

Supplementary Information

Table S1. Lung cancer risk by *CYP2B6*, *CYP2A6* and *CHRNA5-A3-B4* genotype group.

Genotype Group	Cases, <i>n</i>	Controls, <i>n</i>	OR (95% CI) [†]	Adjusted OR (95% CI) [‡]
<i>CYP2B6</i>				
*6/*6	20	25	1.0 (ref)	1.0 (ref)
*1/*1, *1/*6	378	396	1.19 (0.65–2.18)	1.25 (0.68–2.30)
<i>CYP2A6</i>				
reduced metabolizer	72	94	1.0 (ref)	1.0 (ref)
normal metabolizer	326	327	1.30 (0.92–1.83)	1.27 (0.90–1.80)
<i>CHRNA5-A3-B4</i>				
rs1051730 GG/GA	330	372	1.0 (ref)	1.0 (ref)
rs1051730 AA	68	49	1.56 (1.05–2.32)	1.56 (1.05–2.33)

OR: Odds ratio; 95% CI: 95% confidence interval; [†] Odds ratios estimated by logistic regression modeling;

[‡] Adjusted for age, gender, log cigarette pack-years.

Table S2. Lung cancer risk by combined genotype group for each gene pair.

Genotype Group ^a	Cases, <i>n</i>	Controls, <i>n</i>	OR (95% CI) [†]	Adjusted OR (95% CI) [‡]
<i>CYP2B6</i> & <i>CYP2A6</i>				
0 risk genotypes	2	6	1.0 (ref)	1.0 (ref)
1 risk genotype	88	107	2.47 (0.49–12.5)	2.51 (0.49–12.8)
2 risk genotypes	308	308	3.00 (0.60–15.0)	3.03 (0.60–15.2)
0 or 1 risk, pooled ^b	90	113	1.0 (ref)	1.0 (ref)
2 risk genotypes	308	308	1.26 (0.91–1.73)	1.25 (0.91–1.72)
<i>CYP2B6</i> & <i>A5-A3-B4</i>				
0 risk genotypes	16	23	1.0 (ref)	1.0 (ref)
1 risk genotype	318	351	1.30 (0.68–2.51)	1.39 (0.72–2.70)
2 risk genotypes	64	47	1.96 (0.93–4.11)	2.07 (0.98–4.37)
<i>CYP2A6</i> & <i>A5-A3-B4</i>				
0 risk genotypes	64	83	1.0 (ref)	1.0 (ref)
1 risk genotype	274	300	1.18 (0.82–1.71)	1.16 (0.80–1.68)
2 risk genotypes	60	38	2.05 (1.22–3.44)	2.02 (1.19–3.43)

OR: Odds ratio; 95% CI: 95% confidence interval; ^a Risk genotype groups: *CYP2B6* *1/*1, *1/*6; *CYP2A6* normal metabolizer; *CHRNA5-A3-B4* AA; ^b Pooled those with 0 or 1 risk genotypes due to the small size of the 0 risk genotype reference group; [†] Odds ratios estimated by logistic regression modeling; [‡] Adjusted for age, gender, log cigarette pack-years.

Table S3. Combined lung cancer risk by genotype group for all three genes.

Genotype Group ^a	Cases, <i>n</i>	Controls, <i>n</i>	Adjusted OR (95% CI) [†]	<i>p</i> value [‡]
<i>CYP2B6</i> , <i>CYP2A6</i> , <i>A5-A3-B4</i>				
0 risk genotypes	2	5	1.0 (ref)	0.06
1 risk genotype	76	97	2.05 (0.39–10.9)	
2 risk genotypes	264	282	2.43 (0.47–12.7)	
3 risk genotypes	56	37	3.94 (0.72–21.5)	
0 or 1 risk genotype, pooled ^b	78	102	1.0 (ref)	0.03
2 risk genotypes	264	282	1.22 (0.87–1.71)	
3 risk genotypes	56	37	1.97 (1.18–3.30)	

OR: Odds ratio; 95% CI: 95% confidence interval; ^a Risk genotype groups: *CYP2B6* *1/*1, *1/*6; *CYP2A6* normal metabolizer; *CHRNA5-A3-B4* AA; ^b Pooled those with 0 or 1 risk genotypes due to the small size of the 0 risk genotype reference group; [†] Odds ratios estimated by logistic regression modeling and adjusted for age, gender, log cigarette pack-years. [‡] Post-estimation Wald test comparing odds ratios for each risk group.

Table S4. Lung cancer risk within the lighter-smoking stratum (cigarettes per day ≤20).

Genotype Group	Cases, <i>n</i>	Controls, <i>n</i>	OR (95% CI) [†]	Adjusted OR (95% CI) [‡]
<i>CYP2B6</i>				
*6/*6	7	11	1.0 (ref)	1.0 (ref)
*1/*1, *1/*6	192	210	1.44 (0.55–3.78)	1.54 (0.58–4.08)
<i>CYP2A6</i>				
reduced metabolizer	40	65	1.0 (ref)	1.0 (ref)
normal metabolizer	159	156	1.66 (1.05–2.60)	1.65 (1.05–2.60)
<i>CHRNA5-A3-B4</i>				
rs1051730 GG/GA	172	201	1.0 (ref)	1.0 (ref)
rs1051730 AA	27	20	1.58 (0.85–2.91)	1.58 (0.85–2.94)

OR: Odds ratio; 95% CI: 95% confidence interval; [†] Odds ratios estimated by logistic regression modeling.

[‡] Adjusted for age, gender, log cigarette pack-years.