

***Glutathione S-Transferase P1, Maternal Smoking and Asthma in Children: A  
Haplotype-Based Analysis***

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**SUPPLEMENTAL MATERIAL**

Supplemental Material, Table 1. Primers and probes for genotyping four *GSTP1* htSNPs.

GSTP1 SNPs	Base change	Primer/probe sequences
rs6591255	T → A	<p>Forward primer: 5' - CCCCCGATAATAAGTCTCTTAAAAA-3'</p> <p>Reverse primer: 5' -CACCGAAGACACGAGTTTACTTATG-3'</p> <p>T probe: 5'-(6FAM)ACTTTTATTTCT<u>G</u>TTTTTGGG-3'</p> <p>A probe: 5'-(VIC)ACTTTTATTTCA<u>G</u>TTTTTGGG-3'</p>
rs4147581	C → G	<p>Forward primer: 5' -CGCGCCTTGGCATCCT-3'</p> <p>Reverse primer: 5' -CTGGGAAATAGACCACGGTGTAG-3'</p> <p>C probe: 5'-(6FAM)TCCAGCAA<u>A</u>CTTTT-3'</p> <p>G probe: 5'-(VIC)TCCAGCAA<u>A</u>GTTTT-3'</p>
rs1695 (codon 105)	A → G (amino acid:	<p>Forward primer: 5' -CCTGGTGGACATGGTGAATG-3'</p> <p>Reverse primer: 5' -TGCTCACATAGTTGGTGTAGATGA-3'</p>

Ile → Val)

A probe: 5'-(6FAM)TGCAAATACATCTCCCT-3'

G probe: 5'-(VIC)CTGCAAATACGTCTCC-3'

rs749174

C → T

Forward primer: 5'-TCAATGGCCCCCATTGC-3'

Reverse primer: 5'-CGGGTGGGTAAGGAGATAGAGA-3'

C probe: 5'-(6FAM)AGACTCCAAACCAGTGG-3'

T probe: 5'-(VIC)AGACTCCAAACTAGTGG-3'

Supplemental Material, Table 2. Multiple logistic-regression models considering two potential functional *GSTP1* SNPs <sup>a</sup> by the two independent CHS cohorts.

Ethnicity and outcome	Cohort I (recruited in 1993)			Cohort II (recruited in 1996)		
	SNP#1	SNP#3	LRT <sup>b</sup>	SNP#1	SNP#3	LRT <sup>b</sup>
	OR (95% CI)	OR (95% CI)	p-value	OR (95% CI)	OR (95% CI)	p-value
Non-Hispanic + Hispanic whites <sup>c</sup>						
Lifetime diagnosis of asthma	1.2(0.8,1.7)	1.2(0.8,1.6)	0.065	1.6(1.0,2.4) *	0.9(0.6,1.3)	0.074
Early onset asthma	1.1(0.6,1.8)	1.3(0.7,2.1)	0.203	1.3(0.7,2.2)	1.1(0.6,1.9)	0.368
Late onset asthma	1.3(0.8,2.0)	1.1(0.6,1.6)	0.187	2.0(1.1,3.5) *	0.7(0.3,1.1)	0.062
Current wheezing	1.4(1.0,1.9) *	0.9(0.6,1.2)	0.074	1.5(1.0,2.2) *	0.8(0.5,1.1)	0.091
Medication for wheeze	1.5(0.9,2.1)	1.0(0.6,1.5)	0.045	2.2(1.3,3.6) *	0.7(0.4,1.1)	0.007
Non-Hispanic whites <sup>d</sup>						
Lifetime diagnosis of asthma	1.4(0.8,2.2)	1.0(0.6,1.5)	0.117	1.9(1.0,3.3) *	0.9(0.5,1.4)	0.069
Early onset asthma	1.3(0.6,2.6)	1.3(0.6,2.4)	0.142	1.2(0.5,2.6)	1.3(0.6,2.5)	0.405
Late onset asthma	1.4(0.7,2.4)	0.9(0.5,1.5)	0.447	3.2(1.4,7.1) *	0.5(0.2,1.0)	0.017

Current wheezing	1.7(1.1,2.6) *	0.8(0.5,1.2)	0.018	1.6(0.9,2.7)	0.7(0.4,1.1)	0.178
Medication for wheeze	1.7(1.0,3.0) *	0.9(0.5,1.4)	0.045	2.1(1.0,4.1) *	0.7(0.4,1.3)	0.072
Hispanic whites <sup>d</sup>						
Lifetime diagnosis of asthma	1.2(0.7,2.1)	1.6(0.8,3.1)	0.120	1.3(0.7,2.4)	0.9(0.4,1.7)	0.691
Early onset asthma	1.0(0.4,2.1)	1.3(0.5,3.0)	0.861	1.3(0.5,3.0)	1.0(0.4,2.5)	0.790
Late onset asthma	1.6(0.7,3.3)	2.2(0.8,5.7)	0.041	1.2(0.4,2.7)	0.9(0.3,2.2)	0.939
Current wheezing	1.1(0.6,1.7)	1.0(0.5,1.6)	0.968	1.5(0.8,2.6)	1.1(0.5,2.0)	0.342
Medication for wheeze	1.4(0.7,2.5)	1.2(0.5,2.4)	0.446	2.1(0.9,4.5)	0.7(0.3,1.6)	0.143

<sup>a</sup> SNP#1 (rs6591255): T→A; SNP#3 (rs1695): A→G

<sup>b</sup> LRT (likelihood ratio test): comparing the model with the two *GSTPI* SNPs with the model without the *GSTPI* SNPs.

<sup>c</sup> Models are adjusted for communities of residence, gender, age, gestational age, smoke exposure and Hispanic ethnicity.

<sup>d</sup> Models are adjusted for communities of residence, gender, age, gestational age and smoke exposure.

\* p<0.05 although the confidence upper/lower limit is 1.0

Supplemental Material, Table 3. The association of four *GSTP1* htSNPs with asthma and wheezing among 579 child-parent trios from the CHS. <sup>a</sup>

	<u>SNP#1</u>	<u>SNP#2</u>	<u>SNP#3</u>	<u>SNP#4</u>
<u>Outcome</u>	<u>OR (95% CI)</u>	<u>OR (95% CI)</u>	<u>OR (95% CI)</u>	<u>OR (95% CI)</u>
Lifetime diagnosis of asthma	1.6 (1.0, 2.5)	0.8 (0.5, 1.2)	1.2 (0.7, 1.9)	1.8 (1.0, 2.8)
Early onset asthma	1.8 (0.9, 3.2)	0.7 (0.3, 1.1)	1.5 (0.8, 2.7)	1.9 (1.0, 3.4)
Late onset asthma	1.5 (0.8, 2.8)	0.9 (0.5, 1.5)	1.1 (0.5, 2.0)	1.6 (0.8, 3.3)
Current wheezing	1.5 (0.9, 2.2)	0.8 (0.5, 1.2)	1.4 (0.8, 2.1)	2.2 (1.3, 3.5)
Medication for wheeze	1.9 (1.1, 3.1)	0.9 (0.5, 1.3)	1.6 (0.9, 2.7)	2.7 (1.4, 4.7)

<sup>a</sup> Models are adjusted for ethnicity, communities of residence, gender, age, gestational age, smoke exposure and parental mating types.

Supplemental Material, Table 4. Selected characteristics of CHS genetic study participants with and without available DNA.

Demographic characteristics/ Respiratory outcomes	Not in genetic study	In genetic study
Total	3177	3082
Demographic characteristics		
Female, %	50.4	53.3
Age at study entry (yrs)		
8-<10, %	41.2	52.2
10-<12, %	21.6	21.7
12-<14, %	17.8	14.3
14-18, %	19.4	11.8
Gestational Age		
Full term, %	90.7	88.9
<4 weeks early, %	5.8	6.9
≥4 weeks early, %	3.5	4.2
Tobacco-smoke exposure		
<i>In utero</i> , %	19.0	17.0
Respiratory outcomes		
Lifetime diagnosis of asthma, %	13.7	15.0
Current wheezing, %	21.7	23.4

Supplemental Material, Table 5. The comparison of association (odds ratio (OR) and 95% confidence interval (CI)) of common GSTP1 haplotypes between lifetime diagnosis of asthma and current asthma in CHS participants.

Haplotype	Lifetime diagnosis	Current
	of asthma	asthma <sup>a</sup>
<u>All Whites</u>	<u>OR (95% CI)</u>	<u>OR (95% CI)</u>
h0100	1.0	1.0
h0000	1.1 (0.8, 1.4)	0.9 (0.6, 1.5)
h0010	0.9 (0.7, 1.3)	1.3 (0.8, 1.9)
h1000	1.3 (1.0, 1.7)	1.3 (0.8, 1.9)
h1011	1.2 (1.0, 1.5)	1.3 (1.0, 1.7)
Others	1.0 (0.7, 1.6)	1.1 (0.6, 2.1)

<sup>a</sup> Current asthma was defined as lifetime diagnosis of asthma excluding early transient wheezing