Supplementary Table 2. Conservation scores of CYP21A2 amino acid residues predicted by ConSurf. Additional information for figure 3.

- POS: The position of the acid in the sequence.

- SEQ: The acid one letter.

- SCORE: The normalized conservation scores. (ranging from -1.907 to +2.748, where higher values indicate more conserved residues).
- COLOR: The color scale representing the conservation scores (9 - conserved, 1 - variable). Conservation grades were calculated using ConSurf with default parameters based on a multiple sequence alignment of homologous CYP21A2 sequences.
- CONFIDENCE INTERVAL: When using the bayesian method for calculating rates, a confidence interval is assigned to each of the inferred evolutionary conservation scores, next to it are the colors of the lower and upper bounds of the confidence interval

- B/E: Burried (b) or Exposed (e) residue.
- MSA DATA: The number of aligned sequences having an acid (non-gapped) from the overall number of sequences at each position.

- RESIDUE VARIETY: The residues variety at each position of the multiple sequence alignment.

These values correspond to the six rare CYP21A2 variants visualized in Figure 3 (Evolutionary Conservation and Structural Context Figure).

POS	SEQ	SCORE	COLOR	CONFIDENCE INTERVAL	B/E	MSA DATA	RESIDUE VARIETY
10	L	0.953	3	0.427, 1.171 4,3	b	61/100	-
76	R	0.723	4	0.264, 0.859 5,4	e	90/100	K 15%
162	E	0.783	4	0.264, 1.171 5,3	e	100/100	G 4%
274	S	1.683	2	0.859, 1.641 4,2	e	97/100	Y 2%
308	L	-1.019	7	-1.230, -0.892 8,7	b	100/100	V 3%
373	S	0.925	3	0.427, 1.171 4,3	e	100/100	N 4%
387	P	0.433	4	-0.008, 0.622 5,4	b	100/100	L 5%
393	H	-0.648	7	-0.892, -0.510 7,6	b	100/100	Q <1%
401	R	-0.497	6	-0.747, -0.329 7,6	e	99/100	G 1%
436	R	-0.541	6	-0.822, -0.423 7,6	e	98/100	-
494	N	-0.265	6*	-1.097, 0.264 8,5	e	2/100	-