

*Description of Additional Supplementary files:*

- *Supplementary Data 1: Comparison of common records in the IMEx mutations data set, UniProt mutagenesis annotations and the SKEMPI 2.0 database. Effect descriptions have been simplified to facilitate comparison, with deleterious and increasing/causing effects being qualified as 'loss' and 'gain', respectively.*
- *Supplementary Data 2: Annotations with conflicting effects reported in the IMEx mutations data set.*
- *Supplementary Data 3: IMEx data set mutation annotations associated with disease according to UniProtKB and DisGeNET.*
- *Supplementary Data 4: Pathways enriched in PathDIP analysis for each effect group (refers to figure 6c and Supplementary Figure 5).*
- *Supplementary Data 5: Pathway sets used for word clouds (refers to figure 6c and Supplementary Figure 6).*