SUPPLEMENTAL DATA

Naturally Occurring Variations in the Human *Cholinesterase* Genes: Heritability and Association with Cardiovascular and Metabolic Parameters

Anne M. Valle[1,5], Zoran Radić[1,5], Brinda K. Rana[3], Vafa Mahboubi[5], Jennifer Wessel[3], Pei-an Shih[2], Fangwen Rao[2], Daniel T. O'Connor[1,2,4], and Palmer Taylor[1,4,5].

Departments of Pharmacology[1], Medicine[2], Psychiatry[3], Institute for Genomic Medicine[4], and Skaggs School of Pharmacy and Pharmaceutical Sciences[5], University of California at San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0657

Running Title: Human *cholinesterase* variants and cardiovascular function

Corresponding author: Palmer Taylor, Ph.D
Skaggs School of Pharmacy & Pharmaceutical Sciences
University of California at San Diego
9500 Gilman Drive
La Jolla, CA 92093-0657
E-mail: pwtaylor@ucsd.edu
Phone: 858-534-1366

FAX : 858-534-8248

Table S1. *ACHE* SNP Results: Characteristics of single nucleotide polymorphisms discovered upon resequencing of human *ACHE* gene.

AChE gene ID:43

NT_007933.14, Reverse Complement

SNP #	SNP	Location	AA# in mature protein	AA # with signal peptide	dbSNP rs number	Contig position	Euro MA frequency	Afr-Am MA frequency	N
1	C/t	Intron 1	--	--	rs17880615	25727172	0.00	0.04	73
2	G/c	Intron 1	--	--	rs17883799	25727109	0.03	0.00	75
3	C/t	Intron 1	--	--	--	--	0.00	0.02	69
4	C/t	Intron 1	--	--	rs10953305	25726844	0.50	0.21	67
5*	G/a	Exon 2	Arg3Gln	Arg34Gln	rs17881553	25726029	0.00	0.09	74
6	G/c	Exon 2	Asp134His	Asp165His	--	--	0.05	0.02	71
7	G/a	Exon 2	Thr238Thr	Thr269Thr	rs17228581	25725323	0.00	0.05	79
8*	G/a	Exon 2	Glu313Glu	Glu344Glu	rs17880119	25725098	0.00	0.03	77
9*	C/a	Exon 2	His322Asn	His353Asn	rs1799805	25725073	0.03	0.02	76
10	G/a	Intron 2	--	--	--	--	0.00	0.05	76
11	G/c	Intron 2	--	--	--	--	0.00	0.02	78
12*	C/t	Exon 3	Pro446Pro	Pro477Pro	rs7636	25724353	0.03	0.22	76
13	C/g	Exon 5	Pro561Arg	Pro592Arg	rs1799806	25723862	0.42	0.12	77
14	C/a	Intron 5	--	--	--	--	0.00	0.02	75
15	G/a	3'-UTR	--	--	rs17228609	25722024	0.00	0.07	75
16*	C/a	3'-UTR	--	--	rs17228616	25721997	0.06	0.34	75
17	A/g	3'-UTR	--	--	rs2396755	25721796	0.10	0.28	63
18	C/a	3'-UTR	--	--	rs17880700	25721593	0.00	0.23	66
19	C/t	3'-UTR	--	--	rs17885823	25721577	0.00	0.13	67

*SNPs used to impute *ACHE* haplotypes in Table 2. N = number of individuals re-sequenced. AA#: amino acid number. Euro/Afr-Am MA Frequency = minor allele frequency in subjects of European versus African-American ancestry.

Table S2. Kinetic Parameters for wtT547 and Mutant Enzymes.

Enzyme	K_m (mM)	Kss (mM)	b	k_{cat} (10^5/min)
wtT547	0.13 ± 0.01	11 ± 2	0.036 ± 0.03	1.9 ± 0.2
R3Q	0.15 ± 0.02	8.6 ± 1.6	0.086 ± 0.03	1.8 ± 0.1
D134H	0.17 ± 0.02	11 ± 3	0.11 ± 0.04	2.0 ± 0.4
H322N	0.14 ± 0.02	8.4 ± 2.4	0.096 ± 0.04	1.9 ± 0.2
D134H/R136Q	0.14 ± 0.02	16 ± 4	0.062 ± 0.05	1.8 ± 0.1

Values for K_m, K_{ss}, and b were calculated using nonlinear computer fitting according to eq I in figure 4 of the manuscript. k_{cat} was determined by stoichiometric titration of AChE activity with the covalent organophosphate inhibitor SpDMB.

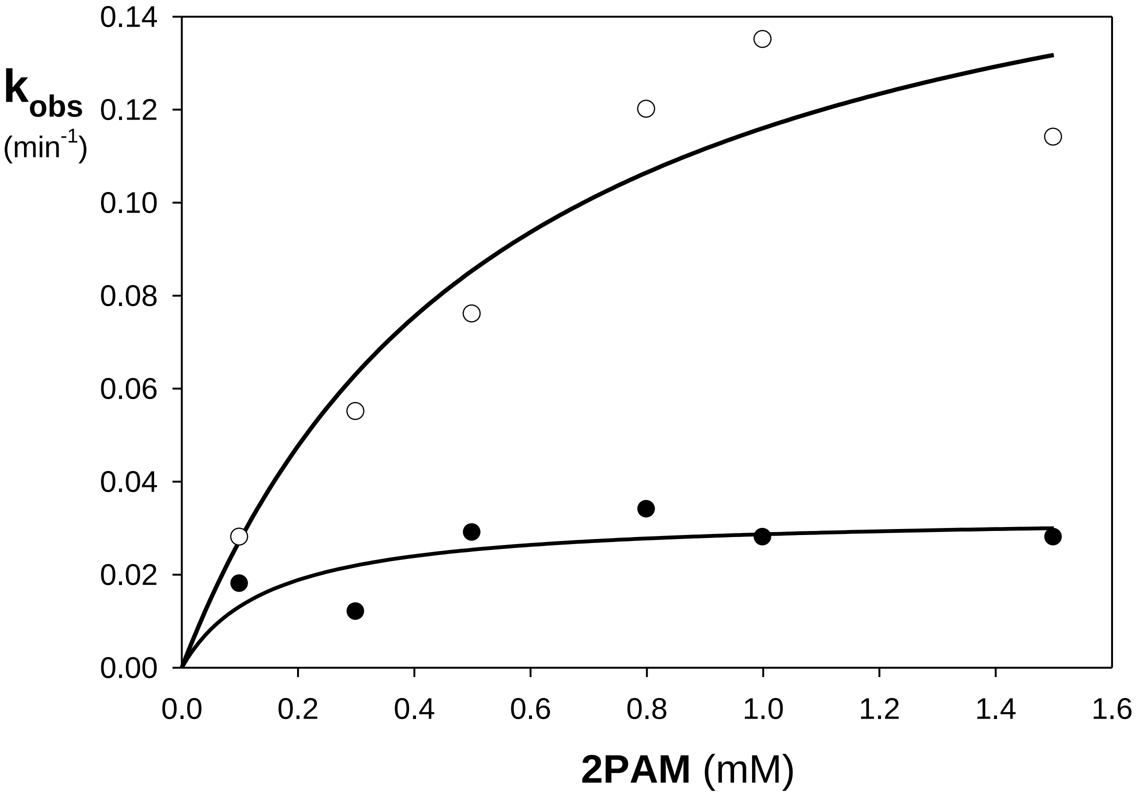

Fig. S1. Reactivation of paraoxon-inhibited wild-type (●) and D134H (○) hAChE by different 2PAM concentrations. Dependence of the first order reactivation rate constants (k_{obs}) determined for individual 2PAM concentrations is given. Nonlinear regression analysis (Kovarik, 2004) yielded the following kinetic constants: k_{+2} = (0.033±0.007) min^{-1}, K_{ox} = (0.15±0.14) mM, k_r = 220 M^{-1}min^{-1} for wild type hAChE and k_{+2} = (0.18±0.04) min^{-1}, K_{ox} = (0.56±0.31) mM, k_r =320 M^{-1}min^{-1} for D134H hAChE.