

## SUPPLEMENTAL MATERIALS

### **The rs35217482 (T755I) single-nucleotide polymorphism in aldehyde oxidase-1 attenuates protein dimer formation and reduces the rates of phthalazine metabolism**

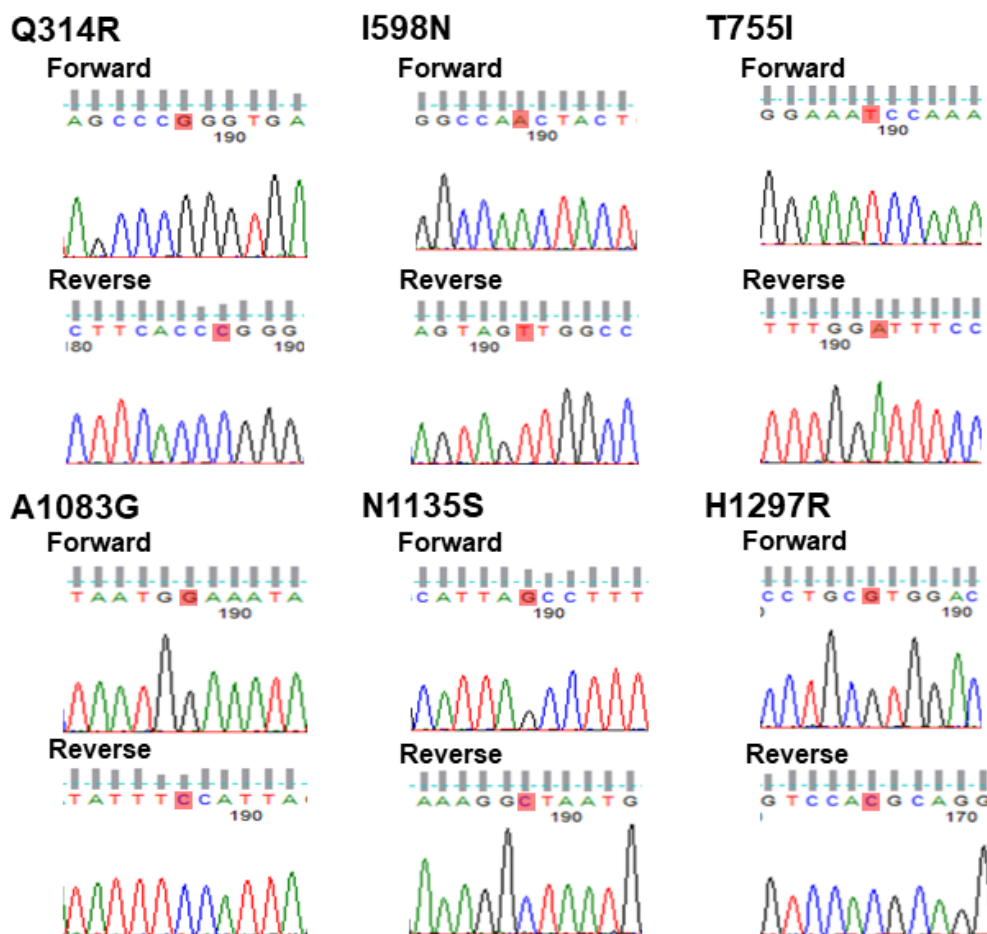
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Drug Metabolism and Disposition

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Supplementary Table 1. Primer sequences for mutagenesis.

Amino Acid Change	Forward primer (5' to 3')	Reverse primer (5' to 3')
Q314R	CTAGCCCCGGGTGAAGGACATTTTGG CTGATG	CTTCACCCGGGCTAGGCTGAGACC AGC
I598N	GAGGCCAACTACTGTGATGACATGC CTCTGG	ACAGTAGTTGGCCTCCCCCGTGGCA TG
T755I	ATGGAAATCCAAAGCATGCTTGTCG TTCCCAAGGG	GCTTTGGATTTCATATAAAAATGTT CTTGACCTCCCATATG
A1083G	CCTAATGGAAATATCTCTGGAGGTT CTGTGGTGGC	GATATTTCATTAGGGACAGTTTCT GTGCTTGTTCCACG
N1135S	AGCATTAGCCTTTCAGCTGTTGGAT ACTTCAGAGG	GCTGAAAGGCTAATGCTTTCATCAA AAGCAGTCTGTG
H1297R	GAGAGAGGCCTGCGTGGACCCTTG AC	GTCAAGGGTCCACGCAGGCCTCTC TC



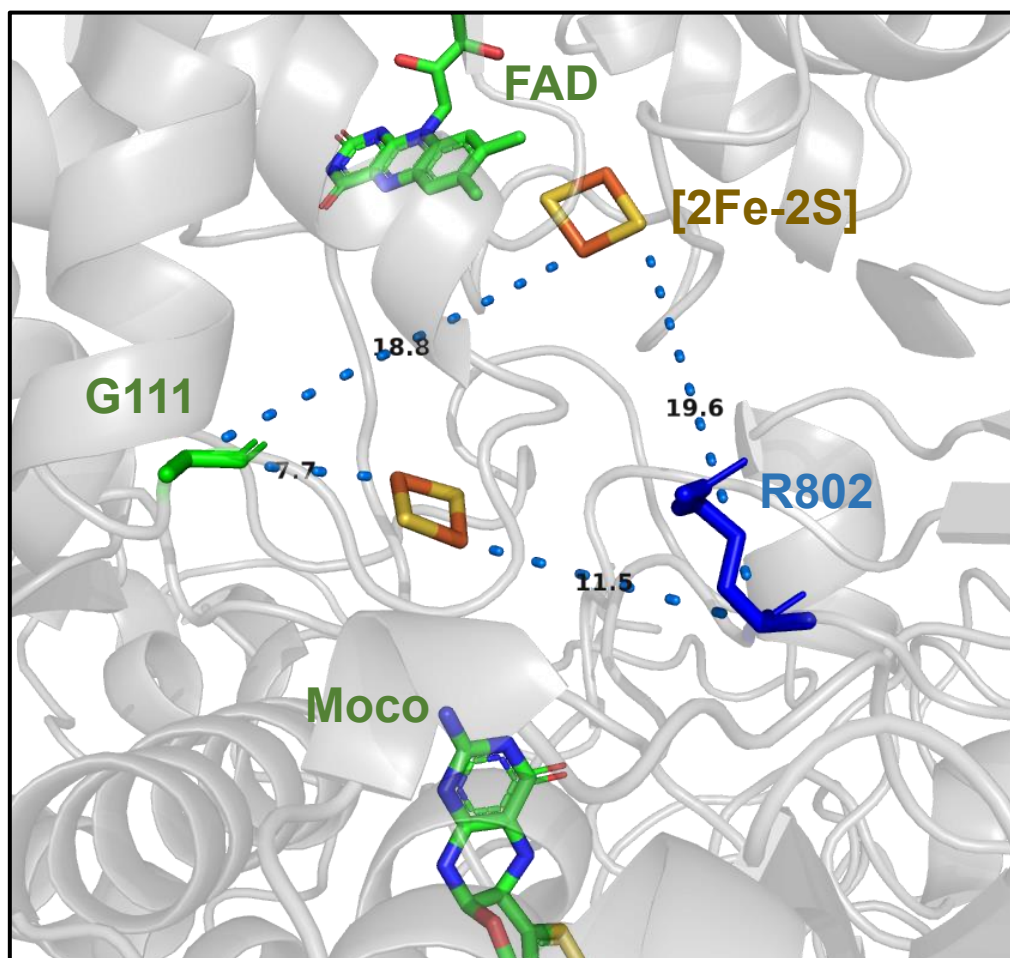
**Supplementary Figure 1. Electropherograms of the AOX1 SNPs: Q314R, I598N, T755I, A1083G, N1135S, and H1297R.**

The locations of SNPs are highlighted in red color.

*Homo sapiens* AOX1 : V D Q I L E G E I H M G G Q E H F Y M E T Q S M L V V P K G E D Q E M D V Y V S T Q : 755  
*Mus musculus* Aox1 : V D Q I L E G E I H I G G Q E H F Y M E T Q S M L V V P K G E D G E I D I Y V S T Q : 750  
*Mus musculus* Aox2 : V D Q V A E G T V H V G G Q E H F Y M E T Q R V L V I P K T E D K E L D M Y V S T Q : 761  
*Mus musculus* Aox3 : A D Q I L E G E V H L G G Q E H F Y M E T Q S V R V V P K G E D K E M D I Y V S S Q : 751  
*Mus musculus* Aox4 : V D Q I V E G E I H V E G Q E H F Y M E T Q T I L A I P Q T E D K E M V L H L G T Q : 753  
*Oryctolagus cuniculus* Aox1 : V D Q I L E G E I H M G G Q E H F Y M E T Q S V L V V P K G E D Q E M D V Y A S T Q : 751  
*Macaca mulatta* Aox1 : V D Q I L E G E I H M G G Q E H F Y M E T Q S M L V V P K G E D Q E M D V Y V S T Q : 755  
*Homo sapiens* XDH : A D N V V S G E I Y I G G Q E H F Y L E T H C T I A V P K G E A G E M E L F V S T Q : 747

**Supplementary Figure 2. Multiple protein sequence alignments of mammalian aldehyde oxidase (AOX) and xanthine dehydrogenase (XDH).**

Alignments were performed using Molecular Evolutionary Genetics Analysis version 11 under default parameters. The conserved threonine of AOX and XDH is highlighted in yellow. Multiple protein sequence alignments were performed among mammalian AOX and XDH (*Homo sapiens* AOX1, NP\_001150; *Mus musculus* Aox1, NP\_033806; *Mus musculus* Aox2, NP\_001008419; *Mus musculus* Aox3, NP\_076106; *Mus musculus* Aox4, NP\_076120; *Oryctolagus cuniculus* Aox1, NP\_001075459; *Macaca mulatta* Aox1, NP\_001268238; and *Homo sapiens* XDH, NP\_000370). Alignments were conducted using Molecular Evolutionary Genetics Analysis version 11 under default parameters (Tamura et al., 2021).



**Supplementary Figure 3. Location of G111 and R802 in wild-type (WT) AOX1.**

AOX1 (PDB:4UHW) is shown as a cartoon, and G111, R802, FAD, Moco, and the [2Fe-2S] cluster are shown as stick representations. The distance from the mutated amino acids to the [2Fe-2S] cluster is denoted by dashed lines.