Supplementary Table 4. FoldX and DUET ΔΔG predictions for CYP21A2 variants.

In FoldX, ΔΔG values > +3SD kcal·mol⁻¹ were provisionally considered destabilization, whereas ΔΔG < –3SD kcal·mol⁻¹ were regarded as stabilization; intermediate values were suggested as neutral. In DUET, ΔΔG values ≥ +1 kcal·mol⁻¹ indicated significantly stabilizing mutations, while values ≤ -1 kcal·mol⁻¹ indicated significantly destabilizing mutations; |ΔΔG | values between 0.5 and 1.0 kcal·mol⁻¹ showed moderate changes. In both cases, the larger absolute ΔΔG value correspond to the greater the predicted magnitude of stability changes.

FoldX ΔΔG predictions (kcal·mol⁻¹) are given as averages ± SD over five independent runs.

SNV	FoldX (Average ± SD, kcal·mol⁻¹)	DUET (ΔΔG predictions, kcal·mol⁻¹)
R76K	0.63±0.10	0.19
E162G	1.80±0.37	-1.78
L308V	2.10±0.07	-2.15
S373N	-0.08±0.08	0.01
P387L	1.50±0.86	0.16
H393Q	4.47±0.02	-1.69
R401G	3.42±0.02	-0.94
R436C	1.16±0.02	-1.58