

**Supplementary Figure 1. Comparison of Fold-X computed (∆∆G) and ENCoM-computed (∆∆Svib).** Each haplotype is represented by a maroon square and their defining missense variants are represented by circles. Figure points that fall within the highlighted region are expected to have neutral effects on protein stability [1]. ∆∆G predicts most of the variants and haplotypes as destabilising to the protein encoded protein structures. Both ∆∆G and ∆∆Svib seem to exhibit a destabilising bias for both haplotype and variants. However, ∆∆Svib predicted more haplotypes and variants to have neutral effects on protein stability than ∆∆G (see also Figure 3A).

**Reference:**

[1]  V. Frappier and R. J. Najmanovich. A coarse-grained elastic network atom contact model and its use in the simulation of protein dynamics and the prediction of the effect of mutations. *PLoS computational biology*, 10(4):e1003569, 2014.