

**Table S1. Characteristics of the study population used in this study.**

| Variables             | Discovery cohort |             | GWAS-NJMU <sup>a</sup> |              | GWAS-SLD <sup>b</sup> |              | GWAS-CADM <sup>c</sup> |              | GWAS-FLCCA <sup>d</sup> |               |
|-----------------------|------------------|-------------|------------------------|--------------|-----------------------|--------------|------------------------|--------------|-------------------------|---------------|
|                       | Case (%)         | Control (%) | Case (%)               | Control (%)  | Case (%)              | Control (%)  | Case (%)               | Control (%)  | Case (%)                | Control (%)   |
| <b>Sample size</b>    | 192              | 278         | 2,331                  | 3,077        | 1,937                 | 1,984        | 3,779                  | 3,837        | 4,796                   | 3,741         |
| <b>Sex</b>            |                  |             |                        |              |                       |              |                        |              |                         |               |
| Male                  | 140 (72.9)       | 198 (71.2)  | 1,711 (73.4)           | 2,086 (67.8) | 1,532 (79.1)          | 1,519 (76.6) | 2,926 (77.4)           | 3,375 (88.0) | --                      | --            |
| Female                | 52 (27.1)        | 80 (28.8)   | 620 (26.6)             | 991 (32.2)   | 405 (20.9)            | 465 (23.4)   | 853 (22.6)             | 462 (12.0)   | 4,796 (100.0)           | 3,741 (100.0) |
| <b>Age (years)</b>    |                  |             |                        |              |                       |              |                        |              |                         |               |
| <60                   | 102 (53.1)       | 144 (51.8)  | 1,111 (47.7)           | 1,429 (46.4) | 423 (21.8)            | 502 (25.3)   | 1,402 (37.1)           | 1,315 (34.3) | 2,408 (50.2)            | 2,023 (54.1)  |
| ≥60                   | 90 (46.9)        | 134 (48.2)  | 1,220 (52.3)           | 1,648 (53.6) | 1,514 (78.2)          | 1,482 (74.7) | 2,377 (62.9)           | 2,522 (65.7) | 2,388 (49.8)            | 1,718 (45.9)  |
| <b>Smoking status</b> |                  |             |                        |              |                       |              |                        |              |                         |               |
| Never                 | 63 (32.8)        | 146 (52.5)  | 838 (36.0)             | 1,755 (57.0) | 138 (7.2)             | 636 (32.1)   | n/a                    | n/a          | 4,796 (100.0)           | 3,741 (100.0) |
| Ever                  | 129 (67.2)       | 132 (47.5)  | 1,493 (64.0)           | 1,322 (43.0) | 1,787 (92.8)          | 1,343 (67.9) | n/a                    | n/a          | --                      | --            |
| <b>Histology</b>      |                  |             |                        |              |                       |              |                        |              |                         |               |
| SCC                   | 63 (32.8)        | --          | 822 (35.3)             | --           | 492 (25.4)            | --           | n/a                    | --           | 660 (13.8)              | --            |
| AD                    | 129(67.2)        | --          | 1304 (55.9)            | --           | 795 (41.0)            | --           | n/a                    | --           | 3469 (72.3)             | --            |
| Others                | 0                | --          | 205 (8.8)              | --           | 650 (33.6)            | --           | n/a                    | --           | 667 (13.9)              | --            |

<sup>a</sup> GWAS-NJMU: Genome-wide Association Study at Nanjing Medical University;

<sup>b</sup> SLD: Environment and Genetics in Lung Cancer Etiology in Italy;

<sup>c</sup> CADM: Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study in Finland, the Prostate, Lung, Colon, Ovary Screening Trial and the Cancer Prevention Study II Nutrition Cohort in the US.

<sup>d</sup> FLCCA: Female Lung Cancer Consortium in Asia.

SCC: Squamous cell carcinoma; AD: Adenocarcinoma; Others: other subtypes or missing; n/a: not available.

**Table S2. The association of significant SNPs identified by previous GWAS and fine-mapping studies with lung cancer risk in this study.**

| First author<br>(Reference) | Previous Study |                  |                        |                        | Targeted Sequence |         |                        |                       |
|-----------------------------|----------------|------------------|------------------------|------------------------|-------------------|---------|------------------------|-----------------------|
|                             | SNP            | Effect<br>Allele | OR(95%CI) <sup>a</sup> | <i>P</i> <sup>a</sup>  | EAF <sup>b</sup>  |         | OR(95%CI) <sup>c</sup> | <i>P</i> <sup>c</sup> |
|                             |                |                  |                        |                        | Case              | Control |                        |                       |
| Hu Z (21725308)             | rs4488809      | T                | 1.26 (1.21–1.32)       | $7.20 \times 10^{-26}$ | 0.55              | 0.47    | 1.31 (1.01-1.75)       | 0.044                 |
| Lan Q (23143601)            | rs4488809      | T                | 1.19 (1.12-1.26)       | $4.00 \times 10^{-9}$  |                   |         |                        |                       |
| Miki (20871597)             | rs10937405     | C                | 1.31 (1.22–1.42)       | $7.26 \times 10^{-12}$ | 0.74              | 0.66    | 1.49 (1.11-2.04)       | 0.009                 |
| Shiraishi (22797724)        | rs10937405     | C                | 1.25 (1.19–1.32)       | $6.92 \times 10^{-17}$ |                   |         |                        |                       |
| Wang Y (24880342)           | rs13314271     | T                | 1.13 (1.09-1.18)       | $7.00 \times 10^{-10}$ | 0.54              | 0.47    | 1.31 (1.00-1.72)       | 0.054                 |

<sup>a</sup> Retrieved from previous papers;

<sup>b</sup> EAF: effect allele frequency;

<sup>c</sup> Logistic regression with adjustment for age, gender and smoking status.

**Table S3. Conditional analysis of GWAS SNVs by rs4488809 and rs10937405.**

| SNP        | Ref/Eff<br>Allele | MAF  |         | Step 1                  |                       | Step 2                  |                       | Step 3                  |                       | Step 4                  |                       |
|------------|-------------------|------|---------|-------------------------|-----------------------|-------------------------|-----------------------|-------------------------|-----------------------|-------------------------|-----------------------|
|            |                   | case | control | OR (95%CI) <sup>a</sup> | <i>P</i> <sup>a</sup> | OR (95%CI) <sup>b</sup> | <i>P</i> <sup>b</sup> | OR (95%CI) <sup>c</sup> | <i>P</i> <sup>c</sup> | OR (95%CI) <sup>d</sup> | <i>P</i> <sup>d</sup> |
| rs4396880  | G/A               | 0.26 | 0.35    | 0.64(0.47-0.87)         | 3.88×10 <sup>-3</sup> | -                       | -                     | 0.65(0.48-0.89)         | 6.10×10 <sup>-3</sup> | -                       | -                     |
| rs3856776  | C/T               | 0.13 | 0.08    | 1.84(1.19-2.85)         | 6.05×10 <sup>-3</sup> | 1.79(1.15-2.77)         | 9.52×10 <sup>-3</sup> | -                       | -                     | -                       | -                     |
| rs4488809  | T/C               | 0.45 | 0.53    | 0.76(0.57-0.99)         | 4.43×10 <sup>-2</sup> | 0.98(0.68-1.41)         | 0.912                 | 0.8(0.61-1.06)          | 0.127                 | 1.08(0.75-1.57)         | 0.678                 |
| rs10937405 | C/T               | 0.26 | 0.34    | 0.67(0.49-0.9)          | 9.27×10 <sup>-3</sup> | 1.99(0.47-8.4)          | 0.348                 | 0.68(0.5-0.93)          | 0.143                 | 2.08(0.49-8.89)         | 0.325                 |
| rs13314271 | C/T               | 0.54 | 0.47    | 1.31(1-1.72)            | 5.45×10 <sup>-2</sup> | 1.01(0.71-1.44)         | 0.963                 | 1.23(0.93-1.63)         | 0.145                 | 0.92(0.64-1.33)         | 0.659                 |

<sup>a</sup> adjusted for age, sex and smoking status.

<sup>b</sup> adjusted for age, sex, smoking status and rs4396880.

<sup>c</sup> adjusted for age, sex, smoking status and rs3856776.

<sup>d</sup> adjusted for age, sex, smoking status, rs4396880 and rs3856776.