**Supplementary Material**

**Table S1.** Detailed information of ESCC tissues samples.

| Items | Detailed information |
|---|---|
| Sources | The TMA chip containing these ESCC tissue samples was purchased from the Shanghai Outdo Biotech Company. |
| Procedure of mIHC experiment | 1) Drying<br>2) Dewaxing<br>3) Antigen repair<br>4) Removal of endogenous peroxidase<br>5) Blocking<br>6) Primary antibody incubation<br>7) Incubation of secondary antibody<br>8) Opal dye color development<br>9) Microwave treatment<br>10) Repeat steps 5)-9) for subsequent indicators until all indicators are labeled.<br>11) DAPI staining and blocking<br>12) Photographic analysis |
| Interpretation of mIHC results | From the analysis report provided by Shanghai Outdo Biotech Company. The analysis report has provided the number of positive cells for each staining molecule, as well as the number of positive cells between two staining molecules. And it can be used directly for statistical analysis. |

mIHC, multiplex immunohistochemistry.

**Table S2.** The difference of CD39 expression in 71 pairs of ESCC cancer tissues and paracancerous tissues.

| Variables (Cancer tissue - paracancerous tissue) | Normality test | | | | | Paired t-test/Wilcoxon signed-rank test |
|---|---|---|---|---|---|---|
| | *P* value | Mean | SD | Median | IQR | *P* value |
| CD39$^+$ count | 0.002** | | | 1035.500 | 3560.500 | 0.013* |
| CD8$^+$ count | <0.001*** | | | -45.000 | 358.750 | 0.196 |
| CD39-expressing CD8$^+$ T cells | 0.200 | 4.832 | 25.007 | | | 0.096 |
| CD39$^+$ in CK$^+$ region | <0.001*** | | | 91.500 | 772.750 | 0.011* |
| CD39$^+$ in CK$^-$ region | <0.001*** | | | 461.500 | 2605.750 | 0.129 |
| CD8$^+$ in CK$^+$ region | <0.001*** | | | -46.500 | 109.750 | <0.001*** |
| CD8$^+$ in CK$^-$ region | <0.001*** | | | 10.500 | 272.250 | 0.445 |
| CD39-expressing CD8$^+$ T cells in CK$^+$ region | 0.200 | 9.155 | 28.179 | | | 0.011* |
| CD39-expressing CD8$^+$ T cells in CK$^-$ region | 0.200 | -12.031 | 31.673 | | | 0.002** |

CD39, extracellular nucleotide triphosphate diphosphate hydrolase 1; CK, cytokeratin; ESCC, esophageal squamous cell carcinoma; IQR, interquartile range; SD, standard deviation. $^*P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

**Table S3.** Points for variables in nomogram models.

| Variables | Points | Total points | Nomogram 1-year | 3-year | 5-year |
|---|---|---|---|---|---|
| Gender | | 244 | 0.3 | | |
| male | 100 | 227 | 0.4 | | |
| female | 0 | 210 | 0.5 | | |
| TNM stage | | 191 | 0.6 | | |
| I + II | 0 | 169 | 0.7 | | |
| III+IV | 74 | 139 | 0.8 | | |
| CD39-expressing CD8$^+$ T cells in CK$^+$ region | | 93 | 0.9 | | |
| ≤77.48% | 0 | 219 | | 0.1 | |
| >77.48% | 64 | 196 | | 0.2 | |
| CD39-expressing CD8$^+$ T cells in CK$^-$ region | | 178 | | 0.3 | |
| ≤59.46% | 0 | 161 | | 0.4 | |
| >59.46% | 78 | 144 | | 0.5 | |
| | | 125 | | 0.6 | |
| | | 103 | | 0.7 | |
| | | 73 | | 0.8 | |
| | | 27 | | 0.9 | |
| | | 210 | | | 0.1 |
| | | 188 | | | 0.2 |
| | | 170 | | | 0.3 |
| | | 153 | | | 0.4 |
| | | 136 | | | 0.5 |
| | | 117 | | | 0.6 |
| | | 94 | | | 0.7 |
| | | 65 | | | 0.8 |
| | | 18 | | | 0.9 |

CD39, extracellular nucleotide triphosphate diphosphate hydrolase 1; CK, cytokeratin.

**Table S4.** Correlation of *ENTPD1* expression with the expression of genetic markers of ESCA TIICs in the TIMER2.0 database.

| Immune cells | Genetic markers | Unadjusted tumor purity | | Adjusted tumor purity | |
|---|---|---|---|---|---|
| | | rho | *P* value [a] | rho | *P* value [a] |
| CD8+ T cell | *CD8A* | 0.496 | <0.001*** | 0.458 | <0.001*** |
| | *CD8B* | 0.461 | <0.001*** | 0.424 | <0.001*** |
| T cell (general) | *CD3D* | 0.536 | <0.001*** | 0.489 | <0.001*** |
| | *CD3E* | 0.565 | <0.001*** | 0.520 | <0.001*** |
| | *CD2* | 0.607 | <0.001*** | 0.570 | <0.001*** |
| B cell | *CD19* | 0.417 | <0.001*** | 0.355 | <0.001*** |
| | *CD79A* | 0.437 | <0.001*** | 0.389 | <0.001*** |
| Monocyte | *CD86* | 0.502 | <0.001*** | 0.458 | <0.001*** |
| | *CD115 (CSF1R)* | 0.641 | <0.001*** | 0.618 | <0.001*** |
| TAM | *CCL2* | 0.529 | <0.001*** | 0.491 | <0.001*** |
| | *CD68* | 0.289 | <0.001*** | 0.252 | <0.001*** |
| | *IL10* | 0.534 | <0.001*** | 0.503 | <0.001*** |
| M1 Macrophage | *INOS (NOS2)* | 0.218 | 0.004** | 0.241 | 0.002** |
| | *IRF5* | -0.081 | 0.303 | -0.136 | 0.086 |
| | *COX2 (PTGS2)* | 0.282 | <0.001*** | 0.257 | <0.001*** |
| M2 Macrophage | *CD163* | 0.611 | <0.001*** | 0.58 | <0.001*** |
| | *VSIG4* | 0.515 | <0.001*** | 0.48 | <0.001*** |
| | *MS4A4A* | 0.617 | <0.001*** | 0.585 | <0.001*** |
| Neutrophils | *CD66b (CEACAM8)* | 0.125 | 0.104 | 0.106 | 0.184 |
| | *CD11b (ITGAM)* | 0.490 | <0.001*** | 0.446 | <0.001*** |
| | *CCR7* | 0.614 | <0.001*** | 0.575 | <0.001*** |
| Natural killer cell | *KIR2DL1* | 0.183 | 0.017* | 0.136 | 0.095 |
| | *KIR2DL3* | 0.195 | 0.011* | 0.179 | 0.025* |
| | *KIR2DL4* | 0.204 | 0.008** | 0.158 | 0.051 |
| | *KIR3DL1* | 0.274 | <0.001*** | 0.231 | 0.003** |
| | *KIR3DL2* | 0.131 | 0.093 | 0.075 | 0.371 |
| | *KIR3DL3* | 0.020 | 0.809 | 0.017 | 0.862 |
| | *KIR2DS4* | 0.123 | 0.118 | 0.106 | 0.202 |
| Dendritic cell | *HLA-DPB1* | 0.603 | <0.001*** | 0.568 | <0.001*** |
| | *HLA-DQB1* | 0.372 | <0.001*** | 0.32 | <0.001*** |
| | *HLA-DRA* | 0.572 | <0.001*** | 0.536 | <0.001*** |
| | *HLA-DPA1* | 0.610 | <0.001*** | 0.581 | <0.001*** |
| | *BDCA-1 (CD1C)* | 0.458 | <0.001*** | 0.408 | <0.001*** |
| | *BDCA-4 (NRP1)* | 0.595 | <0.001*** | 0.565 | <0.001*** |
| | *CD11c (ITGAX)* | 0.620 | <0.001*** | 0.59 | <0.001*** |
| Th1 | *T-bet (TBX21)* | 0.516 | <0.001*** | 0.465 | <0.001*** |
| | *STAT4* | 0.666 | <0.001*** | 0.635 | <0.001*** |
| | *STAT1* | 0.296 | <0.001*** | 0.252 | <0.001*** |
| | *IFN (IFNG)* | 0.370 | <0.001*** | 0.318 | <0.001*** |

| | | | | | |
|---|---|---|---|---|---|
| | TNF | 0.211 | 0.006** | 0.158 | 0.052 |
| Th2 | GATA3 | 0.379 | <0.001*** | 0.33 | <0.001*** |
| | STAT6 | 0.235 | 0.002** | 0.262 | <0.001*** |
| | STAT5A | 0.565 | <0.001*** | 0.542 | <0.001*** |
| | IL13 | 0.429 | <0.001*** | 0.385 | <0.001*** |
| Tfh | BCL6 | 0.005 | 0.948 | -0.009 | 0.923 |
| | IL21 | 0.269 | <0.001*** | 0.219 | 0.005** |
| Th17 | STAT3 | 0.284 | <0.001*** | 0.258 | <0.001*** |
| | IL17A | 0.159 | 0.040* | 0.164 | 0.040* |
| Treg | FOXP3 | 0.676 | <0.001*** | 0.655 | <0.001*** |
| | CCR8 | 0.715 | <0.001*** | 0.691 | <0.001*** |
| | STAT5B | 0.530 | <0.001*** | 0.556 | <0.001*** |
| | TGF (TGFB1) | -0.035 | 0.668 | -0.114 | 0.160 |
| T cell exhaustion | PD-1 (PDCD1) | 0.539 | <0.001*** | 0.503 | <0.001*** |
| | CTLA4 | 0.610 | <0.001*** | 0.575 | <0.001*** |
| | LAG3 | 0.421 | <0.001*** | 0.378 | <0.001*** |
| | TIM-3 (HAVCR2) | 0.647 | <0.001*** | 0.616 | <0.001*** |
| | GZMB | 0.318 | <0.001*** | 0.253 | 0.001** |

*ENTPD1*, ectonucleoside triphosphate diphosphohydrolase 1; ESCA, esophageal carcinoma; TIICs, tumor-infiltrating immune cells; rho, correlation coefficient. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$. [a] Spearman's rank correlation was performed.

**Table S5.** Correlation of *ENTPD1* expression with genetic markers of ESCA TIICs in the GEPIA2 database.

| Immune cells | Genetic markers | Tumor tissues | | Normal tissues | |
|---|---|---|---|---|---|
| | | rho | *P* value [a] | rho | *P* value [a] |
| CD8+ T-Cell | CD8A | 0.490 | <0.001*** | 0.290 | 0.340 |
| | CD8B | 0.460 | <0.001*** | 0.320 | 0.280 |
| Naive T-Cell | CCR7 | 0.600 | <0.001*** | 0.550 | 0.055 |
| | LEF1 | 0.300 | <0.001*** | 0.280 | 0.350 |
| | TCF7 | 0.230 | 0.002** | 0.120 | 0.710 |
| | SELL | 0.660 | <0.001*** | 0.530 | 0.064 |
| Effector T-Cell | CX3CR1 | 0.520 | <0.001*** | 0.740 | 0.005** |
| | FGFBP2 | 0.130 | 0.081 | 0.480 | 0.097 |
| | FCGR3A | 0.520 | <0.001*** | 0.750 | 0.003** |
| Effector memory T-Cell | PDCD1 | 0.570 | <0.001*** | 0.470 | 0.110 |
| | DUSP4 | 0.290 | <0.001*** | -0.320 | 0.280 |
| | GZMK | 0.620 | <0.001*** | 0.220 | 0.460 |
| | GZMA | 0.390 | <0.001*** | 0.500 | 0.079 |
| | IFNG | 0.380 | <0.001*** | 0.250 | 0.410 |
| Central memory T-Cell | CCR7 | 0.600 | <0.001*** | 0.550 | 0.055 |
| | SELL | 0.660 | <0.001*** | 0.530 | 0.064 |
| | IL7R | 0.560 | <0.001*** | 0.170 | 0.580 |
| Resident memory T-Cell | CD69 | 0.640 | <0.001*** | 0.700 | 0.008** |
| | ITGAE | 0.033 | 0.660 | 0.520 | 0.074 |
| | CXCR6 | 0.590 | <0.001*** | -0.110 | 0.710 |
| | MYADM | 0.500 | <0.001*** | 0.750 | 0.004** |
| Exhausted T-Cell | HAVCR2 | 0.680 | <0.001*** | 0.850 | <0.001*** |
| | TIGIT | 0.600 | <0.001*** | 0.430 | 0.140 |
| | LAG3 | 0.400 | <0.001*** | 0.760 | 0.004** |
| | PDCD1 | 0.570 | <0.001*** | 0.470 | 0.110 |
| | CXCL13 | 0.410 | <0.001*** | -0.071 | 0.820 |
| | LAYN | 0.320 | <0.001*** | 0.820 | <0.001*** |
| Resting Treg T-Cell | FOXP3 | 0.690 | <0.001*** | 0.210 | 0.490 |
| | IL2RA | 0.660 | <0.001*** | 0.870 | <0.001*** |
| Effector Treg T-Cell | FOXP3 | 0.690 | <0.001*** | 0.210 | 0.490 |
| | CTLA4 | 0.630 | <0.001*** | 0.200 | 0.520 |
| | CCR8 | 0.720 | <0.001*** | -0.064 | 0.840 |
| | TNFRSF9 | 0.580 | <0.001*** | 0.390 | 0.180 |
| Th1-like | CXCL13 | 0.410 | <0.001*** | -0.071 | 0.820 |
| | HAVCR2 | 0.680 | <0.001*** | 0.850 | <0.001*** |
| | IFNG | 0.380 | <0.001*** | 0.250 | 0.410 |
| | CXCR3 | 0.500 | <0.001*** | 0.470 | 0.110 |

| | | | | |
|---|---|---|---|---|
| BHLHE40 | -0.001 | 0.990 | 0.680 | 0.013[*] |
| CD4 | 0.740 | <0.001[***] | 0.810 | 0.001[**] |

ENTPD1, ectonucleoside triphosphate diphosphohydrolase 1; ESCA, esophageal carcinoma; TIICs, tumor-infiltrating immune cells; rho, correlation coefficient. [*]$P < 0.05$, [**]$P < 0.01$, [***]$P < 0.001$. [a] Spearman's rank correlation was performed.
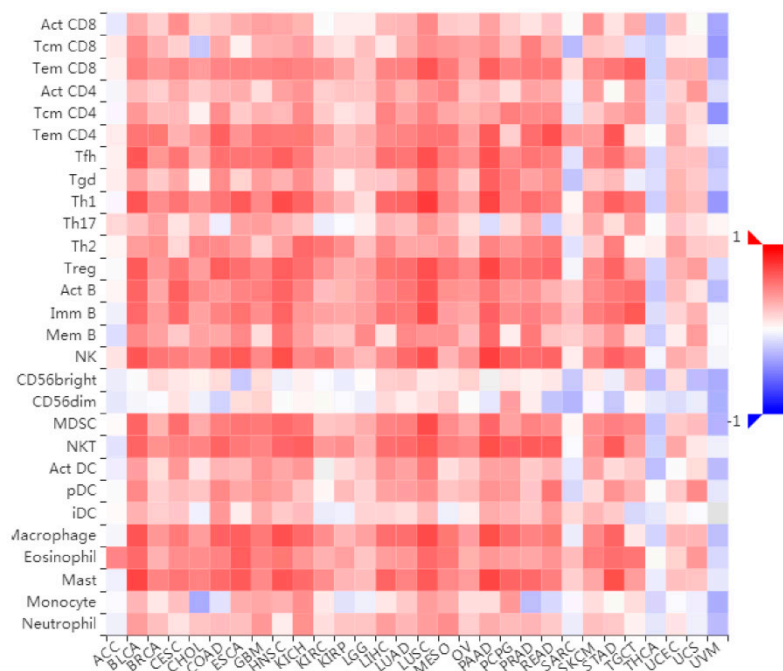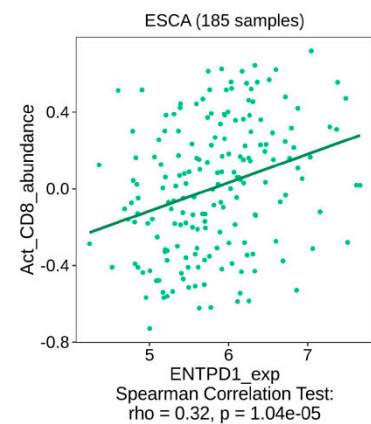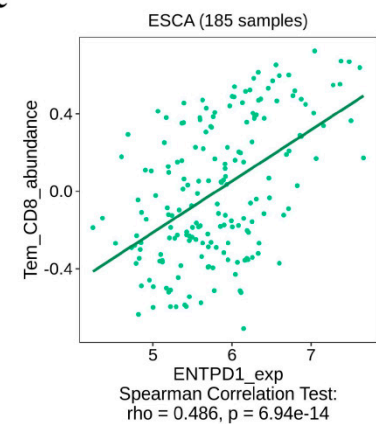
**a**

Act CD8
Tcm CD8
Tem CD8
Act CD4
Tcm CD4
Tem CD4
Tfh
Tgd
Th1
Th17
Th2
Treg
Act B
Imm B
Mem B
NK
CD56bright
CD56dim
MDSC
NKT
Act DC
pDC
iDC
Macrophage
Eosinophil
Mast
Monocyte
Neutrophil

ACC BLCA BRCA CESC CHOL COAD ESCA GBM HNSC KICH KIRC KIRP LGG LIHC LUAD LUSC MESO OV PAAD PCPG PRAD READ SARC SKCM STAD TGCT THCA UCEC UCS UVM

**b**

ESCA (185 samples)

ENTPD1_exp

Spearman Correlation Test:
rho = 0.32, p = 1.04e-05

**c**

ESCA (185 samples)

ENTPD1_exp

Spearman Correlation Test:
rho = 0.486, p = 6.94e-14

**d**

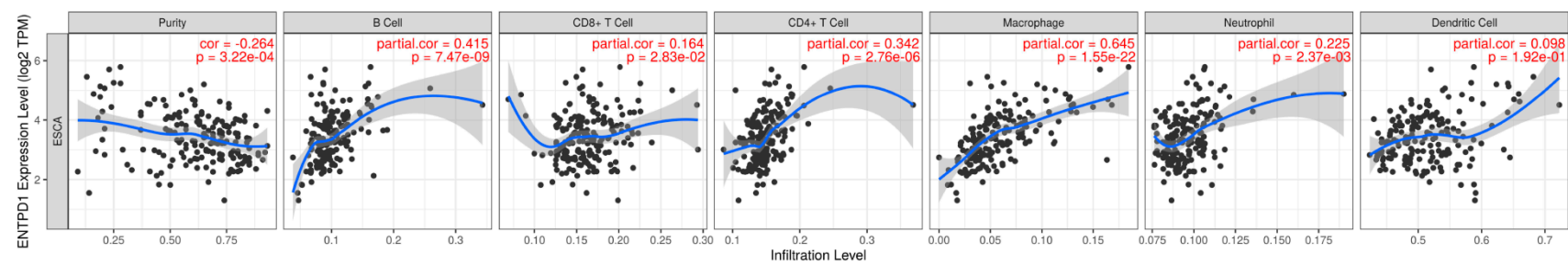| Purity | B Cell | CD8+ T Cell | CD4+ T Cell | Macrophage | Neutrophil | Dendritic Cell |
|---|---|---|---|---|---|---|
| cor = -0.264 | partial.cor = 0.415 | partial.cor = 0.164 | partial.cor = 0.342 | partial.cor = 0.645 | partial.cor = 0.225 | partial.cor = 0.098 |
| p = 3.22e-04 | p = 7.47e-09 | p = 2.83e-02 | p = 2.76e-06 | p = 1.55e-22 | p = 2.37e-03 | p = 1.92e-01 |

ENTPD1 Expression Level (log2 TPM)

Infiltration Level

**Figure S1.** Correlation of *ENTPD1* expression with the abundance of TIICs in ESCA [a]. (**a**) Correlation of *ENTPD1* expression with the abundance of TIICs in the TISIDB database; (**b, c**) Correlation of *ENTPD1* expression with the abundances of active CD8$^+$ T cells and memory CD8$^+$ T cell in the TISIDB database; (**d**) Correlation of *ENTPD1* expression with the abundance of six types of TIICs in the TIMER database. *ENTPD1*, extracellular nucleotide triphosphate diphosphate-1; ESCA, esophageal carcinoma; TIICs, tumor-infiltrating immune cells; rho, correlation coefficient; cor, correlation coefficient. [a] Spearman's rank correlation was performed.
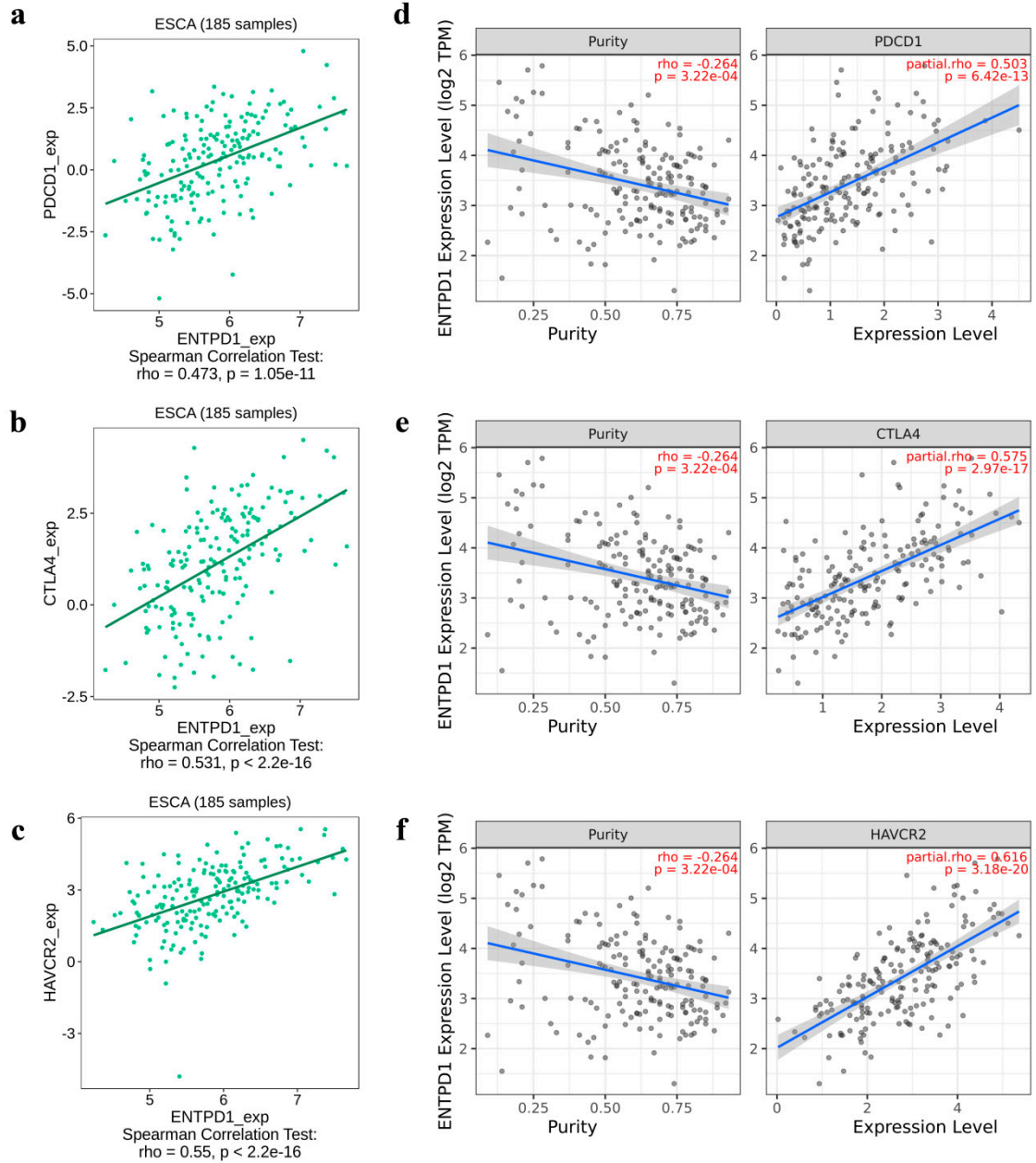
**Figure S2.** Correlation of *ENTPD1* expression with the expression of inhibitory immune checkpoint molecules in ESCA [a]. (**a-c**) Correlation of *ENTPD1* expression with the expression of *PDCD1*, *CTLA4* and *HAVCR2* in the TISIDB database; (**d-f**) Correlation of *ENTPD1* expression with the expression of *PDCD1*, *CTLA4* and *HAVCR2* in the TIMER2.0 database**.** *CTLA4*, cytotoxic T-lymphocyte-associated protein 4; *ENTPD1*, extracellular nucleotide triphosphate diphosphatehydrolase-1; ESCA, esophageal carcinoma; rho, correlation coefficient; *HAVCR2*, hepatitis A virus cellular receptor 2; *PDCD1*, programmed cell death protein 1. [a] Spearman's rank correlation was performed.