**Supplementary Materials:**

**Table S1.** Distribution of candidate genotypes of *MAOA*, *MAOB*, and *COMT* among males with oral cancer, pharyngeal cancer, OPMD and control (N = 530)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Oral cancer**  **(N = 209)** | | **Pharyngeal cancer**  **(N = 88)** | | **OPMD**  **(N = 40)** | | **Control**  **(N = 193)** | | **Oral cancer vs. control** | | | **Pharyngeal cancer vs. control** | | | **OPMD vs. control** | | |
|  |  |  |  |  |  |  |  |  |  | Risk assessment | |  | Risk assessment | |  | Risk assessment | |  |
| SNPs | BQ | N | (%) | N | (%) | N | (%) | N | (%) | AOR | (95%CI)a | *p* | AOR | (95% CI)a | *p* | AOR | (95% CI)a | *p* |
| *MAOA* | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| rs6323 | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| T |  | 72 | (34.5) | 26 | (29.6) | 10 | (25.0) | 89 | (46.1) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| G |  | 137 | (65.6) | 62 | (70.5) | 30 | (75.0) | 104 | (53.9) | 1.80 | (1.09-2.96)\* | 0.022 | 2.75 | (1.42-5.32)\* | 0.003 | 2.97 | (1.30-6.79)\* | 0.010 |
| T | (-) | 9 | (4.3) | 5 | (5.7) | 5 | (12.5) | 57 | (29.5) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| G | (-) | 17 | (8.1) | 9 | (10.2) | 2 | (5.0) | 73 | (37.8) | 1.68 | (0.67-4.25) | 0.271 | 1.97 | (0.54-7.18) | 0.305 | 0.37 | (0.07-2.03) | 0.250 |
| T | (+) | 63 | (30.1) | 21 | (23.9) | 5 | (12.5) | 32 | (16.6) | 17.71 | (6.87-45.66)\* | <0.001 | 5.01 | (1.40-17.88)\* | 0.013 | 1.87 | (0.42-8.28) | 0.411 |
| G | (+) | 120 | (57.4) | 53 | (60.2) | 28 | (70.0) | 31 | (16.1) | 38.89 | (15.19-99.58)\* | <0.001 | 18.07 | (5.26-62.02)\* | <0.001 | 12.72 | (3.56-45.49)\* | <0.001 |
| rs1137070 | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| C |  | 71 | (34.0) | 26 | (29.6) | 10 | (25.0) | 103 | (53.4) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| T |  | 138 | (66.0) | 62 | (70.5) | 30 | (75.0) | 90 | (46.6) | 2.16 | (1.32-3.55)\* | 0.002 | 3.38 | (1.75-6.52)\* | <0.001 | 3.35 | (1.47-7.62)\* | 0.004 |
| C | (-) | 9 | (4.3) | 5 | (5.7) | 5 | (12.5) | 70 | (36.3) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| T | (-) | 17 | (8.1) | 9 | (10.2) | 2 | (5.0) | 60 | (31.1) | 2.13 | (0.84-5.36) | 0.110 | 3.19 | (0.89-11.50) | 0.076 | 0.53 | (0.10-2.89) | 0.461 |
| C | (+) | 62 | (29.7) | 21 | (23.9) | 5 | (12.5) | 33 | (17.1) | 17.84 | (7.16-44.45)\* | <0.001 | 5.67 | (1.69-19.07)\* | 0.005 | 2.23 | (0.53-9.41) | 0.275 |
| T | (+) | 121 | (57.9) | 53 | (60.2) | 28 | (70.0) | 30 | (15.5) | 44.38 | (17.92-109.95)\* | <0.001 | 22.45 | (6.97-72.34)\* | <0.001 | 15.42 | (4.62-51.48)\* | <0.001 |
| rs5906957 | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| G |  | 73 | (34.9) | 31 | (35.2) | 10 | (25.0) | 79 | (40.9) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| A |  | 136 | (65.1) | 57 | (64.8) | 30 | (75.0) | 114 | (59.1) | 1.60 | (0.97-2.64) | 0.068 | 1.93 | (1.01-3.68)\* | 0.047 | 2.58 | (1.12-5.93)\* | 0.025 |
| G | (-) | 9 | (4.3) | 6 | (6.8) | 5 | (12.5) | 48 | (24.9) | 1.0 |  |  | 1.0 |  |  | 1.0 |  |  |
| A | (-) | 17 | (8.1) | 8 | (9.1) | 2 | (5.0) | 82 | (42.5) | 1.34 | (0.52-3.40) | 0.544 | 1.16 | (0.33- 4.12) | 0.822 | 0.27 | (0.05-1.49) | 0.133 |
| G | (+) | 64 | (30.6) | 25 | (28.4) | 5 | (12.5) | 31 | (16.1) | 15.54 | (5.93-40.68)\* | <0.001 | 4.24 | (1.27- 14.24)\* | 0.019 | 1.53 | (0.34-6.88) | 0.578 |
| A | (+) | 119 | (56.9) | 49 | (55.7) | 28 | (70.0) | 32 | (16.6) | 32.50 | (12.60-83.85)\* | <0.001 | 11.70 | (3.58- 38.19)\* | <0.001 | 9.88 | (2.76-35.40)\* | <0.001 |
| *MAOB* | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| rs6324 | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| A |  | 60 | (28.7) | 14 | (15.9) | 4 | (10.0) | 157 | (81.4) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| G |  | 149 | (71.3) | 74 | (84.1) | 36 | (90.0) | 36 | (18.7) | 11.32 | (6.28-20.40)\* | <0.001 | 20.48 | (9.28-45.18)\* | <0.001 | 38.04 | (12.12-119.40)\* | <0.001 |
| A | (-) | 5 | (2.4) | 0 | (0.0) | 1 | (2.5) | 108 | (56.0) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| G | (-) | 21 | (10.1) | 14 | (15.9) | 6 | (15.0) | 22 | (11.4) | 18.30 | (6.02-55.70)\* | <0.001 | NA |  |  | 30.50 | (3.40-273.78)\* | 0.002 |
| A | (+) | 55 | (26.3) | 14 | (15.9) | 3 | (7.5) | 49 | (25.4) | 31.85 | (10.79- 94.03)\* | <0.001 | NA |  |  | 7.90 | (0.74-84.76) | 0.088 |
| G | (+) | 128 | (61.2) | 60 | (68.2) | 30 | (75.0) | 14 | (7.3) | 252.21 | (78.89- 806.31)\* | <0.001 | NA |  |  | 244.40 | (27.74-NA)\* | <0.001 |
| rs1799836 | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| C |  | 40 | (19.1) | 10 | (11.4) | 5 | (12.5) | 34 | (17.6) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| T |  | 169 | (80.9) | 78 | (88.6) | 35 | (87.5) | 159 | (82.4) | 1.14 | (0.62-2.10) | 0.678 | 2.53 | (1.04-6.16)\* | 0.040 | 2.03 | (0.70-5.92) | 0.194 |
| C | (-) | 4 | (1.9) | 1 | (1.1) | 2 | (5.0) | 19 | (9.8) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| T | (-) | 22 | (10.5) | 13 | (14.8) | 5 | (12.5) | 111 | (57.5) | 1.17 | (0.34-4.02) | 0.808 | 2.78 | (0.31-25.11) | 0.364 | 0.44 | (0.08-2.57) | 0.362 |
| C | (+) | 36 | (17.2) | 9 | (10.2) | 3 | (7.5) | 15 | (7.8) | 19.57 | (5.05-75.80)\* | <0.001 | 7.41 | (0.73-75.16) | 0.090 | 1.84 | (0.24-14.30) | 0.562 |
| T | (+) | 147 | (70.3) | 65 | (73.9) | 30 | (75.0) | 48 | (24.9) | 23.90 | (6.93-82.48)\* | <0.001 | 20.25 | (2.33-175.69)\* | 0.006 | 6.31 | (1.20-33.11)\* | 0.029 |
| rs3027452 | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| A |  | 33 | (15.8) | 8 | (9.1) | 5 | (12.5) | 27 | (14.0) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| G |  | 176 | (84.2) | 80 | (90.9) | 35 | (87.5) | 166 | (86.0) | 1.17 | (0.60-2.26) | 0.646 | 2.59 | (0.97-6.87) | 0.057 | 1.61 | (0.54-4.79) | 0.390 |
| A | (-) | 3 | (1.44) | 1 | (1.1) | 2 | (5.0) | 13 | (6.7) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| G | (-) | 23 | (11.0) | 13 | (14.8) | 5 | (12.5) | 117 | (60.6) | 1.00 | (0.24-4.09) | 0.998 | 1.55 | (0.16-14.98) | 0.703 | 0.27 | (0.04-1.60) | 0.148 |
| A | (+) | 30 | (14.4) | 7 | (8.0) | 3 | (7.5) | 14 | (7.3) | 15.56 | (3.37-71.92)\* | <0.001 | 3.80 | (0.34-43.13) | 0.281 | 1.31 | (0.16-10.73) | 0.801 |
| G | (+) | 153 | (73.2) | 67 | (76.1) | 30 | (75.0) | 49 | (25.4) | 21.30 | (5.18-87.57)\* | <0.001 | 12.45 | (1.33-116.49)\* | 0.027 | 3.99 | (0.72-22.15) | 0.113 |
| *COMT* | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| rs4633 | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| T/T | | 9 | (4.3) | 6 | (6.8) | 4 | (10.0) | 17 | (8.8) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| C/T | | 65 | (31.1) | 26 | (29.6) | 7 | (17.5) | 81 | (42.0) | 1.30 | (0.45-3.75) | 0.625 | 0.60 | (0.17-2.07) | 0.415 | 0.30 | (0.07-1.26) | 0.099 |
| C/C | | 135 | (64.6) | 56 | (63.6) | 29 | (72.5) | 95 | (49.2) | 2.27 | (0.82-6.29) | 0.115 | 1.08 | (0.33-3.53) | 0.898 | 1.05 | (0.29-3.78) | 0.946 |
| T/T+C/T | | 74 | (35.4) | 32 | (36.4) | 11 | (27.5) | 98 | (50.8) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| C/C | | 135 | (64.6) | 56 | (63.6) | 29 | (72.5) | 95 | (49.2) | 1.80 | (1.10-2.95)\* | 0.019 | 1.65 | (0.89-3.09) | 0.115 | 2.63 | (1.18-5.85)\* | 0.018 |
| T/T+C/T | (-) | 9 | (4.3) | 4 | (4.6) | 2 | (5.0) | 68 | (35.2) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| C/C | (-) | 17 | (8.1) | 10 | (11.4) | 5 | (12.5) | 62 | (32.1) | 1.76 | (0.70-4.42) | 0.231 | 1.83 | (0.49-6.80) | 0.370 | 2.56 | (0.47-13.99) | 0.278 |
| T/T+C/T | (+) | 65 | (31.1) | 28 | (31.8) | 9 | (22.5) | 30 | (15.5) | 19.66 | (7.87-49.09)\* | <0.001 | 7.66 | (2.20-26.73)\* | 0.001 | 10.14 | (1.83-56.06)\* | 0.008 |
| CC | (+) | 118 | (56.5) | 46 | (52.3) | 24 | (60.0) | 33 | (17.1) | 35.49 | (14.37-87.64)\* | <0.001 | 12.41 | (3.65-42.19)\* | <0.001 | 26.75 | (5.16-138.55)\* | <0.001 |
| rs9605030 | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| C/C | | 130 | (62.2) | 47 | (53.4) | 16 | (40.0) | 115 | (59.6) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| C/T | | 67 | (32.1) | 36 | (40.9) | 20 | (50.0) | 69 | (35.8) | 0.94 | (0.56-1.58) | 0.827 | 1.45 | (0.76-2.76) | 0.265 | 2.46 | (1.12-5.40)\* | 0.025 |
| T/T | | 12 | (5.7) | 5 | (5.7) | 4 | (10.0) | 9 | (4.7) | 1.02 | (0.35-3.02) | 0.972 | 1.21 | (0.31-4.70) | 0.778 | 3.32 | (0.81-13.53) | 0.094 |
| C/C+C/T | | 197 | (94.3) | 83 | (94.3) | 36 | (90.0) | 184 | (95.3) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| T/T | | 12 | (5.7) | 5 | (5.7) | 4 | (10.0) | 9 | (4.7) | 1.04 | (0.36-3.04) | 0.938 | 1.06 | (0.28-4.02) | 0.931 | 2.22 | (0.58-8.51)\* | 0.244 |
| C/C+C/T | (-) | 26 | (12.4) | 14 | (15.9) | 5 | (12.5) | 123 | (63.7) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| T/T | (-) | 0 | (0.0) | 0 | (0.0) | 2 | (5.0) | 7 | (3.6) | NA |  |  | NA |  |  | 4.10 | (0.59-28.42) | 0.153 |
| C/C+C/T | (+) | 171 | (81.8) | 69 | (78.4) | 31 | (77.5) | 61 | (31.6) | 18.45 | (9.63-35.36)\* | <0.001 | 6.28 | (2.80-14.08)\* | <0.001 | 12.49 | (3.89-40.02)\* | <0.001 |
| T/T | (+) | 12 | (5.7) | 5 | (5.7) | 2 | (5.0) | 2 | (1.0) | 40.38 | (7.53-216.62)\* | <0.001 | 16.25 | (2.35-112.37)\* | 0.005 | 32.03 | (3.23-318.00)\* | 0.003 |
| rs9606186 | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| C/C | | 17 | (8.1) | 5 | (5.7) | 3 | (7.5) | 23 | (11.9) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| G/C | | 89 | (42.6) | 36 | (40.9) | 12 | (30.0) | 84 | (43.5) | 2.17 | (0.94-5.00) | 0.068 | 2.60 | (0.78-8.66) | 0.118 | 1.62 | (0.39-6.77) | 0.510 |
| G/G | | 103 | (49.3) | 47 | (53.4) | 25 | (62.5) | 86 | (44.6) | 2.52 | (1.11-5.75)\* | 0.028 | 3.74 | (1.15-12.20)\* | 0.029 | 3.38 | (0.86-13.29) | 0.081 |
| C/C+G/C | | 106 | (50.7) | 41 | (46.6) | 15 | (37.5) | 107 | (55.4) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| G/G | | 103 | (49.3) | 47 | (53.4) | 25 | (62.5) | 86 | (44.6) | 1.36 | (0.84-2.20) | 0.214 | 1.72 | (0.93-3.18) | 0.082 | 2.32 | (1.09-4.93)\* | 0.028 |
| C/C+G/C | (-) | 12 | (5.7) | 7 | (8.0) | 3 | (7.5) | 70 | (36.3) | 1.00 | [Reference] |  | 1.00 | [Reference] |  | 1.00 | [Reference] |  |
| G/G | (-) | 14 | (6.7) | 7 | (8.0) | 4 | (10.0) | 60 | (31.1) | 1.39 | (0.57-3.40) | 0.469 | 1.79 | (0.52-6.21) | 0.359 | 1.52 | (0.32-7.25) | 0.597 |
| C/C+G/C | (+) | 94 | (45.0) | 34 | (38.6) | 12 | (30.0) | 37 | (19.2) | 20.50 | (9.03-46.54)\* | <0.001 | 7.13 | (2.47-20.57)\* | <0.001 | 7.95 | (1.86-33.89)\* | 0.005 |
| G/G | (+) | 89 | (42.6) | 40 | (45.5) | 21 | (52.5) | 26 | (13.5) | 28.30 | (11.92-67.20)\* | <0.001 | 12.46 | (4.24-36.59)\* | <0.001 | 20.61 | (4.89-86.94)\* | <0.001 |

Abbreviations: AOR, adjusted odds ratio; BQ, betel-quid; OPMD, oral potentially malignant disorder; SNP, single nucleotide polymorphism; NA, not applicable owing to limited samples.

a May not total 100% due to rounding.

b AOR was obtained after adjustment for age, race, marital status, educational level, and covariates (alcohol, betel quid, and cigarette uses).

NA, non-appreciable owing to limited samples.

\* *p* < 0.05

**Table S2.** Distribution of selected clinical characteristics of males with oral and pharyngeal cancers between oral and pharynx sites (N = 42)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Variables** | **Oral site**  **(N = 28)** | | **Pharynx site**  **(N = 14)** | |  |  |
|  | N | (%) | N | (%) | Chi-square | Mann- Whitney U |
| *p*-value | *p*-value |
| **Clinical characteristics** |  |  |  |  |  |  |
| TNM Stage |  |  |  |  |  |  |
| II+III | 16 | (57.1) | 8 | (57.1) | 1.000 |  |
| IV | 12 | (42.9) | 6 | (42.9) |  |  |
| Age (years), Mean (SD) | 54.64 | (10.34) | 56.57 | (7.35) | 0.470 |  |
| BMI (kg/m2), Mean (SD) | 25.55 | (3.85) | 22.47 | (4.83) |  | 0.111 |
| Race |  |  |  |  |  |  |
| Minnan | 23 | (82.1) | 10 | (71.4) | 0.425 |  |
| Non-Minnan | 5 | (17.9) | 4 | (28.6) |  |  |
| Marital status |  |  |  |  |  |  |
| Married | 17 | (60.7) | 6 | (42.9) |  |  |
| Unmarried | 11 | (39.3) | 8 | (57.1) | 0.273 |  |
| Occupational status |  |  |  |  |  |  |
| Working | 16 | (57.1) | 5 | (35.7) | 0.190 |  |
| Not working | 12 | (42.9) | 9 | (64.3) |  |  |
| Education level |  |  |  |  |  |  |
| Low (≤ 6 year) | 19 | (67.9) | 11 | (78.6) | 0.469 |  |
| High (> 6 year) | 9 | (32.1) | 3 | (21.4) |  |  |
| Religion status |  |  |  |  |  |  |
| Having a religion | 24 | (85.7) | 11 | (78.6) | 0.558 |  |
| No religion | 4 | (14.3) | 3 | (21.4) |  |  |
| Alcohol drinking status |  |  |  |  |  |  |
| Never | 8 | (28.6) | 2 | (14.3) | 0.306 |  |
| Current or former | 20 | (71.4) | 12 | (85.7) |  |  |
| Age at starting drinking (years), Mean (SD) | 21.53 | (6.49) | 20.44 | (3.81) |  | 0.620 |
| Years of alcohol drinking, Mean (SD) | 30.87 | (10.39) | 34.11 | (11.66) |  | 0.389 |
| BQ chewing status |  |  |  |  |  |  |
| Never | 2 | (7.1) | 3 | (21.4) | 0.178 |  |
| Current or former | 26 | (92.9) | 11 | (78.6) |  |  |
| Age at starting chewing (years), Mean (SD) | 22.80 | (5.80) | 21.78 | (4.87) |  | 0.692 |
| Years of BQ chewing, Mean (SD) | 24.78 | (10.45) | 32.00 | (12.33) |  | 0.061 |
| Average amount of chewing, Mean (SD) | 31.13 | (26.52) | 23.89 | (8.58) |  | 0.903 |
| Cumulative lifetime BQ use (pack-years), Mean (SD) | 78.86 | (74.20) | 71.83 | (32.46) |  | 0.686 |
| Type of BQ material |  |  |  |  |  |  |
| With Piper betel leaf | 17 | (60.7) | 4 | (28.6) |  |  |
| Mixed use (With Piper betel leaf or with inflorescence of Piper betel Linn.) | 11 | (39.3) | 10 | (71.4) | 0.050 |  |
| Cigarette smoking status |  |  |  |  |  |  |
| Never | 2 | (7.1) | 1 | (7.1) | 1.000 |  |
| Current or former | 26 | (92.9) | 13 | (92.9) |  |  |
| Age at starting smoking (years), Mean (SD) | 19.72 | (4.70) | 19.20 | (3.36) |  | 0.554 |
| Years of cigarette smoking, Mean (SD) | 31.84 | (9.04) | 35.30 | (10.86) |  | 0.257 |
| Average amount of smoking, Mean (SD) | 12.86 | (2.57) | 17.00 | (5.38) |  | 0.758 |

BMI: body mass index

SD: standard deviation

BQ: betel quid

**Table S3.**

Associations between MAOA, MAOB, and COMT mRNA expression (N = 42)

|  |  |  |
| --- | --- | --- |
| Biomarkers | Spearman’s Rho correlation coefficient | *p*-value |
| MAOA-MAOB | 0.822\* | <0.001 |
| MAOB-COMT | 0.738\* | <0.001 |
| MAOA-COMT | 0.557\* | <0.001 |

\* *p* < 0.05