

**Table S1.** The context sequence of five MACC1 SNPs in the study.

| Variable  | Assay ID       | Context Sequence  |
|-----------|----------------|---|
| rs3095007 | C__27452671_10 | TACAATGCACTGTGCTAATTTAATG[A/C]<br>CCCCCTTAACTTAATTACATGATTA |
| rs1990172 | C__2632417_10  | TGTTTCCAGGCATGATAATTAAATA[A/C]<br>ATCCAAAAATTGTCTCATAAGGTGG |
| rs4721888 | C__27869756_10 | CCTGTAATATTGCAACTTTTTGAGA[C/G]<br>TTTTCCAGCTTCCATGTCAATCAAA |
| rs975263  | C__2632422_20  | CTTCTGCAAATAGCCTGGCAGATT[C/A]<br>AGAGTCTTTTTAGGTTTGGGGTTGG  |
| rs3735615 | C__27489506_10 | TGACTGAAGGTCTTGTAACACATCT[C/G]<br>TGTAGTTATTTCCATAGTGAGCACT |

**Table S2.** The MACC1 SNPs genotype frequencies of people who were used to cigarette smoking.

| Variable         | Controls<br>(N=636) n (%) | Patients (N=809)<br>n (%) | OR <sup>a</sup> (95% CI) | AOR <sup>b</sup> (95% CI) |
|------------------|---------------------------|---------------------------|--------------------------|---------------------------|
| <b>rs3095007</b> |                           |                           |                          |                           |
| GG               | 530 (83.3%)               | 678 (83.8%)               | 1.00                     | 1.00                      |
| GT               | 100 (15.7%)               | 127 (15.7%)               | 0.993 (0.746-1.321)      | 0.962 (0.680-1.362)       |
| TT               | 6 (0.9%)                  | 4 (0.5%)                  | 0.521 (0.146-1.856)      | 0.373 (0.084-1.657)       |
| GT+TT            | 106 (16.7%)               | 131 (16.2%)               | 0.966 (0.730-1.278)      | 0.924 (0.658-1.298)       |
| <b>rs1990172</b> |                           |                           |                          |                           |
| GG               | 464 (73.0%)               | 609 (75.3%)               | 1.00                     | 1.00                      |
| GT               | 166 (26.1%)               | 183 (22.6%)               | 0.840 (0.659-1.070)      | 0.805 (0.600-1.081)       |
| TT               | 6 (0.9%)                  | 17 (2.1%)                 | 2.159 (0.845-5.518)      | 2.259 (0.731-6.980)       |
| GT+TT            | 172 (27.0%)               | 200 (24.7%)               | 0.886 (0.699-1.123)      | 0.852 (0.639-1.137)       |
| <b>rs4721888</b> |                           |                           |                          |                           |
| GG               | 346 (54.4%)               | 410 (50.7%)               | 1.00                     | 1.00                      |
| GC               | 247 (38.8%)               | 338 (41.8%)               | 1.155 (0.929-1.436)      | 1.289 (0.989-1.681)       |
| CC               | 43 (6.8%)                 | 61 (7.5%)                 | 1.197 (0.790-1.814)      | 1.534 (0.923-2.549)       |
| GC+CC            | 290 (45.6%)               | 399 (49.3%)               | 1.161 (0.943-1.430)      | 1.323 (0.953-1.726)       |
| <b>rs975263</b>  |                           |                           |                          |                           |
| TT               | 442 (69.5%)               | 556 (68.7%)               | 1.00                     | 1.00                      |
| TC               | 178 (28.0%)               | 230 (28.4%)               | 1.027 (0.814-1.296)      | 1.062 (0.801-1.409)       |
| CC               | 16 (2.5%)                 | 23 (2.9%)                 | 1.143 (0.596-2.189)      | 1.000 (0.458-2.180)       |
| TC+CC            | 194 (30.5%)               | 253 (31.3%)               | 1.037 (0.828-1.298)      | 1.057 (0.804-1.389)       |
| <b>rs3735615</b> |                           |                           |                          |                           |
| GG               | 450 (70.8%)               | 581 (71.8%)               | 1.00                     | 1.00                      |
| GC               | 173 (27.2%)               | 217 (26.8%)               | 0.972 (0.768-1.228)      | 0.874 (0.658-1.162)       |
| CC               | 13 (2.0%)                 | 11 (1.4%)                 | 0.655 (0.291-1.477)      | 0.440 (0.165-1.177)       |
| GC+CC            | 186 (29.2%)               | 228 (28.2%)               | 0.949 (0.755-1.194)      | 0.842 (0.637-1.112)       |

<sup>a</sup>The odds ratio (OR) with their 95% confidence intervals were estimated by logistic regression models.

<sup>b</sup>The adjusted odds ratio (AOR) with their 95% confidence intervals were estimated by multiple logistic regression models after controlling for chew betel quid and alcohol consumption.

**Table S3.** The MACC1 SNPs genotype frequencies of people who were used to alcohol drinking.

| Variable         | Controls<br>(N=237) n (%) | Patients (N=490)<br>n (%) | OR <sup>a</sup> (95% CI) | AOR <sup>b</sup> (95% CI) |
|------------------|---------------------------|---------------------------|--------------------------|---------------------------|
| <b>rs3095007</b> |                           |                           |                          |                           |
| GG               | 196 (82.7%)               | 412 (84.1%)               | 1.00                     | 1.00                      |
| GT               | 38 (16.0%)                | 76 (15.5%)                | 0.951 (0.622-1.455)      | 0.847 (0.514-1.395)       |
| TT               | 3 (1.3%)                  | 2 (0.4%)                  | 0.317 (0.053-1.913)      | 0.182 (0.027-1.234)       |
| GT+TT            | 41 (17.3%)                | 78 (15.9%)                | 0.905 (0.598-1.370)      | 0.785 (0.483-1.276)       |
| <b>rs1990172</b> |                           |                           |                          |                           |
| GG               | 171 (72.2%)               | 376 (76.7%)               | 1.00                     | 1.00                      |
| GT               | 63 (26.6%)                | 105 (21.4%)               | 0.758 (0.528-1.087)      | 0.669 (0.437-1.024)       |
| TT               | 3 (1.3%)                  | 9 (1.9%)                  | 1.364 (0.365-5.103)      | 0.717 (0.173-2.965)       |
| GT+TT            | 66 (27.8%)                | 114 (23.3%)               | 0.786 (0.552-1.118)      | 0.672 (0.443-1.019)       |
| <b>rs4721888</b> |                           |                           |                          |                           |
| GG               | 131 (55.3%)               | 254 (51.8%)               | 1.00                     | 1.00                      |
| GC               | 95 (40.1%)                | 199 (40.6%)               | 1.080 (0.782-1.492)      | 1.127 (0.770-1.648)       |
| CC               | 11 (4.6%)                 | 37 (7.6%)                 | 1.735 (0.857-3.512)      | 2.023 (0.889-4.602)       |
| GC+CC            | 106 (44.7%)               | 236 (48.2%)               | 1.148 (0.841-1.568)      | 1.215 (0.842-1.754)       |
| <b>rs975263</b>  |                           |                           |                          |                           |
| TT               | 165 (69.6%)               | 341 (69.6%)               | 1.00                     | 1.00                      |
| TC               | 66 (27.8%)                | 136 (27.8%)               | 0.997 (0.704-1.412)      | 0.922 (0.613-1.389)       |
| CC               | 6 (2.6%)                  | 13 (2.6%)                 | 1.048 (0.391-2.807)      | 0.799 (0.258-2.476)       |
| TC+CC            | 72 (30.4%)                | 149 (30.4%)               | 1.001 (0.715-1.403)      | 0.911 (0.613-1.354)       |
| <b>rs3735615</b> |                           |                           |                          |                           |
| GG               | 166 (70.0%)               | 355 (72.4%)               | 1.00                     | 1.00                      |
| GC               | 65 (27.4%)                | 125 (25.5%)               | 0.899 (0.633-1.278)      | 0.819 (0.541-1.241)       |
| CC               | 6 (2.6%)                  | 10 (2.1%)                 | 0.779 (0.279-2.180)      | 0.423 (0.138-1.294)       |
| GC+CC            | 71 (30.0%)                | 135 (27.6%)               | 0.889 (0.632-1.251)      | 0.775 (0.519-1.159)       |

<sup>a</sup>The odds ratio (OR) with their 95% confidence intervals were estimated by logistic regression models.

<sup>b</sup>The adjusted odds ratio (AOR) with their 95% confidence intervals were estimated by multiple logistic regression models after controlling for chew betel quid and alcohol consumption.

Figure S1

*MACC1* rs4721888

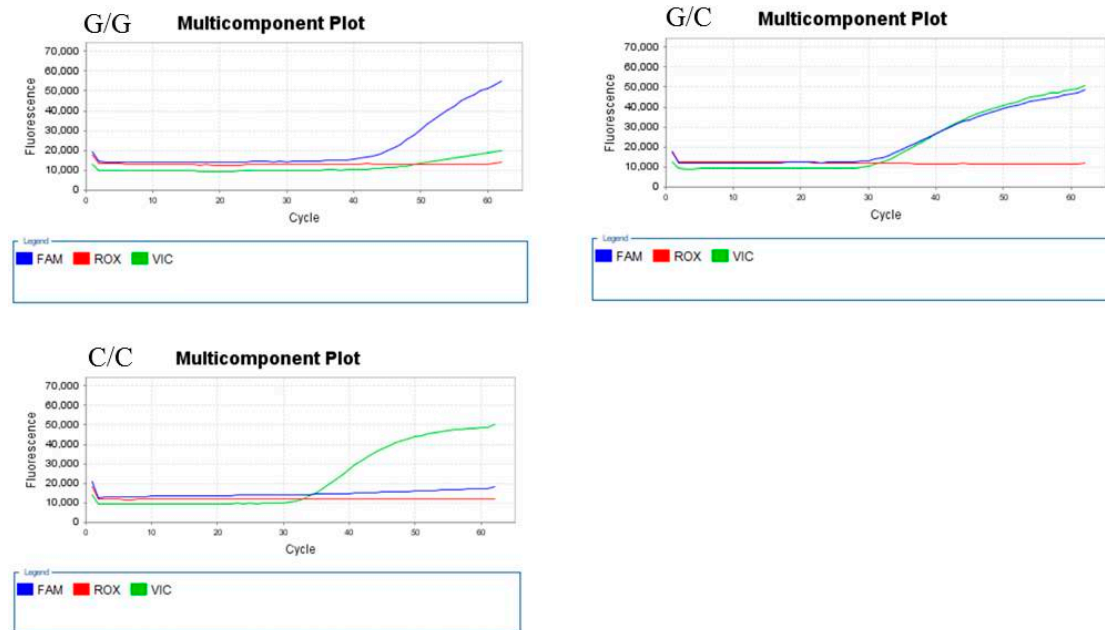


Figure S1: Representative TaqMan assay for *MACC1* rs4721888 genotyping.