

**Figure S1. Classification of MMPs and TIMPs.**



**Figure S2.** Correlation between the expression level of each MMPs/TIMPs gene and clinical stages patients with HNSCC. The expression of MMP11 and MMP23B were increased with the clinical stage. while, the expression of MMP1, MMP3, MMP25 and MMP27 was decreased with clinical stage.



**Figure S3.** Prognostic value of the MMPs/TIMPs mRNA expression in HNSCC patients. Higher expressions of MMP14, MMP20, TIMP1 and TIMP4 were associated with worse prognosis in HNSCC patients. Higher expressions of MMP25 was associated with better prognosis in HNSCC patients. P values by Log-rank test < 0.05 were considered statistically significant.



**Figure S4. Receiver operating characteristic curve (ROC) of the expression level of every MMPs and TIMPs for predicting three-years, and five-year survival rate.**

**Table S1 Differential expression analysis of MMPs and TIMPs in HNSCC cancer tissues compared with adjacent tissues**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Gene symbol | Median  (Cancer) | Median  (Normal) | log2FC | Effect size | P  value | FDR | Regulated |
| MMP1 | 1096.1744 | 94.2352 | 3.5401 | 0.7815 | <0.0001 | <0.0001 | Up |
| MMP2 | 258.7923 | 107.8846 | 1.2623 | 1.5322 | <0.0001 | <0.0001 | Up |
| MMP3 | 190.5372 | 19.6458 | 3.2778 | 0.6158 | <0.0001 | <0.0001 | Up |
| MMP7 | 65.9518 | 127.5980 | -0.9521 | 0.2277 | 0.0001 | 0.0005 | Non |
| MMP8 | 0.5557 | 0.0687 | 3.0155 | 0.2798 | <0.0001 | <0.0001 | Up |
| MMP9 | 259.4681 | 13.1221 | 4.3055 | 0.5947 | <0.0001 | <0.0001 | Up |
| MMP10 | 335.2225 | 39.3918 | 3.0892 | 0.3863 | <0.0001 | <0.0001 | Up |
| MMP11 | 87.5374 | 1.9045 | 5.5224 | 0.5844 | <0.0001 | <0.0001 | Up |
| MMP12 | 124.5092 | 7.1014 | 4.1320 | 0.5738 | <0.0001 | <0.0001 | Up |
| MMP13 | 233.2955 | 2.4264 | 6.5872 | 0.3072 | <0.0001 | <0.0001 | Up |
| MMP14 | 469.2598 | 121.3564 | 1.9511 | 1.4139 | <0.0001 | <0.0001 | Up |
| MMP15 | 20.6828 | 11.9765 | 0.7882 | 1.6896 | <0.0001 | <0.0001 | Non |
| MMP16 | 1.1774 | 0.3746 | 1.6521 | 0.9754 | <0.0001 | <0.0001 | Up |
| MMP17 | 6.5674 | 1.8789 | 1.8054 | 1.1383 | <0.0001 | <0.0001 | Up |
| MMP19 | 10.7771 | 3.3299 | 1.6944 | 1.0898 | <0.0001 | <0.0001 | Up |
| MMP20 | 0.2770 | 0.0863 | 1.6819 | 0.2810 | 0.0081 | 0.0324 | Up |
| MMP21 | 0.0457 | 0.0317 | 0.5291 | 0.4241 | 0.3014 | 0.6027 | Non |
| MMP23A | 0.2618 | 0.3214 | -0.2960 | -3.4235 | 0.0325 | 0.0976 | Non |
| MMP23B | 0.1274 | 0.0456 | 1.4827 | 1.1714 | <0.0001 | <0.0001 | Up |
| MMP24 | 0.6865 | 0.4991 | 0.4599 | 0.2294 | 0.4521 | 0.6027 | Non |
| MMP25 | 3.6272 | 1.7509 | 1.0507 | 2.2801 | <0.0001 | <0.0001 | Up |
| MMP26 | 0.0279 | 0.0024 | 3.5336 | 0.1551 | 0.0040 | 0.0202 | Non |
| MMP27 | 0.4064 | 1.1310 | -1.4764 | 1.2415 | <0.0001 | <0.0001 | Down |
| MMP28 | 47.6682 | 11.8797 | 2.0045 | 0.6883 | <0.0001 | <0.0001 | Up |
| TIMP1 | 409.1440 | 261.5066 | 0.6458 | -10.2192 | <0.0001 | <0.0001 | Non |
| TIMP2 | 125.7125 | 71.2910 | 0.8183 | 0.7626 | 0.0032 | 0.0064 | Non |
| TIMP3 | 5.8858 | 3.5842 | 0.7156 | 0.5850 | 0.0489 | 0.0489 | Non |
| TIMP4 | 1.0984 | 7.6324 | -2.7967 | 0.7319 | <0.0001 | <0.0001 | Down |

Footnote: mRNA expression values are presented as mean transcripts per million (TPM); Log2FC stand for Log2 fold change; P values are calculated using Mann-Whitney test; FDR is the Benjamini–Hochberg false discovery rate (FDR) adjusted P value.

**Table S2 multivariate Cox regression analysis of expression level of MMPs/TIMPs in patients with HNSCC for overall survival.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| GENE | β | HR | SE(β) | z | P value |
| MMP3 | 0.9595 | 2.6104 | 0.3924 | 2.445 | 0.014477 |
| MMP17 | -0.9643 | 0.3812 | 0.4516 | -2.135 | 0.032737 |
| MMP19 | -2.1628 | 0.115 | 0.6274 | -3.448 | 0.000566 |
| MMP24 | -0.8316 | 0.4354 | 0.42 | -1.98 | 0.04771 |
| TIMP1 | 6.0062 | 405.9403 | 2.154 | 2.788 | 0.005297 |