

TSPO is a potential independent prognostic factor associated with cellular respiration and p16 in head and neck squamous cell carcinoma

Sanni Tuominen^{1,2,3}, Linda Nissi⁴, Antti Kukkula², Johannes Routila⁵, Teemu Huusko⁵, Ilmo Leivo⁶, Heikki Minn⁴, Heikki Irjala⁵, Eliisa Löyttyniemi⁷, Sami Ventelä⁵, Maria Sundvall^{2,4} and Tove J. Grönroos^{1,3,4}

¹Preclinical Imaging Laboratory, Turku PET Centre, University of Turku, Turku, Finland

²Cancer Research Unit, Institute of Biomedicine, and FICAN West Cancer Research Laboratory, Turku University Hospital and University of Turku, Turku, Finland

³Medicity Research Laboratory, Faculty of Medicine, University of Turku, Turku, Finland

⁴Department of Clinical Oncology, Turku University Hospital and University of Turku, Turku, Finland

⁵Department of Otorhinolaryngology – Head and Neck Surgery, Turku University Hospital and University of Turku, Turku, Finland

⁶Department of Pathology, Turku University Hospital and University of Turku, Turku, Finland

⁷Department of Biostatistics, Turku University Hospital and University of Turku, Turku, Finland

Supplementary Table S1. The number of patients with HNSCC in subgroups from which *TSPO* expression was available and used in the *in silico* analyses from the TCGA cohort.

		No. of patients	<i>TSPO</i> mRNA level (log ₂ (norm_value+1))	Data version
Sample type	Solid tissue normal	74	44	2019-12-06
	Primary	528	520	
	Total	609	566	
Site	Alveolar ridge	18	18	2019-12-06
	Base of tongue	27	27	
	Buccal mucosa	23	22	
	Floor of mouth	63	62	
	Hard palate	7	7	
	Hypopharynx	10	10	
	Larynx	117	116	
	Lip	3	3	
	Oral cavity	73	73	
	Oral tongue	133	130	
	Oropharynx	9	9	
	Tonsil	45	43	
	Total	528	520	
	Missing	0	0	
T	T1	37	35	2019-12-06
	T2	152	151	
	T3	139	135	
	T4	25	25	
	T4a	156	155	
	T4b	3	3	
	TX	12	12	
	Total	524	516	
	Missing	4	4	
N	N0	246	244	2019-12-06
	N1	85	83	
	N2	19	19	
	N2a	17	17	
	N2b	85	81	
	N2c	45	45	
	N3	9	9	
	NX	18	18	
	Total	524	516	
	Missing	4	4	
Stage	I	21	20	2019-12-06
	II	99	98	
	III	107	105	
	IVA	269	265	
	IVB	11	11	
	IVC	7	7	
	Total	514	506	
	Missing	14	14	
Grade	G1	63	62	2019-12-06
	G2	311	304	
	G3	125	125	
	G4	7	7	
	GX	18	18	
	Total	524	516	
	Missing	4	4	
p16	Negative	74	73	2019-12-06
	Positive	41	38	
	Total	115	111	
	Missing	413	409	

Supplementary Table S2. Top 100 genes with the highest positive expression with *TSPO*.

Correlated gene	Cytoband	Spearman's correlation	p-Value	q-Value
<i>MPST</i>	22q12.3	0.661	1.31E-62	2.64E-58
<i>NOL12</i>	22q13.1	0.604	6.07E-50	6.08E-46
<i>UQCR10</i>	22q12.2	0.597	1.68E-48	1.12E-44
<i>TRABD</i>	22q13.33	0.588	1.02E-46	3.41E-43
<i>RBX1</i>	22q13.2	0.587	1.29E-46	3.71E-43
<i>SMDT1</i>	22q13.2	0.569	3.91E-43	9.81E-40
<i>MCAT</i>	22q13.2	0.567	6.36E-43	1.42E-39
<i>TXN2</i>	22q12.3	0.565	1.97E-42	3.58E-39
<i>NDUFB7</i>	19p13.12	0.562	4.83E-42	6.92E-39
<i>COMTD1</i>	10q22.2	0.559	1.61E-41	1.61E-38
<i>PMVK</i>	1q21.3	0.553	1.75E-40	1.52E-37
<i>PGLS</i>	19p13.11	0.553	1.86E-40	1.55E-37
<i>MIF</i>	22q11.23	0.551	4.66E-40	3.60E-37
<i>NDUFA6</i>	22q13.2	0.548	1.26E-39	9.40E-37
<i>STAP2</i>	19p13.3	0.546	2.63E-39	1.82E-36
<i>RPS19BP1</i>	22q13.1	0.545	4.50E-39	2.79E-36
<i>SNU13</i>	22q13.2	0.545	4.58E-39	2.79E-36
<i>SELENOO</i>	22q13.33	0.543	9.53E-39	5.46E-36
<i>SCO2</i>	22q13.33	0.543	1.08E-38	5.99E-36
<i>MVB12A</i>	19p13.11	0.539	4.05E-38	2.20E-35
<i>GGA1</i>	22q13.1	0.535	1.62E-37	8.35E-35
<i>FBXL15</i>	10q24.32	0.534	2.17E-37	1.09E-34
<i>HSPB1</i>	7q11.23	0.531	6.67E-37	3.04E-34
<i>PMM1</i>	22q13.2	0.531	7.31E-37	3.26E-34
<i>GIPC1</i>	19p13.12	0.531	8.21E-37	3.58E-34
<i>NDUFA13</i>	19p13.11	0.524	1.04E-35	3.78E-33
<i>COPE</i>	19p13.11	0.522	1.78E-35	5.93E-33
<i>COX4I1</i>	16q24.1	0.520	3.16E-35	9.74E-33
<i>RPS15</i>	19p13.3	0.519	4.47E-35	1.32E-32
<i>WDR83OS</i>	19p13.13	0.519	4.93E-35	1.42E-32
<i>ZNF524</i>	19q13.42	0.519	5.35E-35	1.51E-32
<i>VAMP8</i>	2p11.2	0.518	7.03E-35	1.93E-32
<i>AURKAIP1</i>	1p36.33	0.518	8.48E-35	2.24E-32
<i>ATP5F1D</i>	19p13.3	0.517	9.23E-35	2.37E-32
<i>ZMAT5</i>	22q12.2	0.517	1.06E-34	2.65E-32
<i>POLR2F</i>	22q13.1	0.516	1.38E-34	3.37E-32
<i>COX8A</i>	11q13.1	0.516	1.53E-34	3.66E-32
<i>PICK1</i>	22q13.1	0.514	2.60E-34	5.80E-32
<i>RPS9</i>	19q13.42	0.514	3.19E-34	6.94E-32
<i>TRAPPC5</i>	19p13.2	0.513	4.88E-34	1.04E-31
<i>GUK1</i>	1q42.13	0.512	5.28E-34	1.09E-31
<i>TRADD</i>	16q22.1	0.511	7.21E-34	1.46E-31
<i>CCDC124</i>	19p13.11	0.510	1.06E-33	2.09E-31
<i>TEN1</i>	17q25.1	0.509	1.55E-33	2.94E-31
<i>FAM98C</i>	19q13.2	0.509	1.66E-33	3.12E-31
<i>GADD45GIP1</i>	19p13.13	0.507	3.17E-33	5.73E-31
<i>SGSM3</i>	22q13.1	0.504	7.20E-33	1.27E-30
<i>STUB1</i>	16p13.3	0.504	7.58E-33	1.32E-30
<i>HSPB1P1</i>	9q21.13	0.504	9.22E-33	1.58E-30
<i>ILVBL</i>	19p13.12	0.503	1.25E-32	2.08E-30
<i>TRIR</i>	19p13.13	0.502	1.50E-32	2.44E-30
<i>TBC1D22A</i>	22q13.31	0.500	3.31E-32	4.99E-30
<i>NME3</i>	16p13.3	0.499	3.83E-32	5.69E-30
<i>DDT</i>	22q11.23	0.499	4.19E-32	6.18E-30
<i>PRR34-AS1</i>	22q13.31	0.499	4.40E-32	6.44E-30
<i>COQ4</i>	9q34.11	0.498	5.12E-32	7.38E-30

Supplementary Table S2 (continued). Top 100 genes with the highest positive expression with *TSPO*.

Correlated Gene	Cytoband	Spearman's correlation	p-Value	q-Value
<i>MRPS34</i>	16p13.3	0.498	6.72E-32	9.43E-30
<i>RPL36</i>	19p13.3	0.497	7.33E-32	1.02E-29
<i>ECHS1</i>	10q26.3	0.496	1.12E-31	1.53E-29
<i>NDUFA11</i>	19p13.3	0.495	1.61E-31	2.19E-29
<i>PERM1</i>	1p36.33	0.494	1.98E-31	2.65E-29
<i>EDF1</i>	9q34.3	0.493	2.56E-31	3.36E-29
<i>TMEM134</i>	11q13.2	0.493	3.48E-31	4.47E-29
<i>RPL18A</i>	19p13.11	0.492	4.21E-31	5.28E-29
<i>ARF5</i>	7q32.1	0.491	5.20E-31	6.36E-29
<i>COPS9</i>	2q37.3	0.491	5.30E-31	6.45E-29
<i>UBA52</i>	19p13.1-p12	0.490	6.81E-31	8.04E-29
<i>ATP5MK</i>	10q24.33	0.490	7.71E-31	8.99E-29
<i>NDUFS7</i>	19p13.3	0.490	8.12E-31	9.42E-29
<i>SSNA1</i>	9q34.3	0.489	1.08E-30	1.23E-28
<i>UQCRQ</i>	5q31.1	0.489	1.17E-30	1.32E-28
<i>PYM1</i>	12q13.2	0.488	1.30E-30	1.46E-28
<i>S100A16</i>	1q21.3	0.488	1.51E-30	1.68E-28
<i>JOSD2</i>	19q13.33	0.486	2.60E-30	2.82E-28
<i>ALKBH7</i>	19p13.3	0.486	2.96E-30	3.13E-28
<i>COA3</i>	17q21.2	0.485	3.25E-30	3.41E-28
<i>COX6A1</i>	12q24.31	0.485	3.32E-30	3.47E-28
<i>ABHD17A</i>	19p13.3	0.485	3.65E-30	3.79E-28
<i>VPS28</i>	8q24.3	0.485	3.66E-30	3.79E-28
<i>NDUFA7</i>	19p13.2	0.484	4.97E-30	5.06E-28
<i>RPL37A</i>	2q35	0.484	5.40E-30	5.47E-28
<i>NR2F6</i>	19p13.11	0.483	6.41E-30	6.37E-28
<i>RAB24</i>	5q35.3	0.483	7.64E-30	7.55E-28
<i>RPL34</i>	4q25	0.482	8.64E-30	8.41E-28
<i>TMEM191A</i>	22q11.21	0.482	9.02E-30	8.69E-28
<i>CCDC12</i>	3p21.31	0.481	1.34E-29	1.27E-27
<i>TOMM22</i>	22q13.1	0.480	1.86E-29	1.73E-27
<i>INKA1</i>	3p21.31	0.478	3.10E-29	2.76E-27
<i>MRPL41</i>	9q34.3	0.477	4.76E-29	4.13E-27
<i>TST</i>	22q12.3	0.476	4.99E-29	4.28E-27
<i>RPS19</i>	19q13.2	0.475	7.68E-29	6.44E-27
<i>COX7A2</i>	6q14.1	0.474	9.64E-29	7.83E-27
<i>PRDX5</i>	11q13.1	0.474	9.96E-29	8.02E-27
<i>SNRPD3</i>	22q11.23	0.474	1.13E-28	9.00E-27
<i>UQCR11</i>	19p13.3	0.474	1.13E-28	9.00E-27
<i>NUDT8</i>	11q13.2	0.474	1.18E-28	9.36E-27
<i>UBL5</i>	19p13.2	0.473	1.48E-28	1.16E-26
<i>TRMU</i>	22q13.31	0.473	1.50E-28	1.17E-26
<i>ATF4</i>	22q13.1	0.473	1.52E-28	1.18E-26
<i>YIF1B</i>	19q13.2	0.473	1.59E-28	1.22E-26

Supplementary Table S3. Top 100 genes with the highest negative expression with *TSPO*.

Correlated gene	Cytoband	Spearman's correlation	p-Value	q-Value
<i>ROCK2</i>	2p25.1	-0.597	2.26E-48	1.13E-44
<i>ROCK1</i>	18q11.1	-0.593	1.38E-47	5.54E-44
<i>RIF1</i>	2q23.3	-0.566	1.17E-42	2.35E-39
<i>TRIM44</i>	11p13	-0.564	2.17E-42	3.59E-39
<i>NEU3</i>	11q13.4	-0.564	2.33E-42	3.59E-39
<i>HELZ</i>	17q24.2	-0.561	7.18E-42	8.85E-39
<i>TTBK2</i>	15q15.2	-0.561	7.23E-42	8.85E-39
<i>ZNF281</i>	1q32.1	-0.561	7.50E-42	8.85E-39
<i>ZKSCAN8</i>	6p21	-0.561	9.75E-42	1.09E-38
<i>TAF1L</i>	9p21.1	-0.560	1.43E-41	1.51E-38
<i>MED13</i>	17q23.2	-0.556	7.10E-41	6.78E-38
<i>NF1</i>	17q11.2	-0.555	8.61E-41	7.85E-38
<i>LATS1</i>	6q25.1	-0.552	2.64E-40	2.12E-37
<i>ATRX</i>	Xq21.1	-0.547	2.08E-39	1.49E-36
<i>RGPD4</i>	2q12.3	-0.546	3.40E-39	2.28E-36
<i>PHLPP2</i>	16q22.2	-0.545	4.07E-39	2.63E-36
<i>MAP3K2</i>	2q14.3	-0.544	5.41E-39	3.19E-36
<i>MED1</i>	17q12	-0.538	6.24E-38	3.29E-35
<i>UBR1</i>	15q15.2	-0.534	2.75E-37	1.35E-34
<i>TCF12</i>	15q21.3	-0.533	3.38E-37	1.61E-34
<i>MACF1</i>	1p34.3	-0.532	4.99E-37	2.33E-34
<i>RGPD3</i>	2q12.2	-0.530	1.12E-36	4.77E-34
<i>RAD54L2</i>	3p21.2	-0.529	1.76E-36	7.34E-34
<i>LIMS1</i>	2q12.3	-0.528	2.38E-36	9.72E-34
<i>MIGA1</i>	1p31.1	-0.528	2.55E-36	1.02E-33
<i>CCNT1</i>	12q13.11-q13.12	-0.526	4.15E-36	1.63E-33
<i>ERCC6L2</i>	9q22.32	-0.526	5.17E-36	1.99E-33
<i>ERCC4</i>	16p13.12	-0.524	8.16E-36	3.09E-33
<i>GCC2</i>	2q12.3	-0.524	8.32E-36	3.09E-33
<i>ZNF81</i>	Xp11.23	-0.523	1.48E-35	5.22E-33
<i>ASAP1</i>	8q24.21-q24.22	-0.523	1.48E-35	5.22E-33
<i>PIK3C2A</i>	11p15.1	-0.522	1.57E-35	5.45E-33
<i>ZNF106</i>	15q15.1	-0.522	1.61E-35	5.47E-33
<i>ASXL2</i>	2p23.3	-0.522	1.84E-35	6.05E-33
<i>RBM27</i>	5q32	-0.522	1.92E-35	6.20E-33
<i>GPATCH8</i>	17q21.31	-0.522	2.04E-35	6.51E-33
<i>ADAT1</i>	16q23.1	-0.522	2.13E-35	6.67E-33
<i>SMURF2</i>	17q23.3-q24.1	-0.520	4.26E-35	1.28E-32
<i>TAOK1</i>	17q11.2	-0.520	4.28E-35	1.28E-32
<i>BBX</i>	3q13.12	-0.519	4.94E-35	1.42E-32
<i>INTS2</i>	17q23.2	-0.519	5.98E-35	1.67E-32
<i>ZSCAN29</i>	15q15.3	-0.518	7.38E-35	2.00E-32
<i>PPP1R12A</i>	12q21.2-q21.31	-0.518	8.16E-35	2.18E-32
<i>YLPM1</i>	14q24.3	-0.518	8.69E-35	2.26E-32
<i>DHX33</i>	17p13.2	-0.517	1.03E-34	2.63E-32
<i>PHF3</i>	6q12	-0.516	1.37E-34	3.37E-32
<i>FAM168A</i>	11q13.4	-0.516	1.41E-34	3.41E-32
<i>DPP8</i>	15q22.31	-0.515	1.93E-34	4.56E-32
<i>ADAM10</i>	15q21.3	-0.515	1.98E-34	4.61E-32
<i>BIRC6</i>	2p22.3	-0.515	2.09E-34	4.83E-32
<i>UGGT1</i>	2q14.3	-0.515	2.31E-34	5.26E-32
<i>CBL</i>	11q23.3	-0.515	2.42E-34	5.46E-32
<i>REST</i>	4q12	-0.514	2.96E-34	6.53E-32
<i>TGFBRAP1</i>	2q12.1-q12.2	-0.514	3.22E-34	6.94E-32
<i>N4BP2</i>	4p14	-0.512	5.19E-34	1.09E-31
<i>MDN1</i>	6q15	-0.512	5.28E-34	1.09E-31

Supplementary Table S3 (continued). Top 100 genes with the highest negative expression with *TSPO*.

Correlated gene	Cytoband	Spearman's correlation	p-Value	q-Value
<i>PTPN11</i>	12q24.13	-0.512	6.29E-34	1.29E-31
<i>MGAT5</i>	2q21.2-q21.3	-0.510	1.03E-33	2.07E-31
<i>PDE3A</i>	12p12.2	-0.510	1.04E-33	2.07E-31
<i>TAF1</i>	Xq13.1	-0.510	1.10E-33	2.15E-31
<i>KIRREL1</i>	1q23.1	-0.510	1.17E-33	2.26E-31
<i>CASP8AP2</i>	6q15	-0.510	1.33E-33	2.54E-31
<i>ANKRD40</i>	17q21.33	-0.509	1.81E-33	3.36E-31
<i>KLHL11</i>	17q21.2	-0.508	2.35E-33	4.33E-31
<i>MGA</i>	15q15	-0.508	2.42E-33	4.41E-31
<i>MYO9A</i>	15q23	-0.505	6.12E-33	1.10E-30
<i>SPTBN1</i>	2p16.2	-0.505	7.14E-33	1.27E-30
<i>ZFR</i>	5p13.3	-0.504	8.16E-33	1.41E-30
<i>CKAP5</i>	11p11.2	-0.504	9.53E-33	1.62E-30
<i>REV3L</i>	6q21	-0.503	1.09E-32	1.84E-30
<i>MED13L</i>	12q24.21	-0.503	1.34E-32	2.21E-30
<i>PDPR</i>	16q22.1	-0.502	1.39E-32	2.29E-30
<i>RAB11FIP2</i>	10q26.11	-0.501	1.92E-32	3.11E-30
<i>RASSF8</i>	12p12.1	-0.501	2.66E-32	4.28E-30
<i>UBXN7</i>	3q29	-0.500	2.74E-32	4.36E-30
<i>TBCEL</i>	11q23.3	-0.500	2.77E-32	4.37E-30
<i>PRKDC</i>	8q11.21	-0.500	2.79E-32	4.38E-30
<i>GTF2A1</i>	14q31.1	-0.500	2.87E-32	4.42E-30
<i>MTR</i>	1q43	-0.500	2.87E-32	4.42E-30
<i>ATF2</i>	2q31.1	-0.500	3.10E-32	4.74E-30
<i>TEAD1</i>	11p15.3	-0.500	3.30E-32	4.99E-30
<i>CEP170</i>	1q43	-0.500	3.39E-32	5.07E-30
<i>STK4</i>	20q13.12	-0.499	5.08E-32	7.38E-30
<i>IL6ST</i>	5q11.2	-0.498	5.48E-32	7.85E-30
<i>SEL1L</i>	14q31	-0.498	6.00E-32	8.50E-30
<i>TRIO</i>	5p15.2	-0.498	6.02E-32	8.50E-30
<i>ADNP</i>	20q13.13	-0.496	1.01E-31	1.39E-29
<i>CDC27</i>	17q21.32	-0.496	1.08E-31	1.48E-29
<i>TP53BP1</i>	15q15.3	-0.495	1.69E-31	2.28E-29
<i>SHPRH</i>	6q24.3	-0.494	2.10E-31	2.79E-29
<i>CDK12</i>	17q12	-0.494	2.24E-31	2.96E-29
<i>KDM5A</i>	12p13.33	-0.493	2.59E-31	3.37E-29
<i>ANKRD36BP1</i>	1q24.2	-0.493	2.91E-31	3.76E-29
<i>SLX4IP</i>	20p12.2	-0.492	3.72E-31	4.75E-29
<i>SON</i>	21q22.11	-0.492	3.97E-31	5.04E-29
<i>SMG1</i>	16p12.3	-0.492	4.13E-31	5.21E-29
<i>PCNX1</i>	14q24.2	-0.492	4.37E-31	5.44E-29
<i>PALM2AKAP2</i>	9q31.3	-0.492	4.69E-31	5.81E-29
<i>RANBP2</i>	2q13	-0.491	4.84E-31	5.95E-29
<i>TGOLN2</i>	2p11.2	-0.491	5.45E-31	6.59E-29

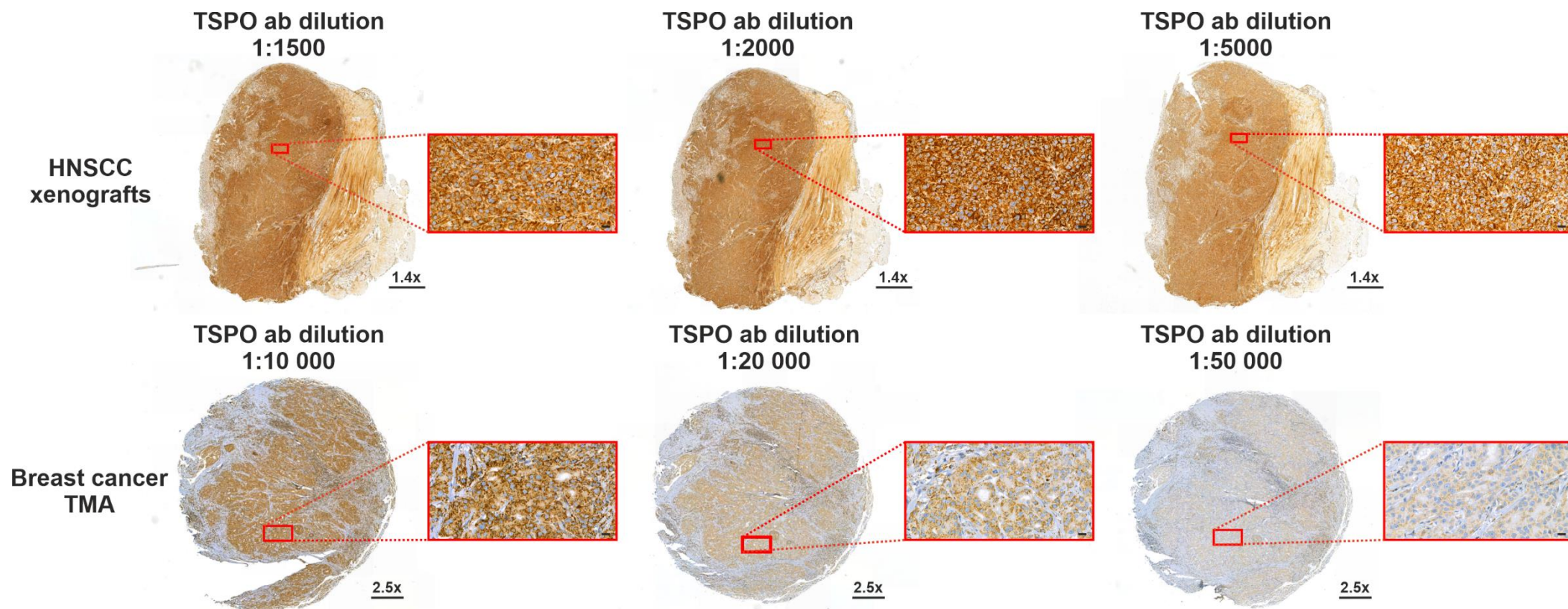
Supplementary Table S4. Univariate survival analyses of TSPO expression and clinicopathological features of patients with HNSCC in the TMA patient cohort.

	TSPO expression	OS		DSS		DFS		
		Survival effect HR (95% CI)	p-value	Survival effect HR (95% CI)	p-value	Survival effect HR (95% CI)	p-value	
T	T1–T2	Low	1	-	1	-	1	-
		High	0.687 (0.476–0.992)	0.045	0.469 (0.289–0.760)	0.002	0.627 (0.414–0.949)	0.027
	T3–T4	Low	1	-	1	-	1	-
		High	0.864 (0.632–1.180)	0.357	0.822 (0.575–1.174)	0.281	1.209 (0.767–1.905)	0.413
N	N0	Low	1	-	1	-	1	-
		High	0.713 (0.502–1.012)	0.058	0.567 (0.355–0.908)	0.018	0.868 (0.553–1.361)	0.537
	N+	Low	1	-	1	-	1	-
		High	0.722 (0.526–0.992)	0.044	0.658 (0.459–0.941)	0.022	0.715 (0.469–1.089)	0.118
Stage	0–II	Low	1	-	1	-	1	-
		High	0.733 (0.461–1.164)	0.188	0.430 (0.222–0.835)	0.013	0.613 (0.365–1.031)	0.065
	III–IV	Low	1	-	1	-	1	-
		High	0.764 (0.582–1.003)	0.053	0.722 (0.527–0.988)	0.042	0.939 (0.646–1.364)	0.740
Grade	G1	Low	1	-	1	-	1	-
		High	0.766 (0.470–1.251)	0.287	0.554 (0.297–1.033)	0.063	0.674 (0.384–1.181)	0.168
	G2	Low	1	-	1	-	1	-
		High	0.629 (0.440–0.899)	0.011	0.571 (0.376–0.868)	0.009	0.706 (0.451–1.106)	0.128
	G3	Low	1	-	1	-	1	-
		High	0.772 (0.493–1.209)	0.258	0.667 (0.390–1.139)	0.138	1.029 (0.539–1.965)	0.931

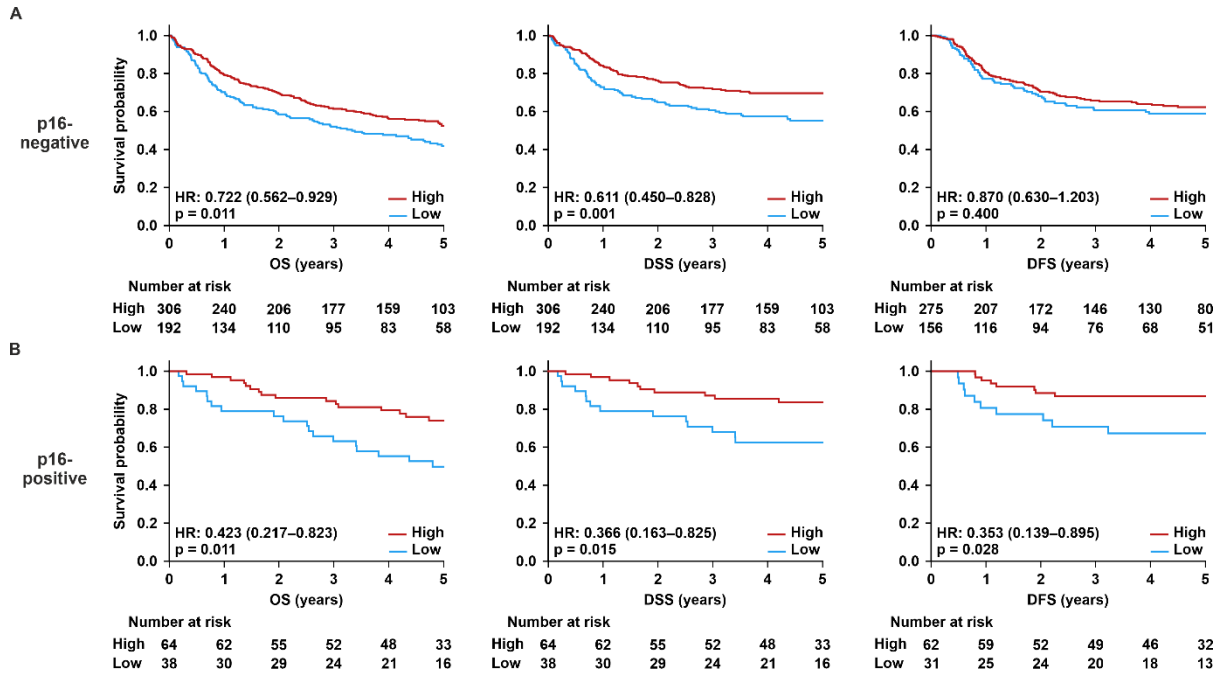
TSPO staining intensity scores of 0–1 were considered low and scores 2–3 as high. Statistical significance was calculated using Cox’s proportional hazard model. p-values < 0.05 were considered statistically significant (shown in bold). OS = overall survival, DSS = disease-specific survival, DFS = disease-free survival, HR = hazard ratio, CI = confidence interval.

Supplementary Table S7. Abbreviations for cancer types listed in Figure 4D.

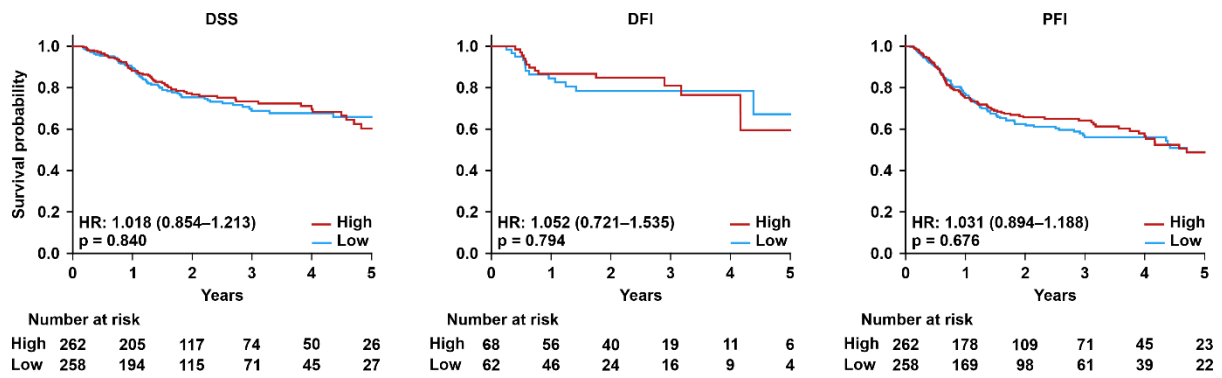
Abbreviation	Cancer
ACC	Adrenocortical carcinoma
BLCA	Bladder urothelial carcinoma
BRCA	Breast invasive carcinoma
CESC	Cervical and endocervical cancers
CHOL	Cholangiocarcinoma
COAD	Colon adenocarcinoma
ESCA	Esophageal carcinoma
KICH	Kidney chromophobe
KIRC	Kidney renal clear cell carcinoma
KIRP	Kidney renal papillary cell carcinoma
LIHC	Liver hepatocellular carcinoma
LUAD	Lung adenocarcinoma
LUSC	Lung squamous cell carcinoma
MESO	Mesothelioma
OV	Ovarian serous cystadenocarcinoma
PAAD	Pancreatic adenocarcinoma
PCPG	Pheochromocytoma and paraganglioma
PRAD	Prostate adenocarcinoma
READ	Rectum adenocarcinoma
SARC	Sarcoma
SKCM	Skin cutaneous melanoma
STAD	Stomach adenocarcinoma
THCA	Thyroid carcinoma
UCEC	Uterine corpus endometrial carcinoma
UCS	Uterine carcinosarcoma
UVM	Uveal melanoma



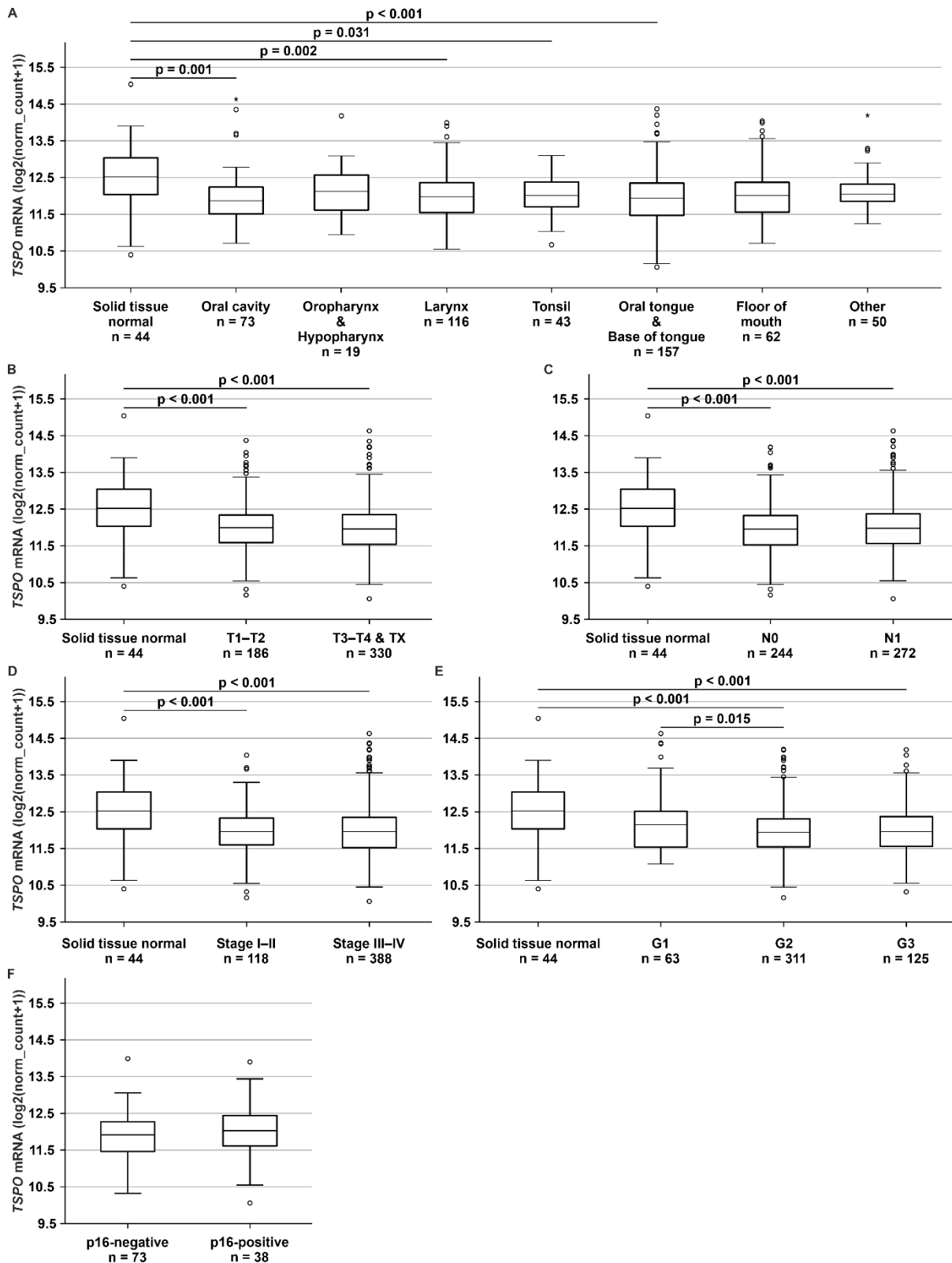
Supplementary Fig. S1 TSPO IHC optimization. TSPO IHC staining with different antibody (monoclonal rabbit TSPO antibody, Abcam ab109497) dilutions were performed to find the optimal antibody dilution for TMA IHC stainings. Stainings were done with HNSCC xenograft tumors and breast cancer TMAs. 1:50 000 dilution was found to be the most optimal for stainings. Scale bars for xenograft tumors: 1000 μm (whole section) and 20 μm (inset). Scale bars for breast cancer TMA sections: 500 μm (whole section) and 20 μm (inset).



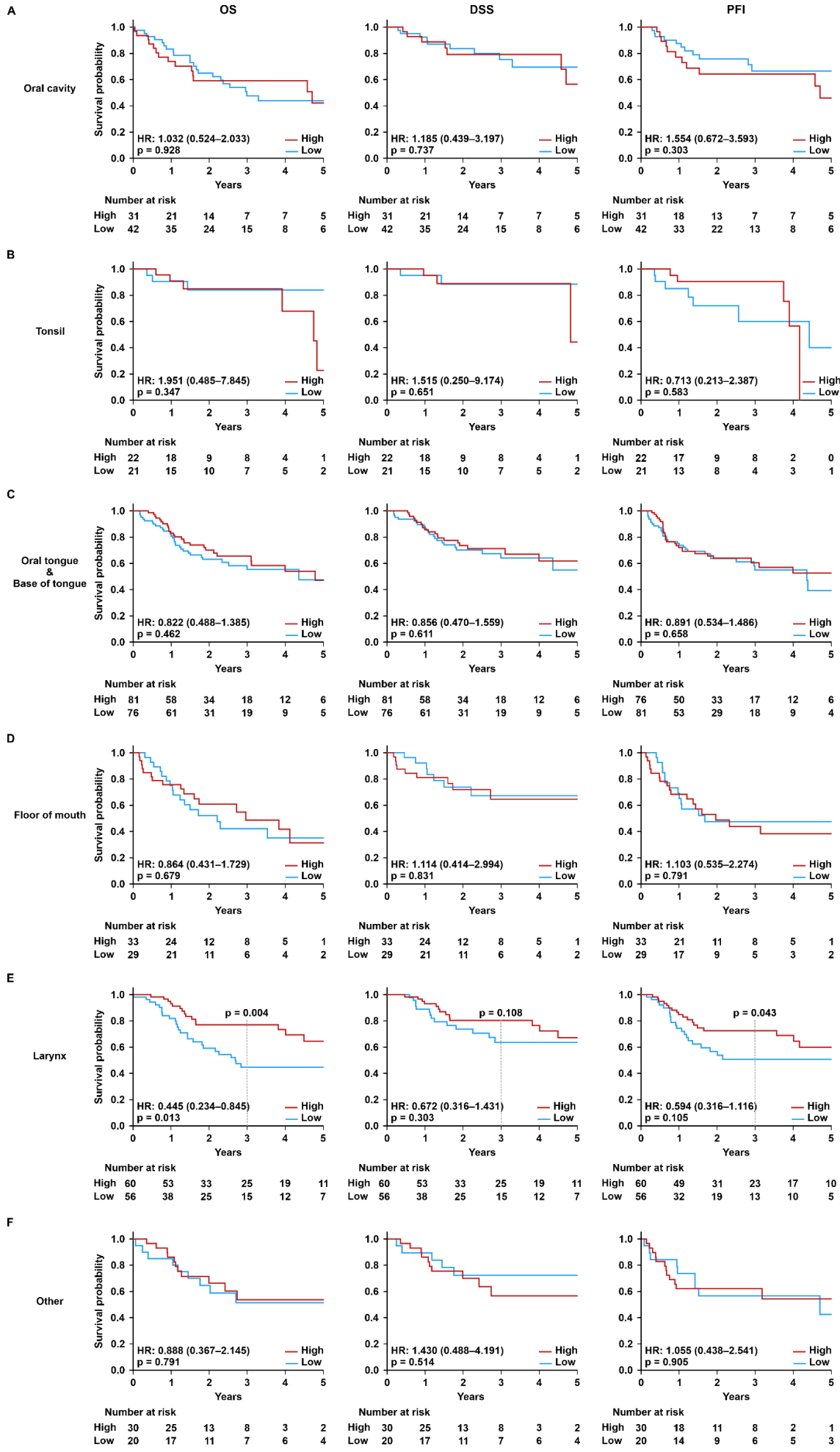
Supplementary Fig. S2 Effect of p16 and TSP0 expression on survival in the TMA cohort. Prognostic trends with HR (95% CI) for 5-year overall survival (OS), disease-specific survival (DSS), and disease-free survival (DFS) divided into low and high (staining intensity scores of 0–1 and 2–3, respectively) TSP0 tumor expression in patients with (A) p16-negative or (B) p16-positive tumors. Statistical significance was calculated using Cox’s proportional hazard model. p-values < 0.05 were considered statistically significant.



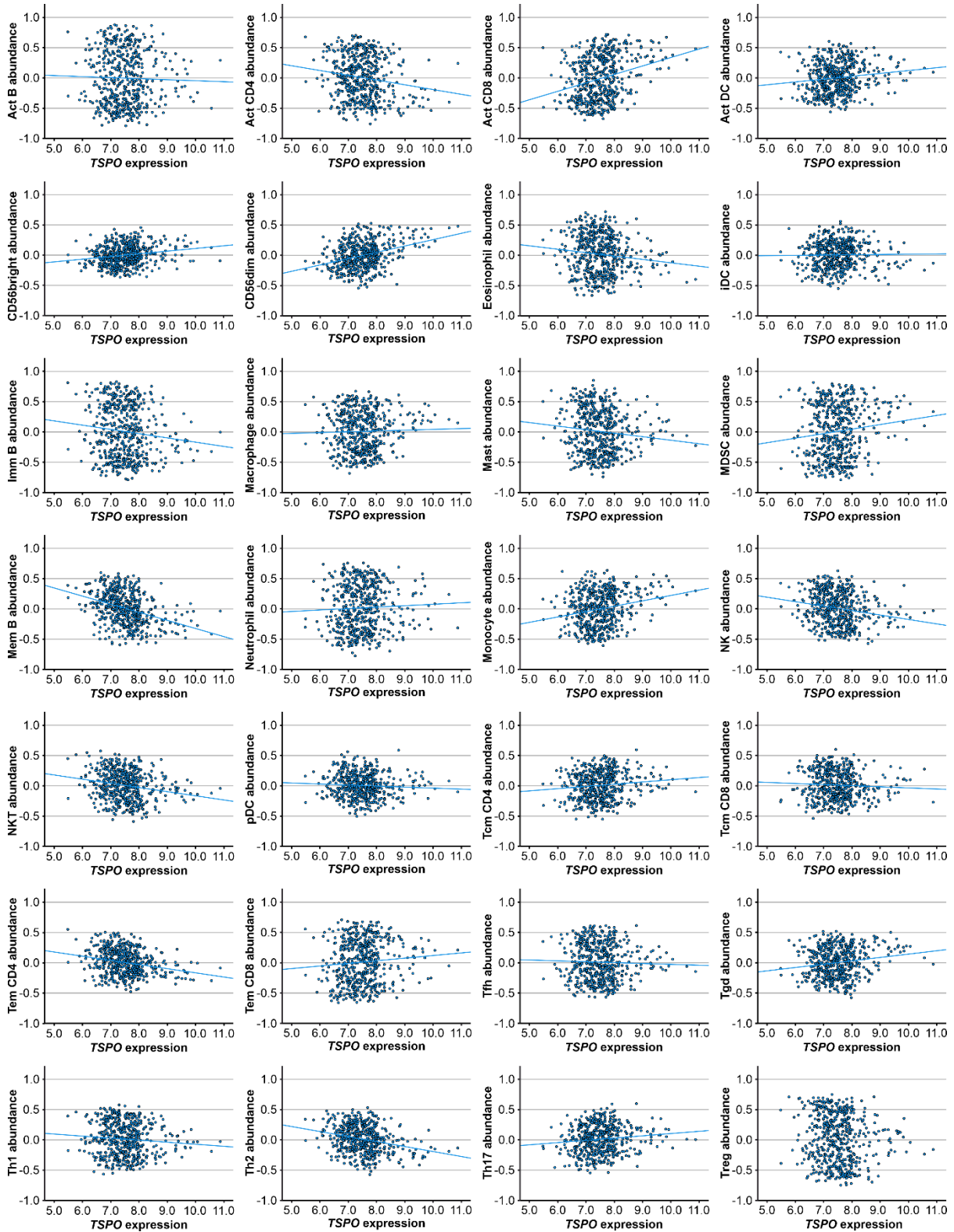
Supplementary Fig. S3 Effect of *TSPO* expression on survival in the TCGA HNSCC cohort. Prognostic trends with HR (95% CI) for 5-year disease-specific survival (DSS), disease-free interval (DFI), and progression-free interval (PFI) in low (below median) and high (equal to or above median) *TSPO* expression in all patients. Statistical significance was calculated using Cox's proportional hazard model. p-values < 0.05 were considered statistically significant.



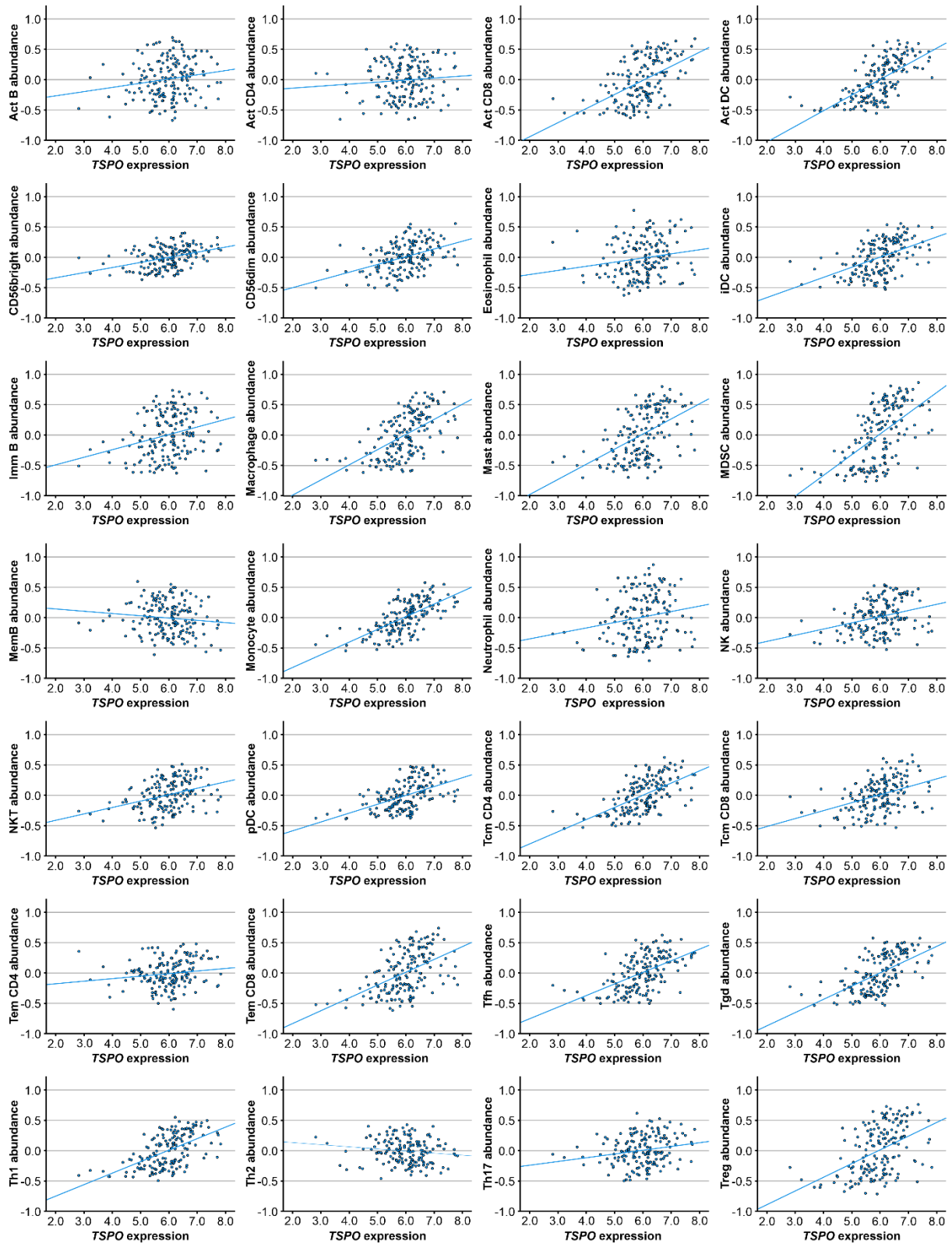
Supplementary Fig. S4 *TSPO* expression in clinicopathological subgroups from the TCGA HNSCC cohort. Boxplots visualizing *TSPO* expression according to (A) primary tumor site, (B) T classification, (C) N classification, (D) overall stage, (E) grade, and (F) p16 status. The box ranges from Q1 (first quartile) to Q3 (third quartile) of the median distribution, and the whiskers represent the range between minimum and maximum. Dots represent outlier values. Independent samples t-test (for comparing two groups) or one-way ANOVA with Bonferroni post hoc tests (for comparing more than two groups) was used to analyze differences in *TSPO* expression. p-values < 0.05 were considered statistically significant.



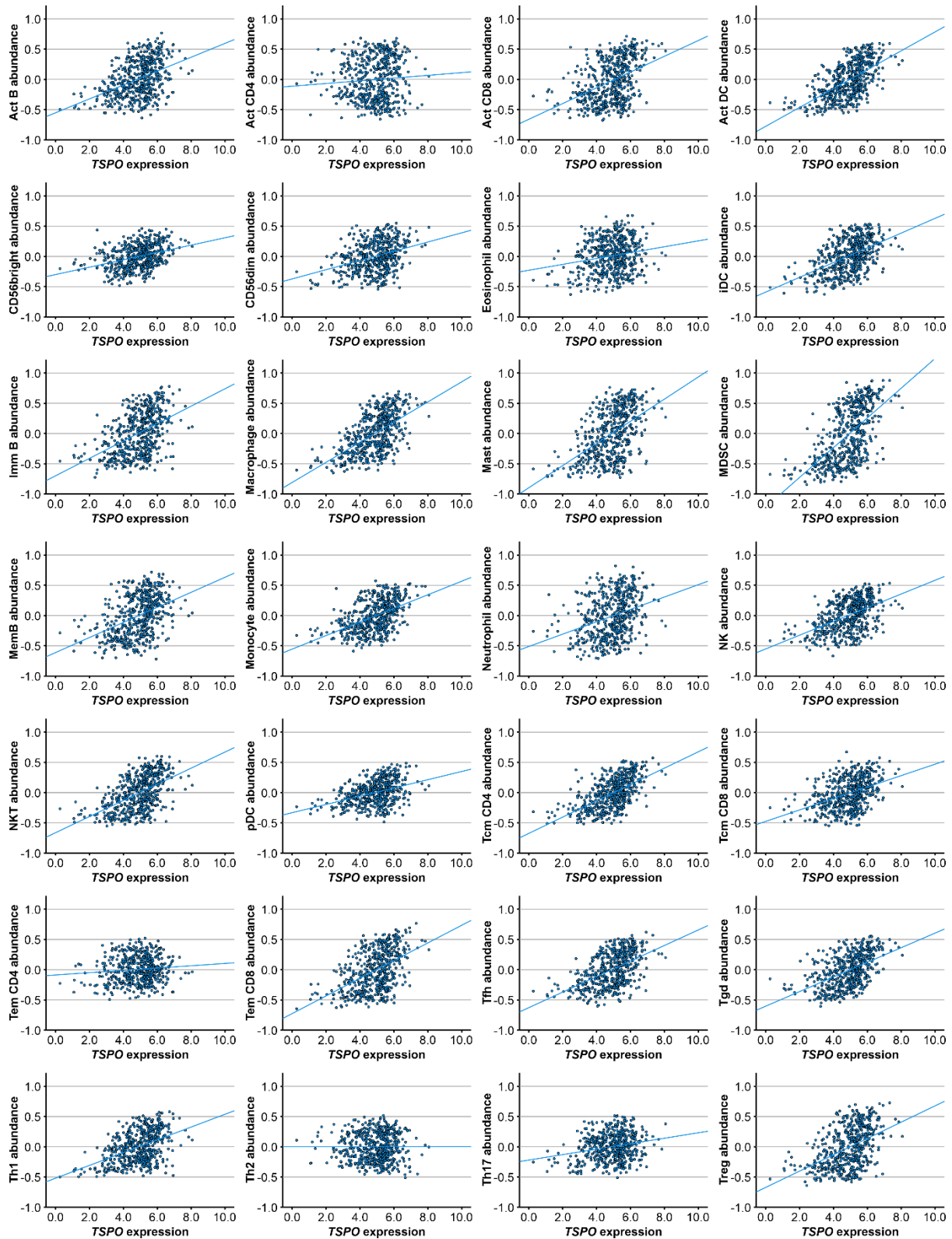
Supplementary Fig. S5 *TSPO* expression and site-specific survival analyses from the HNSCC TCGA cohort. Prognostic trends with HR (95% CI) for 5-year overall survival (OS), disease-specific survival (DSS), and progression-free interval (PFI) for *TSPO* expression in (A) oral cavity, (B) tonsil, (C) oral tongue and base of tongue, (D) floor of mouth, (E) larynx, and (F) other tumor sites. *TSPO* expression was divided into low (expression below median) and high (expression equal to or above median). Statistical significance was calculated using Cox's proportional hazard model. p-values < 0.05 were considered statistically significant.



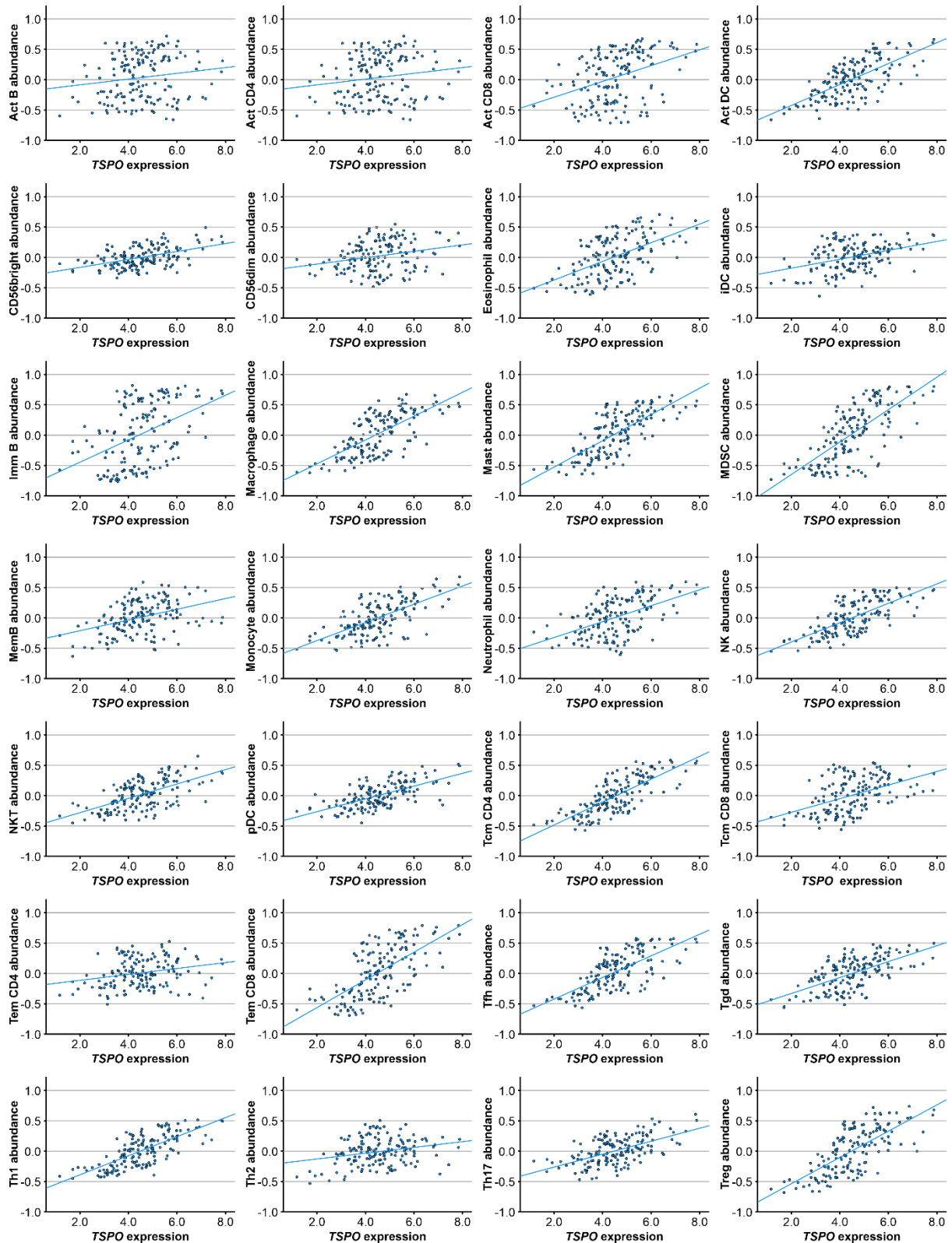
Supplementary Fig. S6 Scatter plots of immune cell abundance in relation to *TSPO* expression in HNSCC. The heatmap is shown in Figure 4D. Act = activated, IDC = interstitial dendritic cell, Imm = immature, MDSC = myeloid-derived suppressor cell, Mem = memory, NK = natural killer cell, NKT = natural killer T cell, pDC = plasmacytoid dendritic cell, Tcm = central memory cell, Tem = effector memory cell, Tfh = T follicular helper cell, Tgd = gamma delta T cell, Th1 = type 1 T helper cell, Th2 = type 2 T helper cell, Th17 = type 17 T helper cell, Treg = regulatory T cell.



Supplementary Fig. S7 Scatter plots of immune cell abundance in relation to *TSPO* expression in glioblastoma (GBM). The heatmap is shown in Figure 4D. Act = activated, IDC = interstitial dendritic cell, Imm = immature, MDSC = myeloid-derived suppressor cell, Mem = memory, NK = natural killer cell, NKT = natural killer T cell, pDC = plasmacytoid dendritic cell, Tcm = central memory cell, Tem = effector memory cell, Tfh = T follicular helper cell, Tgd = gamma delta T cell, Th1 = type 1 T helper cell, Th2 = type 2 T helper cell, Th17 = type 17 T helper cell, Treg = regulatory T cell.



Supplementary Fig. S8 Scatter plots of immune cell abundance in relation to *TSPO* expression in lower grade glioma (LGG). The heatmap is shown in Figure 4D. Act = activated, IDC = interstitial dendritic cell, Imm = immature, MDSC = myeloid-derived suppressor cell, Mem = memory, NK = natural killer cell, NKT = natural killer T cell, pDC = plasmacytoid dendritic cell, Tcm = central memory cell, Tem = effector memory cell, Tfh = T follicular helper cell, Tgd = gamma delta T cell, Th1 = type 1 T helper cell, Th2 = type 2 T helper cell, Th17 = type 17 T helper cell, Treg = regulatory T cell.



Supplementary Fig. S9 Scatter plots of immune cell abundance in relation to *TSPO* expression in testicular germ cell tumors (TGCT). The heatmap is shown in Figure 4D. Act = activated, IDC = interstitial dendritic cell, Imm = immature, MDSC = myeloid-derived suppressor cell, Mem = memory, NK = natural killer cell, NKT = natural killer T cell, pDC = plasmacytoid dendritic cell, Tcm = central memory cell, Tem = effector memory cell, Tfh = T follicular helper cell, Tgd = gamma delta T cell, Th1 = type 1 T helper cell, Th2 = type 2 T helper cell, Th17 = type 17 T helper cell, Treg = regulatory T cell.