

Supplemental Material

An Investigation of Modifying Effects of Metallothionein Single Nucleotide Polymorphisms on the Association between Mercury Exposure and Biomarker Levels

Author and Affiliations

Yi Wang¹, Jaclyn M. Goodrich¹, Brenda Gillespie², Robert Werner^{1,3}, Niladri Basu¹, Alfred Franzblau^{1*}

¹ Department of Environmental Health Sciences, School of Public Health, University of Michigan, Ann Arbor

² Department of Biostatistics, School of Public Health, University of Michigan, Ann Arbor

³ Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor

University of Michigan School of Public Health, 1415 Washington Heights, Ann Arbor, MI USA 48109

* Corresponding author:

Alfred Franzblau, M.D.

M6023 SPH II, 1415 Washington Heights, University of Michigan School of Public Health, Ann Arbor, MI 48109-2029, USA

Email: af Franz@umich.edu

Office: +1 (734)936-0758 Fax: +1 (734)763-8095

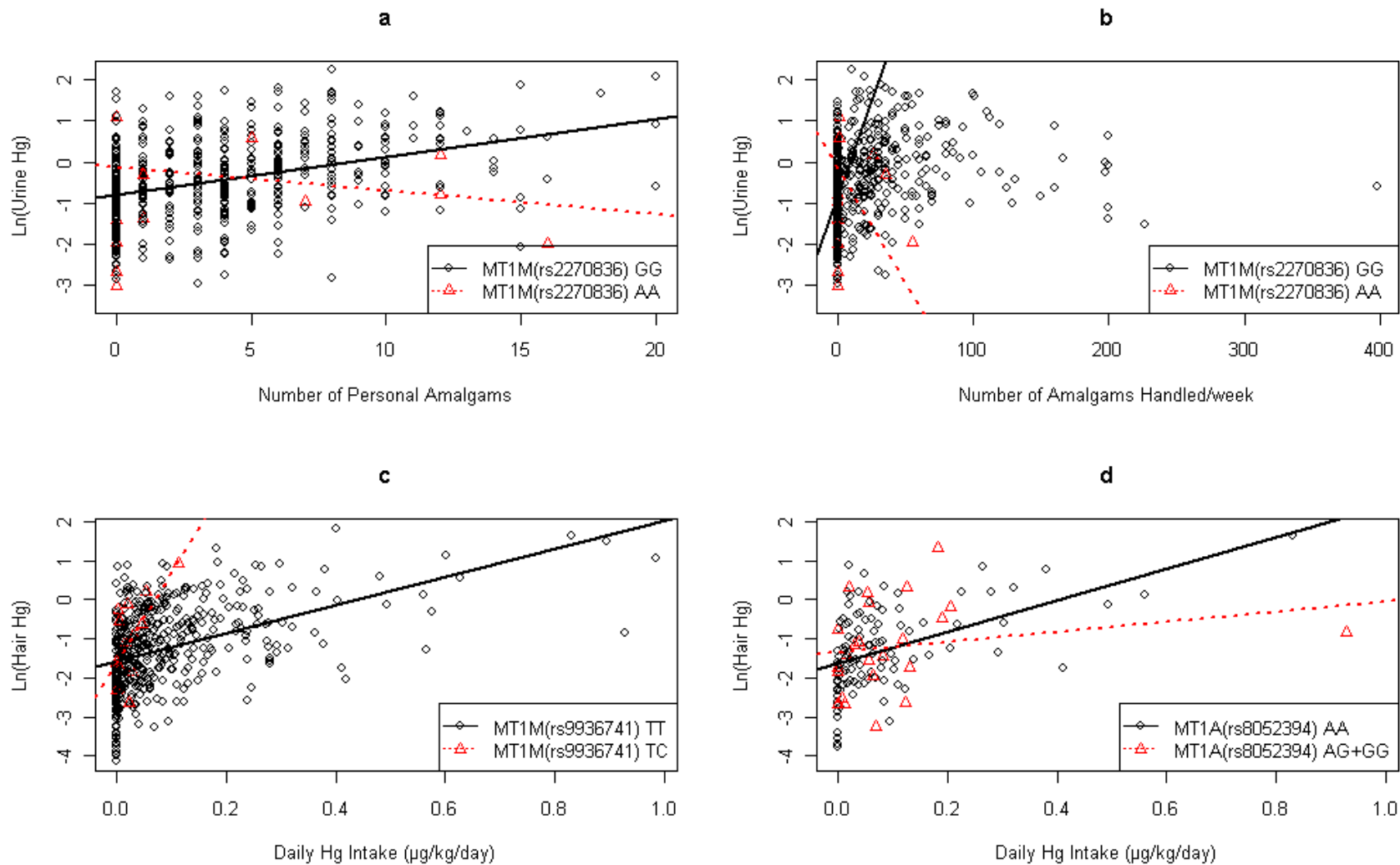
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Supplemental Material, Table 1. Summary of Average Hg Concentrations in Fish species

Fish Species	Average Concentration (µg Hg/g)	Source	Year of Data	Number of Samples Averaged
Tuna White(canned)	0.356	FDA Monitoring Program ^a	2003	27
Tuna Light(canned)	0.258	FDA monitoring program	2003	12
Tuna Fresh	0.647	FDA monitoring program	2001-2004	9
Salmon	0.015	FDA monitoring program	2003	1
Shrimp	0.028	FDA monitoring program	1993-1995	2
Cod	0.084	FDA monitoring program	2004	19
Crab	0.049	FDA monitoring program	2004-2005	4
Scallop	0	FDA monitoring program	1991	1
Mussel	0.091	Mierzykowski et al. 2001	-	-
Halibut	0.232	FDA monitoring program	2004	14
Lobster	0.224	FDA monitoring program	2004	10
Clam	0	FDA monitoring program	1991-1993	6
Oyster	0.014	FDA monitoring program	2004	4
Perch	0.005	FDA monitoring program	1991, 1994	6
Perch Freshwater	0.141	FDA monitoring program	1991, 1995	5
Trout	0.111	FDA monitoring program	2002-2004	17
Carp	0.271	FDA monitoring program	1993	1
Walleye	0.065	FDA monitoring program	1991-1994	4
Seabass	0.679	FDA monitoring program	1996-1997	3
Fresh Seabass	0.38	Bahnick et al. 1994	-	-
Pike	0.31	Bahnick et al. 1994	-	-
Swordfish	1.312	FDA monitoring program	2002-2004	13
Red Snapper	0.193	FDA monitoring program	2002-2004	36
Shark	1.086	FDA monitoring program	1992-2000	29
King Mackerel	0.73	American Heart Association Fish 101 ^b	-	-
Porgy	0.522	NOAA Technical Report 1978	-	-
Tilapia	0.01	FDA monitoring program	1991-1992	9
Whitefish	0.074	FDA monitoring program	2002-2004	19

^a US Food and Drug Administration 1990-2010

^b American Heart Association 20 May 2010

Supplemental Material, Table 2. Arithmetic Mean Urine Hg levels ($\mu\text{g/L}$) Stratified by Levels of Elemental Hg Exposures from Occupational Practice and Personal Amalgam

Amalgam handled/wk (N)	Urine Hg (SD)($\mu\text{g/L}$)*	Personal amalgam (N)	Urine Hg (SD) ($\mu\text{g/L}$)*
0 (215)	0.70(0.71)	0 (128)	0.61(0.79)
1-20 (102)	1.16(1.48)	1-3 (127)	0.91(0.90)
21-45 (102)	1.36(1.32)	4-6 (132)	1.11(1.32)
≥ 46 (82)	1.50(1.62)	≥ 7 (114)	1.67(1.61)

* Cochran-Armitage trend test : $p < 0.05$

SD: standard deviation

Supplemental Material, Table 3. Mean Hair Hg Levels ($\mu\text{g/g}$) Stratified by Levels of Estimated Methylmercury Intake from Dietary Fish Consumption

Hair Hg ($\mu\text{g/g}$)	Daily MeHg Intake (I) ($\mu\text{g/kg/day}$)	Mean Hair Hg
	(N)	(SD)*
	0 \leq I<0.01 (145)	0.22 (0.28)
	0.01 \leq I<0.05 (137)	0.39 (0.39)
	0.05 \leq I<0.12 (112)	0.56 (0.48)
	I \geq 0.12 (109)	0.91 (1.02)

* Cochran-Armitage linear trend test: $p < 0.05$
SD: standard deviation

Supplemental Material, Table 4: Arithmetic Mean Urinary Hg Levels ($\mu\text{g/L}$) and Hair Hg Levels ($\mu\text{g/g}$) Stratified by Genotypes of Selected Metallothionein SNPs

SNP name	db SNP	N	Mean Urinary Hg ($\mu\text{g/L}$)				Mean Hair Hg ($\mu\text{g/g}$)				
			Homozygote (N)	Heterozygote (N)	Homozygote variant (N)	ANOVA <i>p</i>	N	Homozygote (N)	Heterozygote (N)	Homozygote variant (N)	ANOVA <i>p</i>
SNPs Analyzed in Both 2009-2010											
MT2A 3'UTR(G>C)	rs10636	464	1.04(251)	1.04(171)	1.22(42)	0.65	473	0.50(254)	0.43(174)	0.57(45)	0.28
MTF1 3'UTR(G>A)	rs473279	463	1.04(215)	1.06(206)	1.17(42)	0.81	472	0.47(217)	0.51(212)	0.43(43)	0.64
MT1M 3'UTR(T>C)	rs9936741	465	1.05(449)	1.09(16)	-	0.88	474	0.48(459)	0.55(15)	-	0.65
MT1M 3'UTR(G>A)	rs2270836	460	1.04(329)	1.10(120)	0.98(11)	0.88	469	0.47(337)	0.51(122)	0.33(10)	0.69
MT1A missense(A>C)	rs11640851	447	1.03(190)	1.09(202)	0.97(55)	0.76	454	0.44(194)	0.51(205)	0.52(55)	0.51
SNPs Analyzed in 2009											
MTF1 3'UTR(T>C)	rs3748682	220	1.17(125)	1.05(81)	1.15(14)	0.78	221	0.48(127)	0.63(81)	0.44(13)	0.30
MT1M missense(A>C)	rs1827210	221	1.09(162)	1.22(51)	1.13(9)	0.81	223	0.50(165)	0.67(50)	0.32(8)	0.26
MT1G 3'UTR(G>T)	rs12315	222	1.11(201)	1.18(20)	0.54(1)	0.87	223	0.53(202)	0.56(20)	1.72(1)	0.26
MT1E 3'UTR(G>T)	rs708274	223	1.12(171)	1.13(49)	0.48(3)	0.67	224	0.55(174)	0.50(47)	0.34(3)	0.81
MT4 missense(G>A)	rs11643815	221	1.07(167)	1.20(51)	1.96(3)	0.39	222	0.53(166)	0.55(52)	0.33(4)	0.84
SNPs Analyzed in 2010											
MT2A 5'UTR(A>G)	rs28366003	239	1.03(213)	0.76(24)	0.34(2)	0.40	247	0.44(220)	0.39(25)	0.43(2)	0.88
MT1A missense(A>G)	rs8052394	131	0.95(109)	0.89(21)	0.28(1)	0.82	136	0.50(113)	0.44(22)	0.16(1)	0.87
MT1A 5'near gene(C>G)	rs9922957	234	1.02(180)	0.95(50)	0.69(4)	0.82	242	0.45(184)	0.37(54)	0.43(4)	0.60

^aWhen number of homozygote variant is smaller than 9 and 8 for urine Hg and hair Hg, respectively, the ANOVA results shown are for comparing homozygote and the pooled heterozygote and homozygote variant.

Supplemental Material, Table 5: Coefficients and p Values from Multivariate Linear Regression Models of Natural Log-transformed Urinary Hg Predicted against Exposure Surrogates of Elemental Hg, SNP Genotypes and Exposure-SNP Interactions

SNP name	db SNP	R ²	Base model						SNP main effects				
			Personal Amalgam		Amalgam handled/week		Nondentist		Heterozygote		Homozygote variant		
			β	<i>p</i>	β	<i>p</i>	β	<i>p</i>	β	<i>p</i>	β	<i>p</i>	
2009-2010													
MT2A 3'UTR(G>C)	rs10636	0.24	0.080	<0.0001	0.06	0.37	-0.54	0.0002	-0.19	0.41	-0.02	0.96	
MTF1 3'UTR(G>A)	rs473279	0.24	0.086	<0.0001	0.18	0.01	-0.28	0.06	0.36	0.11	0.28	0.43	
MT1M 3'UTR(T>C)	rs9936741	0.24	0.081	<0.0001	0.13	0.01	-0.42	<0.0001	0.52	0.44	-	-	
MT1M 3'UTR(G>A)	rs2270836	0.25	0.085	<0.0001	0.11	0.04	-0.38	0.001	-0.04	0.87	1.85	0.01	
MT1A missense(A>C)	rs11640851	0.24	0.084	<0.0001	0.15	0.02	-0.40	0.007	0.12	0.60	0.36	0.32	
2009													
MTF1 3'UTR(T>C)	rs3748682	0.24	0.069	<0.0001	0.04	0.71	-0.69	0.003	-0.62	0.10	-0.32	0.75	
MT1M missense(A>C)	rs1827210	0.24	0.068	<0.0001	0.14	0.13	-0.37	0.08	-0.33	0.42	1.00	0.20	
MT1G 3'UTR(G>T)	rs12315	0.24	0.063	<0.0001	0.15	0.06	-0.41	0.02	-0.34	0.54	-	-	
MT1E 3'UTR(G>T)	rs708274	0.23	0.076	<0.0001	0.15	0.09	-0.32	0.11	0.21	0.61	-	-	
MT4 missense(G>A)	rs11643815	0.23	0.063	<0.0001	0.13	0.14	-0.39	0.04	-0.40	0.38	-	-	
2010													
MT2A 5'UTR(A>G)	rs28366003	0.26	0.091	<0.0001	0.09	0.13	-0.54	0.0001	-0.43	0.32	-	-	
MT1A missense(A>G)	rs8052394	0.23	0.127	<0.0001	0.06	0.4	-0.43	0.02	0.46	0.40	-	-	
MT1A 5'near gene(C>G)	rs9922957	0.24	0.100	<0.0001	0.048	0.45	-0.48	0.0007	0.06	0.87	-	-	

Supplemental Material, Table 5 (Cont.): Coefficients and p Values from Multivariate Linear Regression Models of Natural Log-transformed Urinary Hg Predicted against Exposure Surrogates of Elemental Hg, SNP Genotypes and Exposure-SNP Interactions

SNP name	db SNP	SNP-exposure interactions											
		Amalgam X heterozygote		Amalgam handled X heterozygote		Nondentist X heterozygote		Amalgam X homozygote variant		Amalgam handled X homozygote variant		Nondentist X homozygote variant	
		β	<i>p</i>	β	<i>p</i>	β	<i>p</i>	β	<i>p</i>	β	<i>p</i>	β	<i>p</i>
2009-2010													
MT2A 3'UTR(G>C)	rs10636	-0.005	0.80	0.13	0.17	0.23	0.29	0.04	0.27	0.007	0.96	-0.002	0.99
MTF1 3'UTR(G>A)	rs473279	-0.012	0.55	-0.15	0.12	-0.36	0.09	0.004	0.91	-0.11	0.49	-0.20	0.56
MT1M 3'UTR(T>C)	rs9936741	-0.01	0.86	-0.22	0.41	-0.60	0.27	-	-	-	-	-	-
MT1M 3'UTR(G>A)	rs2270836	-0.002	0.92	0.11	0.32	-0.03	0.90	-0.25	0.02	-0.97	0.01	-0.05	0.94
MT1A missense(A>C)	rs11640851	-0.003	0.88	-0.055	0.58	-0.09	0.70	-0.013	0.71	-0.12	0.40	-0.13	0.69
2009													
MTF1 3'UTR(T>C)	rs3748682	0.011	0.73	0.23	0.18	0.68	0.06	0.02	0.86	0.20	0.60	0.56	0.43
MT1M missense(A>C)	rs1827210	0.009	0.76	0.25	0.20	0.25	0.55	-0.01	0.90	-0.63	0.15	-0.41	0.54
MT1G 3'UTR(G>T)	rs12315	0.06	0.13	-0.20	0.63	-0.12	0.84	-	-	-	-	-	-
MT1E 3'UTR(G>T)	rs708274	-0.009	0.78	0.03	0.90	-0.24	0.56	-	-	-	-	-	-
MT4 missense(G>A)	rs11643815	0.04	0.23	0.15	0.45	0.16	0.72	-	-	-	-	-	-
2010													
MT2A 5'UTR(A>G)	rs28366003	0.03	0.60	-0.08	0.63	0.45	0.22	-	-	-	-	-	-
MT1A missense(A>G)	rs8052394	-0.09	0.09	0.04	0.86	-0.05	0.92	-	-	-	-	-	-
MT1A 5'near gene(C>G)	rs9922957	-0.03	0.45	0.08	0.56	-0.04	0.90	-	-	-	-	-	-

^a When number of homozygote variant is smaller than 9, the ANOVA results shown is for comparing homozygote and the pooled heterozygote and homozygote variant.

Supplemental Material, Table 6: Coefficients and p Values from Multivariate Linear Regression Models of Natural Log-transformed Hair Hg Predicted by Estimated Methylmercury Exposure, SNP Genotypes and Intake-SNP Interactions

SNP Name	db SNP	Base model			SNP main effects				SNP-intake interactions				
		R ²	Estimated Daily MeHg Intake		Heterozygote		Homozygote variant		Intake X Heterozygote		Intake X homozygote variant		
			β	p	β	p	β	p	β	p	β	p	
2009-2010													
MT2A 3'UTR(G>C)	rs10636	0.19	3.52	<0.0001	-0.15	0.17	-0.10	0.56	0.38	0.65	0.45	0.68	
MTF1 3'UTR(G>A)	rs473279	0.19	4.52	<0.0001	0.13	0.23	-0.14	0.50	1.42	0.06	0.15	0.93	
MT1M 3'UTR(T>C)	rs9936741	0.20	3.69	<0.0001	-0.03	0.92	-	-	19.3	0.02	-	-	
MT1M 3'UTR(G>A)	rs2270836	0.19	3.93	<0.0001	-0.04	0.72	-0.14	0.78	-0.67	0.36	-5.33	0.68	
MT1A missense(A>C)	rs11640851	0.18	3.74	<0.0001	-0.007	0.95	-0.09	0.61	-0.24	0.78	-0.22	0.84	
2009													
MTF1 3'UTR(T>C)	rs3748682	0.24	4.97	<0.0001	0.32	0.06	0.21	0.57	-1.63	0.13	1.23	0.73	
MT1M missense(A>C)	rs1827210	0.23	4.4	<0.0001	0.05	0.81	-0.05	0.93	-0.61	0.56	-1.36	0.98	
MT1G 3'UTR(G>T)	rs12315	0.23	4.21	<0.0001	0.30	0.38	-	-	-1.45	0.52	-	-	
MT1E 3'UTR(G>T)	rs708274	0.24	4.79	<0.0001	-0.05	0.77	-	-	-1.57	0.13	-	-	
MT4 missense(G>A)	rs11643815	0.24	3.97	<0.0001	-0.23	0.21	-	-	0.73	0.54	-	-	
2010													
MT2A 5'UTR(A>G)	rs28366003	0.14	3.08	<0.0001	-0.17	0.51	-	-	0.97	0.60	-	-	
MT1A missense(A>G)	rs8052394	0.21	4.04	<0.0001	0.21	0.40	-	-	-300	0.02	-	-	
MT1A 5'near gene(C>G)	rs9922957	0.15	3.52	<0.0001	-0.22	0.19	-	-	-1.04	0.36	-	-	

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