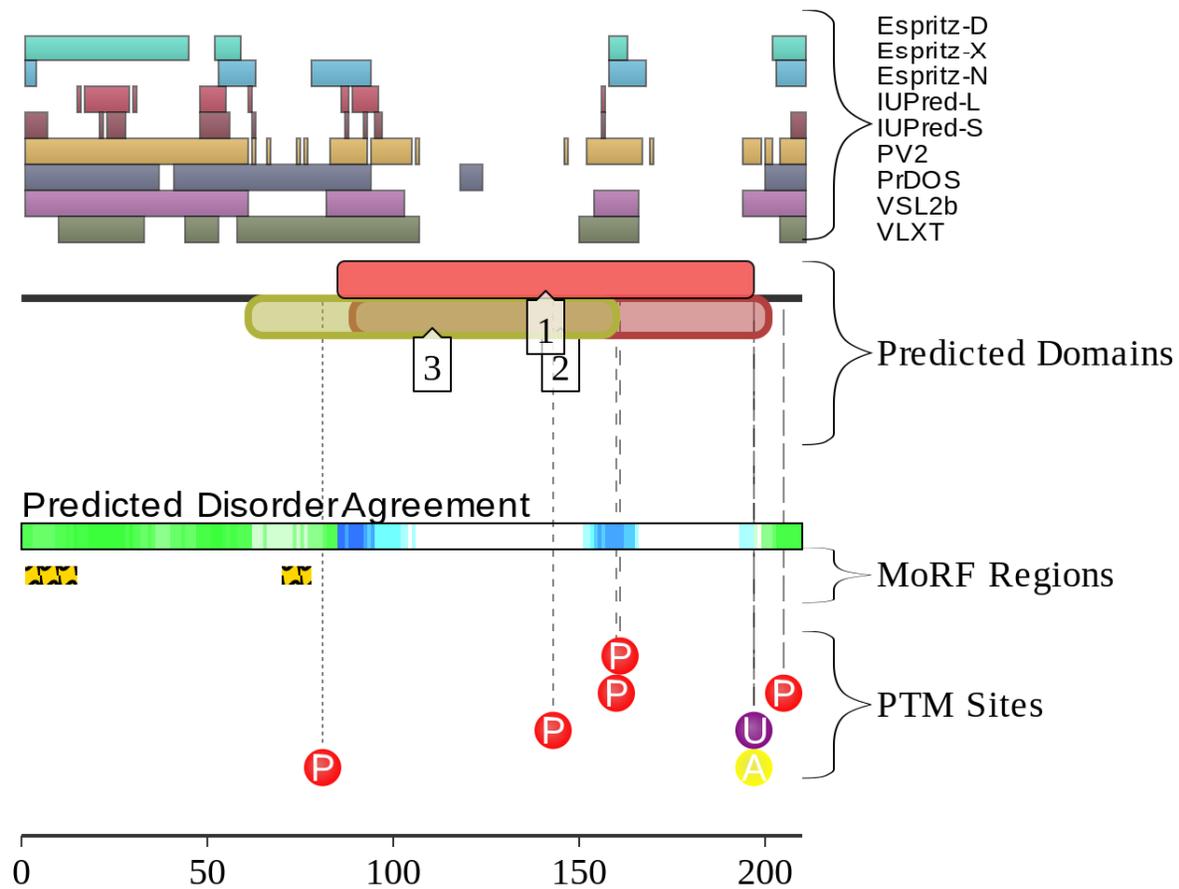


Figure S1X. D²P² output for C9orf72 (UniProt ID: Q96LT7)



Key:

- Predicted SCOP Structure
- ⋮ Weaker Support
- Pfam Conserved Domain
- Predicted Disorder
- ⚡ Predicted MoRFs
- Ⓞ Curated PTM Site

Disorder:

- Espritz-D
- Espritz-X
- Espritz-N
- IUPred-L
- IUPred-S
- PV2
- PrDOS
- VSL2b
- VLXT

Superfamilies:

- [1] Frataxin/Nqo15-like

Pfams:

- [2] Frataxin-like domain
- [3] PB004571 (Pfam-B)

Figure S1Y. D²P² output for frataxin (UniProt ID: Q16595)

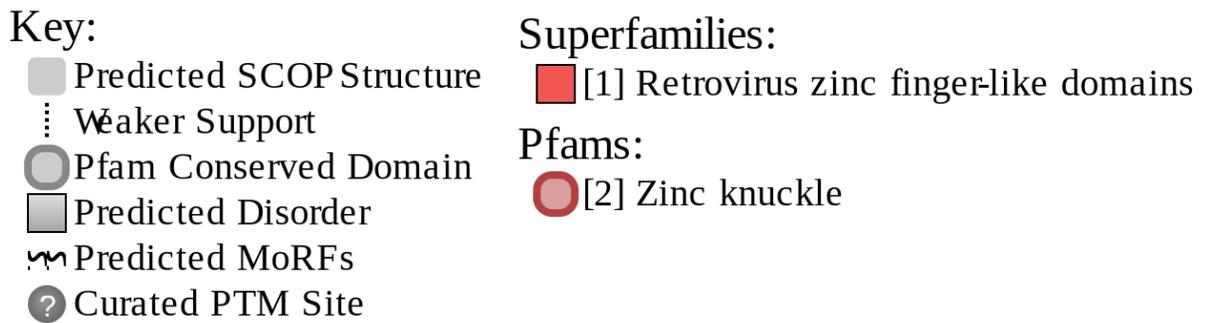
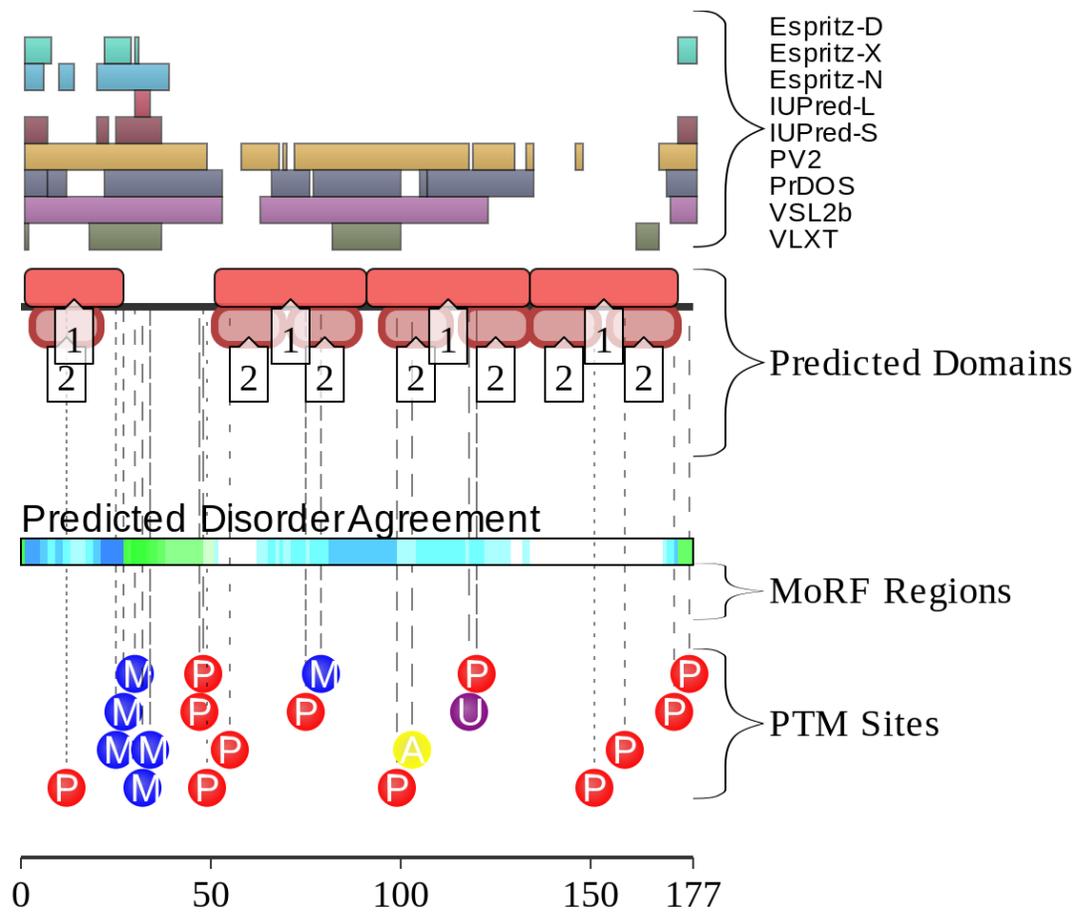


Figure S1Z. D²P² output for cellular nucleic acid-binding protein (CNBP, UniProt ID: P62633)

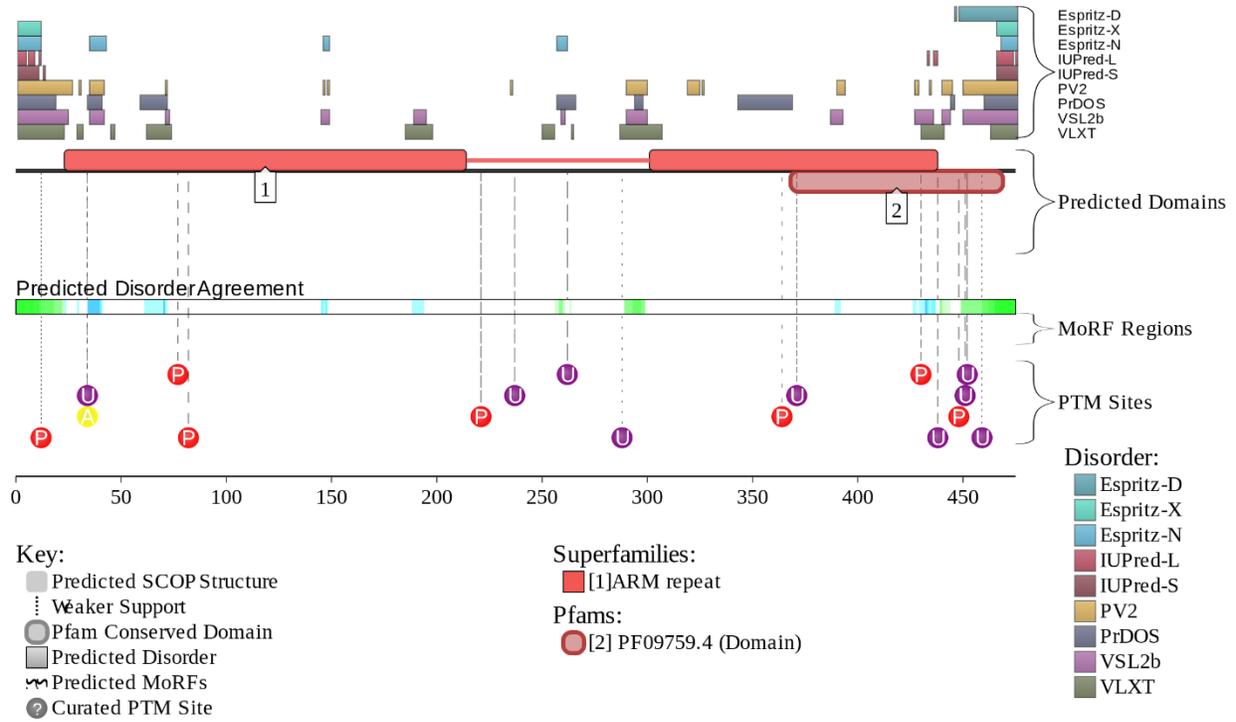


Figure S1a. D²P² output for ataxin-10 (UniProt ID: Q9UBB4)

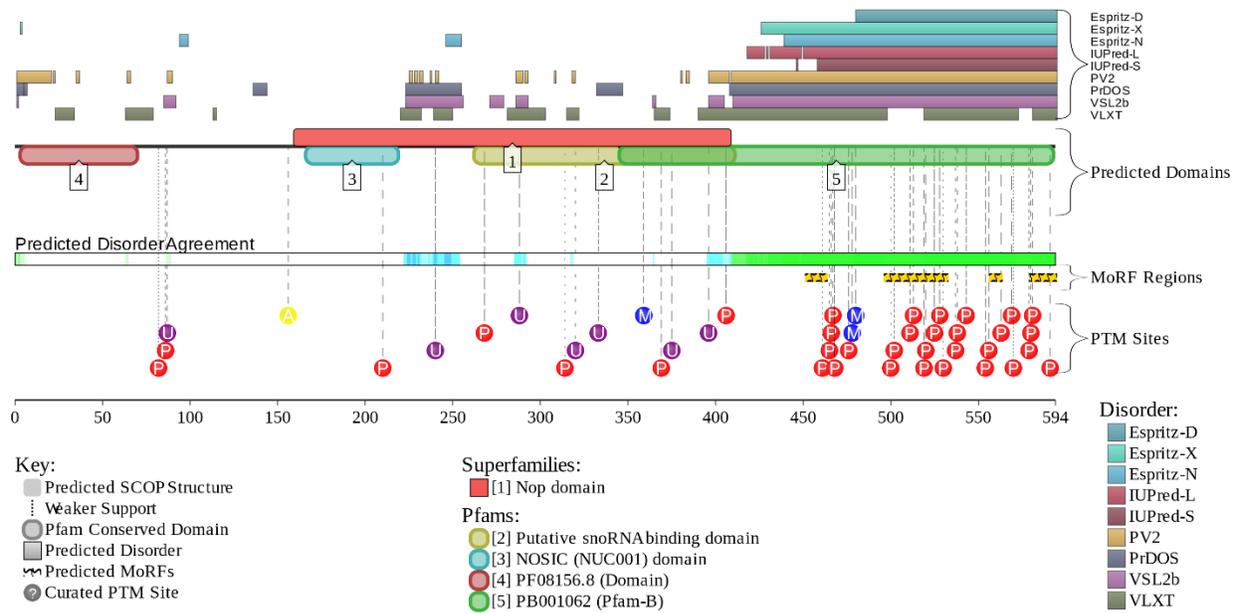


Figure S1b. D²P² output for nucleolar protein 56 (UniProt ID: O00567)

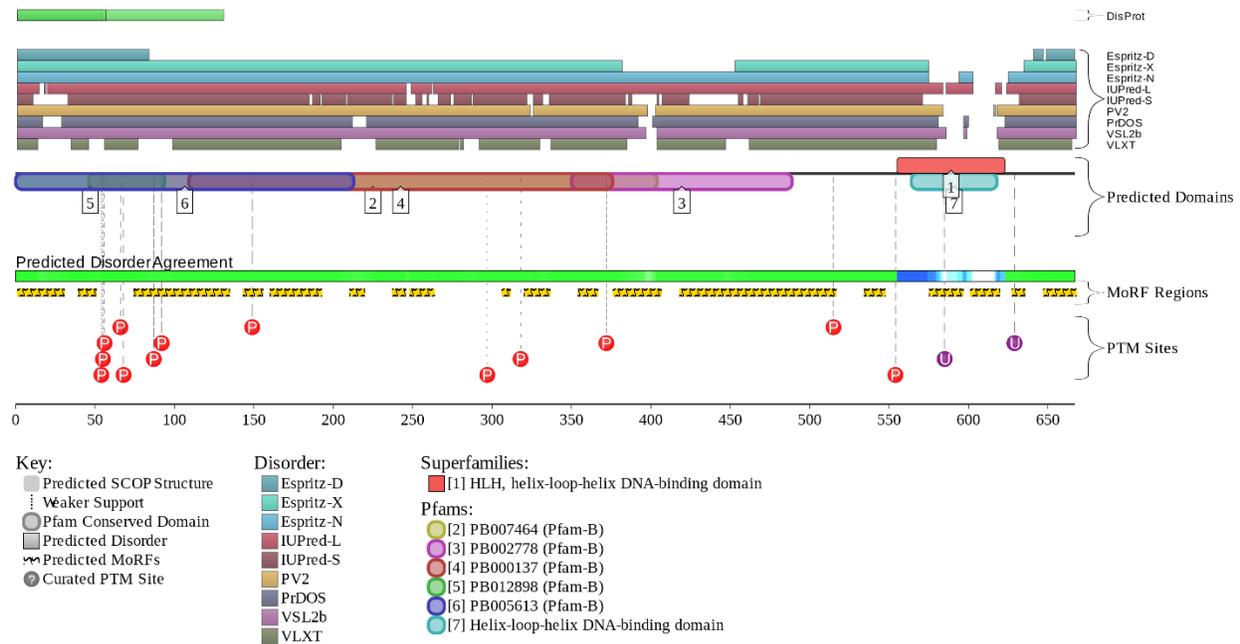


Figure S1c. D²P² output for transcription factor 4 (UniProt ID: P15884)

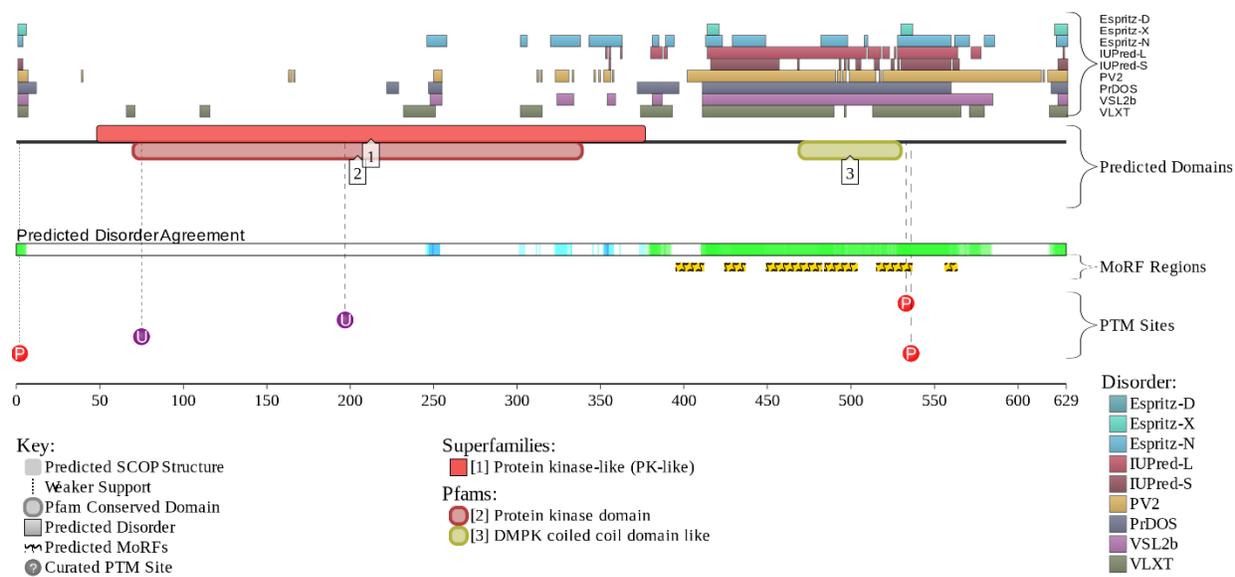


Figure S1d. D²P² output for myotonin-protein kinase (UniProt ID: Q09013)

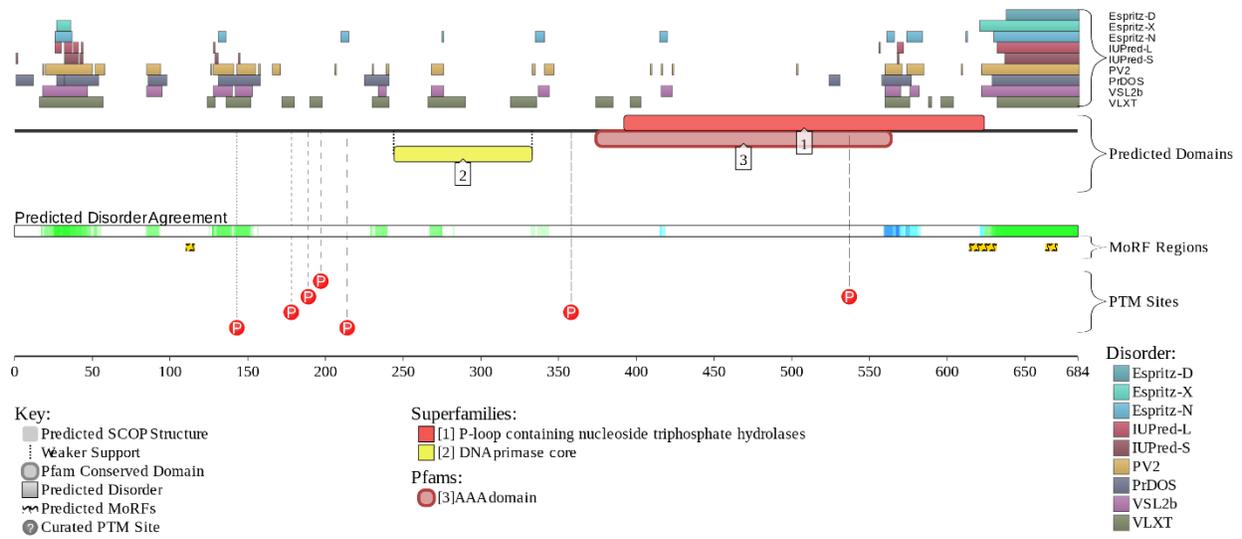


Figure S1e. D²P² output for mitochondrial twinkle protein (UniProt ID: Q96RR1)

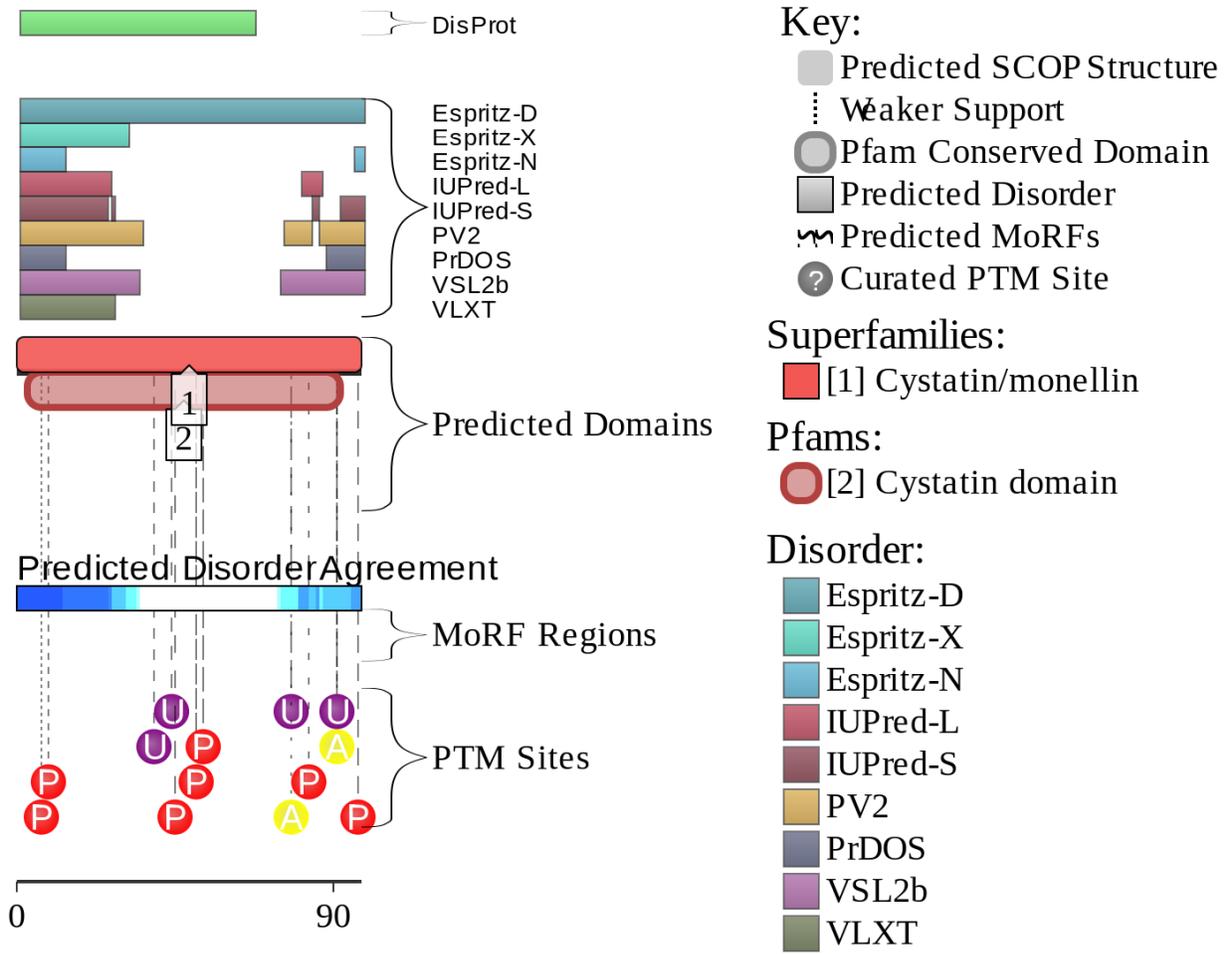


Figure S1f. D²P² output for cystatin-B (UniProt ID: P04080)

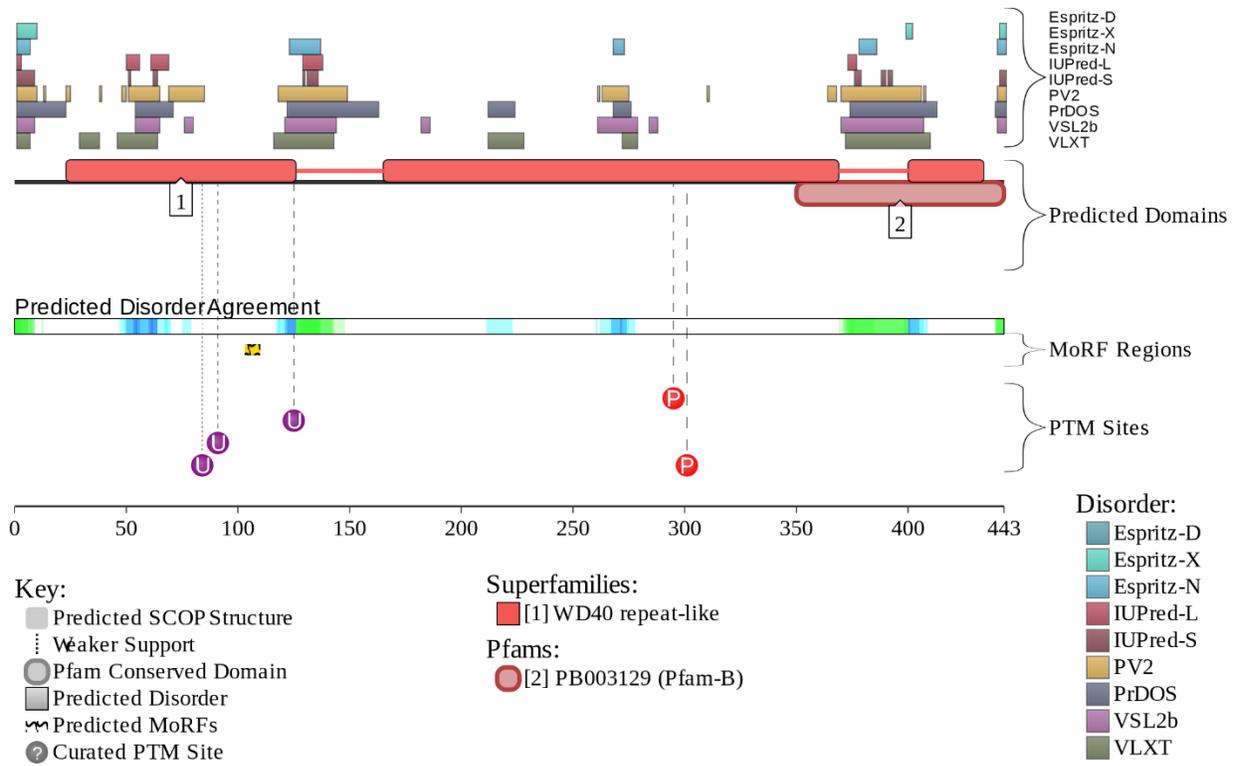


Figure S1g. Serine/threonine-protein phosphatase 2A 55 kDa regulatory subunit B β isoform (PPP2R2B, UniProt ID: Q00005).