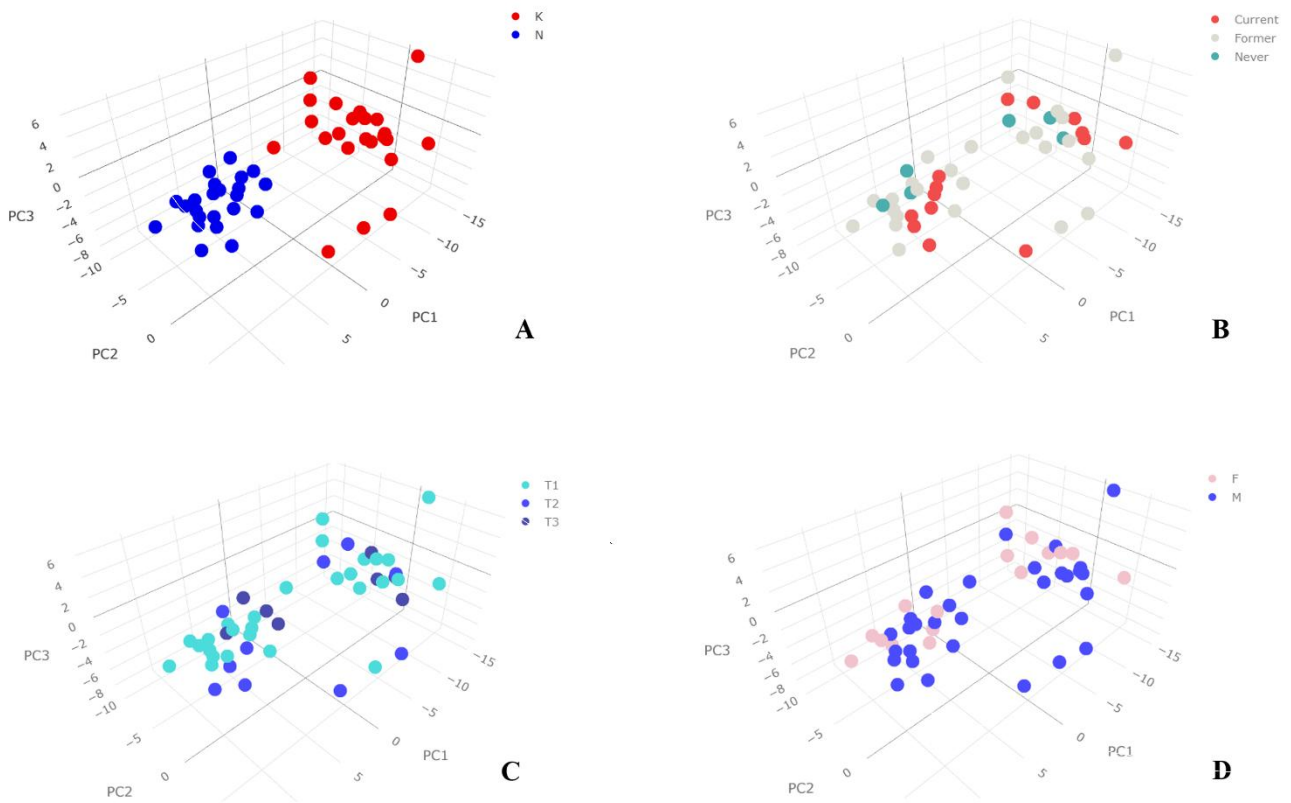
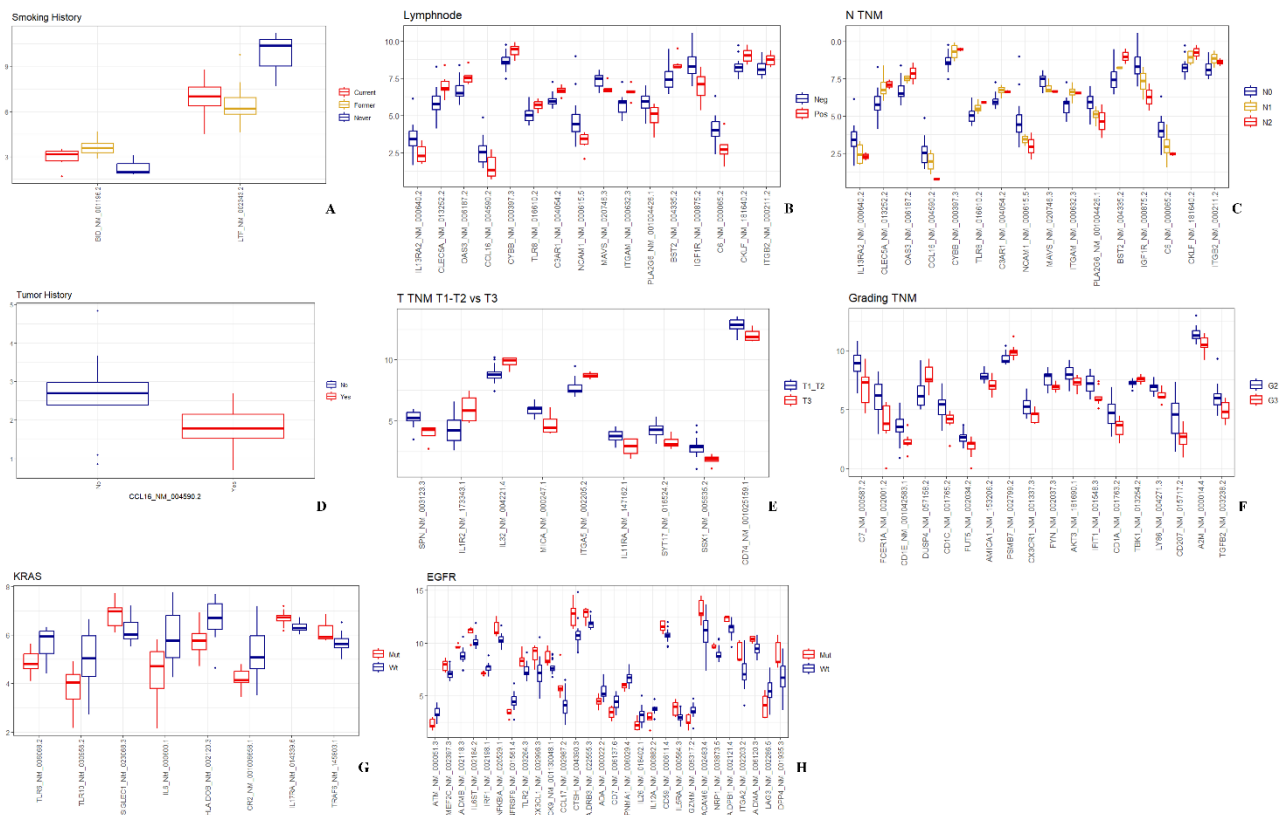




Supplementary Figure S1: Supplementary Figure S1. PCA of the 65-gene signature annotated by clinical characteristics. (A) Three-dimensional PCA representation of tumour (K, red) and patient-matched adjacent non-tumour (N, blue) samples. (B-D) The same PCA annotated by smoking history (B), pathological T category (T1-T3; C), and sex (D), respectively. No dominant visual grouping by smoking history, T category or sex was apparent.



Supplementary figure S2: GLM-significant transcript abundance shifts across clinical and molecular features. Boxplots showing gradual and partially overlapping expression shifts of selected transcripts across smoking history (A), lymph-node involvement (B), pathological N category (N0-N2, tumour history (D), pathological T category ((T1-T2 versus T3; E), tumour grade (G2 versus G3; F), and *KRAS* and *EGFR* mutation status (G-H). The plots illustrate gradual and partially overlapping transcript-abundance distributions across the clinical and molecular categories represented in the cohort.

Pathway Map Folders	Network Objects
---------------------	-----------------

Table S4

Export to image											Reorder enrichment profile			Total results: 50		
#	Map folders	0	2	4	6	8	10	12	14	16	log (fold-enr)	p-value	FCR	Ratio		
1	Immune system response											3.874e-13		35/222		
2	Inflammatory response											1.688e-10	1.023e-9	32/189		
3	Apoptosis											2.032e-4	9.822e-4	25/231		
4	Lung cancer											3.015e-4	1.747e-3	27/267		

Table S1

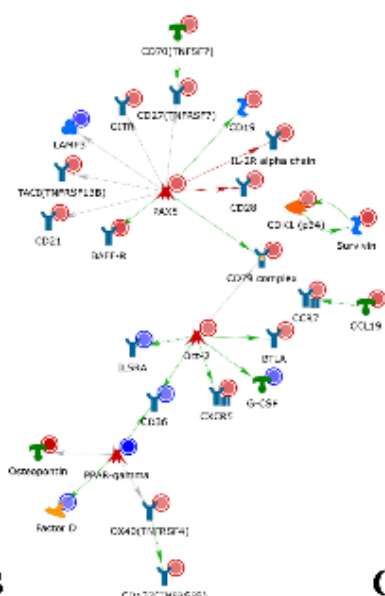
[illegible]

Table SII

The screenshot shows the 'SubNetwork' window in the 'NetworkMiner' application. The window displays a list of subnetworks with columns for ID, Name, and Score. The list is sorted by Score in descending order. The top subnetworks are highlighted in red. The 'SubNetwork' window is open over the 'NetworkMiner' main window, which shows a network graph and a list of nodes.

ID	Name	Score
1	1.0776	0.1
2	1.0776	0.1
3	1.0776	0.1
4	1.0776	0.1
5	1.0776	0.1
6	1.0776	0.1
7	1.0776	0.1
8	1.0776	0.1
9	1.0776	0.1
10	1.0776	0.1
11	1.0776	0.1
12	1.0776	0.1
13	1.0776	0.1
14	1.0776	0.1
15	1.0776	0.1
16	1.0776	0.1
17	1.0776	0.1
18	1.0776	0.1
19	1.0776	0.1
20	1.0776	0.1
21	1.0776	0.1
22	1.0776	0.1
23	1.0776	0.1
24	1.0776	0.1
25	1.0776	0.1
26	1.0776	0.1
27	1.0776	0.1
28	1.0776	0.1
29	1.0776	0.1
30	1.0776	0.1
31	1.0776	0.1
32	1.0776	0.1
33	1.0776	0.1
34	1.0776	0.1
35	1.0776	0.1
36	1.0776	0.1
37	1.0776	0.1
38	1.0776	0.1
39	1.0776	0.1
40	1.0776	0.1
41	1.0776	0.1
42	1.0776	0.1
43	1.0776	0.1
44	1.0776	0.1
45	1.0776	0.1
46	1.0776	0.1
47	1.0776	0.1
48	1.0776	0.1
49	1.0776	0.1
50	1.0776	0.1
51	1.0776	0.1
52	1.0776	0.1
53	1.0776	0.1
54	1.0776	0.1
55	1.0776	0.1
56	1.0776	0.1
57	1.0776	0.1
58	1.0776	0.1
59	1.0776	0.1
60	1.0776	0.1
61	1.0776	0.1
62	1.0776	0.1
63	1.0776	0.1
64	1.0776	0.1
65	1.0776	0.1
66	1.0776	0.1
67	1.0776	0.1
68	1.0776	0.1
69	1.0776	0.1
70	1.0776	0.1
71	1.0776	0.1
72	1.0776	0.1
73	1.0776	0.1
74	1.0776	0.1
75	1.0776	0.1
76	1.0776	0.1
77	1.0776	0.1
78	1.0776	0.1
79	1.0776	0.1
80	1.0776	0.1
81	1.0776	0.1
82	1.0776	0.1
83	1.0776	0.1
84	1.0776	0.1
85	1.0776	0.1
86	1.0776	0.1
87	1.0776	0.1
88	1.0776	0.1
89	1.0776	0.1
90	1.0776	0.1
91	1.0776	0.1
92	1.0776	0.1
93	1.0776	0.1
94	1.0776	0.1
95	1.0776	0.1
96	1.0776	0.1
97	1.0776	0.1
98	1.0776	0.1
99	1.0776	0.1
100	1.0776	0.1

Table SIII

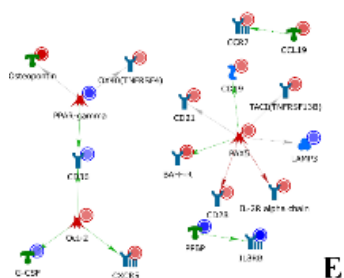
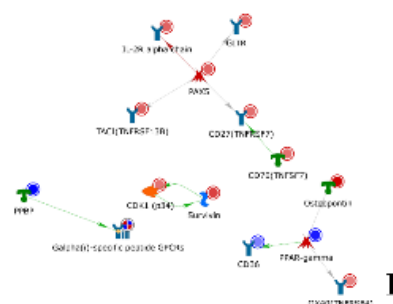
[illegible]

Table SIV

The screenshot shows the AWS IAM console 'Users' page. The table contains the following data:

User Name	Created	Last Sign-In
1 root	1/2/2016	1/2/2016
2 root	1/2/2016	1/2/2016
3 root	1/2/2016	1/2/2016
4 root	1/2/2016	1/2/2016
5 root	1/2/2016	1/2/2016
6 root	1/2/2016	1/2/2016
7 root	1/2/2016	1/2/2016
8 root	1/2/2016	1/2/2016
9 root	1/2/2016	1/2/2016
10 root	1/2/2016	1/2/2016
11 root	1/2/2016	1/2/2016
12 root	1/2/2016	1/2/2016
13 root	1/2/2016	1/2/2016
14 root	1/2/2016	1/2/2016
15 root	1/2/2016	1/2/2016
16 root	1/2/2016	1/2/2016
17 root	1/2/2016	1/2/2016
18 root	1/2/2016	1/2/2016
19 root	1/2/2016	1/2/2016
20 root	1/2/2016	1/2/2016
21 root	1/2/2016	1/2/2016
22 root	1/2/2016	1/2/2016
23 root	1/2/2016	1/2/2016
24 root	1/2/2016	1/2/2016
25 root	1/2/2016	1/2/2016
26 root	1/2/2016	1/2/2016



response“ (n = 38), “*inflammatory response*“ (n = 32), “*apoptosis*“ (n = 25), and “*lung cancer*“ (n = 27), respectively. For each term, the first column shows the DEGs, whereas the second column shows their expression levels as Log_2FC [FC = LUAD samples (K)/nontumour samples (N)]. The colors of the rows indicate changes in expression, from brilliant red (upregulated in K) to dark blue (downregulated in K). Gene order follows the MetaCore output and does not imply ranking by expression. Panels C, E, G, and I display the corresponding direct interaction networks (DINs) generated from the DEGs listed in panels B, D, F, and H, respectively. For each DIN, red and blue bubbles indicate up- or downregulated factors, matching the colour scale of the associated Table SI-IV panels. The percentage of DEGs establishing at least one direct functional interaction within the same term cluster, and thus included in the corresponding DIN, was 80% for *the immune system response*, 60% for *the inflammatory response*, 50% for *apoptosis*, and 52% for *lung cancer*. According to the tool and reported in decreasing order of relevance, the most functionally relevant DEG-encoded proteins in the C, E, G, and I networks were (C) PAX5, Oct-2, PPAR-gamma, OX40 (TNFRSF4), and survivin; (E) PAX5, PPAR-gamma, Oct-2, CD36, and LAMP3; (G) PPAR-gamma, survivin, CDK1 (p34), CXCL13, and CXCR5; and (I) PAX5, PPAR-gamma, CD27 (TNFRSF7), CDK1 (p34), and survivin. Proteins with the highest recurrence in the DINs are highlighted in bold. Network edges indicate the type of interaction: green = activation, red = inhibition, gray = unspecified or unknown, and the arrow indicates the direction of the interaction.

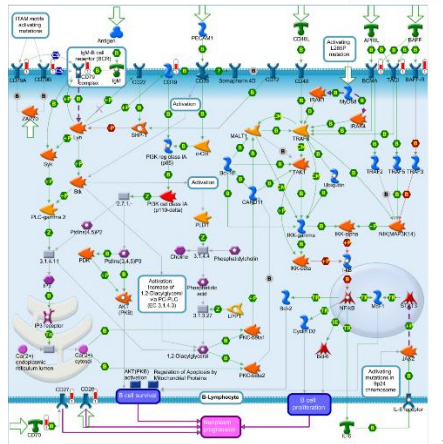
Table S5

#	Terms	0	2	4	6	8	log(p-value)	p-value	FDR	Ratio
1	B cell signaling in hematological malignancies							2.867e-12	1.356e-9	83/77
2	Immune response_T cell co-signaling secondary scheme							1.942e-10	4.592e-8	8/55
3	Immune response_Differentiation and clonal expansion of CD4+ T cells							1.146e-6	6.021e-5	5/39
4	Role of tumor-infiltrating B cells in anti-tumor immunity							4.876e-6	1.942e-4	6/91
5	Immune response_T cell subsets_cell surface markers							4.927e-6	1.942e-4	5/52
6	Regulatory cells and tumor cells intercellular interaction							1.7732e-5	5.851e-4	5/67
7	Immune response_Differentiation of natural regulatory T cells							2.323e-5	7.344e-4	4/35
8	Immune response_Generation of memory CD4+ T cells							2.917e-5	8.115e-4	4/37
9	Apoptosis and survival_Anti-apoptotic TNF- α /Bcl-2/Bcl-XL pathway							2.906e-4	6.873e-3	3/27
10	Immune response_BAFF-induced signaling							1.905e-3	2.336e-2	3/51

1. B cell signaling in hematological malignancies

Table SV

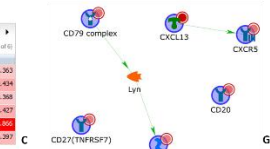
#	Terms	0	2	4	6	8	log(p-value)	p-value	FDR	Ratio
1	CD28							0.303		
2	CD28(TNFRSF18)							0.304		
3	CD28							0.303		
4	CD28							0.303		
5	CD28(TNFRSF18)							0.303		
6	CD28(TNFRSF18)							0.304		
7	CD28(TNFRSF18)							0.303		
8	CD28							0.303		
9	CD28							0.303		
10	CD28(TNFRSF18)							0.303		



4. Role of tumor-infiltrating B cells in anti-tumor immunity

Table SVI

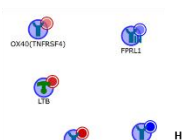
#	Terms	0	2	4	6	8	log(p-value)	p-value	FDR	Ratio
1	CD28							0.303		
2	CD28							0.304		
3	CD28(TNFRSF18)							0.303		
4	CD28							0.303		
5	CD28(TNFRSF18)							0.304		
6	CD28							0.303		



6. B-regulatory cells and tumor cells intercellular interaction

Table SVII

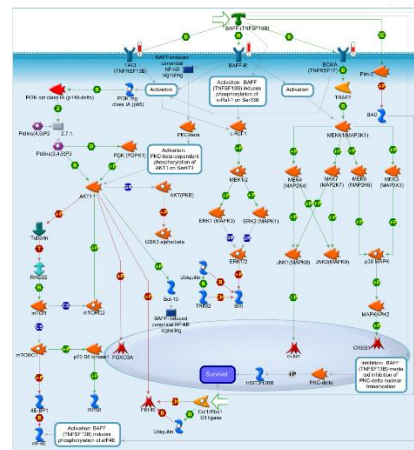
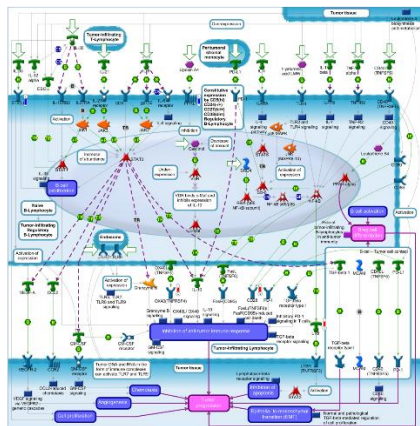
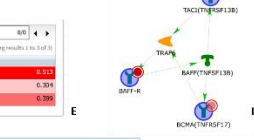
#	Terms	0	2	4	6	8	log(p-value)	p-value	FDR	Ratio
1	CD28							0.303		
2	CD28							0.304		
3	CD28							0.303		
4	CD28(TNFRSF18)							0.303		
5	CD28							0.303		



10. Immune response_BAFF-induced signaling

Table SVIII

#	Terms	0	2	4	6	8	log(p-value)	p-value	FDR	Ratio
1	BAFF							0.303		
2	CD28(TNFRSF18)							0.304		
3	CD28(TNFRSF18)							0.303		



Supplementary Figure S4: (A) Table S5 listing terms from the MetaCore “pathway maps” ontology significantly enriched among those annotating the 65 DEGs. (B-M) Panels B, C, D, and E show MetaCore Tables SV-VIII listing the DEGs (n) annotated with the enriched terms “*B-cell signalling in hematological malignancies*” (n = 9), “*role of tumor-infiltrating B-cells in antitumour immunity*”

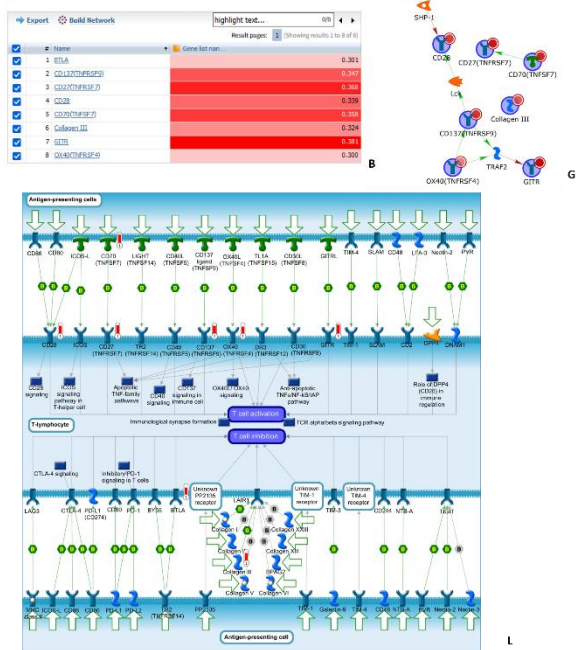
(n = 6), “*B-regulatory cell and tumor cell intercellular interactions*” (n = 5), and “*immune response_BAFF-induced signalling*” (n = 3), respectively. For each enriched term, the third column of Tables SV-VIII reports the DEGs, whereas the fourth column shows their expression levels as Log_2FC [FC = LUAD samples (K)/nontumour samples (N)]. The row colours of the fourth column indicate expression changes, from brilliant red (upregulated in K) to dark blue (downregulated in K). The gene order follows the MetaCore output and does not imply ranking by expression. Panels F, G, H and I display the corresponding shortest path networks (SPNs) generated from the DEGs listed in panels B, C, D, and E, respectively, by using the MetaCore net building tool. All DEGs from “*B-cell signalling in hematological malignancies*” and all DEGs from “*immune response_BAFF-induced signalling*” maps resulted, within each group, connectable through at least one direct or indirect functional interaction within each group, leading to the generation of the corresponding SPNs. Similarly, two-thirds of the factors “*involved in the role of tumor-infiltrating B-cells in antitumour immunity*” establish functional interactions. In contrast, neither direct nor indirect connections were observed among the DEGs belonging to the “*B-regulatory cell and tumor cell intercellular interaction*” pathway map. In each SPN, red and blue bubbles indicate up- or downregulated factors, matching the colour scale of the associated Table SV-VIII panels. Panels J, K, L, and M show MetaCore pathway maps significantly enriched in DEGs. Within each map, DEGs are highlighted by vertical bars displayed adjacent to the corresponding protein symbols. The bar color and height reflect the tumour (K) versus nontumour (N) expression ratio: red bars indicate higher expression in K than in N, whereas blue bars denote the opposite condition. The magnitude of differential expression is proportional to bar height, with larger differences between K and N resulting in taller bars. Network proteins are represented by distinct symbols indicating their functional class, edges depict functional relationships between proteins, and arrowheads indicate the directionality of interactions. Edge colors denote the nature of the interaction (green = activation, red = inhibition, gray = unspecified or unknown).

Table S6

#	Maps	0	2	4	6	8	-log(p-value)	p-value	FDR	Ratio
1	B cell survival in hematological malignancies						2.867e-12	1.356e-9	10/77	
2	Immune response_T cell co-signaling receptors, schema						1.940e-10	4.592e-8	8/95	
3	Immune response_Differentiation and clonal expansion of CD8+ T cells						1.146e-6	6.021e-5	5/39	
4	Role of tumor-infiltrating B cells in anti-tumor immunity						4.876e-6	1.942e-4	6/91	
5	Immune response_T cell subsets: cell surface markers						4.927e-6	1.942e-4	5/52	
6	Regulatory cells and tumor cells intercellular interaction						1.732e-5	5.851e-4	5/67	
7	Immune response_Differentiation of natural regulatory T cells						2.329e-5	7.344e-4	4/35	
8	Immune response_Generation of memory CD4+ T cells						2.917e-5	8.115e-4	4/37	
9	Apoptosis and survival_Anti-apoptotic TRAF3/RIP-4/5AP pathway						2.906e-4	6.873e-3	3/27	
10	Immune response_3AP-induced apoptosis						1.905e-3	2.318e-2	3/51	

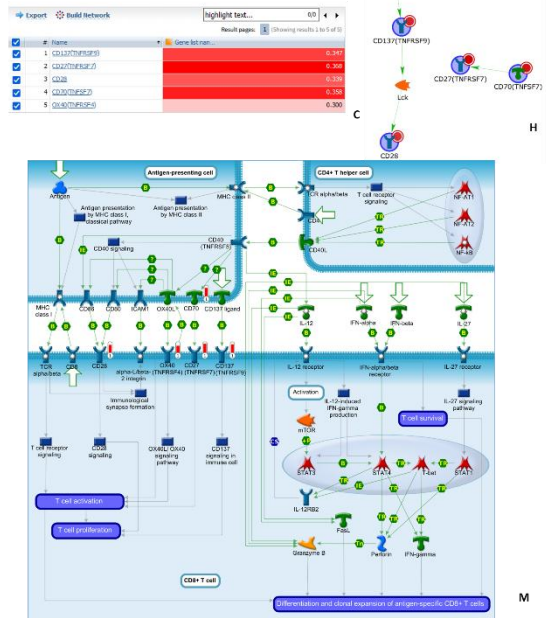
2. Immune response_T cell co-signaling receptors, schema

Table SIX



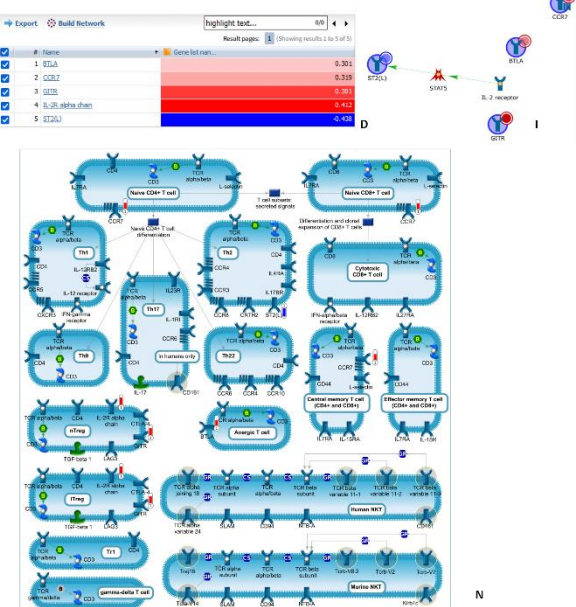
3. Immune response_Differentiation and clonal expansion of CD8+ T cells

Table SX



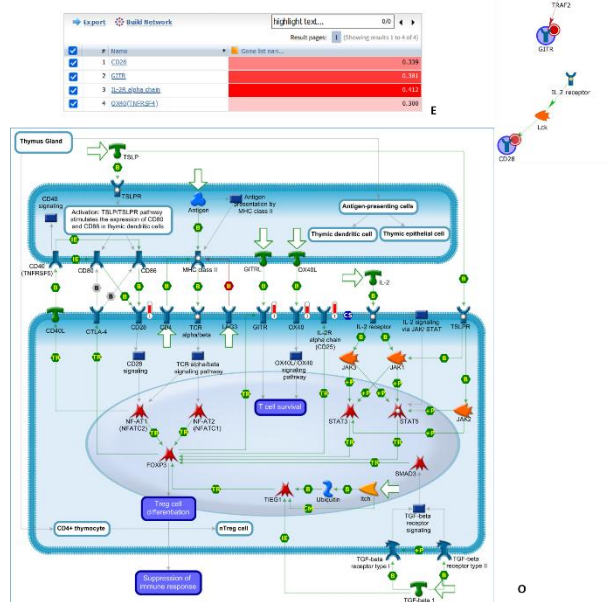
5. Immune response_T cell subsets: cell surface markers

Table SXI

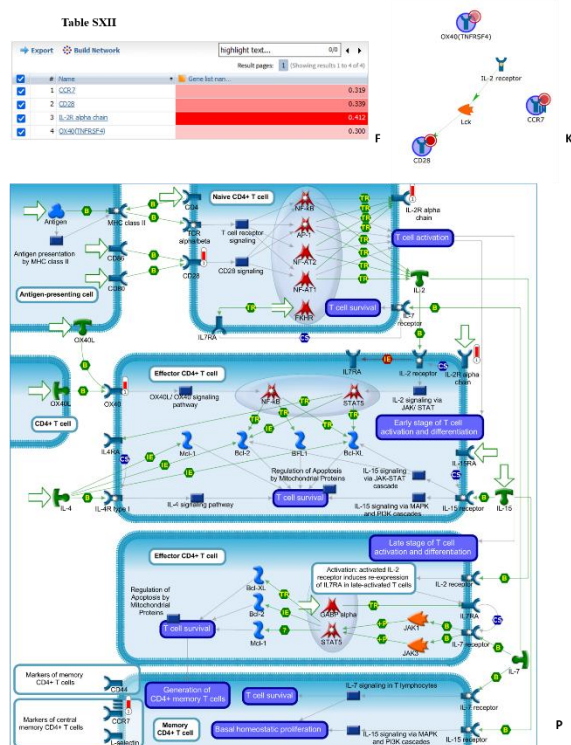


7. Immune response_Differentiation of natural regulatory T cells

Table SXII



8. Immune response_Generation of memory CD4+ T cells



Supplementary Figure S5: (A) Table S6 reporting terms from the MetaCore “pathway maps” ontology significantly enriched among those annotating the 65 detected DEGs. (B-N) Panels B, C, D, E, and F show MetaCore Tables IX--XIII listing the DEGs (n) annotated with the enriched terms: “*immune response_T-cell cosignaling receptors, schema*” (n = 8), “*immune response_Differentiation and clonal expansion of CD8+ T cells*” (n = 5), “*immune response_T-cell subsets: cell surface markers*” (n = 5), “*immune response_Differentiation of natural regulatory T cells*” (n = 4), and “*immune response_Generation of memory CD4+ T cells*” (n = 4), respectively. For each enriched term, the third column of Tables IX--XIII shows the DEGs, whereas the fourth column shows their expression levels as Log₂FC [FC = LUAD samples (K)/nontumour samples (N)]. The row colours of the fourth column indicate expression changes, from brilliant red (upregulated in K) to dark blue (downregulated in K). The gene order follows the MetaCore output and does not imply ranking by expression. Panels G, H, I, J, and K display the corresponding shortest path networks (SPNs) generated from the DEGs listed in panels B, C, D, E, and F, respectively, by using the MetaCore net building tool. Within each group, DEGs were evaluated for their ability to establish direct or indirect

functional interactions leading to SPN generation. In each SPN, red and blue bubbles indicate up- or downregulated factors, matching the colour scale of the associated Table IX-XIII panels. Panels L, M, N, O, and P show MetaCore pathway maps significantly enriched with DEGs. Within each map, DEGs are highlighted by vertical bars displayed adjacent to the corresponding protein symbols. The bar color and height reflect the tumour (K) versus nontumour (N) expression ratio: red bars indicate higher expression in K than in N, whereas blue bars denote the opposite condition. The magnitude of differential expression is proportional to bar height, with larger differences between K and N resulting in taller bars. Network proteins are represented by distinct symbols indicating their functional class, edges depict functional relationships between proteins, and arrowheads indicate the directionality of interactions. Edge colors denote the nature of the interaction (green = activation, red = inhibition, gray = unspecified or unknown).

Age, n (%) - median age: 72	
≤72 years	12 (52%)
> 72 years	11 (48%)
Gender, n (%)	
Male	15 (65%)
Female	8 (35%)
Smoking Status, n (%)	
Former	13 (57%)
Current	7 (30%)
Never	3 (13%)
Work, n (%)	
Indoor	16 (70%)
Outdoor	5 (22%)
Unknown	2 (9%)
Dimension, n (%) - Median: 2 cm	
≤ 2 cm	13 (57%)
> 2 cm	10 (43%)
Histotype	
ADK	21 (91%)
ADK enteric type	1 (4%)
ADK multiple (5 foci)	1 (4%)
Vascular invasion, n (%)	
Yes	2 (9%)
No	21 (91%)
Necrosis, n (%)	
Yes	3 (13%)
No	20 (87%)
History of tumor, n (%)	
Yes	10 (43%)
No	13 (57%)
Lymph node metastasis, n (%)	
Yes	6 (26%)
No	17 (74%)
(Growth) Pattern, n (%)	
Solid	5 (22%)
Acinar	16 (70%)
Papillary	2 (9%)
pTNM, n (%)	
T1-T2	19 (83%)
T3-T4	4 (17%)

Supplementary Table S1: Anamnestic characteristics of patients enrolled in the study.

Gene Symbol	Entrez ID	Gene	Gene name	Log ₂ FC#	p.value\$	BH-FDR*	K Mean±(SD) ¥	N Mean±(SD) ¥
MME	4311	MME_NM_000902.2	membrane metalloendopeptidase	-0.56	1.48E-17	1.14E-14	6.78±(1.11)	9.97±(0.62)
SPP1	6696	SPP1_NM_000582.2	secreted phosphoprotein 1	0.80	3.40E-15	1.31E-12	12.74±(2.08)	7.29±(1.62)
CXCL13	10563	CXCL13_NM_006419.2	C-X-C motif chemokine ligand 13	0.87	2.60E-13	5.00E-11	9.41±(1.92)	5.16±(1.26)
CFD	1675	CFD_NM_001928.2	complement factor D	-0.31	1.71E-12	2.43E-10	8.72±(0.98)	10.78±(0.61)
BIRC5	332	BIRC5_NM_001168.2	baculoviral IAP repeat containing 5	0.55	4.30E-12	4.73E-10	8.21±(1.38)	5.61±(0.59)
IL2RA	3559	IL2RA_NM_000417.1	interleukin 2 receptor subunit alpha	0.41	9.19E-12	8.84E-10	7.74±(0.98)	5.82±(0.59)
MARCO	8685	MARCO_NM_006770.3	macrophage receptor with collagenous structure	-0.38	1.43E-11	1.22E-09	9.80±(1.53)	12.72±(0.88)
CD36	948	CD36_NM_001001548.2	CD36 molecule (CD36 blood group)	-0.31	1.77E-11	1.36E-09	9.05±(1.22)	11.23±(0.53)
CXCR2	3579	CXCR2_NM_001557.2	C-X-C motif chemokine receptor 2	-0.42	3.28E-11	1.88E-09	5.98±(0.92)	8.00±(0.86)
SPN	6693	SPN_NM_003123.3	sialophorin	-0.32	3.43E-11	1.88E-09	6.81±(0.80)	8.50±(0.67)
FPR2	2358	FPR2_NM_001462.3	formyl peptide receptor 2	-0.37	5.79E-11	2.62E-09	7.21±(1.09)	9.29±(0.74)
LAMP3	27074	LAMP3_NM_014398.3	lysosomal associated membrane protein 3	-0.34	5.75E-11	2.62E-09	9.68±(1.42)	12.21±(0.77)
COL3A1	1281	COL3A1_NM_000090.3	collagen type III alpha 1 chain	0.32	8.49E-11	3.44E-09	13.82±(1.62)	11.04±(0.84)
MNX1	3110	MNX1_NM_005515.3	motor neuron and pancreas homeobox 1	0.67	8.41E-11	3.44E-09	5.29±(1.10)	3.33±(0.64)
PPARG	5468	PPARG_NM_015869.3	peroxisome proliferator activated receptor gamma	-0.37	6.22E-10	1.78E-08	6.38±(1.12)	8.27±(0.61)
TAL1	6886	TAL1_NM_003189.2	TAL bHLH transcription factor 1, erythroid differentiation factor	-0.34	9.64E-10	2.47E-08	5.55±(0.85)	7.04±(0.55)
IL1RL1	9173	IL1RL1_NM_016232.4	interleukin 1 receptor like 1	-0.44	1.98E-09	4.48E-08	6.89±(1.03)	9.33±(1.45)
CDK1	983	CDK1_NM_001786.4	cyclin dependent kinase 1	0.34	3.65E-09	7.40E-08	9.20±(1.30)	7.25±(0.60)
THY1	7070	THY1_NM_006288.2	Thy-1 cell surface antigen	0.34	4.95E-09	9.78E-08	10.34±(1.32)	8.14±(1.02)
TTK	7272	TTK_NM_003318.3	TTK protein kinase	0.51	6.68E-09	1.29E-07	6.88±(1.43)	4.82±(0.62)
PBK	55872	PBK_NM_018492.2	PDZ binding kinase	0.58	2.16E-08	3.62E-07	6.35±(1.49)	4.26±(0.71)
TNFRSF18	8784	TNFRSF18_NM_004195.2	TNF receptor superfamily member 18	0.38	3.24E-08	5.24E-07	6.90±(0.93)	5.30±(0.90)
PLA2G1B	5319	PLA2G1B_NM_000928.2	phospholipase A2 group IB	-0.42	4.76E-08	7.19E-07	6.76±(1.58)	9.05±(1.04)

CCL19	6363	CCL19_NM_006274.2	C-C motif chemokine ligand 19	0.44	5.83E-08	8.63E-07	9.32±(1.70)	6.86±(1.18)
CEACAM1	634	CEACAM1_NM_001712.3	CEA cell adhesion molecule 1	0.37	1.25E-07	1.69E-06	7.45±(1.25)	5.77±(0.68)
IL22RA2	116379	IL22RA2_NM_181310.1	interleukin 22 receptor subunit alpha 2	0.37	1.43E-07	1.90E-06	6.05±(0.99)	4.68±(0.58)
C8B	732	C8B_NM_000066.2	complement C8 beta chain	-0.47	1.71E-07	2.24E-06	5.62±(1.45)	7.81±(1.32)
CR2	1380	CR2_NM_001006658.1	complement C3d receptor 2	0.37	1.90E-07	2.43E-06	6.56±(1.03)	5.08±(0.73)
CAMP	820	CAMP_NM_004345.3	cathelicidin antimicrobial peptide	-0.38	2.12E-07	2.64E-06	4.70±(0.86)	6.11±(0.92)
CD28	940	CD28_NM_001243078.1	CD28 molecule	0.34	2.24E-07	2.73E-06	5.37±(0.54)	4.25±(0.79)
TNFRSF4	7293	TNFRSF4_NM_003327.2	TNF receptor superfamily member 4	0.30	2.27E-07	2.73E-06	6.66±(0.71)	5.41±(0.81)
CD79A	973	CD79A_NM_001783.3	CD79a molecule	0.43	4.38E-07	4.96E-06	8.53±(1.71)	6.34±(1.11)
BTLA	151888	BTLA_NM_181780.2	B and T lymphocyte associated	0.30	5.26E-07	5.70E-06	6.84±(1.05)	5.56±(0.50)
LTB	4050	LTB_NM_002341.1	lymphotoxin beta	0.33	8.73E-07	8.73E-06	7.92±(1.29)	6.31±(0.81)
LRRN3	54674	LRRN3_NM_001099660.1	leucine rich repeat neuronal 3	-0.42	9.51E-07	9.27E-06	6.21±(1.80)	8.29±(0.81)
TNFRSF13C	115650	TNFRSF13C_NM_052945.3	TNF receptor superfamily member 13C	0.51	1.03E-06	9.89E-06	6.46±(1.55)	4.52±(1.04)
F12	2161	F12_NM_000505.3	coagulation factor XII	0.49	1.14E-06	1.07E-05	6.01±(1.40)	4.27±(0.86)
LILRA4	23547	LILRA4_NM_012276.3	leukocyte immunoglobulin like receptor A4	0.39	1.65E-06	1.46E-05	4.81±(0.56)	3.66±(0.92)
CD27	939	CD27_NM_001242.4	CD27 molecule	0.37	2.01E-06	1.76E-05	7.24±(1.23)	5.61±(1.08)
TNFRSF9	3604	TNFRSF9_NM_001561.4	TNF receptor superfamily member 9	0.35	2.07E-06	1.79E-05	6.07±(0.89)	4.77±(0.88)
CCL22	6367	CCL22_NM_002990.3	C-C motif chemokine ligand 22	0.34	2.29E-06	1.92E-05	6.56±(0.90)	5.19±(0.99)
TNFRSF17	608	TNFRSF17_NM_001192.2	TNF receptor superfamily member 17	0.30	2.39E-06	1.98E-05	7.26±(1.04)	5.88±(0.91)
POU2F2	5452	POU2F2_NM_002698.2	POU class 2 homeobox 2	0.33	3.71E-06	2.83E-05	6.32±(1.07)	5.03±(0.76)
CXCL14	9547	CXCL14_NM_004887.4	C-X-C motif chemokine ligand 14	0.46	3.78E-06	2.85E-05	9.40±(2.23)	6.83±(1.37)
CD79B	974	CD79B_NM_021602.2	CD79b molecule	0.31	4.24E-06	3.14E-05	7.59±(1.24)	6.12±(0.81)
IL5RA	3568	IL5RA_NM_000564.3	interleukin 5 receptor subunit alpha	-0.31	4.49E-06	3.21E-05	4.93±(0.68)	6.12±(1.01)
S100A12	6283	S100A12_NM_005621.1	S100 calcium binding protein A12	-0.32	4.50E-06	3.21E-05	6.44±(1.06)	8.03±(1.28)
CD19	930	CD19_NM_001770.4	CD19 molecule	0.36	5.16E-06	3.60E-05	6.89±(1.34)	5.35±(0.83)
IL1A	3552	IL1A_NM_000575.3	interleukin 1 alpha	-0.37	6.14E-06	4.08E-05	4.94±(1.12)	6.39±(0.93)
TLR10	81793	TLR10_NM_030956.2	toll like receptor 10	0.42	7.12E-06	4.65E-05	6.13±(1.27)	4.58±(0.98)

PAX5	5079	PAX5_NM_016734.1	paired box 5	0.41	1.13E-05	6.89E-05	5.44±(1.18)	4.09±(0.90)
CCR7	1236	CCR7_NM_001838.2	C-C motif chemokine receptor 7	0.32	1.23E-05	7.32E-05	6.20±(1.07)	4.97±(0.80)
CXCR5	643	CXCR5_NM_001716.3	C-X-C motif chemokine receptor 5	0.40	2.41E-05	1.32E-04	4.80±(0.94)	3.64±(0.89)
PMCH	5367	PMCH_NM_002674.2	pro-melanin concentrating hormone	0.33	3.52E-05	1.88E-04	4.86±(0.92)	3.85±(0.73)
ICAM4	3386	ICAM4_NM_001039132.1	intercellular adhesion molecule 4 (Landsteiner-Wiener blood group)	-0.33	3.61E-05	1.92E-04	6.42±(1.38)	8.07±(1.34)
MS4A1	931	MS4A1_NM_152866.2	membrane spanning 4-domains A1	0.43	3.97E-05	2.09E-04	6.87±(1.81)	5.09±(1.04)
PPBP	5473	PPBP_NM_002704.2	pro-platelet basic protein	-0.39	7.55E-05	3.50E-04	6.01±(1.88)	7.88±(1.29)
IL1RL2	8808	IL1RL2_NM_003854.2	interleukin 1 receptor like 2	0.30	1.30E-04	5.68E-04	5.41±(1.03)	4.38±(0.74)
CD70	970	CD70_NM_001252.2	CD70 molecule	0.36	3.49E-04	1.38E-03	4.64±(0.96)	3.62±(1.03)
TNFRSF13B	23495	TNFRSF13B_NM_012452.2	TNF receptor superfamily member 13B	0.40	3.53E-04	1.39E-03	5.273±(1.39)	4.00±(1.07)
BLK	640	BLK_NM_001715.2	BLK proto-oncogene, Src family tyrosine kinase	0.35	4.91E-04	1.84E-03	4.80±(0.93)	3.76±(1.10)
PRAME	23532	PRAME_NM_006115.3	PRAME nuclear receptor transcriptional regulator	0.52	8.10E-04	2.85E-03	5.65±(2.40)	3.95±(0.82)
MPPED1	758	MPPED1_NM_001044370.1	metallophosphoesterase domain containing 1	0.30	4.73E-03	1.36E-02	4.57±(1.22)	3.70±(1.00)
AMBP	259	AMBP_NM_001633.3	alpha-1-microglobulin/bikunin precursor	0.32	7.38E-03	1.96E-02	6.25±(2.19)	5.01±(0.90)
CSF3	1440	CSF3_NM_000759.3	colony stimulating factor 3	-0.32	1.14E-02	2.81E-02	3.83±(1.16)	4.78±(1.51)

Supplementary Table S2: DEGs detected comparing nanosting transcriptomic profiles of tumour (K) and matching non-tumour (N) samples from 23 LUAD patients. # Log2(K/N); § Limma p value, * Benjamini-Hochberg FDR adjusted p value; ¥ Expression mean ± standard deviation (SD) of K and N samples.

Endogenous_CCL16_NM_004590.2	80,00	-1,42	4,45E-02	61,67	0,47	5,28E-01	82,35	-1,87	3,27E-02	52,22	-0,14	8,09E-01	52,07	0,19	6,91E-01	82,35	-1,87	3,27E-02	58,73	-0,57	2,75E-01	60,53	-0,53	4,27E-01
Endogenous_BST2_NM_004335.2	52,31	-0,32	5,60E-01	63,33	-0,51	5,00E-01	93,14	-2,20	4,40E-02	72,22	-1,20	1,45E-01	52,89	0,01	9,92E-01	93,14	-2,20	4,40E-02	67,46	0,99	1,19E-01	52,63	-0,01	9,85E-01
Endogenous_C3AR1_NM_004054.2	55,38	0,23	7,94E-01	63,33	0,56	6,83E-01	89,22	3,20	2,54E-02	56,67	-0,35	7,48E-01	72,73	1,87	9,72E-02	89,22	3,20	2,54E-02	51,59	0,05	9,59E-01	59,21	-0,48	6,88E-01
Endogenous_C6_NM_000065.2	68,46	-0,74	1,23E-01	65,00	0,74	2,74E-01	82,35	-1,67	3,06E-02	73,33	0,48	3,39E-01	50,41	-0,14	7,46E-01	82,35	-1,67	3,06E-02	70,63	-0,87	8,87E-02	51,32	-0,16	7,59E-01
Endogenous_KCIF_NM_181640.2	63,85	0,87	2,23E-01	65,00	-0,59	5,32E-01	87,25	-2,20	2,82E-02	73,33	1,25	1,41E-01	53,72	-0,31	6,52E-01	87,25	-2,20	2,82E-02	56,35	0,30	6,59E-01	62,68	0,38	6,54E-01
Endogenous_CLEC5A_NM_013252.2	59,23	-0,21	6,23E-01	56,67	0,29	6,52E-01	85,29	1,44	2,24E-02	63,33	0,23	6,46E-01	57,85	-0,06	8,86E-01	85,29	1,44	2,24E-02	58,73	0,19	6,65E-01	71,05	0,45	4,17E-01
Endogenous_CYBB_NM_000397.3	71,54	0,67	7,12E-02	55,00	-0,30	7,76E-01	85,29	2,81	2,58E-02	60,00	-0,26	7,64E-01	57,02	0,33	6,77E-01	85,29	2,81	2,58E-02	60,32	0,46	5,37E-01	50,00	0,15	8,76E-01
Endogenous_IGF1R_NM_000875.2	64,62	-0,24	5,14E-01	76,67	0,75	2,05E-01	85,29	-1,89	3,71E-02	66,67	-0,49	2,93E-01	61,16	0,37	3,70E-01	85,29	-1,89	3,71E-02	62,70	0,12	7,38E-01	57,89	0,08	8,66E-01
Endogenous_IL13RA2_NM_000640.2	64,62	0,61	1,88E-01	76,67	-1,34	9,15E-02	82,35	-1,39	4,92E-02	65,56	0,70	1,82E-01	58,68	-0,43	3,24E-01	82,35	-1,39	4,92E-02	65,08	-0,52	2,70E-01	63,16	-0,48	4,29E-01
Endogenous_IL26_NM_018402.1	77,69	-1,57	3,97E-02	58,33	0,44	6,06E-01	60,78	-0,57	3,89E-01	84,44	-2,15	4,77E-02	63,64	-0,76	2,05E-01	60,78	-0,57	3,89E-01	79,37	1,41	5,63E-02	60,53	0,24	7,32E-01
Endogenous_ITGAM_NM_000632.3	60,00	0,45	4,86E-01	61,67	-0,43	6,44E-01	86,27	2,79	2,98E-02	54,44	-0,08	9,13E-01	52,07	0,16	8,09E-01	86,27	2,79	2,98E-02	50,79	0,03	9,59E-01	60,53	0,45	5,92E-01
Endogenous_ITGB2_NM_000211.2	55,38	0,52	5,11E-01	56,67	0,23	8,39E-01	82,35	2,26	4,40E-02	57,78	0,60	2,73E-01	55,37	0,52	5,28E-01	82,35	2,26	4,40E-02	66,67	-1,12	2,01E-01	55,26	-0,32	7,57E-01
Endogenous_LY86_NM_004271.3	76,92	2,08	4,28E-02	60,00	-0,89	4,64E-01	53,92	0,15	8,62E-01	65,56	1,42	1,92E-01	52,07	-0,13	8,67E-01	53,92	0,15	8,62E-01	84,13	-2,63	2,14E-02	72,37	-2,08	1,09E-01
Endogenous_MAV5_NM_020746.3	56,15	-0,50	5,61E-01	61,67	0,81	5,33E-01	80,39	-2,84	4,22E-02	54,44	-0,27	7,94E-01	51,24	-0,08	9,24E-01	80,39	-2,84	4,22E-02	60,32	0,60	4,92E-01	59,21	-0,93	4,26E-01
Endogenous_NKCM1_NM_000615.5	59,23	0,28	3,74E-01	65,00	-0,16	6,76E-01	87,25	-2,14	4,32E-02	62,22	0,05	8,85E-01	64,46	-0,76	2,05E-01	87,25	-2,14	4,32E-02	71,43	-0,41	2,83E-01	82,89	-1,12	1,46E-01
Endogenous_OAS3_NM_006187.2	56,15	-0,40	4,82E-01	50,00	0,15	8,52E-01	87,25	1,90	3,33E-02	71,11	-1,08	1,91E-01	65,29	0,53	3,56E-01	87,25	1,90	3,33E-02	63,49	0,68	2,51E-01	57,89	0,06	9,31E-01
Endogenous_PLA2G6_NM_001004426.1	65,38	-0,55	3,14E-01	73,33	0,92	2,22E-01	82,35	2,26	4,40E-02	60,00	-0,23	7,23E-01	51,24	0,21	7,09E-01	82,35	-1,53	4,58E-02	53,97	-0,40	9,44E-01	65,79	-0,58	3,79E-01
Endogenous_TLR8_NM_016610.2	56,92	0,51	5,12E-01	60,00	0,36	7,52E-01	83,33	2,80	3,53E-02	71,11	-1,50	1,66E-01	58,68	0,47	5,72E-01	83,33	2,80	3,53E-02	71,43	1,60	8,71E-02	67,11	1,11	3,07E-01
Endogenous_A2M_NM_000014.4	58,46	0,66	2,73E-01	66,67	-1,40	1,43E-01	56,86	-0,44	4,86E-01	76,67	1,60	8,51E-02	50,41	0,04	9,45E-01	56,86	-0,44	4,86E-01	84,13	-2,54	2,80E-02	52,63	-0,40	9,57E-01
Endogenous_CR2_NM_001006558.1	57,69	0,33	6,63E-01	60,00	-0,29	7,18E-01	50,00	-0,17	7,87E-01	85,56	-3,35	4,61E-02	51,24	0,04	9,44E-01	50,00	-0,17	7,87E-01	66,67	0,57	3,41E-01	71,05	0,96	2,14E-01
Endogenous_AKT3_NM_181690.1	50,00	0,18	7,48E-01	58,33	-0,38	6,56E-01	65,69	-0,79	2,59E-01	57,78	-0,12	8,63E-01	54,55	-0,15	6,92E-01	65,69	-0,79	2,59E-01	80,95	-2,01	3,42E-02	51,32	-0,08	9,15E-01
Endogenous_AMICA1_NM_0153206.2	70,77	1,41	1,00E-01	70,00	-1,27	2,89E-01	55,88	-0,26	7,30E-01	85,56	2,22	7,06E-02	52,89	0,34	7,21E-01	55,88	-0,26	7,30E-01	85,71	-3,51	2,41E-02	64,47	-0,37	9,15E-01
Endogenous_ATM_NM_000051.3	51,54	-0,18	7,65E-01	68,33	0,92	3,24E-01	67,65	-0,81	2,65E-01	93,33	-3,54	2,00E-02	63,64	0,66	2,99E-01	67,65	-0,81	2,65E-01	61,11	-0,42	5,02E-01	53,95	0,29	7,15E-01
Endogenous_BID_NM_001196.2	56,92	-0,50	4,11E-01	88,33	2,33	3,95E-02	53,92	-0,21	7,44E-01	60,00	-0,90	2,17E-01	69,42	-0,93	2,06E-01	53,92	-0,21	7,44E-01	50,79	0,02	9,78E-01	64,47	0,12	8,73E-01
Endogenous_C7_NM_000587.2	60,77	0,28	3,14E-01	81,67	-1,12	1,25E-01	68,63	-0,33	2,80E-01	66,67	0,44	2,40E-01	52,07	0,07	7,81E-01	68,63	-0,33	2,80E-01	81,75	-0,88	2,20E-02	67,11	-0,39	2,72E-01
Endogenous_CCL17_NM_002987.2	65,38	0,27	3,82E-01	55,00	-0,15	7,18E-01	63,73	0,18	5,73E-01	85,56	1,23	4,62E-02	51,72	-0,26	4,09E-01	63,73	0,18	5,73E-01	50,79	-0,02	9,46E-01	63,16	-0,30	5,04E-01
Endogenous_CD1A_NM_001763.2	62,31	0,36	3,56E-01	58,33	0,21	7,07E-01	53,92	-0,06	8,83E-01	67,67	0,42	3,58E-01	61,16	0,37	2,78E-01	53,92	-0,06	8,83E-01	80,95	-1,33	3,12E-02	82,89	-1,34	7,51E-02
Endogenous_CD1C_NM_001765.2	69,23	0,69	1,31E-01	65,00	-0,72	2,51E-01	63,73	-0,28	5,13E-01	81,11	1,23	6,24E-02	61,16	-0,28	4,72E-01	63,73	-0,28	5,13E-01	81,75	-1,49	3,26E-02	77,63	-1,19	8,44E-02
Endogenous_CD1E_NM_001042583.1	60,77	0,23	5,44E-01	58,33	-0,23	6,76E-01	53,92	0,11	7,98E-01	75,56	0,66	1,89E-01	51,24	-0,13	7,38E-01	53,92	0,11	7,98E-01	80,16	-1,17	3,47E-02	77,63	-0,92	1,40E-01
Endogenous_CD207_NM_0015717.2	54,62	0,06	8,95E-01	68,33	0,30	4,77E-01	54,90	0,03	9,18E-01	70,00	-0,14	3,33E-01	52,07	0,10	6,87E-01	54,90	0,03	9,18E-01	82,54	-0,88	2,79E-02	80,26	-1,00	1,08E-01
Endogenous_CD59_NM_000611.4	61,54	0,53	4,13E-01	60,00	-0,41	7,36E-01	62,75	0,56	4,38E-01	87,78	2,34	3,23E-02	63,64	0,56	3,99E-01	62,75	0,56	4,38E-01	50,79	0,11	8,63E-01	51,32	0,04	9,56E-01
Endogenous_CDT1_NM_006137.6	58,46	-0,41	4,66E-01	58,33	0,29	7,20E-01	53,92	-0,06	8,83E-01	86,67	-2,43	3,49E-02	55,37	-0,15	7,91E-01	53,92	-0,06	8,83E-01	74,60	1,40	5,36E-02	64,47	-0,52	4,79E-01
Endogenous_CDT4_NM_001025159.1	69,23	1,37	1,02E-01	53,33	-0,35	7,41E-01	56,86	0,29	7,22E-01	82,22	3,11	5,37E-02	52,07	0,24	7,25E-01	56,86	0,29	7,22E-01	59,52	-0,55	4,39E-01	84,21	-2,51	4,32E-02
Endogenous_CEACAM6_NM_002483.4	56,15	-0,16	5,38E-01	60,00	0,37	3,14E-01	57,84	0,24	4,40E-01	85,56	1,14	4,44E-02	56,20	-0,06	8,18E-01	57,84	0,24	4,40E-01	53,17	0,04	8,87E-01	60,53	0,36	3,37E-01
Endogenous_CR2_NM_001006558.1	54,62	0,06	8,95E-01	73,33	-0,66	2,44E-01	79,41	-2,49	7,35E-02	66,67	0,14	7,79E-01	82,64	-2,02	4,47E-02	79,41	-2,49	7,35E-02	65,87	-0,53	3,04E-01	57,89	0,39	4,59E-01
Endogenous_CTSX_NM_004390.3	66,92	0,44	1,87E-01	60,00	0,02	9,63E-01	58,82	-0,36	3,68E-01	91,11	0,95	3,46E-02	61,98	0,18	5,53E-01	58,82	-0,36	3,68E-01	63,49	-0,22	4,92E-01	68,42	-0,67	2,46E-01
Endogenous_CX3CL1_NM_002996.3	63,08	0,31	3,40E-01	71,67	-0,51	2,88E-01	68,63	0,50	1,89E-01	86,67	1,14	3,70E-02	57,78	-0,11	7,29E-01	68,63	0,50	1,89E-01	65,87	-0,38	2,64E-01	60,53	-0,26	5,43E-01
Endogenous_CX3CR1_NM_001337.3	71,54	1,13	8,98E-02	73,33	-1,46	1,24E-01	55,88	0,17	7,79E-01	74,44	1,36	8,95E-02	71,90	0,81	1,88E-01	55,88	0,17	7,79E-01	80,95	-2,09	2,49E-02	71,05	-1,29	1,80E-01
Endogenous_DOCCK9_NM_001130048.1	52,31	0,14	8,03E-01	55,00	0,24	7,86E-01	67,65	-1,18	1,92E-01	86,67	1,83	3,47E-02	53,72	0,01	9,79E-01	67,65	-1,18	1,92E-01	61,11	-0,64	3,29E-01	52,63	-0,40	6,32E-01
Endogenous_DPP4_NM_001395.3	50,00	0,06	8,03E-01	58,33	-0,12	7,48E-01	69,61	0,36	2,46E-01	85,56	1,10	3,61E-02	59,50	0,19	4,63E-01	69,61	0,36	2,46E-01	71,43	-0,55	9,02E-02	53,95	-0,08	9,06E-01
Endogenous_DUSP4_NM_057158.2	55,38	-0,17	6,07E-01	58,33	0,32	5,28E-01	68,63	-0,57	1,78E-01	81,11	-1,26	5,51E-02	56,20	0,19	5,60E-01	68,63	-0,57	1,78E-01	81,75	0,92	3,11E-02	67,11	0,40	3,55E-01
Endogenous_FCER1A_NM_002001.2	64,62	0,34	1,93E-01	60,00	-0,29	4,37E-01	55,88	-0,05	8,44E-01	78,89	0,78	6,37E-02	61,24	0,05	8,14E-01	55,88	-0,05	8,44E-01	80,16	-0,83	2,95E-02	69,74	-0,52	1,19E-01
Endogenous_FUT5_NM_002034.2	56,15	-0,19	7,30E-01	53,33	0,45	5,38E-01	57,84	-0,36	5,49E-01	52,22	-0,17	7,94E-01	56,20	0,92	2,38E-01	57,84	-0,36	5,49E-01	84,92	-2,79	4,52E-02	97,37	-6,66	7,34E-02
Endogenous_FYN_NM_002037.3	56,92	0,19	7,74E-01	51,67	0,14	8,90E-01	52,94	0,25	7,37E-01	52,22	-0,08	8,15E-01	51,24	0,02	9,71E-01	52,94	0,25	7,37E-01	84,92	-2,94	2,31E			

expressed in pairwise tumour-versus-adjacent non-tumour comparisons are highlighted in blue in the gene-name column.

Gene	Tumor_history			Smoking_history			Lymphnode			EGFR			KRAS			N_TNM			Grading_TNM			I_TNM_T1-2vsT3		
	AUC	Coef	p.value	AUC	Coef	p.value	AUC	Coef	p.value	AUC	Coef	p.value	AUC	Coef	p.value	AUC	Coef	p.value	AUC	Coef	p.value	AUC	Coef	p.value
ATM_NM_1	59.23	-0.53	4.13E-01	53.33	0.06	9.50E-01	85.29	-2.88	3.26E-02	61.11	0.59	4.55E-01	52.89	-0.06	9.25E-01	85.29	-2.88	3.26E-02	58.73	-0.85	2.27E-01	51.32	0.05	9.49E-01
BATF_NM_1	86.15	-2.56	2.39E-02	73.33	1.34	2.52E-01	50.00	0.41	5.71E-01	61.11	0.38	6.17E-01	53.72	0.35	5.99E-01	50.00	0.41	5.71E-01	53.97	-0.22	7.39E-01	61.84	0.44	5.94E-01
BCL2L1_N	83.08	-6.11	2.39E-02	51.67	0.36	8.74E-01	55.88	-1.00	9.39E-01	50.00	1.47	3.89E-01	71.07	-3.01	1.28E-01	55.88	-1.00	9.39E-01	53.17	-0.21	8.91E-01	69.74	0.81	6.55E-01
BST12_N	86.15	4.23	1.21E-02	73.33	-2.56	2.10E-01	55.88	-0.63	6.23E-01	61.11	-1.08	4.39E-01	57.02	-3.01	4.72E-01	55.88	-0.63	6.23E-01	50.79	0.03	9.78E-01	56.58	0.55	7.09E-01
BTLA_NM_1	65.38	-1.31	2.08E-01	58.33	-0.10	9.42E-01	53.92	-0.05	9.60E-01	70.00	0.74	4.90E-01	52.07	0.15	8.72E-01	53.92	-0.05	9.60E-01	50.79	0.17	8.55E-01	96.05	7.07	4.97E-02
CAMP_NM_1	53.08	-0.25	6.12E-01	50.00	0.08	9.07E-01	56.86	-0.57	3.87E-01	51.11	0.00	1.00E+00	66.12	0.76	1.97E-01	56.86	-0.57	3.87E-01	85.71	-2.46	2.99E-02	63.16	-0.64	4.20E-01
CCL16_N	80.00	-1.80	2.39E-02	65.00	0.53	4.92E-01	53.92	0.06	9.15E-01	61.11	0.08	8.94E-01	52.07	-0.14	7.80E-01	53.92	0.06	9.15E-01	80.95	1.54	3.67E-02	61.84	0.57	4.73E-01
CD27_NM_1	53.08	-0.24	5.69E-01	66.67	-0.32	5.96E-01	59.80	0.26	5.82E-01	61.11	-0.53	3.38E-01	59.50	-0.45	3.20E-01	59.80	0.26	5.82E-01	82.54	1.77	4.26E-02	89.47	1.89	7.03E-02
CD40LG_1	66.15	1.14	1.34E-01	75.00	-1.93	1.23E-01	57.84	0.39	5.99E-01	83.33	2.25	5.45E-02	52.07	0.11	8.69E-01	57.84	0.39	5.99E-01	50.79	-0.14	8.27E-01	89.47	2.82	4.66E-02
CDBA_NM_1	55.38	-0.17	7.20E-01	73.33	0.96	2.41E-01	53.92	0.14	8.05E-01	90.00	-2.06	3.41E-02	52.07	0.11	8.69E-01	57.84	0.39	5.99E-01	50.79	-0.14	8.27E-01	89.47	2.82	4.66E-02
CDKN1A_1	89.23	-3.77	3.29E-02	83.33	4.00	7.56E-02	51.96	-0.07	9.02E-01	66.67	-0.77	3.17E-01	66.12	-0.60	2.65E-01	51.96	-0.07	9.02E-01	65.74	0.10	8.32E-01	65.79	-0.63	3.50E-01
CEACAM1	52.31	0.32	6.50E-01	75.00	-1.44	2.71E-01	53.92	0.25	7.57E-01	67.78	-0.14	8.60E-01	81.82	-2.93	4.56E-02	53.92	0.25	7.57E-01	61.11	0.27	5.62E-01	57.89	-0.66	4.16E-01
COL3A1_N	53.08	-0.13	7.97E-01	50.00	-0.01	9.86E-01	56.86	0.36	5.49E-01	57.78	-0.49	4.45E-01	55.37	0.30	5.66E-01	56.86	0.36	5.49E-01	66.67	0.70	2.20E-01	94.74	3.67	3.78E-02
CR2_NM_1	73.08	-1.72	7.11E-02	61.67	0.86	4.53E-01	57.84	0.56	4.19E-01	52.22	-0.05	9.51E-01	54.55	-0.17	7.88E-01	57.84	0.56	4.19E-01	71.43	1.60	5.28E-02	89.47	2.18	3.29E-02
CTAG1B_N	53.08	0.18	7.29E-01	71.67	-0.94	2.93E-01	64.71	-0.95	1.56E-01	51.11	0.13	8.35E-01	58.68	0.65	2.65E-01	64.71	-0.95	1.56E-01	83.33	-2.44	3.04E-02	56.58	-0.35	5.94E-01
CXCL13_N	58.46	-0.50	2.25E-01	65.00	-0.12	8.17E-01	56.82	0.26	5.03E-01	58.89	-0.50	3.59E-01	68.60	-0.61	1.39E-01	56.82	0.26	5.03E-01	79.37	1.12	2.97E-02	88.16	1.47	2.16E-02
FEZ1_NM_1	81.54	2.64	2.36E-02	90.00	-3.74	6.57E-02	61.76	0.65	4.67E-01	61.11	0.88	3.61E-01	56.20	-0.50	5.41E-01	61.76	0.65	4.67E-01	57.14	-0.11	8.93E-01	53.95	-0.16	8.74E-01
GZMK_NM_1	64.62	0.51	4.28E-01	75.00	-1.70	3.04E-01	69.61	1.01	2.15E-01	56.67	-0.46	5.29E-01	52.89	0.34	5.87E-01	69.61	1.01	2.15E-01	60.32	0.73	2.92E-01	89.47	2.95	4.08E-02
IFIT2_NM_1	82.31	3.02	3.77E-02	91.67	-4.70	7.82E-02	56.86	-0.84	4.12E-01	63.33	0.67	5.63E-01	55.37	-0.36	7.03E-01	56.86	-0.84	4.12E-01	58.73	-0.73	4.34E-01	60.53	0.79	5.38E-01
IFIT7_NM_1	83.85	3.30	3.98E-02	93.33	-3.83	1.70E-01	51.96	-0.42	6.15E-01	70.00	0.35	6.17E-01	52.07	-0.38	5.71E-01	51.96	-0.42	6.15E-01	74.60	-2.10	7.86E-02	53.95	-0.17	8.51E-01
IFNA7_NM_1	54.62	0.29	6.75E-01	66.67	0.82	4.38E-01	68.63	-1.26	1.61E-01	62.22	-0.54	5.23E-01	83.47	2.86	3.20E-02	68.63	-1.26	1.61E-01	65.08	-1.31	1.15E-01	63.16	-0.91	3.43E-01
IFNG_NM_1	61.54	-0.46	4.75E-01	61.67	0.27	7.69E-01	52.94	-0.23	7.50E-01	58.89	-0.39	6.13E-01	81.82	2.02	3.60E-02	52.94	-0.23	7.50E-01	72.22	-1.85	4.42E-02	57.89	0.19	8.17E-01
IL15_NM_1	83.08	5.89	2.14E-02	80.00	-5.67	1.06E-01	50.98	-0.31	8.44E-01	65.56	2.16	2.72E-01	81.82	3.56	3.80E-01	50.98	-0.31	8.44E-01	50.98	-1.21	4.07E-01	55.26	1.16	5.55E-01
IL15RA_NM_1	59.23	0.94	3.69E-01	70.00	-2.01	3.04E-01	52.94	0.50	6.66E-01	58.89	-0.96	4.04E-01	81.82	-3.56	2.40E-02	52.94	0.50	6.66E-01	75.40	2.38	7.57E-02	60.53	1.00	4.90E-01
IL1A_NM_1	63.08	-0.11	8.22E-01	68.33	0.54	4.04E-01	57.84	-0.37	4.80E-01	50.00	0.04	9.48E-01	61.16	0.43	4.09E-01	57.84	-0.37	4.80E-01	55.56	0.02	9.64E-01	89.47	-1.77	3.00E-02
IL1B_NM_1	60.77	-0.17	6.99E-01	56.67	0.19	7.62E-01	56.86	-0.31	5.18E-01	51.11	0.11	8.36E-01	55.37	-0.12	7.91E-01	56.86	-0.31	5.18E-01	50.79	-0.05	9.14E-01	82.89	-1.92	3.47E-02
IL1RAP_NM_1	80.77	-3.90	3.15E-02	66.67	2.05	3.07E-01	53.92	-0.80	4.95E-01	53.33	-0.15	8.95E-01	59.50	-1.22	2.56E-01	53.92	-0.80	4.95E-01	56.35	-0.30	7.59E-01	65.79	-1.86	2.74E-01
IL25_NM_1	54.62	-0.31	6.51E-01	65.00	0.78	4.07E-01	69.61	-1.24	1.61E-01	75.56	1.67	1.10E-01	62.81	0.87	2.39E-01	69.61	-1.24	1.61E-01	80.16	-2.06	2.91E-02	56.58	-0.40	6.65E-01
ISG15_NM_1	86.15	3.85	2.01E-02	88.33	-5.61	2.00E-01	61.76	0.10	8.84E-01	68.89	0.52	4.68E-01	50.41	-0.40	5.66E-01	61.76	0.10	8.84E-01	73.02	-2.09	8.12E-02	51.32	-0.32	7.38E-01
KLRC1_N	58.46	-0.29	6.50E-01	51.67	-0.14	8.85E-01	60.78	0.60	4.40E-01	50.00	0.22	7.91E-01	57.85	0.50	4.53E-01	60.78	0.60	4.40E-01	59.52	0.58	4.04E-01	55.26	0.32	7.11E-01
LILRA5_N	51.54	-0.31	6.47E-01	58.33	0.37	6.97E-01	65.69	-0.69	3.67E-01	50.00	0.22	7.91E-01	59.50	0.36	5.93E-01	65.69	-0.69	3.67E-01	51.59	-0.22	7.43E-01	51.59	-0.22	7.43E-01
LRRN3_N	87.69	2.70	6.38E-03	83.33	-1.85	1.10E-01	51.96	-0.13	8.31E-01	73.33	-1.98	1.02E-01	57.02	-0.29	7.48E-01	51.96	-0.13	8.31E-01	51.59	-0.08	8.81E-01	52.63	-0.23	7.56E-01
NFATC4_N	54.62	0.07	9.33E-01	61.67	0.39	7.60E-01	70.59	1.41	2.51E-01	73.33	-1.98	1.02E-01	57.02	-0.29	7.48E-01	70.59	1.41	2.51E-01	82.54	4.27	3.16E-02	86.84	5.13	8.16E-02
PASD1_N	59.23	0.61	3.00E-01	51.67	-0.33	6.98E-01	56.86	0.41	5.27E-01	58.89	-0.07	9.05E-01	52.07	0.37	4.96E-01	56.86	0.41	5.27E-01	74.60	-1.57	4.62E-02	92.11	-2.38	4.24E-02
PDCD1LG	86.15	5.91	1.78E-02	56.67	-1.21	4.63E-01	50.98	0.62	5.63E-01	56.67	0.18	8.66E-01	52.07	0.03	9.73E-01	50.98	0.62	5.63E-01	57.94	-0.37	6.63E-01	78.95	-1.10	2.81E-01
PPARG_N	50.77	-0.15	8.30E-01	78.33	2.84	1.22E-01	59.80	-0.29	7.12E-01	66.67	-0.88	3.43E-01	59.50	0.69	3.53E-01	59.80	-0.29	7.12E-01	60.32	-0.53	4.67E-01	90.79	-4.47	4.84E-02
PSMB9_N	80.77	4.83	2.89E-02	88.33	-5.76	9.34E-02	50.00	-0.64	7.00E-01	73.33	2.72	1.88E-01	52.07	0.30	8.45E-01	50.00	-0.64	7.00E-01	65.08	-2.18	1.92E-01	61.84	1.38	4.97E-01
PTGDR2_1	69.23	-1.48	6.27E-02	96.67	3.87	3.90E-02	52.94	-0.36	5.84E-01	74.44	-1.19	1.13E-01	61.16	0.69	3.42E-01	52.94	-0.36	5.84E-01	70.63	0.90	2.07E-01	56.58	-0.33	6.58E-01
RAG1_NM_1	83.85	3.74	1.74E-02	81.67	-2.73	1.48E-01	54.90	-0.42	7.16E-01	60.00	1.02	4.19E-01	56.20	-0.69	5.26E-01	54.90	-0.42	7.16E-01	56.35	-0.25	8.10E-01	57.89	0.73	5.88E-01
SLM2B2_N	60.00	-1.07	2.42E-01	65.00	1.66	2.09E-01	64.71	-1.53	1.51E-01	70.00	-2.01	9.75E-02	57.85	0.69	4.89E-01	64.71	-1.53	1.51E-01	61.11	-0.98	2.84E-01	84.21	-3.26	4.97E-02
SLM1F1_N	65.38	-0.29	6.34E-01	66.67	0.39	6.26E-01	59.80	0.29	6.95E-01	68.89	-0.40	5.58E-01	65.29	0.54	4.18E-01	59.80	0.29	6.95E-01	63.49	0.20	7.55E-01	94.74	4.39	2.32E-02
SPP1_NM_1	70.77	-0.57	7.30E-02	90.00	1.47	8.46E-02	72.55	0.63	1.07E-01	84.44	-0.93	4.61E-02	60.33	0.32	2.67E-01	72.55	0.63	1.07E-01	59.52	0.20	4.81E-01	65.79	0.57	1.87E-01
STAT1_NM_1	86.15	6.61	3.12E-02	90.00	-6.89	5.67E-02	53.92	-0.16	9.10E-01	56.67	1.24	4.33E-01	61.16	1.13	3.78E-01	53.92	-0.16	9.10E-01	63.49	-2.07	1.49E-01	53.95	-0.03	9.86E-01
TGF2B_N	81.54	2.92	2.62E-02	83.33	-2.14	1.46E-01	62.75	0.81	3.31E-01	58.89	0.63	4.56E-01	55.37	0.03	9.51E-01	62.75	0.81	3.31E-01	5					

Supplementary Table S3B: GLM-significant transcripts associated with clinicopathological and oncogenic features in non-tumour samples. GLM estimates are reported in cells across feature-specific column blocks. Associations meeting the predefined thresholds of an absolute regression coefficient ≥ 0.6 , nominal $p \leq 0.05$ and AUC ≥ 0.80 are highlighted in yellow.

Vars	Tumor history							EGFR							N_TNM					
	K			N				K			N				K			N		
	AUC	Coef	p.value	AUC	Coef	p.value		AUC	Coef	p.value	AUC	Coef	p.value		AUC	Coef	p.value	AUC	Coef	p.value
ATM_NM_000051.3	51,54	-0,18	7,65E-01	59,23	-0,53	4,13E-01		93,33	-3,54	2,00E-02	61,11	0,59	4,55E-01		67,65	-0,81	2,65E-01	85,29	-2,88	3,26E-02
BST2_NM_004335.2	52,31	-0,32	5,60E-01	86,15	4,23	1,21E-02		72,22	-1,20	1,45E-01	61,11	-1,08	4,39E-01		93,14	2,20	4,40E-02	55,88	-0,63	6,23E-01
CR2_NM_001006658.1	54,62	0,06	8,95E-01	73,08	-1,72	7,11E-02		66,67	0,14	7,79E-01	52,22	-0,05	9,51E-01		79,41	-2,49	7,35E-02	57,84	0,56	4,19E-01
IFIT1_NM_001548.3	53,85	0,11	8,13E-01	83,85	3,30	3,98E-02		62,22	0,62	2,97E-01	70,00	0,35	6,17E-01		53,92	0,21	6,91E-01	51,96	-0,42	6,15E-01
TGFB2_NM_003238.2	55,38	0,31	4,14E-01	81,54	2,92	2,62E-02		80,00	0,67	1,49E-01	58,89	0,63	4,56E-01		54,90	-0,03	9,50E-01	62,75	0,81	3,31E-01

Vars	Smoking history							KRAS							Grading_TNM					
	K			N				K			N				K			N		
	AUC	Coef	p.value	AUC	Coef	p.value		AUC	Coef	p.value	AUC	Coef	p.value		AUC	Coef	p.value	AUC	Coef	p.value
ATM_NM_000051.3	68,33	0,92	3,24E-01	53,33	0,06	9,50E-01		63,64	0,66	2,99E-01	52,89	-0,06	9,25E-01		61,11	-0,42	5,02E-01	58,73	-0,85	2,27E-01
BST2_NM_004335.2	63,33	-0,51	5,00E-01	73,33	-2,56	2,10E-01		52,89	0,01	9,92E-01	57,02	0,40	7,25E-01		67,46	0,99	1,19E-01	50,79	0,03	9,78E-01
CR2_NM_001006658.1	73,33	-0,66	2,44E-01	61,67	0,86	4,53E-01		82,64	-2,02	4,47E-02	54,55	-0,17	7,88E-01		65,87	-0,53	3,04E-01	71,43	1,60	5,28E-02
IFIT1_NM_001548.3	58,33	0,30	6,62E-01	93,33	-3,83	1,70E-01		64,46	0,64	2,06E-01	52,07	-0,38	5,71E-01		85,71	-1,86	1,45E-02	74,60	-2,10	7,86E-02
TGFB2_NM_003238.2	60,00	-0,12	8,17E-01	83,33	-2,14	1,46E-01		74,38	0,89	9,16E-02	55,37	0,03	9,51E-01		80,95	-1,45	3,84E-02	54,76	-0,05	9,32E-01

Vars	Lymphnode							T_TNM_T1andT2_vs_T3						
	K			N				K			N			
	AUC	Coef	p.value	AUC	Coef	p.value		AUC	Coef	p.value	AUC	Coef	p.value	
ATM_NM_000051.3	67,65	-0,81	2,65E-01	85,29	-2,88	3,26E-02		53,95	0,29	7,15E-01	51,32	0,05	9,49E-01	
BST2_NM_004335.2	93,14	2,20	4,40E-02	55,88	-0,63	6,23E-01		52,63	-0,01	9,85E-01	56,58	0,55	7,09E-01	
CR2_NM_001006658.1	79,41	-2,49	7,35E-02	57,84	0,56	4,19E-01		57,89	0,39	4,59E-01	89,47	2,18	3,28E-02	
IFIT1_NM_001548.3	53,92	0,21	6,91E-01	51,96	-0,42	6,15E-01		88,16	-2,05	7,64E-02	53,95	-0,17	8,51E-01	
TGFB2_NM_003238.2	54,90	-0,03	9,50E-01	62,75	0,81	3,31E-01		63,16	-0,45	4,37E-01	56,58	0,40	6,38E-01	

Supplementary Table S3C: Common GLM-significant transcripts detected in both tumour (K, red bar) and non-tumour (N, blue bar) tissues, associated with clinicopathological and oncogenic features in non-tumour samples. GLM estimates are reported in cells across feature-specific column blocks. Associations meeting the predefined thresholds of an absolute regression coefficient ≥ 0.6 , nominal $p \leq 0.05$ and $AUC \geq 0.80$ are highlighted in yellow.

Gene	Common Name / Alias	Category	Luad Cox-ph Z-score	Lusc Cox-ph Z-score	Direction In Luad	Direction In Lusc
CDK1	Cyclin-dependent kinase 1	Hub gene	-0.90	+2.44	Favorable	Unfavorable
PAX5	Paired box protein Pax-5	Hub gene	-1.73	+1.03	Favorable	Unfavorable
POU2F2	POU domain class 2 TF 2 / OCT-2	Hub gene	-0.27	+1.41	Favorable	Unfavorable
TAL1	T-cell acute lymphocytic leukemia protein 1	Hub gene	-0.89	+2.30	Favorable	Unfavorable
PPARG	Peroxisome proliferator-activated receptor γ	Hub gene	+0.78	-1.99	Unfavorable	Favorable
TNFSF13B	BAFF	BAFF-APRIL axis	-0.75	+1.19	Favorable	Unfavorable
TNFRSF13C	BAFF-R	BAFF-APRIL axis	-1.26	+0.78	Favorable	Unfavorable
TNFRSF13B	TACI	BAFF-APRIL axis	-0.70	+0.70	Favorable	Unfavorable
TNFRSF17	BCMA	BAFF-APRIL axis	-0.63	+0.80	Favorable	Unfavorable
TNFSF13	APRIL	BAFF-APRIL axis	+0.65	-1.94	Unfavorable	Favorable

Supplementary Table S4: Association of hub genes and BAFF/APRIL axis components with anti-PD-1 therapy outcomes in LUAD and LUSC cohorts. Cox proportional hazards z-scores from the Cancer Immunology Data Engine (CIDE; cide.ccr.cancer.gov) for the Ravi et al. (2023) cohort are shown for lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC). Negative z-scores indicate that higher gene expression is associated with more favorable survival outcomes under anti-PD-1 therapy (favorable); positive z-scores indicate association with worse outcomes (unfavorable). Genes are grouped as hub genes identified by network analysis (coordinating ~75% of differentially expressed genes) or components of the BAFF/APRIL signaling axis. The direction column summarizes the clinical association for each histotype.