Table S1 Correlations between the expression of each ADAMTSLs gene across all 33 cancer types tested with Pearson correlation tests

Variable	ADAMTSL1	ADAMTSL2	ADAMTSL3	ADAMTSL4	ADAMTSL5	THSD4	PAPLN
ADAMTSL1 _r	1	0.12	0.18	0.01	–0.08	0.22	–0.04
ADAMTSL1 _p	–	4.0e–32	7.2e–73	0.16	2.2e–17	2.6e–113	2.5e–05
ADAMTSL2_r	0.12	1	0.23	–0.07	–0.14	0.02	0.16
ADAMTSL2_p	4.0e–32	–	1.1e–125	3.3e–11	6.7e–45	0.028	1.2e–62
ADAMTSL3_r	0.18	0.23	1	0.16	–0.14	0.19	0.32
ADAMTSL3_p	7.2e–73	1.1e–125	–	2.2e–59	1.04e–45	1.6e–83	2.9e–245
ADAMTSL4_r	0.01	–0.07	0.16	1	0.25	–0.08	0.21
ADAMTSL4_p	0.16	3.3e–11	2.2e–59	–	1.6e–143	2.3e–17	1.6e–105
ADAMTSL5_r	–0.08	–0.14	–0.14	0.25	1	0.01	–0.02
ADAMTSL5_p	2.2e–17	6.7e–45	1.04e–45	1.6e–143	–	0.58	0.037
THSD4_r	0.22	0.02	0.19	–0.08	0.01	1	0.03
THSD4_p	2.6e–113	0.028	1.6e–83	2.3e–17	0.58	–	0.0049
PAPLN _r	–0.04	0.16	0.32	0.21	–0.02	0.03	1
PAPLN _p	2.5e–05	1.2e–62	2.9e–245	1.6e–105	0.037	0.0049	–

r, correlation coefficient; P, P values for the correlation test. ADAMTSLs: A disintegrin-like and metalloproteinase domain with thrombospondin type 1 motifs (ADAMTS)-like proteins.

Table S2 Correlations between ADAMTSLs and tumor stemness scores (RNAss and DNAss) and tumor infiltration scores (stromal scores, immune scores and estimate scores) across all 33 cancer types tested with Pearson correlation test

Variable	ADAMTSL1	ADAMTSL2	ADAMTSL3	ADAMTSL4	ADAMTSL5	THSD4	PAPLN
RNAss_r	–0.308	–0.429	–0.443	–0.176	0.127	–0.244	–0.402
RNAss_p	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
DNAss_r	–0.070	–0.121	–0.074	0.091	0.181	–0.165	–0.228
DNAss_p	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Stromal scores_r	0.294	0.257	0.313	0.287	–0.002	0.100	0.242
Stromal score_p	<0.001	<0.001	<0.001	<0.001	0.838	<0.001	<0.001
Immune scores_r	–0.011	–0.039	0.089	0.359	0.002	–0.206	0.279
Immune scores_p	0.245	<0.001	<0.001	<0.001	0.802	<0.001	<0.001
Estimate scores_r	0.141	0.106	0.213	0.365	<0.001	–0.076	0.293
Estimate scores_p	<0.001	<0.001	<0.001	<0.001	0.960	<0.001	<0.001

r, correlation coefficient; P, P values for the correlation test. ADAMTSLs, A disintegrin-like and metalloproteinase domain with thrombospondin type 1 motifs (ADAMTS)-like proteins; RNAss, RNA stemness; DNAss, DNA stemness.

Table S3 The list of significantly correlated genes and drugs with |r|>0.4 and P<0.01

Gene	Drug name	Correlation coefficient	P value
ADAMTSL1	Simvastatin	0.6338	5.45E–08
ADAMTSL1	Procarbazine	0.6018	3.67E–07
ADAMTSL1	Olaparib	0.5670	2.32E–06
ADAMTSL1	Staurosporine	0.5299	1.34E–05
ADAMTSL1	By-Product of CUDC-305	–0.4715	0.00014
ADAMTSL1	Testolactone	0.4542	0.00027
ADAMTSL1	Wortmannin	0.4036	0.0014
ADAMTSL2	Alectinib	0.4914	6.71E–05
ADAMTSL2	Etoposide	0.4194	0.00085
ADAMTSL2	Pipobroman	0.4023	0.0014
ADAMTSL3	AZD-9291	0.6721	4.10E–09
ADAMTSL3	Ibrutinib	0.6497	1.95E–08
ADAMTSL3	Afatinib	0.5974	4.68E–07
ADAMTSL3	Lapatinib	0.5684	2.17E–06
ADAMTSL3	Erlotinib	0.5454	6.60E–06
ADAMTSL3	Gefitinib	0.4557	0.00025
ADAMTSL4	Eribulin mesilate	–0.4089	0.0012
ADAMTSL4	Homoharringtonine	–0.4037	0.0014
ADAMTSL5	Palbociclib	–0.4521	0.00029
ADAMTSL5	Perifosine	–0.4314	0.00058
THSD4	Carmustine	–0.4682	0.00016
THSD4	Vincristine	–0.4510	0.00030
THSD4	Lomustine	–0.4096	0.0012
THSD4	Curcumin	–0.4072	0.0012
THSD4	Triciribine phosphate	0.4051	0.0013
PAPLN	AZD-9291	0.4517	0.00029
PAPLN	Erlotinib	0.4097	0.0011

r, correlation coefficient; P, P values for the correlation test.

Table S4 Correlations between ADAMTSLs and immune blockade molecules across all 33 cancer types tested with Pearson correlation tests

Variable	ADAMTSL1	ADAMTSL2	ADAMTSL3	ADAMTSL4	ADAMTSL5	THSD4	PAPLN
PDCD1LG2_r	0.24	0.02	0.17	0.36	0.051	−0.0058	0.27
PDCD1LG2_p	<2.2e−16	0.04	<2.2e−16	<2.2e−16	7e−08	0.54	<2.2e−16
PDCD1_r	0.026	−0.02	0.048	0.27	0.096	−0.091	0.27
PDCD1_p	0.0061	0.035	4.9e−07	<2.2e−16	<2.2e−16	<2.2e−16	<2.2e−16
CTLA4_r	0.056	−0.08	−0.018	0.28	0.23	−0.091	0.18
CTLA4_p	3.1e−09	<2.2e−16	0.058	<2.2e−16	<2.2e−16	<2.2e−16	<2.2e−16
LAG3_r	0.053	−0.13	−0.02	0.22	0.087	−0.099	0.091
LAG3_p	2.6e−08	<2.2e−16	0.039	<2.2e−16	<2.2e−16	<2.2e−16	<2.2e−16
HAVCR2_r	0.12	0.12	0.16	0.25	−0.12	−0.12	0.34
HAVCR2_p	<2.2e−16	<2.2e−16	<2.2e−16	<2.2e−16	<2.2e−16	<2.2e−16	<2.2e−16
CD274_r	0.01	0.017	0.089	0.25	0.088	−0.019	0.3
CD274_p	0.28	0.072	<2.2e−16	<2.2e−16	<2.2e−16	0.044	<2.2e−16

r, correlation coefficient; P, P values for the correlation test. ADAMTSLs, A disintegrin-like and metalloproteinase domain with thrombospondin type 1 motifs (ADAMTS)-like proteins.
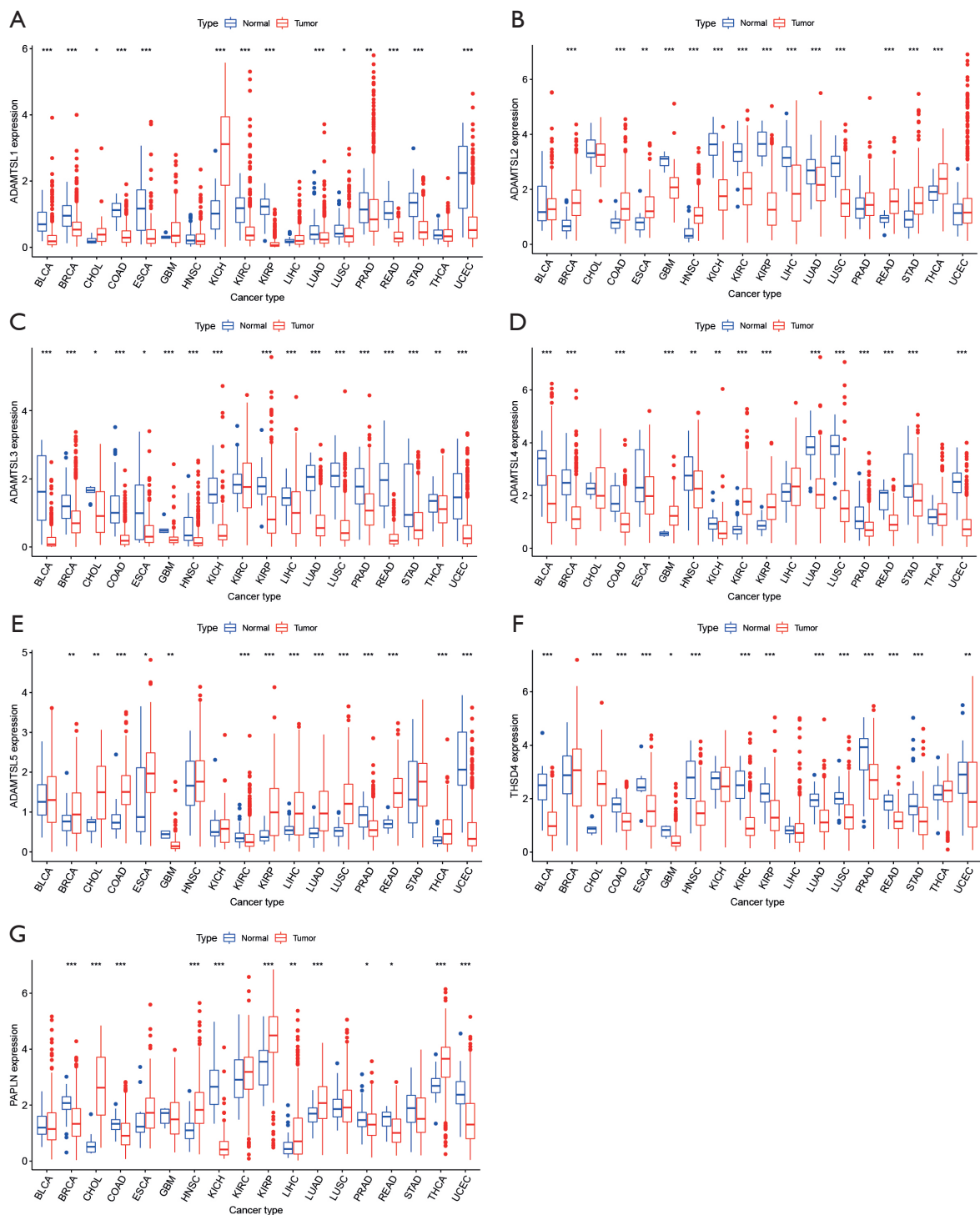
Figure 1 The mRNA expression levels of ADAMTSL genes in each cancer type between tumor and normal tissues. (A) ADAMTSL1, (B) ADAMTSL2, (C) ADAMTSL3, (D) ADAMTSL4, (E) [ADAMTSL5, (F) THSD4, (G) PAPLN. *, P<0.05; **, P<0.01; ***, P<0.001. ADAMTSLs, A disintegrin-like and metalloproteinase domain with thrombospondin type 1 motifs (ADAMTS)-like proteins; THSD4, thrombospondin type 1 domain containing 4; PAPLN, papilin.
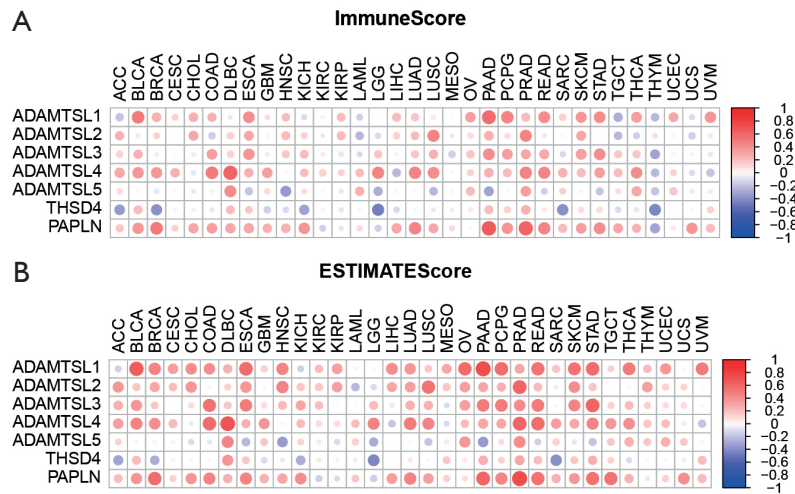
Figure S2 Correlation matrix plots to show the association between the expression of ADAMTSLs and immune score and estimate scores based on ESTIMATE algorithm. (A) Immune score, (B) estimate score. Spearman correlation was used for testing. The size of the dots represents the absolute value of the correlation coefficients. The bigger the size is, the higher the correlation is (higher absolute correlation coefficient). ADAMTSLs, A disintegrin-like and metalloproteinase domain with thrombospondin type 1 motifs (ADAMTS)-like proteins; ESTIMATE, estimation of stromal and immune cells in malignant tumor tissues using expression data.
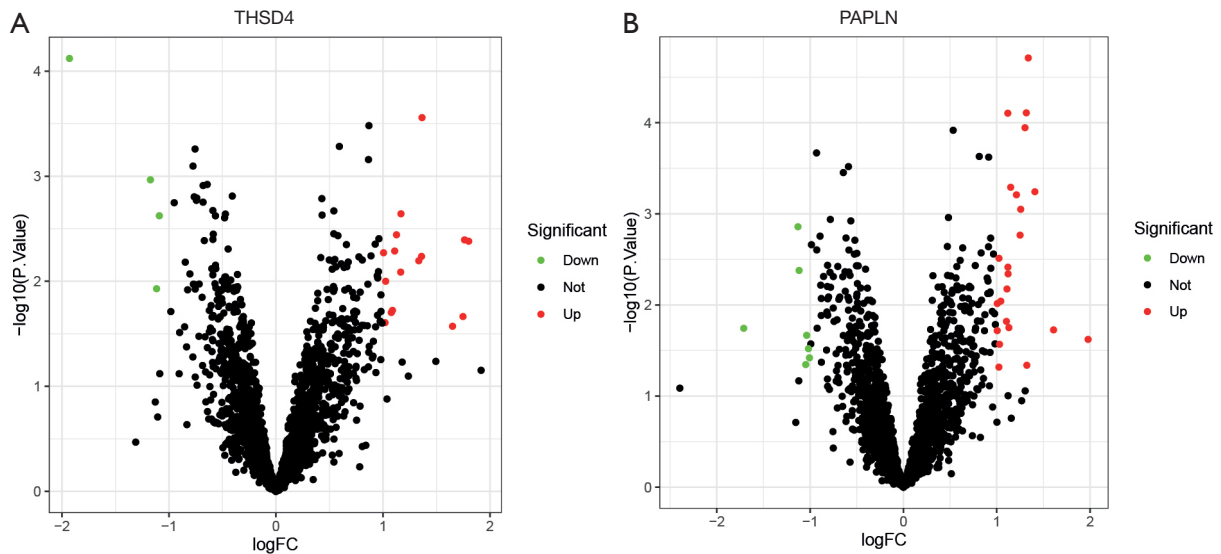

Figure S3 Volcano map showing the THSD4 or PAPLN-related proteins by proteomic analysis of 18 LUAD patients. (A) THSD4, (B) PAPLN. Red dots represent genes that were significantly upregulated; green dots represent genes that were significantly downregulated; black dots represent genes for which no significant differences were observed. LUAD, lung adenocarcinoma; THSD4, thrombospondin type 1 domain containing 4; PAPLN, Papilin.