

Supplemental Tables and Figures

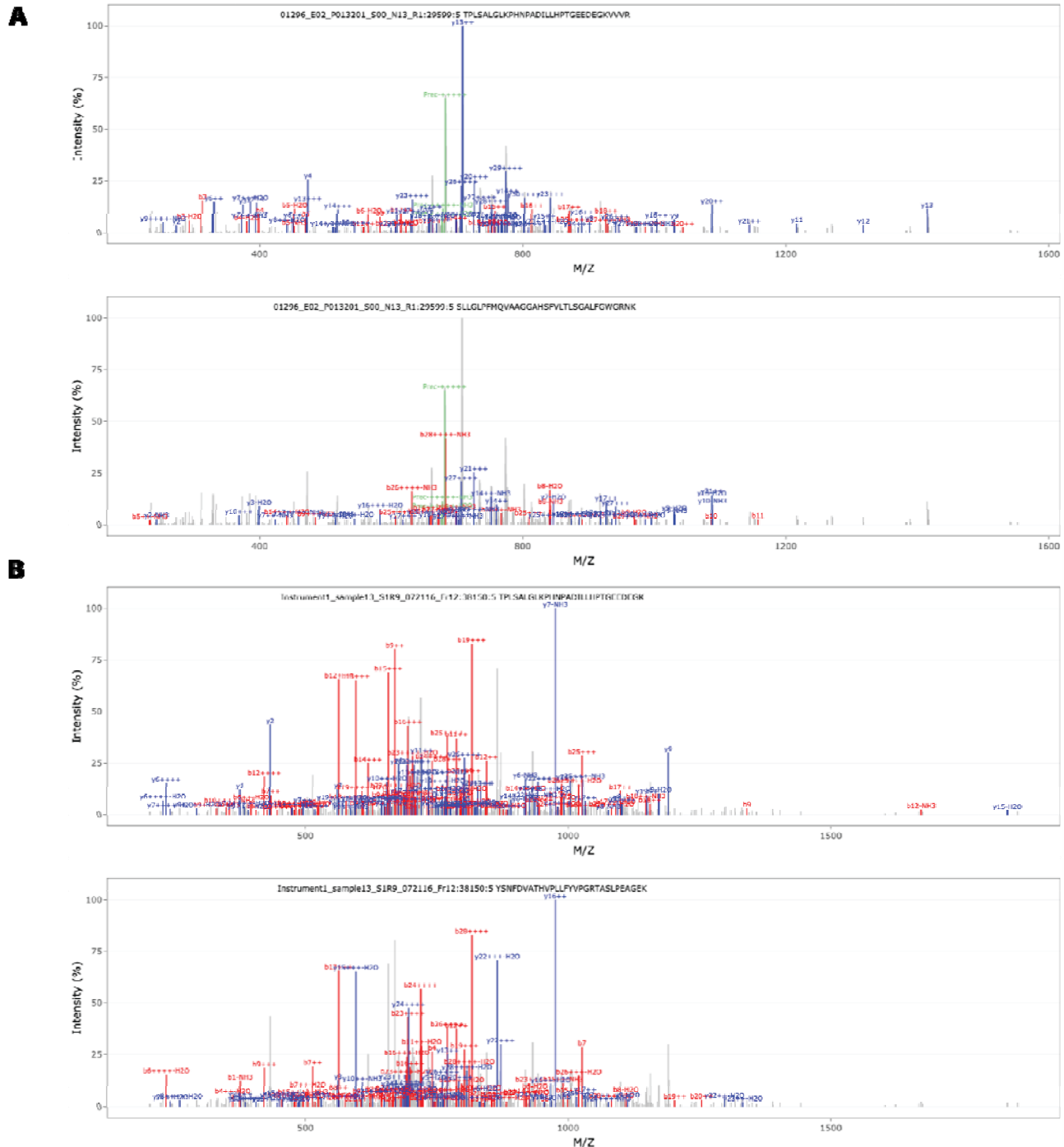
Supplemental Table S1: limma results from canonical database search using MSFragger/Philosopher in PXD008722

Supplemental Table S2: limma results from JCAST canonical + isoform database search using MSFragger/Philosopher in PXD008722

Supplemental Table S3: limma results for alternative isoforms quantified in validation data

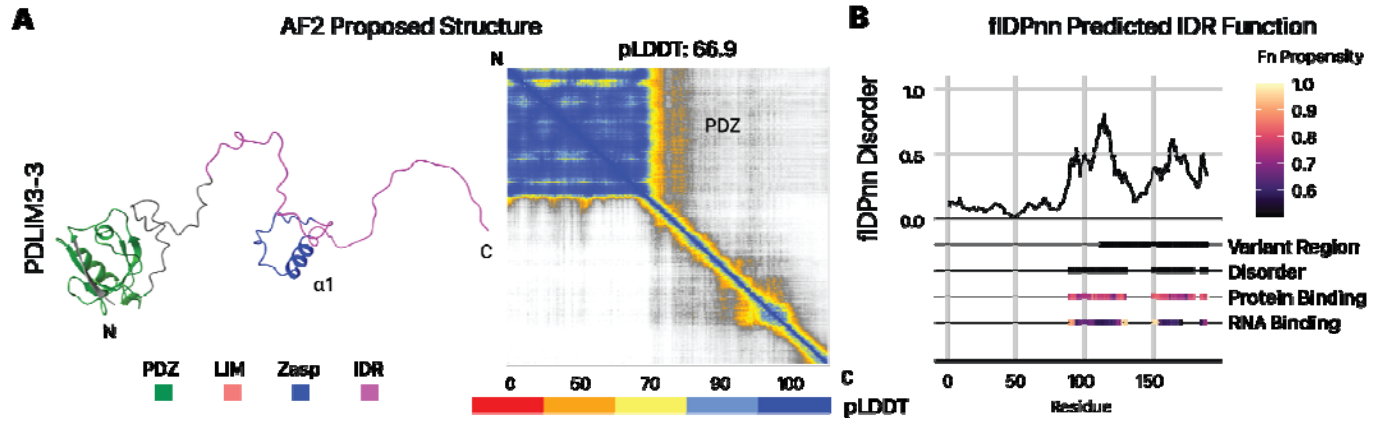
Supplemental Table S4: All identified isoforms by Comet/Percolator and MSFragger/Philosopher

Supplemental Table S5: Annotated protein features in identified isoforms.

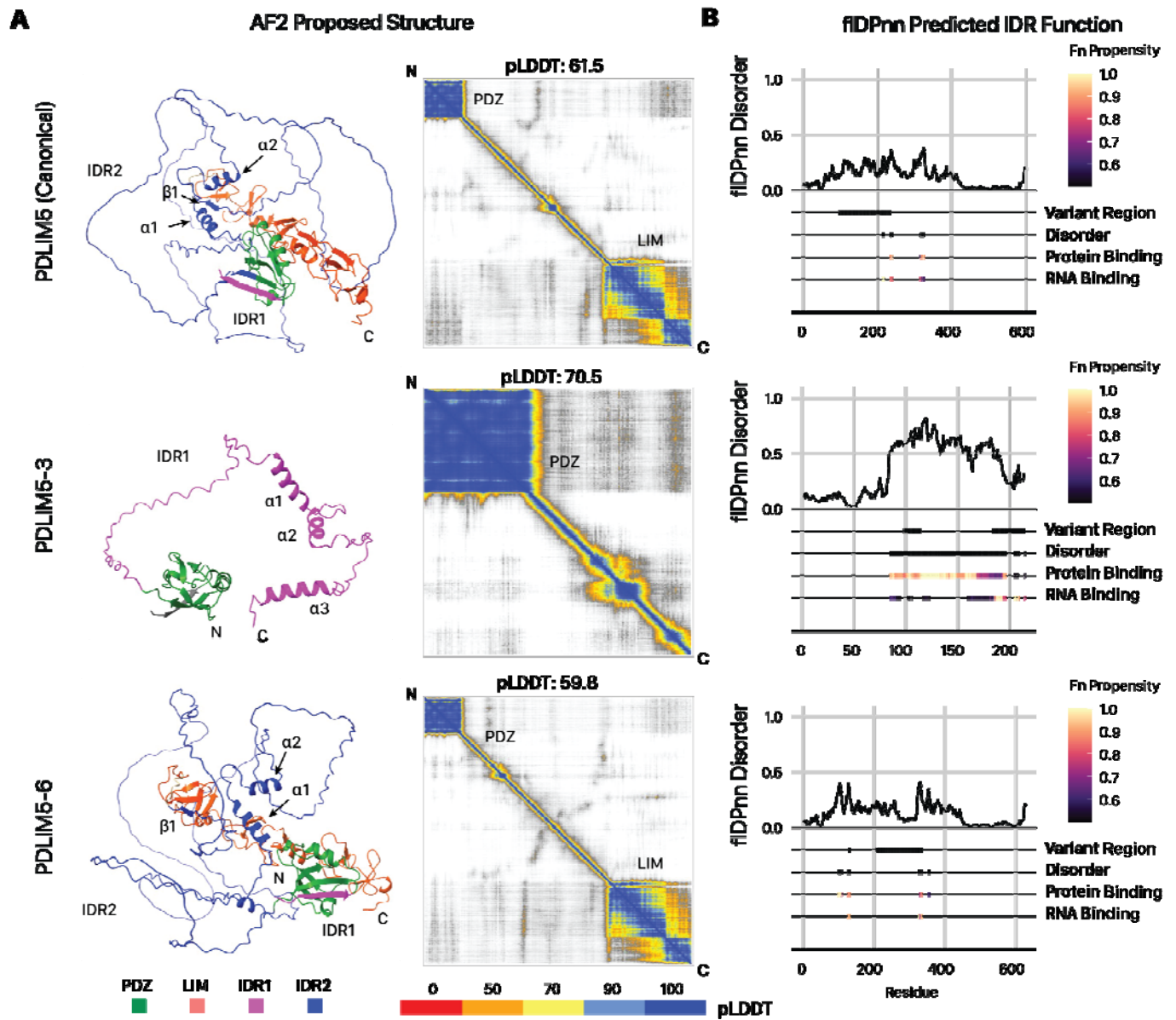


Supplemental Figure S1: PepQuery2 peptide-spectrum matches for two undocumented tensin-1 -J1 isoform peptides. **A.** Peptide spectrum match of the splice junction peptide

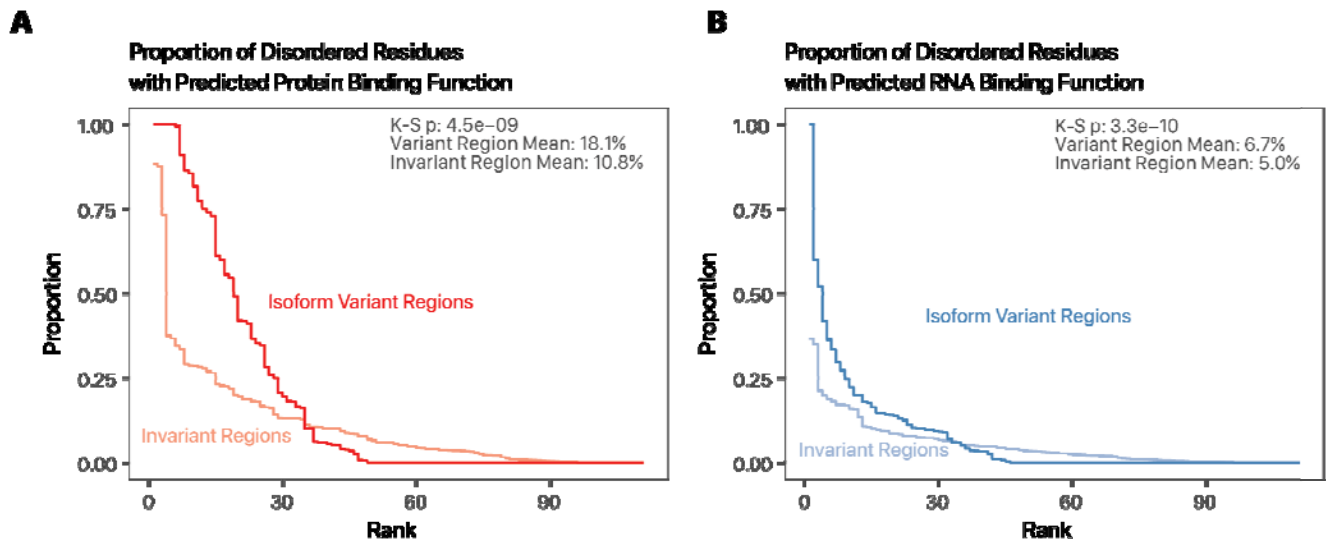
TPLSALGLKPHNPADILLHPTGEEDEGKVVVR against the “29_healthy_human_tissues” (PXD010154) dataset (hyperscore 83.29) (top) and the corresponding peptide spectrum match from the canonical database search (bottom). **B.** Peptide spectrum match of the splice junction peptide TPLSALGLKPHNPADILLHPTGEEDEGK against the “GTEx_32_Tissues_Proteome” (PXD016999) dataset (hyperscore 99.63) (top) and the corresponding peptide spectrum match from the canonical database search (bottom).



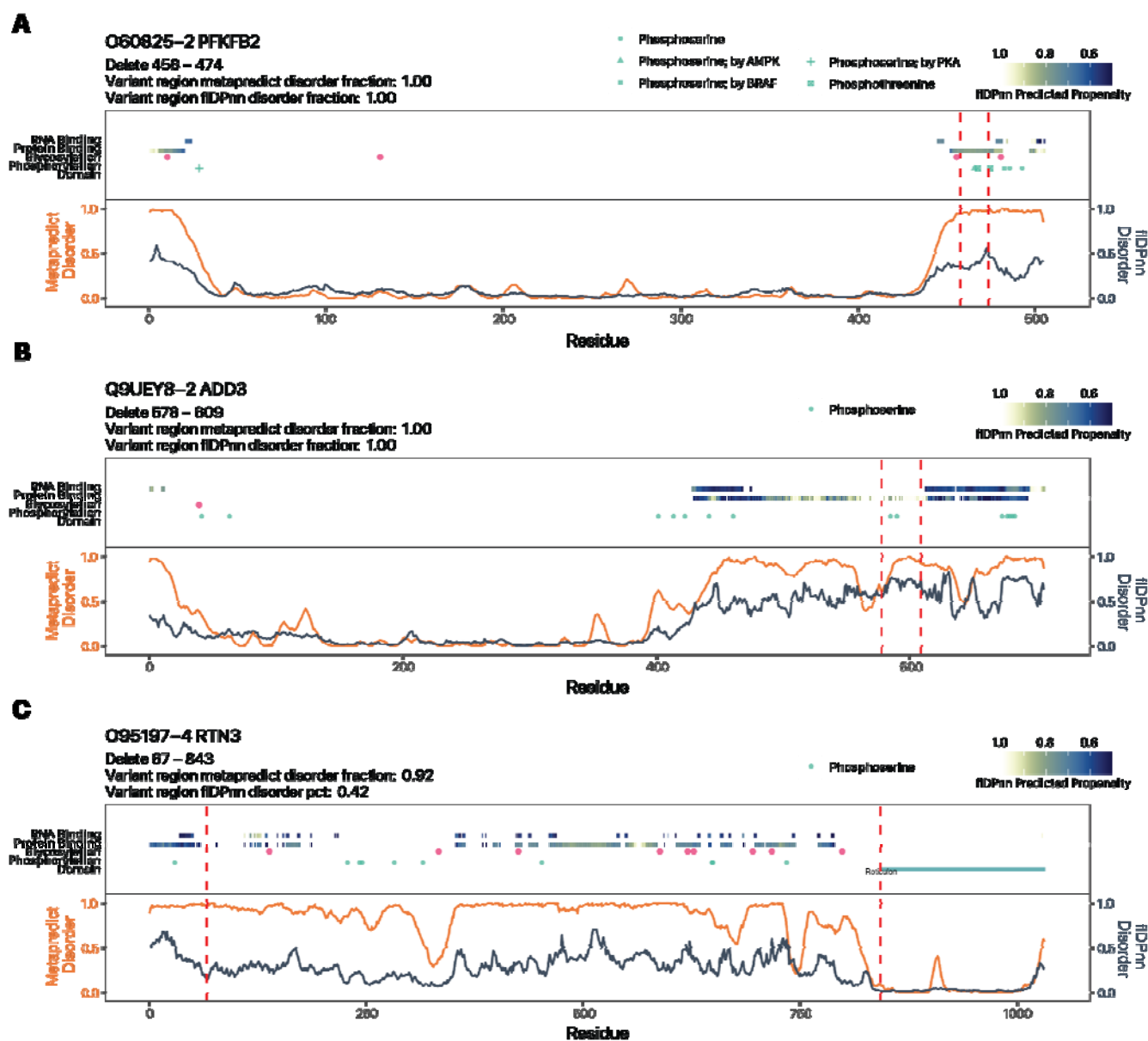
Supplemental Figure S2: A. AlphaFold2 proposed structure and **B.** fIDPnn predicted sequence disorders and functional features for the PDLIM3-3 isoform. See legends for Figure 2 for additional details.



Supplemental Figure S3: A. AlphaFold2 proposed structure and **B.** fIDPnn predicted sequence disorders and functional features for the PDLIM5 sequence and the -3 and -6 alternative isoforms. See legends for Figure 2 for additional details.



Supplemental Figure S4: Proportion of residues within fIDPnn predicted IDRs that are associated with **A.** protein binding or **B.** RNA binding function. K-S: two-sample Kolmogorov-Smirnov test. Darker line: IDR residues within isoform variant regions; lighter line: outside the isoform variant regions.



Supplemental Figure S5: Alternative isoforms with deleted variant regions from canonical sequences show evidence of IDR remodeling. Three isoforms with variant regions removed from the canonical sequences are shown: **A.** PFKFB2-2; **B.** ADD3-2; **C.** RTN3-4. See legends for Figure 5 for additional details.