|  |  |  |
| --- | --- | --- |
| **Supplementary Table S1:** TCGA cohort of patients with OPSCC | | |
|  |  | TCGA cohort OPSCC  n = 76 [100.0%] |
| sex |  |  |
|  | male | 66 (86.8) |
|  | female | 10 (13.2) |
| age median (range) |  | 56 (35-79) |
| HPV status\* |  |  |
|  | negative | 25 (32.9) |
|  | positive | 51 (67.1) |
| site |  |  |
|  | tonsil | 43 (56.6) |
|  | base of the tongue | 25 (32.9) |
|  | oropharynx | 8 (10.5) |
| tumor stage (cT/pT) \*\* |  |  |
|  | T1 | 12 (15.8) |
|  | T2 | 33 (43.4) |
|  | T3 | 21 (27.6) |
|  | T4 | 10 (13.2) |
| lymph node status (cN/pN) \*\* |  |  |
|  | pN0/cN0 | 18 (23.7) |
|  | pN/cN+ | 59 (76.3) |
| distant metastases |  |  |
|  | M0 | 70 (92.1) |
|  | M1 | 1 (1.3) |
|  | Mx | 5 (6.6) |
| Grade |  |  |
|  | 1 | 5 (6.6) |
|  | 2 | 30 (39.5) |
|  | 3 | 22 (28.9) |
|  | 4 | 6 (7.9) |
|  | NA | 13 (17.1) |
| \* Verification of HPV DNA; \*\* in case of discordant results, the pathological classification (pN/pT) was used for further analysis. | | |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Supplementary Table S2:** Cologne University Hospital OPSCC cohort | | | | |
|  |  | total cohort  (%) | HPV-negative  (%) | HPV-positive  (%) |
|  |  | n = 209 | n = 106 | n = 102 |
| sex |  |  |  |  |
|  | male | 170 | 88 | 81 |
|  | female | 39 | 18 | 21 |
| age median in years (range) |  | 62 (42-95) | 61.5 (43-95) | 61.5 (42-82) |
| HPV status |  |  |  |  |
|  | HPV-negative | 106 (51.0) | 106 (100.0) | 0 (0.0) |
|  | HPV-positive | 102 (49.0) | 0 (0.0) | 102 (100.0) |
| alcohol history |  |  |  |  |
|  | no abuse | 141 | 56 | 84 |
|  | abuse | 67 | 50 | 17 |
|  | NA | 1 | 0 | 1 |
| nicotine history |  |  |  |  |
|  | no abuse | 66 | 20 | 47 |
|  | abuse | 143 | 86 | 55 |
| localization |  |  |  |  |
|  | tonsil | 146 | 68 | 78 |
|  | bottom of the tongue | 51 | 27 | 23 |
|  | other | 12 | 11 | 1 |
| tumor stage |  |  |  |  |
|  | T1 | 38 | 27 | 11 |
|  | T2 | 76 | 38 | 38 |
|  | T3 | 45 | 19 | 25 |
|  | T4 | 50 | 22 | 28 |
| lymph node status |  |  |  |  |
|  | pN0/cN0 | 49 | 27 | 22 |
|  | pN/cN+ | 160 | 79 | 80 |
| distant metastases |  |  |  |  |
|  | M0 | 196 | 101 | 94 |
|  | M1 | 10 | 4 | 6 |
|  | Mx | 3 | 1 | 2 |
| Grade |  |  |  |  |
|  | 1 | 2 | 1 | 1 |
|  | 2 | 108 | 61 | 47 |
|  | 3 | 58 | 24 | 34 |
|  | 4 | 1 | 0 | 1 |
|  | NA | 40 | 20 | 19 |
| treatment: upfront surgery |  |  |  |  |
|  | yes | 123 | 69 | 54 |
|  | no | 64 | 29 | 35 |
|  | NA | 22 | 8 | 13 |

|  |  |  |
| --- | --- | --- |
| **Supplementary Table S3:** DESeq2 analysis of *H2AXhigh-* and *H2AXlow* OPSCC | | |
|  | *H2AXhigh* OPSCC | *H2AXlow* OPSCC |
| dysregulated genes | 16970 (100%) | 17460 (100%) |
| significantly dysregulated\* | 9788 (57.7%) | 10565 (60.5%) |
| significantly upregulated\*\* | 1106 (6.5%) | 871 (5.0%) |
| significantly downregulated\*\* | 1580 (9.3%) | 1422 (8.1%) |
| significantly upregulated, exclusive | 555 (3.3%) | 320 (1.8%) |
| significantly downregulated, exclusive | 511 (3.0%) | 353 (2.0%) |
| \*p adjusted ≤ 0.05 (Wald test, Bonferroni correction); \*\*upregulated: log2 Fold Change≥ 2.0; downregulated: log2 Fold Change ≤ -2.0 | | |