Supplementary Information for:

Computational Saturation Screen Reveals the Landscape of Mutations in Human Fumarate Hydratase

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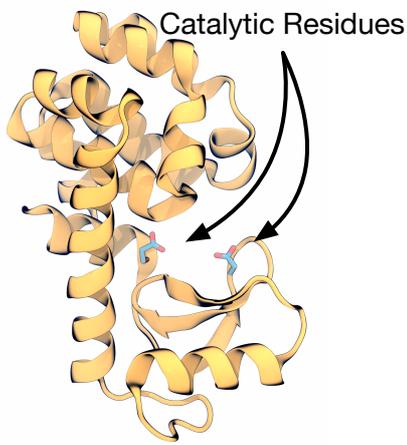2 Wellcome Trust Sanger Institute, Hinxton, CB10 1SA, UK

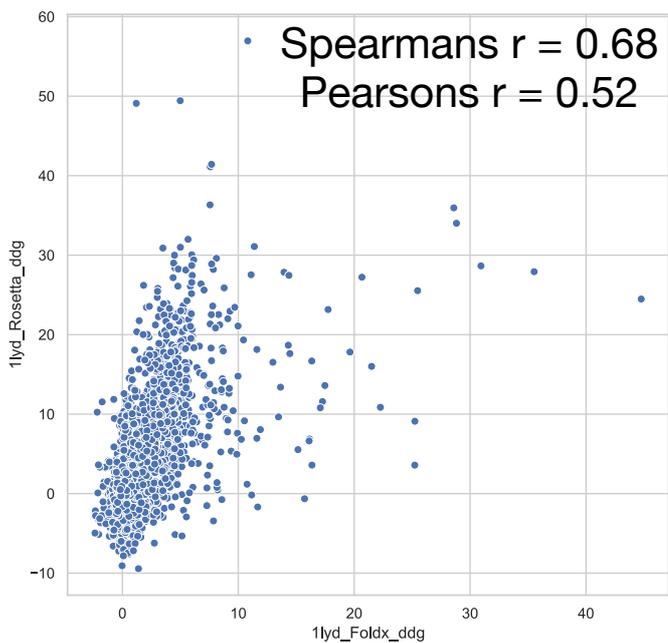Figure S1: Structure of bacterial T4 lysozyme

Figure S2: Spearman's rank correlation for delta-delta G calculated by rosetta and foldx for T4 lysozyme.
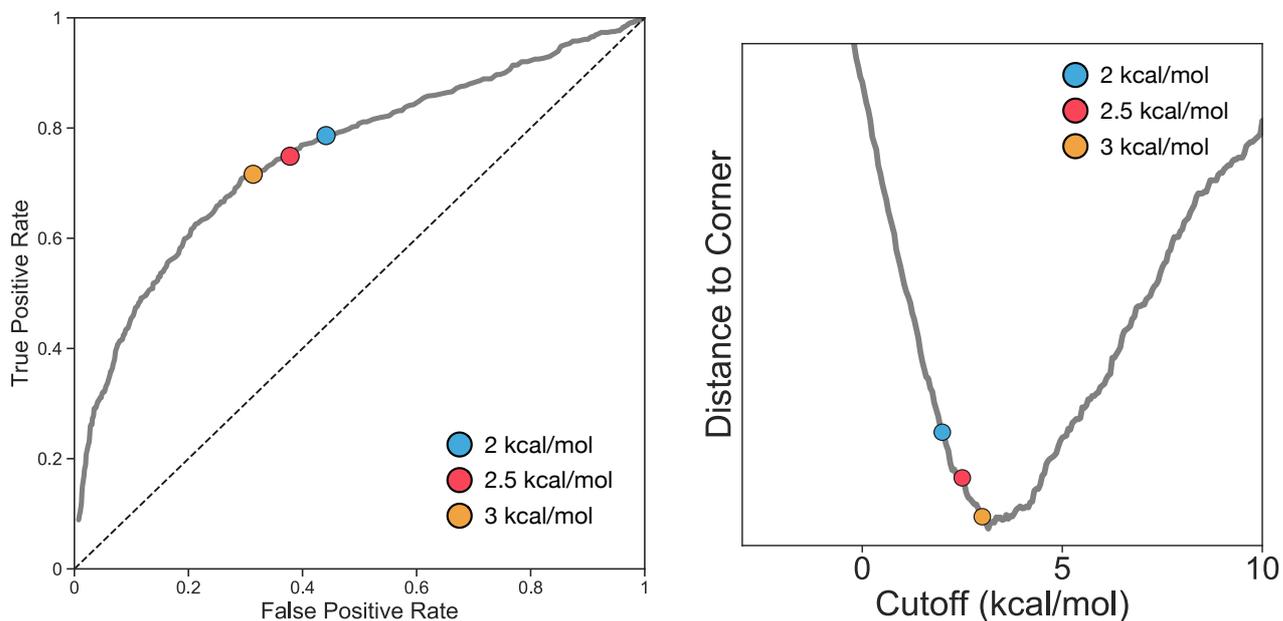

Figure S3: ROC analysis for destabilising cutoffs for measured mutations in T4 lysozyme. Left: ROC curve. Right: Distance to corner.
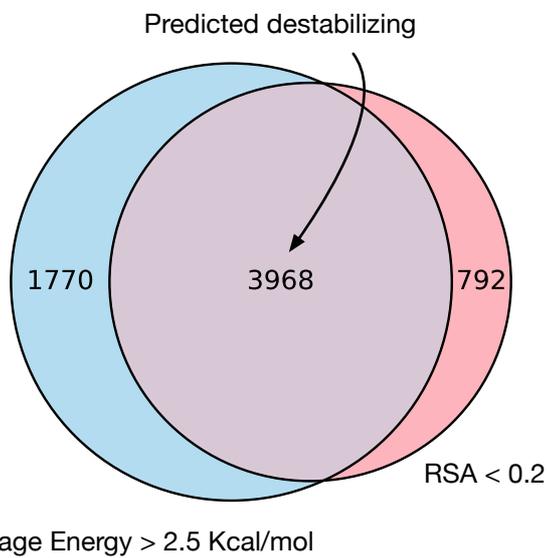
Figure S4: Venn showing the numbers of possible mutations in FH in residues with an RSA < 0.2 (red), and with a destabilising ΔΔG (blue), resulting in predicted destabilising mutations (purple).
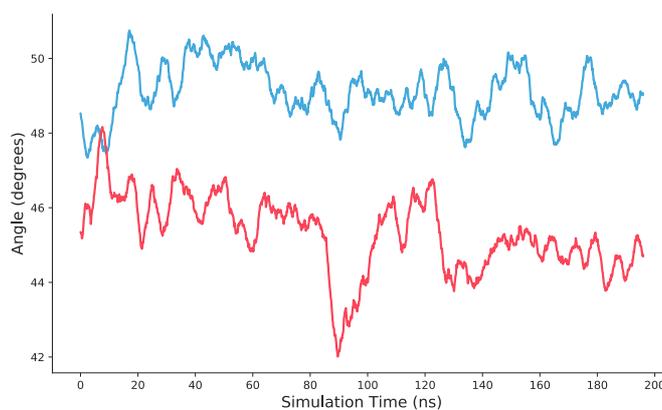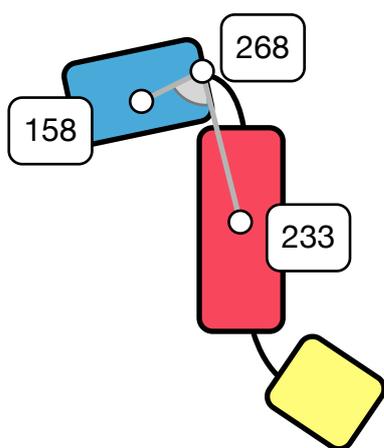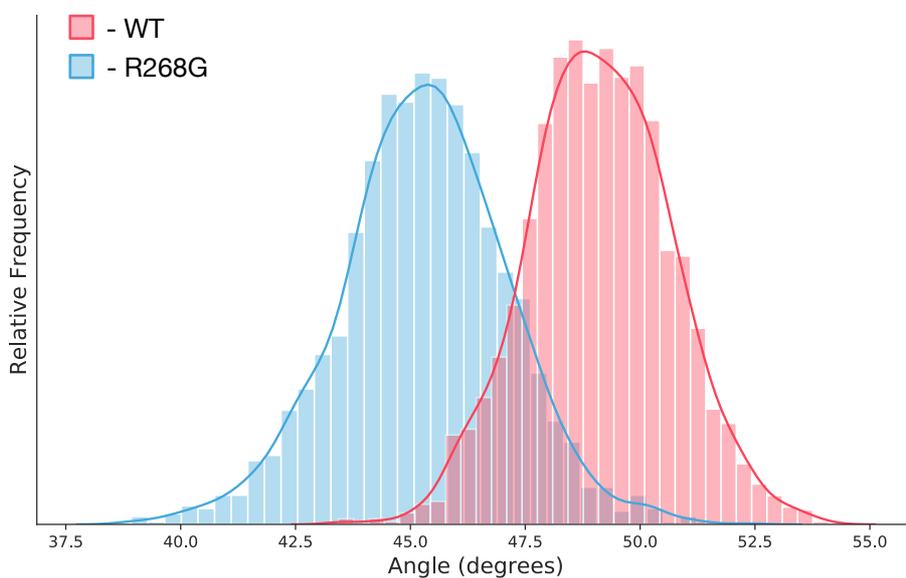

Figure S5: Molecular dynamics of WT (red) vs R268G Mutant form of FH (blue). Shown is the angle between residues 158, 268, and 331.

Table S1: Mutational clusters for all non-benign mutations in the FH mutation database

Table S2: Classification for all possible mutations in FH

Table S3: Classification for all mutations in T4 Lysozyme measured in Rennel et al.

Table S4: Prediction for all mutations in the FH mutation database

Table S5: Prediction for all mutations in FH in the Cancer Cell Line Encyclopedia