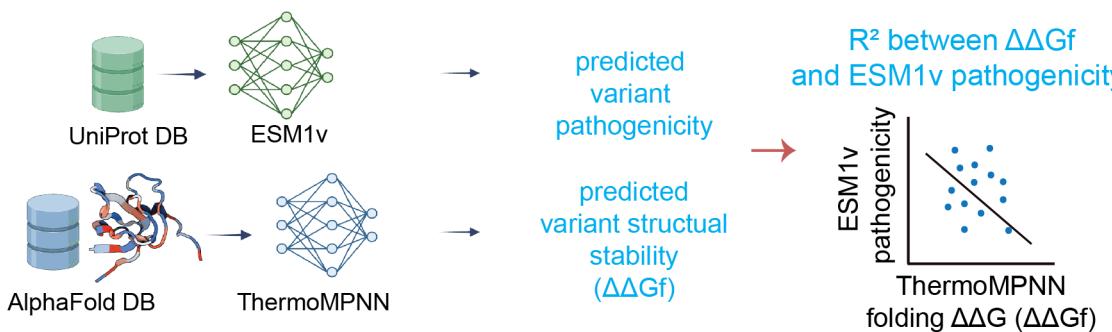
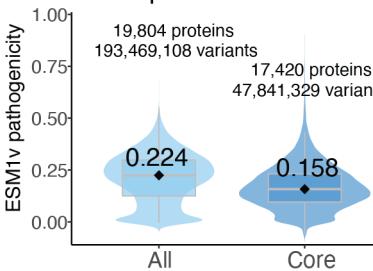
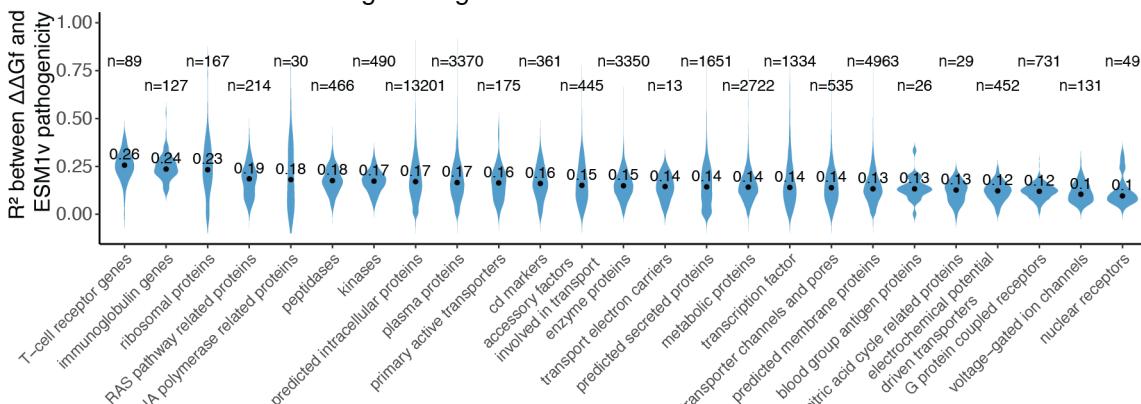
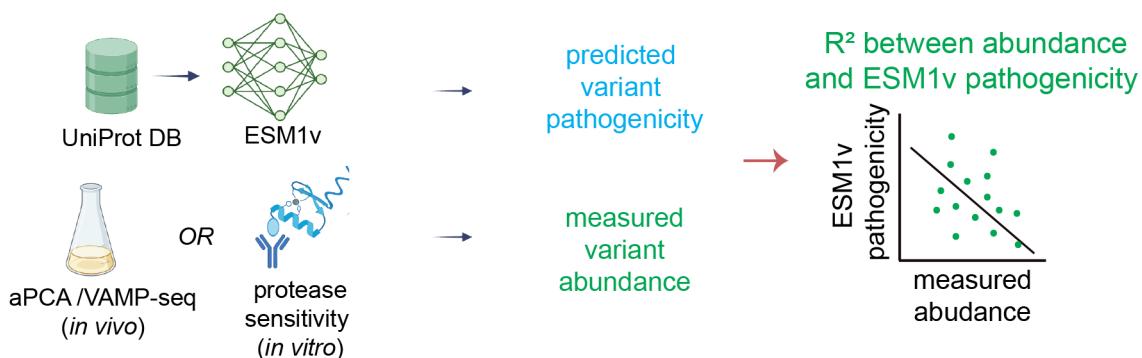


**A****19,804 full-length human proteins****B Human Proteome**

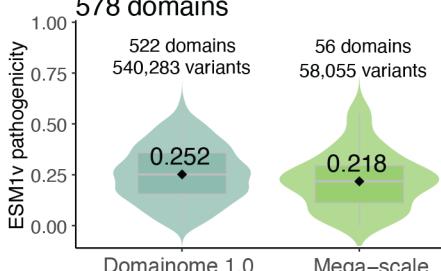
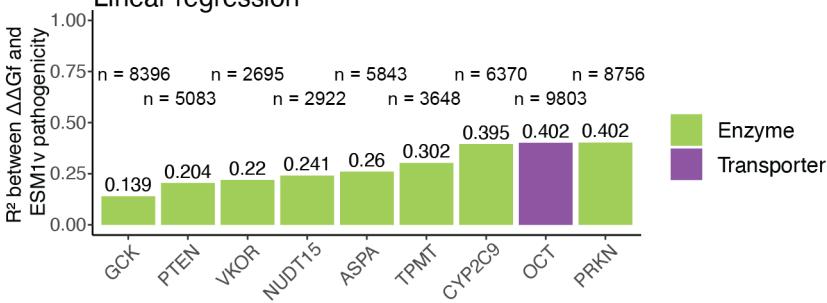
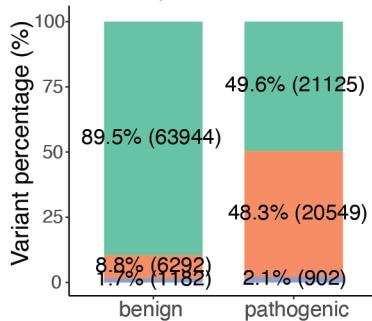
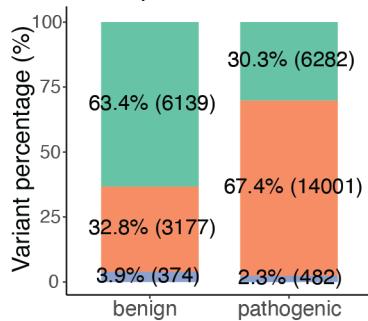
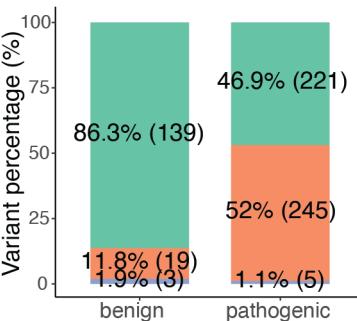
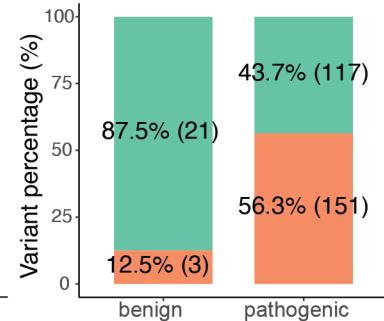
19804 proteins

**C 47,841,329 Variants (Protein Cores)**

Protein cores excluding binding sites

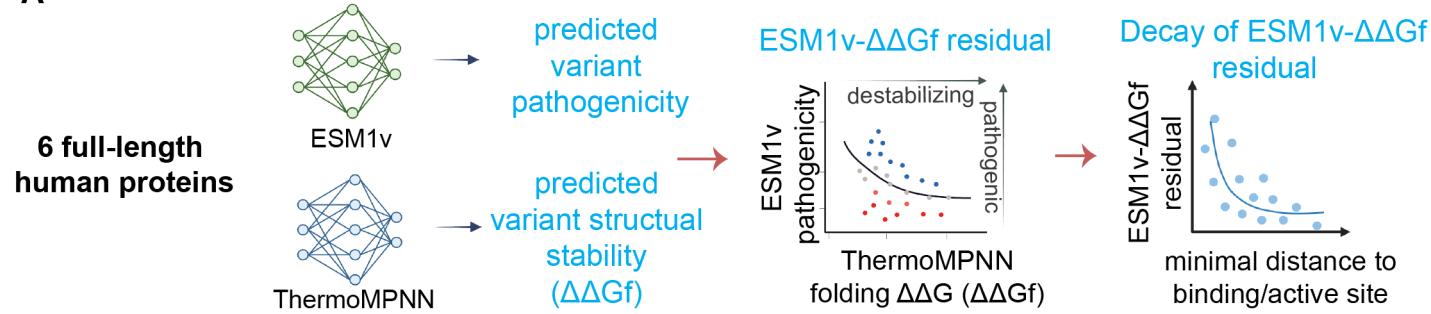
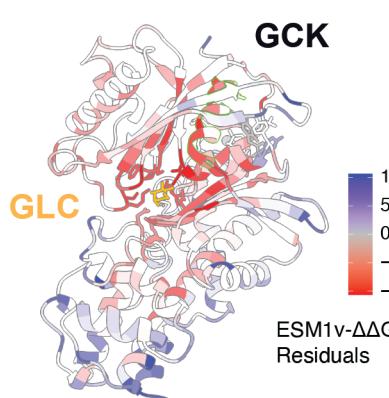
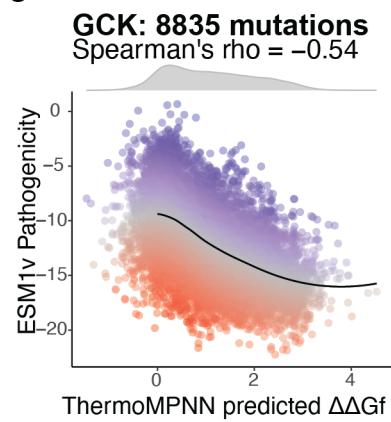
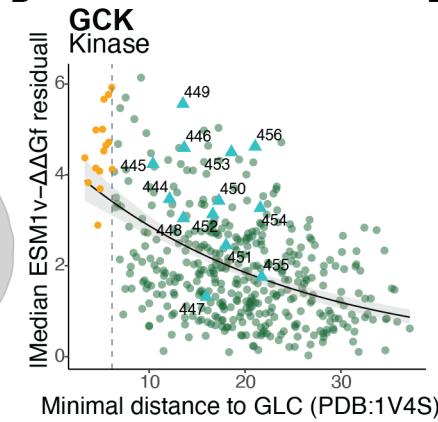
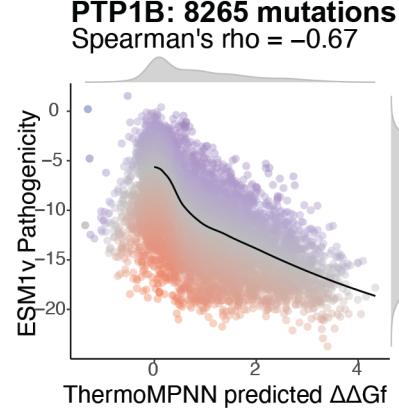
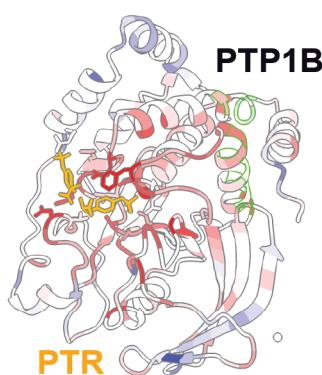
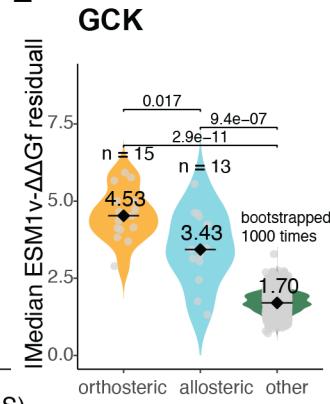
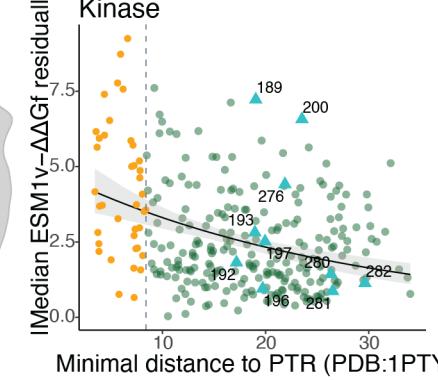
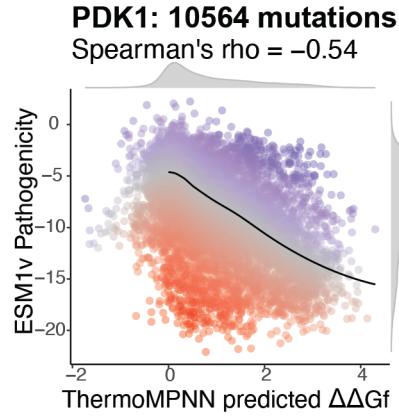
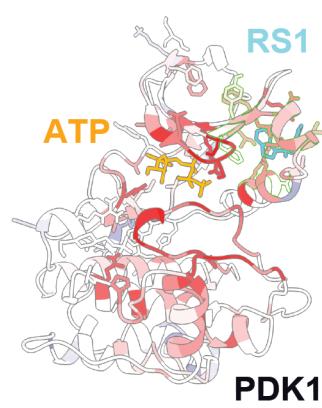
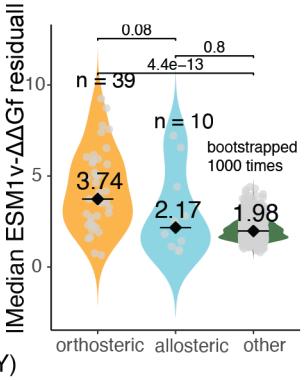
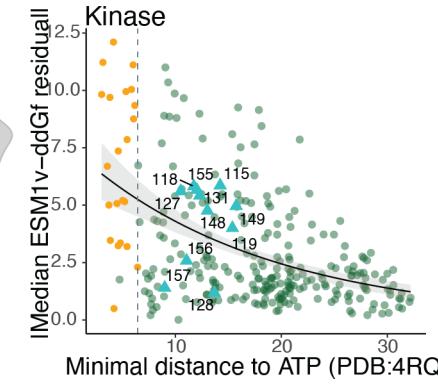
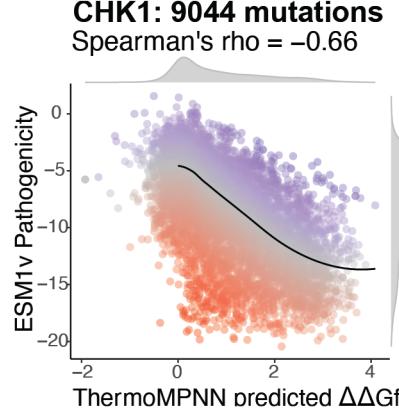
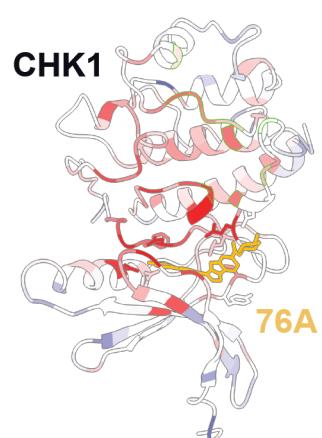
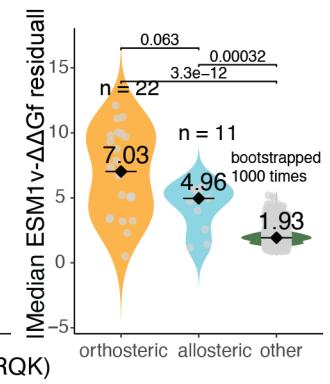
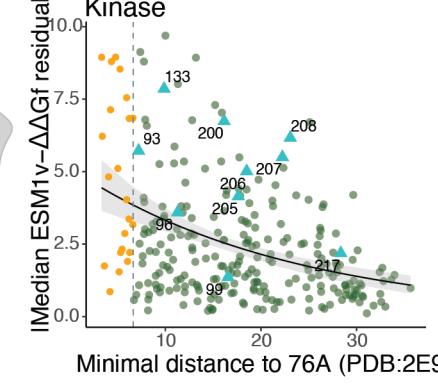
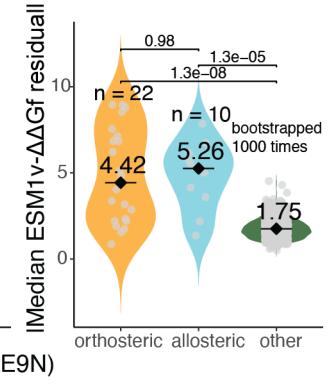
**D****578 protein domains + 9 full-length proteins****E Protein Domains**

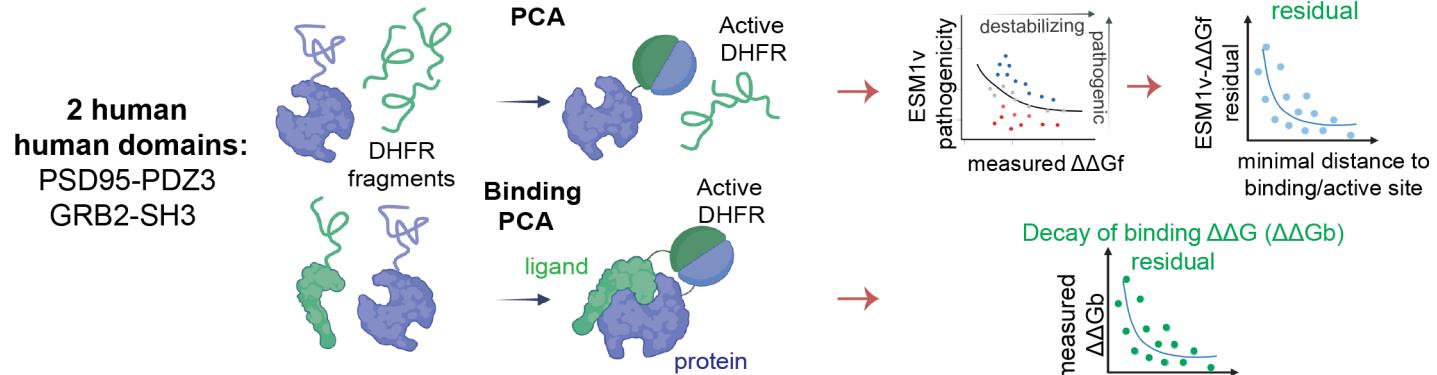
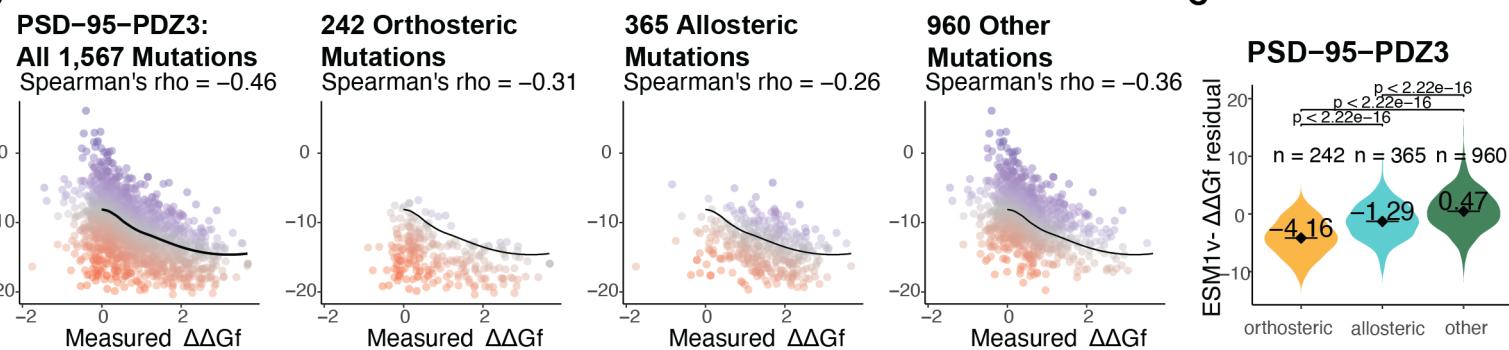
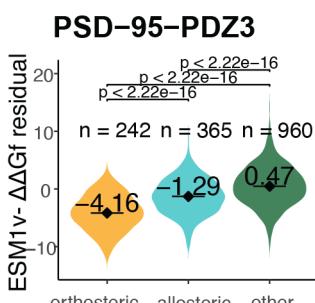
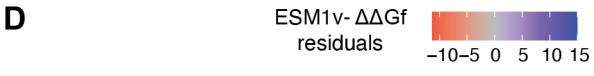
578 domains

**F****VAMP-seq Datasets: 9 Full-length Human Proteins**  
Linear regression**G****113,994 ClinVar Variants**  
12,336 proteins**30,455 ClinVar Variants**  
5,286 proteins**Domainome**  
632 variants**VAMP-seq Datasets**  
292 ClinVar variants

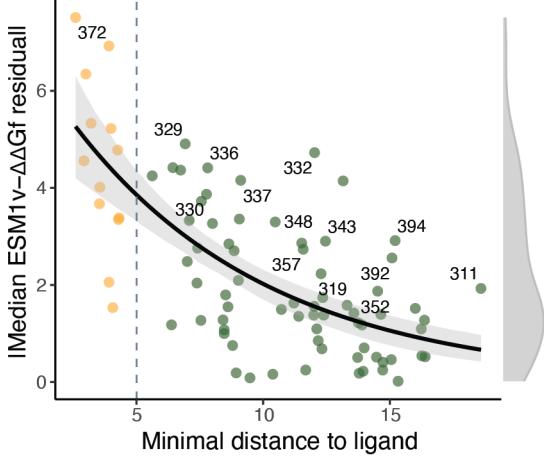
WT-like      destabilizing      stabilizing

**Fig 1**

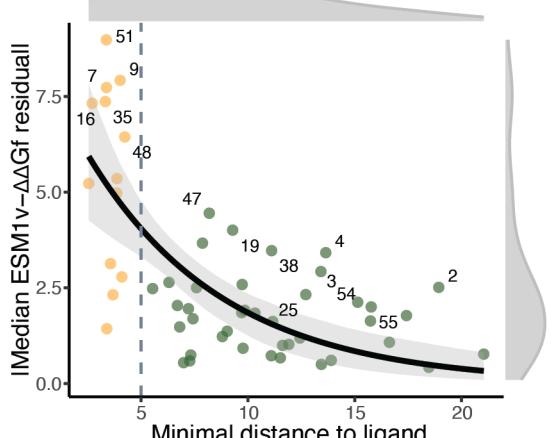
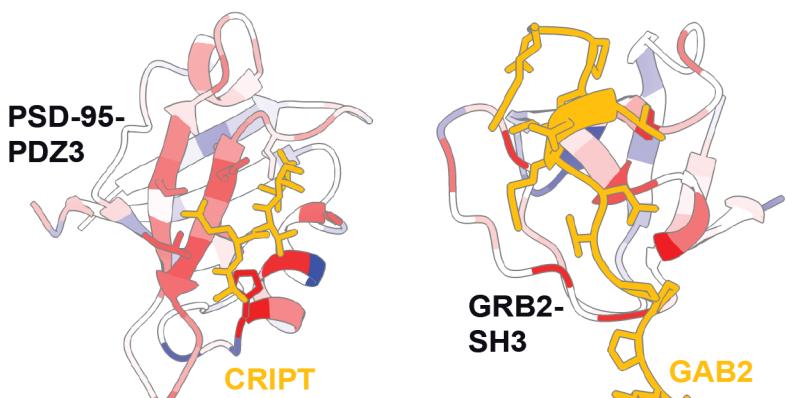
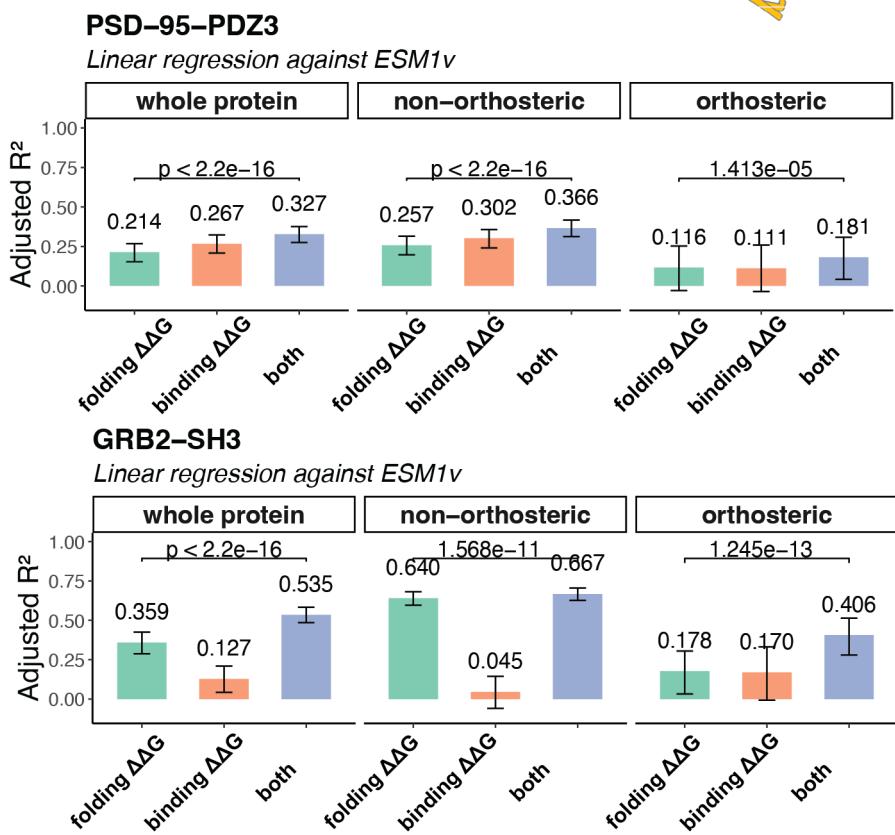
**A****B****C****D****E****D****E****D****E****D****E****Fig 2**

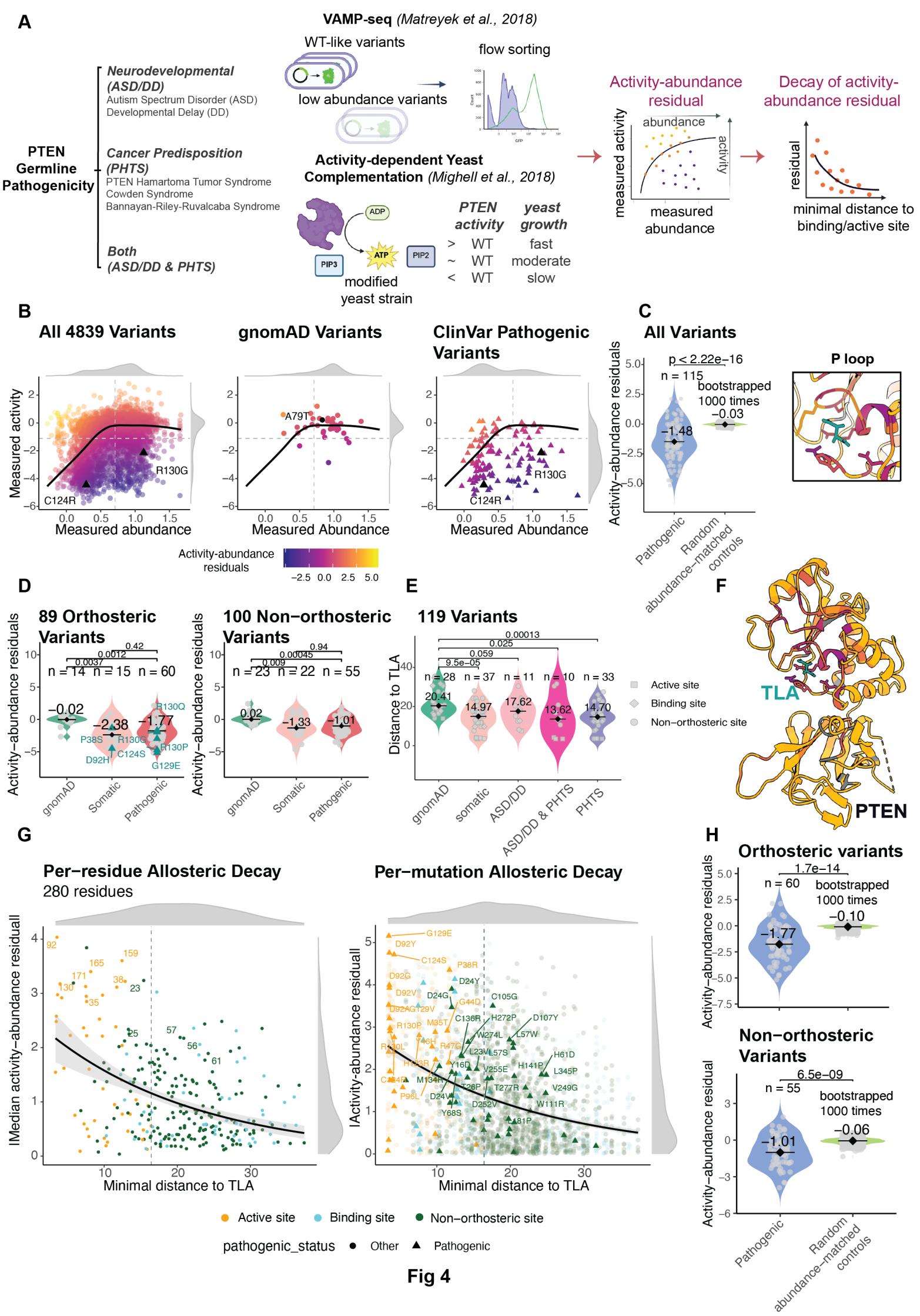
**A****B****C****D**

#### PSD-95-PDZ3: Allosteric Decay

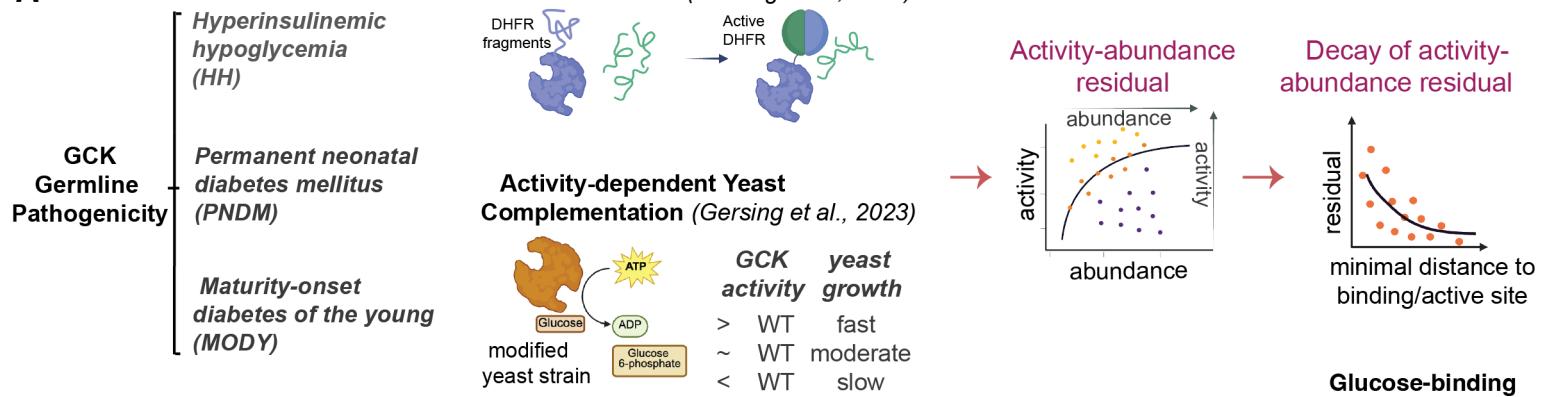
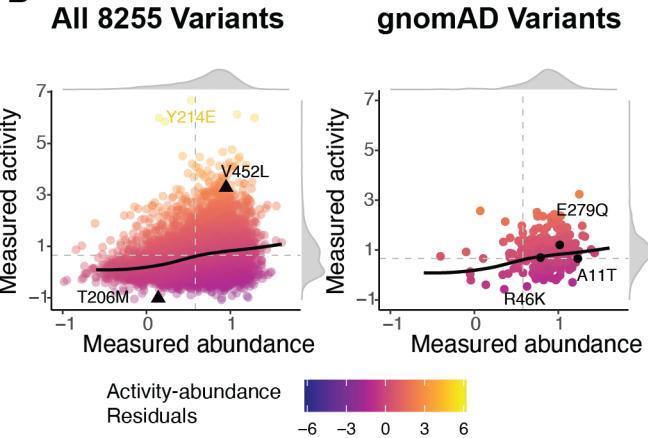
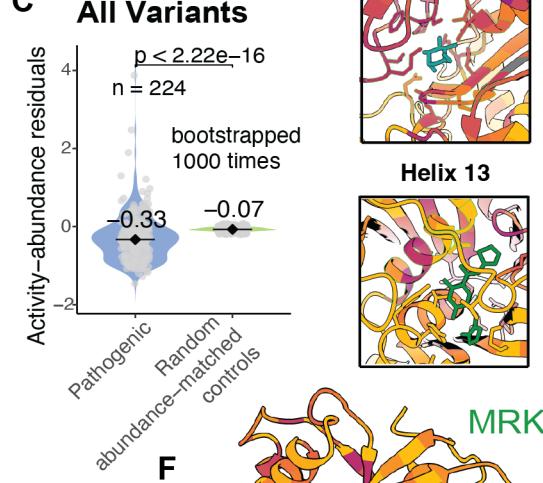
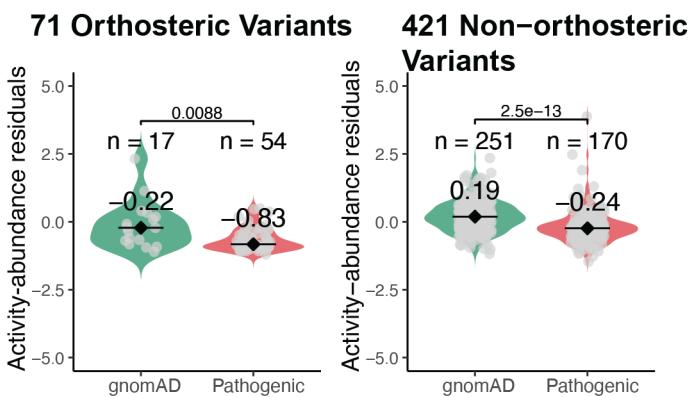
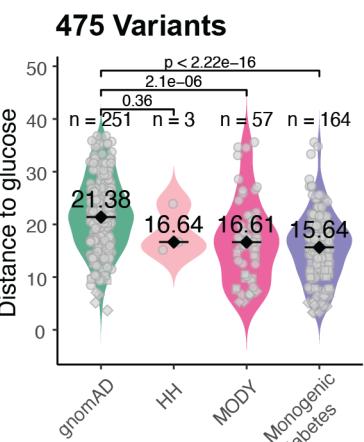
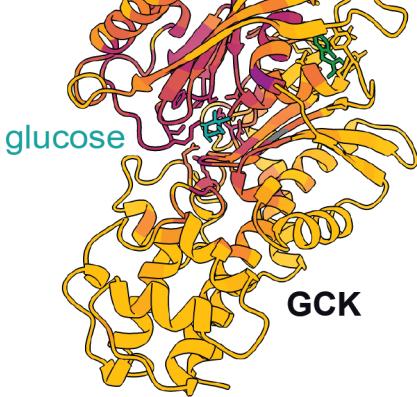
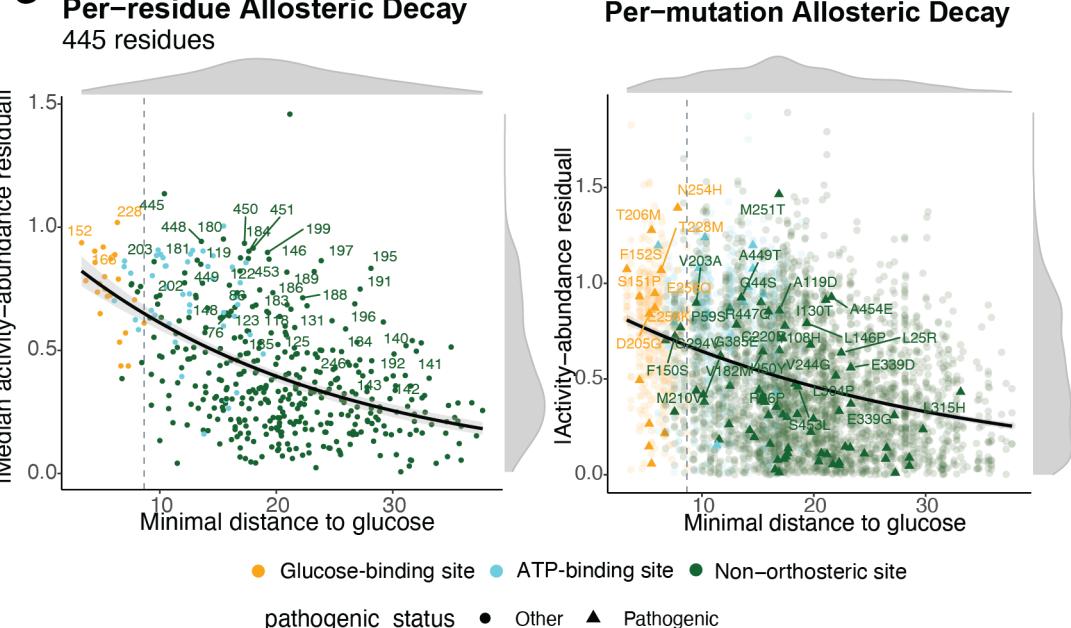
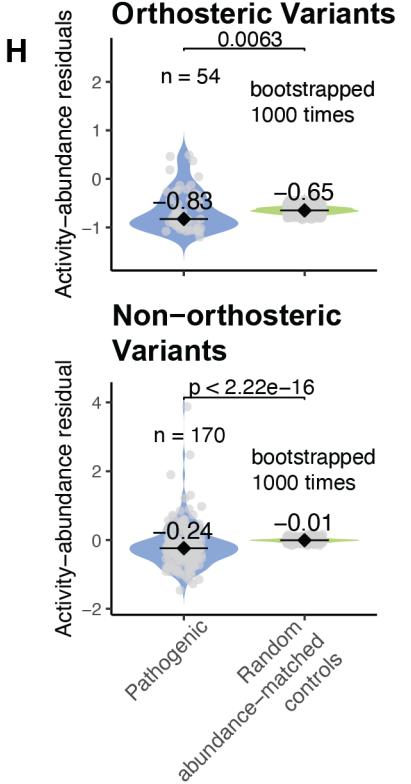


#### GRB2-SH3: Allosteric Decay

**E****F****Fig 3**



**Fig 4**

**A****B****C****D****E****F****G****H****Fig 5**