

Tolerated or enriched	811	59
Depleted	406	361
	Stabilizing	Destabilizing

**Figure 3 - Figure Supplement 3. Truth table comparing functional results to predicted stability.**

Comparison of functional results to computationally predicted change in stability ( $\Delta\Delta G$ , see methods). Substitutions are binned as tolerated or enriched if maximum  $F_D > 0.1$  and depleted if  $F_D < 0.1$  across any strain. Substitutions are considered stabilizing if predicted  $\Delta\Delta G$  was  $<10$  and destabilizing if  $>10$ .