**Supplementary Information**

**Supplemental Figure Legends**

**S1. Tandem mass spectrum and corresponding iTRAQ reporter ions.** A).Tandem mass spectrum identifying a peptide from HLA-DPA1. B). iTRAQ reporter ions for the HLA-DPA1 peptide.

**S2. TsMHCII expression in PTC was downregulated by BRAFV600E at the transcriptional level.** A) Real-time PCR detection of CIITA and tsMHCII in BCPAP and K1 cells after treatment by PLX4032 for 72 h; abbreviations used: Ctrl=untreated cells, PLX4032=BRAF inhibitor treated cells. B) Transcript levels of CIITA and tsMHCII in BCPAP and K1 cells after treatment by U0126 72 h; abbreviations used: Ctrl=untreated cells, U0126=MEK inhibitor treated cells.

**S3. BRAFV600E-upregulated TGF-β1 altered tsMHCII expression.** A) Time course expression of CIITA and tsMHCII in BCPAP and K1 by real-time PCR. B) Quantitative detection of TGF-β1 in the extracellular medium of BCPAP and K1 cells over time via ELISA. C) ELISA quantification of secreted TGF-β1 after treatment with PLX4032; abbreviations used: Ctrl=untreated cells, PLX4032=BRAF inhibitor treatment. D) Transcript levels of CIITA and tsMHCII in BCPAP and K1 cells after treatment with TGF-β1 (10 ng/ml) for 72 h. E) Transcript levels oftsMHCII in BCPAP and K1 cells after treatment with PLX4032 alone or combined with TGF-β1.

**S4. TGF-β1 mediates downregulation of tsMHCII in BRAFV600E PTC cells via SMAD3.** Western blot analysis of p-SMAD3 and SMAD3 expression in BCPAP and K1 cells treated for 48 h with or without C) PLX4032, D) U0126, A) TGF-β1, or B) SIS3, respectively. E) Real-time PCR detection of CIITA and tsMHCII transcripts in BCPAP and K1 cells after treatment by 10 µM SIS3 for 48 h. F) Transcript level of CIITA and tsMHCII in BRAFV600E transfected TPC1 cells after treatment by DOX or combination DOX and SIS3 for 48 hr. Untreated cell controls are labeled as “Ctrl” in the figure.

**S5. TIMER web tool analysis of tsMCHII components in various cancers.** Violin plots depict the association between mRNA expression of A) HLA-DQA1, B) HLA-DRA, and C) HLA-DPA1 in various tumor types. Red boxes highlight the association between tsMCHII genes and thyroid carcinomas.

**S6. Representative hematoxylin and eosin staining in mouse liver (left) and kidney (right) specimens.**

**Supplementary Table 1. Correlation between MHCII expression and clinicopathological factors in PTC patients**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | Low expression | | High expression | | X2 | *P* |
| Age |  |  |  |  |  |  |
| <55 | 36 | | 33 | | 0.028 | 0.867 |
| ≥55 | 62 | | 54 | |  |  |
| Sex |  |  |  |  |  |  |
| Female | 74 | | 58 | | 1.763 | 0.184 |
| Male | 24 | | 29 | |  |  |
| CD4 T cell infiltration | | | | |  |  |
| Present | 17 | | 28 | | 5.511 | 0.019 |
| Absent | 81 | | 59 | |  |  |
| BRAF V600E mutation | | | |  |  |  |
| Present | 59 | | 34 | | 8.226 | 0.004 |
| Absent | 39 | | 53 | |  |  |
| Multifocality | | |  |  |  |  |
| Present | 30 | | 28 | | 0.053 | 0.818 |
| Absent | 68 | | 59 | |  |  |
| Tumour stage | |  |  |  |  |  |
| T1/2 | 82 | | 85 | | 10.325 | 0.001 |
| T3/4 | 16 | | 2 | |  |  |
| Lymph node metastasis | | | | |  |  |
| N0 | 37 | | 52 | | 8.947 | 0.003 |
| N1a/b | 51 | | 35 | |  |  |
| AJCC stage | | |  |  |  |  |
| I+II | 86 | | 86 | | 8.684 | 0.003 |
| III+IV | 12 | | 1 | |  |  |
| Recurrence | | |  |  |  |  |
| Absent | 70 | | 85 | | 23.414 | <0.001 |
| Present | 28 | | 2 | |  |  |

**Supplementary Table 2. Hazard ratios of disease specific survival and overall survivalaccording to the xpression of tsMHCII in patients with PTC**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variable | Disease-speciﬁc Survival | | Overall Survival | |
|  | P-value | HR（95% CI） | P-value | HR（95% CI） |
| Female | 0.608 | 1.311 (0.466-3.690) | 0.392 | 1.501 (0.592-3.807) |
| Stage III+IV | <0.001 | 15.305 (4.578-51.166) | <0.001 | 18.201 (6.381-51.917) |
| Multifocality | 0.820 | 0.885 (0.307-2.549) | 0.613 | 0.783 (0.302-2.025) |
| BRAF mutation | 0.012 | 4.612 (1.405-15.141) | 0.001 | 5.524 (1.942-15.719) |
| MHC II expression | 0.038 | 0.205 (0.046-0.917) | 0.024 | 0.240 (0.070-0.827) |
| CD4 T-cell infiltration | 0.872 | 0.903 (0.258-3.154) | 0.904 | 0.935 (0.315-2.774) |
| Abbreviations: CI=Confidence Interval; HR=Hazard Ratio | | | | |

**Supplementary Table 3. Hazard Ratios of overall survival according to mRNA levels of CIITA using TIMER webtool**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | 95% CI | |  |
|  | HR | Lower | Uper | *P* |
| CIITA | 0.504 | 0.27 | 0.938 | 0.031 |
| Purity | 14.540 | 1.286 | >100 | 0.031 |
| Stage I | Ref. | - | - | - |
| Stage II | 6.304 | 0.738 | 53.849 | 0.093 |
| Stage III | 11.326 | 1.883 | 68.117 | 0.008 |
| Stage IV | 41.385 | 5.495 | >100 | <0.001 |
| mate | 1.109 | 0.312 | 3.930 | 0.874 |
| B-cell | 0.006 | <0.001 | >100 | 0.312 |
| CD8 T-cell | <0.001 | <0.001 | 0.500 | 0.041 |
| CD4 T-cell | 0.021 | <0.001 | >100 | 0.046 |
| Marcrophage | <0.001 | <0.001 | >100 | 0.211 |
| Neutrophage | 0.050 | <0.001 | >100 | 0.983 |
| Dendritic | >100 | >100 | >100 | 0.007 |
| Abbreviations: CI=Confidence Interval; HR=Hazard Ratio | | | | |

**Supplementary Table 4. Clinicopathological characteristics of patients with PTC**

|  |  |
| --- | --- |
| Patient Characteristics | N=185 |
| Age |  |
| ≥55 | 116 (62.7%) |
| Sex |  |
| Female | 132 (71.4%) |
| Tumour stage |  |
| T3/4 | 18 (9.7%) |
| Lymph node metastasis |  |
| N1a/b | 96 (51.9%) |
| Multifocality |  |
| Present | 58 (31.4%) |
| AJCC stage |  |
| III+IV | 13 (7.0%) |
| BRAF mutation |  |
| Present | 93 (50.3%) |
| CD4 T cell infiltration |  |
| Present | 45 (24.3%) |
| Recurrence |  |
| Present | 30 (16.2%) |
| Overall mortality | 28 (15.1%) |
| Disease-specific mortality | 21 (11.4%) |
| Follow-up years, median (range) | 68 (20-72) |