Supplementary table 1. Stratified analysis of the GOLD spirometric grade on association between the SNPs and COPD risk.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| SNP | Model | Genotype | Ⅰ + Ⅱ  | Ⅲ + Ⅳ | OR (95% CI) | *p-*value |
| rs10245353 | Codominant | C/C | 78 (43.3%) | 57 (42.5%) | 1 |  |
|  |  | C/A | 74 (41.1%) | 57 (42.5%) | 1.05 (0.65-1.71) | 0.97 |
|  |  | A/A | 28 (15.6%) | 20 (14.9%) | 0.98 (0.50-1.91) |  |
|  | Dominant | C/C | 78 (43.3%) | 57 (42.5%) | 1 |  |
|  |  | C/A-A/A | 102 (56.7%) | 77 (57.5%) | 1.03 (0.66-1.62) | 0.89 |
|  | Recessive | C/C-C/A | 152 (84.4%) | 114 (85.1%) | 1 |  |
|  |  | A/A | 28 (15.6%) | 20 (14.9%) | 0.95 (0.51-1.78) | 0.88 |
|  | Overdominant | C/C-A/A | 106 (58.9%) | 77 (57.5%) | 1 |  |
|  |  | C/A | 74 (41.1%) | 57 (42.5%) | 1.06 (0.67-1.67) | 0.8 |
|  | Log-additive | --- | --- | --- | 1.00 (0.73-1.37) | 0.98 |
| rs2290263 | --- | A/A | 161 (89%) | 117 (87.3%) | 1 |  |
|  |  | A/G | 20 (11.1%) | 17 (12.7%) | 1.17 (0.59-2.33) | 0.66 |
|  | Codominant | G/G | 82 (45.3%) | 63 (47%) | 1 |  |
| rs4719841  |  | A/G | 85 (47%) | 61 (45.5%) | 0.93 (0.59-1.49) | 0.96 |
|  |  | A/A | 14 (7.7%) | 10 (7.5%) | 0.93 (0.39-2.23) |  |
|  | Dominant | G/G | 82 (45.3%) | 63 (47%) | 1 |  |
|  |  | A/G-A/A | 99 (54.7%) | 71 (53%) | 0.93 (0.60-1.46) | 0.76 |
|  | Recessive | G/G-A/G | 167 (92.3%) | 124 (92.5%) | 1 |  |
|  |  | A/A | 14 (7.7%) | 10 (7.5%) | 0.96 (0.41-2.24) | 0.93 |
|  | Overdominant | G/G-A/A | 96 (53%) | 73 (54.5%) | 1 |  |
|  |  | A/G | 85 (47%) | 61 (45.5%) | 0.94 (0.60-1.48) | 0.8 |
|  | Log-additive | --- | --- | --- | 0.95 (0.66-1.36) | 0.78 |
| rs7780562 | Codominant | C/C | 87 (48.9%) | 76 (57.6%) | 1 |  |
|  |  | C/A | 80 (44.9%) | 47 (35.6%) | 0.67 (0.42-1.08) | 0.25 |
|  |  | A/A | 11 (6.2%) | 9 (6.8%) | 0.94 (0.37-2.38) |  |
|  | Dominant | C/C | 87 (48.9%) | 76 (57.6%) | 1 |  |
|  |  | C/A-A/A | 91 (51.1%) | 56 (42.4%) | 0.70 (0.45-1.11) | 0.13 |
|  | Recessive | C/C-C/A | 167 (93.8%) | 123 (93.2%) | 1 |  |
|  |  | A/A | 11 (6.2%) | 9 (6.8%) | 1.11 (0.45-2.76) | 0.82 |
|  | Overdominant | C/C-A/A | 98 (55.1%) | 85 (64.4%) | 1 |  |
|  |  | C/A | 80 (44.9%) | 47 (35.6%) | 0.68 (0.43-1.08) | 0.097 |
|  | Log-additive | --- | --- | --- | 0.81 (0.56-1.17) | 0.25 |
| rs78750958  | Codominant | G/G | 83 (45.9%) | 66 (49.2%) | 1 |  |
|  |  | A/G | 84 (46.4%) | 59 (44%) | 0.88 (0.56-1.40) | 0.82 |
|  |  | A/A | 14 (7.7%) | 9 (6.7%) | 0.81 (0.33-1.98) |  |
|  | Dominant | G/G | 83 (45.9%) | 66 (49.2%) | 1 |  |
|  |  | A/G-A/A | 98 (54.1%) | 68 (50.8%) | 0.87 (0.56-1.36) | 0.55 |
|  | Recessive | G/G-A/G | 167 (92.3%) | 125 (93.3%) | 1 |  |
|  |  | A/A | 14 (7.7%) | 9 (6.7%) | 0.86 (0.36-2.05) | 0.73 |
|  | Overdominant | G/G-A/A | 97 (53.6%) | 75 (56%) | 1 |  |
|  |  | A/G | 84 (46.4%) | 59 (44%) | 0.91 (0.58-1.42) | 0.67 |
|  | Log-additive | --- | --- | --- | 0.89 (0.62-1.28) | 0.53 |
| rs7934083  | Codominant | T/T | 145 (81.5%) | 104 (77.6%) | 1 |  |
|  |  | C/T | 31 (17.4%) | 29 (21.6%) | 1.30 (0.74-2.30) | 0.62 |
|  |  | C/C | 2 (1.1%) | 1 (0.8%) | 0.70 (0.06-7.79) |  |
|  | Dominant | T/T | 145 (81.5%) | 104 (77.6%) | 1 |  |
|  |  | C/T-C/C | 33 (18.5%) | 30 (22.4%) | 1.27 (0.73-2.21) | 0.4 |
|  | Recessive | T/T-C/T | 176 (98.9%) | 133 (99.2%) | 1 |  |
|  |  | C/C | 2 (1.1%) | 1 (0.8%) | 0.66 (0.06-7.37) | 0.73 |
|  | Overdominant | T/T-C/C | 147 (82.6%) | 105 (78.4%) | 1 |  |
|  |  | C/T | 31 (17.4%) | 29 (21.6%) | 1.31 (0.74-2.30) | 0.35 |
|  | Log-additive | --- | --- | --- | 1.20 (0.72-2.02) | 0.48 |

SNP: single-nucleotide polymorphism; OR, odds ratio; CI, confidence interval; COPD : chronic obstructive pulmonary disease.

I+II and III+IV are the severity of COPD by GOLD Spirometric grade.

Bonferroniʼs multiple adjustment was applied, with *p* < 0.0017（0.05/30）

Bold indicates a statistically significant SNP (*p* < 0.0017)*.*

Supplementary table 2 MDR analysis of SNP-SNP interactions in relation with COPD risk.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Model | Testing Bal. Acc | CVC | OR (95% CI) | p-value |
| rs4719841 | 0.546 | 6/10 | 1.84(1.33-2.54) | *p* =**0.0002** |
| rs4719841,rs7934083 | 0.562 | 8/10 | 2.31(1.65-3.23) | *p* < **0.0001** |
| rs4719841,rs7934083,rs78750958 | 0.618 | 10/10 | 2.93(2.11-4.05) | *p* < **0.0001** |
| rs10245353,rs4719841,rs7780562,rs78750958 | 0.549 | 5/10 | 3.4(2.45-4.72) | *p* < **0.0001** |
| rs10245353,rs4719841,rs7780562,rs7934083,rs78750958 | 0.527 | 10/10 | 5.13(3.58-7.34) | *p* < **0.0001** |
| rs10245353,rs2290263,rs4719841,rs7780562,rs7934083,rs78750958 | 0.543 | 10/10 | 5.88(4.13-8.37) | *p* < **0.0001** |

SNP: single-nucleotide polymorphism; OR, odds ratio; CI, confidence interval; COPD: chronic obstructive pulmonary disease.

MDR, multifactor dimensionality reduction; Bal. Acc., balanced accuracy; CVC, cross–validation consistency; OR, odds ratio; CI, confidence interval.

*p* values were calculated using χ2 tests.

*p <* 0.05 indicates statistical significance.