

Supplementary Table 1. Hallmark of angiogenesis.

Gene symbol
APOH
APP
CCND2
COL3A1
COL5A2
CXCL6
FGFR1
FSTL1
ITGAV
JAG1
JAG2
KCNJ8
LPL
LRPAP1
LUM
MSX1
NRP1
OLR1
PDGFA
PF4
PGLYRP1
POSTN
PRG2
PTK2
S100A4
SERPINA5
SLCO2A1
SPP1
STC1
THBD
TIMP1
TNFRSF21
VAV2
VCAN
VEGFA
VTN

Supplementary Table 2. Common cancer-related signature

Gene Signature	Genes Symbol
CD8 T effector	CD8A, CXCL10, CXCL9, GZMA, GZMB, IFNG, PRF1, TBX21
DNA damage repair	ALKBH2, ALKBH3, APEX1, APEX2, APLF, ATM, ATR, ATRIP, BLM, BRCA1, BRCA2, BRIP1, CCNH, CDK7, CETN2, CHAF1A, CHEK1, CHEK2, CLK2, DCLRE1C, DDB1, DDB2, DUT, ENDOV, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, ERCC6, ERCC8, FAN1, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCL, FANCM, GTF2H1, GTF2H2, GTF2H3, GTF2H4, GTF2H5, H2AFX, HLTF, HUS1, LIG1, LIG3, LIG4, MBD4, MDC1, MGMT, MLH1, MLH3, MMS19, MNAT1, MPG, MSH2, MSH3, MSH4, MSH5, MSH6, MUTYH, NEIL1, NEIL2, NEIL3, NHEJ1, NTHL1, NUDT1, OGG1, PALB2, PARP1, PARP2, PARP3, PCNA, PER1, PMS1, PMS2, PNKP, POLB, POLD1, POLE, POLG, POLH, POLL, POLM, POLQ, PRKDC, RAD1, RAD17, RAD18, RAD23A, RAD23B, RAD51C, RAD9A, RECQL4, RECQL5, RIF1, RNF168, RNF4, RNF8, RPA1, RPA2, RPA3, RPA4, RRM2B, SETMAR, SHPRH, SMUG1, TDP1, TDP2, TOPBP1, TP53, TREX1, UBE2A, UBE2B, UBE2N, UBE2V2, UNG, UVSSA, WRN, XAB2, XPA, XPC, XRCC1, XRCC4, XRCC5, XRCC6
Pan-F-TBRS	ACTA2, ACTG2, ADAM12, ADAM19, CNN1, COL4A1, CTGF, CTPS1, FAM101B, FSTL3, HSPB1, IGFBP3, PXDC1, SEMA7A, SH3PXD2A, TAGLN, TGFB1, TNS1, TPM1
Antigen processing machinery	B2M, HLA-A, HLA-B, HLA-C, TAP1, TAP2
Immune checkpoint	CD274, CTLA4, HAVCR2, LAG3, PDCD1, PDCD1LG2, TIGIT
EMT1	CLDN3, CLDN7, CLDN4, CDH1, VIM, TWIST1, ZEB1, ZEB2
EMT2	AXL, FAP, LOXL2, ROR2, TAGLN, TWIST2, WNT5A
EMT3	FOXF1, GATA6, SOX9, TWIST1, ZEB1, ZEB2
FGFR3-related genes	FGFR3, TP63, WNT7B
KEGG discovered histones	HIST1H2AG, HIST1H2AI, HIST1H2BL, HIST2H2BF
Fanconi anemia	APITD1, ATR, ATRIP, BLM, BRCA1, BRCA2, BRIP1, C17orf70, C19orf40, EME1, EME2, ERCC1, ERCC4, FAN1, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, HES1, MLH1, MUS81, PALB2, PMS2, POLH, POLI, POLK, POLN, RAD51, RAD51C, REV1, REV3L, RMI1,

	RMI2, RPA1, RPA2, RPA3, RPA4, SLX4, STRA13, TELO2, TOP3A, TOP3B, UBE2T, USP1, WDR48
Cell cycle	ABL1, ANAPC1, ANAPC10, ANAPC11, ANAPC13, ANAPC2, ANAPC4, ANAPC5, ANAPC7, ATM, ATR, BUB1, BUB1B, BUB3, CCNA1, CCNA2, CCNB1, CCNB2, CCNB3, CCND1, CCND2, CCND3, CCNE1, CCNE2, CCNH, CDC14A, CDC14B, CDC16, CDC20, CDC23, CDC25A, CDC25B, CDC25C, CDC26, CDC27, CDC45, CDC6, CDC7, CDK1, CDK2, CDK4, CDK6, CDK7, CDKN1A, CDKN1B, CDKN1C, CDKN2A, CDKN2B, CDKN2C, CDKN2D, CHEK1, CHEK2, CREBBP, CUL1, DBF4, E2F1, E2F2, E2F3, E2F4, E2F5, EP300, ESPL1, FZR1, GADD45A, GADD45B, GADD45G, GSK3B, HDAC1, HDAC2, MAD1L1, MAD2L1, MAD2L2, MCM2, MCM3, MCM4, MCM5, MCM6, MCM7, MDM2, MYC, ORC1, ORC2, ORC3, ORC4, ORC5, ORC6, PCNA, PKMYT1, PLK1, PRKDC, PTTG1, PTTG2, RAD21, RB1, RBL1, RBL2, RBX1, SFN, SKP1, SKP2, SMAD2, SMAD3, SMAD4, SMC1A, SMC1B, SMC3, STAG1, STAG2, TFDP1, TFDP2, TGFB1, TGFB2, TGFB3, TP53, TTK, WEE1, YWHAB, YWHAE, YWHAG, YWHAH, YWHAQ, YWHAZ, ZBTB17
DNA replication	DNA2, FEN1, LIG1, MCM2, MCM3, MCM4, MCM5, MCM6, MCM7, PCNA, POLA1, POLA2, POLD1, POLD2, POLD3, POLD4, POLE, POLE2, POLE3, POLE4, PRIM1, PRIM2, RFC1, RFC2, RFC3, RFC4, RFC5, RNASEH1, RNASEH2A, RNASEH2B, RNASEH2C, RPA1, RPA2, RPA3, RPA4, SSBP1
Nucleotide excision repair	CCNH, CDK7, CETN2, CUL4A, CUL4B, DDB1, DDB2, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, ERCC6, ERCC8, GTF2H1, GTF2H2, GTF2H3, GTF2H4, GTF2H5, LIG1, MNAT1, PCNA, POLD1, POLD2, POLD3, POLD4, POLE, POLE2, POLE3, POLE4, RAD23A, RAD23B, RBX1, RFC1, RFC2, RFC3, RFC4, RFC5, RPA1, RPA2, RPA3, RPA4, XPA, XPC
Homologous recombination	BLM, BRCA2, EME1, MRE11A, MUS81, NBN, POLD1, POLD2, POLD3, POLD4, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54B, RAD54L, RPA1, RPA2, RPA3, RPA4, SHFM1, SSBP1, TOP3A, TOP3B, XRCC2, XRCC3
Mismatch repair	EXO1, LIG1, MLH1, MLH3, MSH2, MSH3, MSH6, PCNA, PMS2, POLD1, POLD2, POLD3, POLD4, RFC1, RFC2, RFC3, RFC4, RFC5, RPA1, RPA2, RPA3, RPA4, SSBP1
WNT target	EFNB3, MYC, TCF12, VEGFA
Cell cycle regulators	ATM, CCND1, CCNE1, CDKN1A, CDKN2A, E2F3, FBXW7, MDM2, RB1, TP53

Supplementary Table 3. Prognostic analysis of 32 angiogenesis-related genes using a univariate Cox regression model.

ID	HR	95% CI	p.value
WAS	0.601	(0.405-0.893)	0.012
OPN3	1.46	(1.15-1.85)	0.0022
CYFIP2	1.38	(1.09-1.76)	0.0077
GNA15	0.68	(0.471-0.982)	0.04
MMP2	0.711	(0.509-0.994)	0.046
CYTH4	0.651	(0.449-0.944)	0.024
ANXA13	2.62	(1.63-4.23)	0.00007 3
CDK6	0.542	(0.366-0.803)	0.0023
PTN	0.809	(0.679-0.963)	0.017
ITK	1.6	(1.18-2.18)	0.0028
NCKAP1L	0.558	(0.355-0.876)	0.011
WDFY4	0.335	(0.114-0.986)	0.047
LOXL1	0.722	(0.572-0.911)	0.006
GFPT2	0.705	(0.501-0.992)	0.045
TMCC2	1.61	(1.14-2.26)	0.0065
EGFR	0.635	(0.433-0.932)	0.021
ARL11	0.316	(0.117-0.852)	0.023
TSPAN18	0.645	(0.463-0.9)	0.0098
CHMP4C	1.31	(1.04-1.65)	0.024
WDR72	1.72	(1.28-2.31)	0.00033
SOST	1.23	(1.08-1.39)	0.0015
GNG4	1.44	(1.14-1.84)	0.0028
COL22A1	1.36	(1.11-1.67)	0.0031
COL8A2	0.809	(0.661-0.989)	0.039
GNG12	0.679	(0.482-0.958)	0.028
SYT12	1.56	(1.14-2.15)	0.006
ARSJ	0.546	(0.305-0.978)	0.042
EPHB3	0.606	(0.41-0.895)	0.012
HIST3H2BB	1.81	(1.12-2.92)	0.015
CACNA1E	2.48	(1.2-5.11)	0.014
IFITM5	1.24	(1.03-1.48)	0.022
CTB_4E7.1	1.52	(1.19-1.93)	0.00072

Supplementary Table 4. The Anotation cell markers of single cell data.

Cell type	Markers
osteoblastic cell	COL1A1, CDH11, RUNX2, ALPL
Osteoclast	CTSK, MMP9, ACP5
Myeloid cells	LYZ, CD68, CD74, CD14, FCGR3A
Fibroblast	COL1A1, LUM, DCN, VIM
Myoblast	MYLPF, MYL1
TIL	IL7R, CD3D, NKG7, CD2, CD3E, CD3G, GNLY, KLRD1, KLRB1, MS4A1, CD79A
Endothelial cell	PECAM1, VWF, EGFL7, PLVAP

Reference

Zhou Y, Yang D, Yang Q, et al. Single-cell RNA landscape of intratumoral heterogeneity and immunosuppressive microenvironment in advanced osteosarcoma. *Nat Commun.* 2020 Dec 10;11(1):6322.

Liu Y, Feng W, Dai Y, et al. Single-Cell Transcriptomics Reveals the Complexity of the Tumor Microenvironment of Treatment-Naive Osteosarcoma. *Front Oncol.* 2021 Jul 21;11:709210.

Drug	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448	449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525	526	527	528	529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565	566	567	568	569	570	571	572	573	574	575	576	577	578	579	580	581	582	583	584	585	586	587	588	589	590	591	592	593	594	595	596	597	598	599	600	601	602	603	604	605	606	607	608	609	610	611	612	613	614	615	616	617	618	619	620	621	622	623	624	625	626	627	628	629	630	631	632	633	634	635	636	637	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	653	654	655	656	657	658	659	660	661	662	663	664	665	666	667	668	669	670	671	672	673	674	675	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700	701	702	703	704	705	706	707	708	709	710	711	712	713	714	715	716	717	718	719	720	721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736	737	738	739	740	741	742	743	744	745	746	747	748	749	750	751	752	753	754	755	756	757	758	759	760	761	762	763	764	765	766	767	768	769	770	771	772	773	774	775	776	777	778	779	780	781	782	783	784	785	786	787	788	789	790	791	792	793	794	795	796	797	798	799	800	801	802	803	804	805	806	807	808	809	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	832	833	834	835	836	837	838	839	840	841	842	843	844	845	846	847	848	849	850	851	852	853	854	855	856	857	858	859	860	861	862	863	864	865	866	867	868	869	870	871	872	873	874	875	876	877	878	879	880	881	882	883	884	885	886	887	888	889	890	891	892	893	894	895	896	897	898	899	900	901	902	903	904	905	906	907	908	909	910	911	912	913	914	915	916	917	918	919	920	921	922	923	924	925	926	927	928	929	930	931	932	933	934	935	936	937	938	939	940	941	942	943	944	945	946	947	948	949	950	951	952	953	954	955	956	957	958	959	960	961	962	963	964	965	966	967	968	969	970	971	972	973	974	975	976	977	978	979	980	981	982	983	984	985	986	987	988	989	990	991	992	993	994	995	996	997	998	999	1000
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Supplementary Table 7. The drug names and corresponding targets

Drug Name	Pathway Name	Targets
MN-64	WNT signaling	TNKS1, TNKS2
Venetoclax	Apoptosis regulation	BCL2
AGI-5198	Metabolism	IDH1 (R132H)
AZD3759	EGFR signaling	EGFR
NVP-ADW742	IGF1R signaling	IGF1R
P22077	Protein stability and degradation	USP7, USP47
WEHI-539	Apoptosis regulation	BCL-XL
Foretinib	RTK signaling	MET, KDR, TIE2, VEGFR3/FLT4, RON, PDGFR, FGFR1, EGFR
Rapamycin	PI3K/MTOR signaling	MTORC1
PRIMA-1MET	p53 pathway	TP53 activation
Talazoparib	Genome integrity	PARP1, PARP2
Trametinib	ERK MAPK signaling	MEK1, MEK2
Luminespib	Protein stability and degradation	HSP90
CZC24832	PI3K/MTOR signaling	PI3Kgamma
PFI3	Chromatin other	Polybromo 1, SMARCA4, SMARCA2
Wnt-C59	WNT signaling	PORCN
OTX015	Chromatin other	BRD2, BRD3, BRD4
AGI-6780	Metabolism	IDH2 R140Q mutant
IRAK4_4710	Other, kinases	IRAK4
Uprosertib	PI3K/MTOR signaling	AKT1, AKT2, AKT3
Olaparib	Genome integrity	PARP1, PARP2
Axitinib	RTK signaling	PDGFR, KIT, VEGFR
Buparlisib	PI3K/MTOR signaling	PI3Kalpha, PI3Kdelta, PI3Kbeta, PI3Kgamma
Afuresertib	PI3K/MTOR signaling	AKT1, AKT2, AKT3
Osimertinib	EGFR signaling	EGFR
Savolitinib	RTK signaling	MET

Pyridostatin	DNA replication	G-quadruplex stabiliser
Ulixertinib	ERK MAPK signaling	ERK1, ERK2
Vinorelbine	Mitosis	Microtubule destabiliser
ZM447439	Mitosis	AURKA, AURKB
AZD8055	PI3K/MTOR signaling	MTORC1, MTORC2
Crizotinib	RTK signaling	MET, ALK, ROS1
Temozolomide	DNA replication	DNA alkylating agent
AZD1208	Other, kinases	PIM1, PIM2, PIM3
LCL161	Apoptosis regulation	XIAP, IAP1, IAP2
Vincristine	-	-
Podophyllotoxin bromide	Unclassified	-
OSI-027	PI3K/MTOR signaling	MTORC1, MTORC2
Ibrutinib	Other, kinases	BTK
Docetaxel	Mitosis	Microtubule stabiliser
Vorinostat	Chromatin histone acetylation	HDAC inhibitor Class I, IIa, IIb, IV
Gallibiscoquinazole	Unclassified	-
OF-1	Chromatin histone acetylation	BRPF1B, BRPF2
Cediranib	RTK signaling	VEGFR, FLT1, FLT2, FLT3, FLT4, KIT, PDGFRB
Telomerase Inhibitor IX	Genome integrity	Telomerase
UMI-77	Apoptosis regulation	MCL1
Sepantronium bromide	Apoptosis regulation	BIRC5
MIM1	Apoptosis regulation	MCL1
5-Fluorouracil	Other	Antimetabolite (DNA & RNA)
Niraparib	Genome integrity	PARP1, PARP2
BMS-345541	Other	IKK-1, IKK-2
XAV939	WNT signaling	TNKS1, TNKS2
AZD1332	RTK signaling	NTRK1, NTRK2, NTRK3
Sapitinib	EGFR signaling	EGFR, ERBB2, ERBB3
Taselisib	PI3K/MTOR signaling	PI3K (beta sparing)
Staurosporine	RTK signaling	Broad spectrum kinase inhibitor
NU7441	Genome integrity	DNAPK

ULK1_4989	Other, kinases	ULK1
VSP34_8731	Other	VSP34
BMS-754807	IGF1R signaling	IGF1R, IR
Camptothecin	DNA replication	TOP1
Vinblastine	Mitosis	Microtubule destabiliser
Gefitinib	EGFR signaling	EGFR
SB216763	WNT signaling	GSK3A, GSK3B
Daporinad	Metabolism	NAMPT
Tozasertib	Mitosis	AURKA, AURKB, AURKC, others
ABT737	Apoptosis regulation	BCL2, BCL-XL, BCL-W, BCL-B, BFL1
Dactinomycin	Other	RNA polymerase
GNE-317	PI3K/MTOR signaling	PI3Kalpha
WIKI4	WNT signaling	TNKS1, TNKS2
AMG-319	PI3K/MTOR signaling	PI3K (beta sparing)
Pictilisib	PI3K/MTOR signaling	PI3K (class 1)
Sorafenib	Other, kinases	PDGFR, KIT, VEGFR, RAF
Oxaliplatin	DNA replication	DNA alkylating agent
GSK1904529A	IGF1R signaling	IGF1R, IR
Erlotinib	EGFR signaling	EGFR
MK-1775	Cell cycle	WEE1, PLK1
Gemcitabine	DNA replication	Pyrimidine antimetabolite
YK-4-279	Other	RNA helicase A
Teniposide	DNA replication	-
Fulvestrant	Hormone-related	ESR
CDK9_5576	Cell cycle	CDK9
IGF1R_3801	IGF1R signaling	IGFR1
JAK_8517	Other, kinases	JAK1, JAK2
Zoledronate	Other	
AT13148	PI3K/MTOR signaling	AKT1
AZD7762	Cell cycle	CHEK1, CHEK2
AZD6482	PI3K/MTOR signaling	PI3Kbeta
SB505124	RTK signaling	TGFBR1, ACVR1B, ACVR1C
Obatoclox Mesylate	Apoptosis regulation	BCL2, BCL-XL, BCL-W, MCL1
Dinaciclib	Cell cycle	CDK1, CDK2, CDK5, CDK9

Fulvestrant	Hormone-related	ESR
AZ960	Other, kinases	JAK2, JAK3
Alpelisib	PI3K/MTOR signaling	PI3Kalpha
Wee1 Inhibitor	Cell cycle	WEE1, CHEK1
Nelarabine	DNA replication	-
Dihydrorotenone	Unclassified	-
PRT062607	Other, kinases	SYK
Ribociclib	Cell cycle	CDK4, CDK6
Picolinici-acid	Other	Inflammatory related
PAK_5339	Cytoskeleton	PAK1, PAK2
Acetalax	Unclassified	-
GSK591	Chromatin histone methylation	PMRT5
VE821	Genome integrity	ATR
JQ1	Chromatin other	BRD2, BRD3, BRD4, BRDT
Navitoclax	Apoptosis regulation	BCL2, BCL-XL, BCL-W
Elephantin	Unclassified	-
Sinularin	Unclassified	-
Sabutoclax	Apoptosis regulation	BCL2, BCL-XL, BFL1, MCL1
AZD5363	Other, kinases	AKT1, AKT2, AKT3, ROCK2
GSK2578215A	Other, kinases	LRRK2
MK-8776	Cell cycle	CHEK1, CHEK2, CDK2
Mirin	Genome integrity	MRE11
Alisertib	Mitosis	AURKA
Dactolisib	PI3K/MTOR signaling	PI3K (class 1), MTORC1, MTORC2
Selumetinib	ERK MAPK signaling	MEK1, MEK2
BMS-536924	IGF1R signaling	IGF1R, IR
Bortezomib	Protein stability and degradation	Proteasome
EPZ004777	Chromatin histone methylation	DOT1L
Dabrafenib	ERK MAPK signaling	BRAF
Pevonedistat	Other	NAE
PLX-4720	ERK MAPK signaling	BRAF
LGK974	WNT signaling	PORCN
VE-822	Genome integrity	ATR
GSK2606414	Metabolism	PERK

ML323	Protein stability and degradation	USP1, UAF1
JAK1_8709	Other, kinases	JAK1
TAF1_5496	Other	TAF1
Oxaliplatin	DNA replication	DNA alkylating agent
Nilotinib	ABL signaling	ABL
Afatinib	EGFR signaling	EGFR, ERBB2
LY2109761	Other	TGFB1
MG-132	Protein stability and degradation	Proteasome, CAPN1
BDP-00009066	Cytoskeleton	MRCKB_HUMAN
AZD8186	PI3K/MTOR signaling	PI3Kalpha, PI3Kbeta
Ipatasertib	PI3K/MTOR signaling	AKT1, AKT, AKT3
GDC0810	Hormone-related	ESR1, ESR2
BPD-00008900	Other	-
GSK343	Chromatin histone methylation	EZH2
BIBR-1532	Genome integrity	TERT
Nutlin-3a (-)	p53 pathway	MDM2
Tamoxifen	Hormone-related	ESR1
Cyclophosphamide	DNA replication	Alkylating agent
Lapatinib	EGFR signaling	EGFR, ERBB2
Topotecan	DNA replication	TOP1
Mitoxantrone	DNA replication	TOP2
Dactinomycin	Other	RNA polymerase
AZD5582	Apoptosis regulation	XIAP, cIAP
I-BET-762	Chromatin other	BRD2, BRD3, BRD4
AZD5153	Chromatin other	BRD4
Eg5_9814	Other	KSP11
ERK_2440	ERK MAPK signaling	ERK1, ERK2
AZD5991	Apoptosis regulation	MCL1
AZ6102	WNT signaling	TNKS1, TNKS2
Cisplatin	DNA replication	DNA crosslinker
Cytarabine	Other	Antimetabolite
KRAS (G12C) Inhibitor-12	ERK MAPK signaling	KRAS (G12C)
Ulixertinib	ERK MAPK signaling	ERK1, ERK2
AZD6738	Genome integrity	ATR
I-BRD9	Chromatin other	BRD9
MIRA-1	p53 pathway	TP53
PD173074	RTK signaling	FGFR1, FGFR2, FGFR3

RO-3306	Cell cycle	CDK1
MK-2206	PI3K/MTOR signaling	AKT1, AKT2
Palbociclib	Cell cycle	CDK4, CDK6
PD0325901	ERK MAPK signaling	MEK1, MEK2
Dasatinib	Other, kinases	ABL, SRC, Ephrins, PDGFR, KIT
Paclitaxel	Mitosis	Microtubule stabiliser
BI-2536	Cell cycle	PLK1, PLK2, PLK3
Irinotecan	DNA replication	TOP1
AZD5438	Cell cycle	CDK2
IAP_5620	Other	IAP
AZD2014	PI3K/MTOR signaling	mTORC1, mTORC2
Ruxolitinib	Other, kinases	JAK1, JAK2
Linsitinib	IGF1R signaling	IGF1R
Epirubicin	DNA replication	Anthracycline
Uprosertib	PI3K/MTOR signaling	AKT1, AKT2, AKT3
Doramapimod	JNK and p38 signaling	p38, JNK2
Fludarabine	DNA replication	Antimetabolite
Docetaxel	Mitosis	Microtubule stabiliser
EPZ5676	Chromatin histone methylation	DOT1L
SCH772984	ERK MAPK signaling	ERK1, ERK2
IWP-2	WNT signaling	PORCN
Leflunomide	DNA replication	Pyrimidine synthesis inhibitor
Entinostat	Chromatin histone acetylation	HDAC1, HDAC3
WZ4003	Other, kinases	NUAK1, NUAK2
PCI-34051	Chromatin histone acetylation	HDAC8, HDAC6, HDAC1
RVX-208	Chromatin other	BRD4
Entospletinib	Other, kinases	SYK
CDK9_5038	Cell cycle	CDK9
ERK_6604	ERK MAPK signaling	ERK1, ERK2
AZD4547	RTK signaling	FGFR1, FGFR2, FGFR3
Carmustine	-	-
VX-11e	ERK MAPK signaling	ERK2
LJI308	PI3K/MTOR signaling	RSK2, RSK1, RSK3
KU-55933	Genome integrity	ATM
PF-4708671	PI3K/MTOR signaling	S6K1
GSK269962A	Cytoskeleton	ROCK1, ROCK2

Supplementary Table 8. The samples included in the analyses

TARGET-OS cohort	GSE21257 cohort
TARGET-40-PASKZZ-01A	GSM530667
TARGET-40-PALWWX-01A	GSM530899
TARGET-40-PAMEKS-01A	GSM531283
TARGET-40-PAMLKS-01A	GSM531284
TARGET-40-PAMRHD-01A	GSM531285
TARGET-40-PAMYYJ-01A	GSM531286
TARGET-40-PANMIG-01A	GSM531287
TARGET-40-PANPUM-01A	GSM531288
TARGET-40-PANZHX-01A	GSM531289
TARGET-40-PAPIJR-01A	GSM531290
TARGET-40-PAPKWD-01A	GSM531292
TARGET-40-PAPNVD-01A	GSM531293
TARGET-40-PAPWWC-01A	GSM531295
TARGET-40-PAPXGT-01A	GSM531296
TARGET-40-PARBGW-01A	GSM531297
TARGET-40-PARDAX-01A	GSM531299
TARGET-40-PARFTG-01A	GSM531300
TARGET-40-PARGTM-01A	GSM531301
TARGET-40-PARJXU-01A	GSM531302
TARGET-40-PARKAF-01A	GSM531303
TARGET-40-PASEBY-01A	GSM531305
TARGET-40-PASEFS-01A	GSM531306
TARGET-40-PASFCV-01A	GSM531307
TARGET-40-PASSLM-01A	GSM531308
TARGET-40-PASUUH-01A	GSM531309
TARGET-40-PASYUK-01A	GSM531310
TARGET-40-PATAWV-01A	GSM531311
TARGET-40-PATJVI-01A	GSM531312
TARGET-40-PATKSS-01A	GSM531313
TARGET-40-PATMIF-01A	GSM531319
TARGET-40-PATMPU-01A	GSM531320
TARGET-40-PATPBS-01A	GSM531321
TARGET-40-PASNZV-01A	GSM531322
TARGET-40-PASRNE-01A	GSM531323
TARGET-40-PATEEM-01A	GSM531324
TARGET-40-PATUXZ-01A	GSM531325
TARGET-40-PAUBIT-01A	GSM531326
TARGET-40-PAUTWB-01A	GSM531327
TARGET-40-PAUTYB-01A	GSM531328
TARGET-40-PAUUML-01A	GSM531329
TARGET-40-PAUVUL-01A	GSM531330
TARGET-40-PAUXPZ-01A	GSM531331

TARGET-40-PAUYTT-01A	GSM531332
TARGET-40-PAVALD-01A	GSM531333
TARGET-40-PAVCLP-01A	GSM531334
TARGET-40-PAVDTY-01A	GSM531335
TARGET-40-PAVECB-01A	GSM531351
TARGET-40-PATMXR-01A	
TARGET-40-0A4HLD-01A	
TARGET-40-0A4HMC-01A	
TARGET-40-0A4HX8-01A	
TARGET-40-0A4HXS-01A	
TARGET-40-0A4HY5-01A	
TARGET-40-0A4I0Q-01A	
TARGET-40-0A4I0W-01A	
TARGET-40-0A4I3S-01A	
TARGET-40-0A4I42-01A	
TARGET-40-0A4I48-01A	
TARGET-40-0A4I4M-01A	
TARGET-40-0A4I4O-01A	
TARGET-40-0A4I5B-01A	
TARGET-40-0A4I6O-01A	
TARGET-40-0A4I8U-01A	
TARGET-40-PAKFVX-01A	
TARGET-40-PAKXLD-01A	
TARGET-40-PAKZZK-01A	
TARGET-40-PALECC-01A	
TARGET-40-PALFYN-01A	
TARGET-40-PALHRL-01A	
TARGET-40-PALKDP-01A	
TARGET-40-PALKGN-01A	
TARGET-40-PALZGU-01A	
TARGET-40-PAMHLF-01A	
TARGET-40-PAMHYN-01A	
TARGET-40-PAMJXS-01A	
TARGET-40-PAMTCM-01A	
TARGET-40-PANGPE-01A	
TARGET-40-PANGRW-01A	
TARGET-40-PANSEN-01A	
TARGET-40-PANVJJ-01A	
TARGET-40-PANXSC-01A	
TARGET-40-PANZZJ-01A	
TARGET-40-0A4I65-01A	
TARGET-40-0A4I9K-01A	

Supplementary Table 9. The cancer immunity cycle and representative genes

Genes	Steps	Cycle	Type	Immune cell type
IL10	1	Release of cancer antigens	positive	Multiple
TGFB1	1	Release of cancer antigens	positive	Multiple
HMGB1	1	Release of cancer antigens	positive	Multiple
ANXA1	1	Release of cancer antigens	positive	Multiple
CALR	1	Release of cancer antigens	positive	Multiple
CXCL10	1	Release of cancer antigens	positive	Multiple
PDIA3	1	Release of cancer antigens	positive	Multiple
HSPA1A	1	Release of cancer antigens	positive	Multiple
HSPA1B	1	Release of cancer antigens	positive	Multiple
HSPA2	1	Release of cancer antigens	positive	Multiple
HSPA8	1	Release of cancer antigens	positive	Multiple
HSPA4	1	Release of cancer antigens	positive	Multiple
HSPA14	1	Release of cancer antigens	positive	Multiple
HSPA5	1	Release of cancer antigens	positive	Multiple
HSPA6	1	Release of cancer antigens	positive	Multiple
HSPA9	1	Release of cancer antigens	positive	Multiple
HSPA13	1	Release of cancer antigens	positive	Multiple
HSPA7	1	Release of cancer antigens	positive	Multiple
HSPA8	1	Release of cancer antigens	positive	Multiple
HSPA12A	1	Release of cancer antigens	positive	Multiple
HSPA12B	1	Release of cancer antigens	positive	Multiple
HSP90AA1	1	Release of cancer antigens	positive	Multiple
HSP90AB1	1	Release of cancer antigens	positive	Multiple
HSP90B1	1	Release of cancer antigens	positive	Multiple
IFNA2	1	Release of cancer antigens	positive	Multiple
IFNA1	1	Release of cancer antigens	positive	Multiple
IFNA13	1	Release of cancer antigens	positive	Multiple
IFNA6	1	Release of cancer antigens	positive	Multiple
IFNA21	1	Release of cancer antigens	positive	Multiple
IFNA4	1	Release of cancer antigens	positive	Multiple
IFNA8	1	Release of cancer antigens	positive	Multiple
IFNA5	1	Release of cancer antigens	positive	Multiple
IFNA7	1	Release of cancer antigens	positive	Multiple
IFNA14	1	Release of cancer antigens	positive	Multiple
IFNA16	1	Release of cancer antigens	positive	Multiple
IFNA10	1	Release of cancer antigens	positive	Multiple
IFNA17	1	Release of cancer antigens	positive	Multiple
IFNB1	1	Release of cancer antigens	positive	Multiple
IFNE	1	Release of cancer antigens	positive	Multiple
IFNW1	1	Release of cancer antigens	positive	Multiple
TNF	2	Cancer antigen presentation	positive	Multiple

IL1A	2	Cancer antigen presentation	positive	Multiple
IL1B	2	Cancer antigen presentation	positive	Multiple
IFNA2	2	Cancer antigen presentation	positive	Multiple
IFNA1	2	Cancer antigen presentation	positive	Multiple
IFNA13	2	Cancer antigen presentation	positive	Multiple
IFNA6	2	Cancer antigen presentation	positive	Multiple
IFNA21	2	Cancer antigen presentation	positive	Multiple
IFNA4	2	Cancer antigen presentation	positive	Multiple
IFNA8	2	Cancer antigen presentation	positive	Multiple
IFNA5	2	Cancer antigen presentation	positive	Multiple
IFNA7	2	Cancer antigen presentation	positive	Multiple
IFNA14	2	Cancer antigen presentation	positive	Multiple
IFNA16	2	Cancer antigen presentation	positive	Multiple
IFNA10	2	Cancer antigen presentation	positive	Multiple
IFNA17	2	Cancer antigen presentation	positive	Multiple
CD40LG	2	Cancer antigen presentation	positive	Multiple
CD40	2	Cancer antigen presentation	positive	Multiple
NT5C	2	Cancer antigen presentation	positive	Multiple
HMGB1	2	Cancer antigen presentation	positive	Multiple
TLR1	2	Cancer antigen presentation	positive	Multiple
TLR2	2	Cancer antigen presentation	positive	Multiple
TLR3	2	Cancer antigen presentation	positive	Multiple
TLR4	2	Cancer antigen presentation	positive	Multiple
TLR5	2	Cancer antigen presentation	positive	Multiple
TLR6	2	Cancer antigen presentation	positive	Multiple
TLR7	2	Cancer antigen presentation	positive	Multiple
TLR8	2	Cancer antigen presentation	positive	Multiple
TLR9	2	Cancer antigen presentation	positive	Multiple
TLR10	2	Cancer antigen presentation	positive	Multiple
HCAA	2	Cancer antigen presentation	positive	Multiple
B2M	2	Cancer antigen presentation	positive	Multiple
TAP1	2	Cancer antigen presentation	positive	Multiple
IL10	2	Cancer antigen presentation	negative	Multiple
IL4	2	Cancer antigen presentation	negative	Multiple
IL13	2	Cancer antigen presentation	negative	Multiple
CD3D	3	Priming and activation	positive	Multiple
CD3E	3	Priming and activation	positive	Multiple
CD3G	3	Priming and activation	positive	Multiple
CD247	3	Priming and activation	positive	Multiple
CD28	3	Priming and activation	positive	Multiple
TNFRSF9	3	Priming and activation	positive	Multiple
TNFSF9	3	Priming and activation	positive	Multiple
TNFRSF4	3	Priming and activation	positive	Multiple
TNFSF4	3	Priming and activation	positive	Multiple

CD27	3	Priming and activation	positive	Multiple
CD70	3	Priming and activation	positive	Multiple
TNFRSF14	3	Priming and activation	positive	Multiple
TNFSF14	3	Priming and activation	positive	Multiple
CD40	3	Priming and activation	positive	Multiple
CD40LG	3	Priming and activation	positive	Multiple
TNFRSF18	3	Priming and activation	positive	Multiple
TNFSF18	3	Priming and activation	positive	Multiple
TNFRSF25	3	Priming and activation	positive	Multiple
TNFSF15	3	Priming and activation	positive	Multiple
TNFRSF8	3	Priming and activation	positive	Multiple
TNFSF8	3	Priming and activation	positive	Multiple
HAVCR1	3	Priming and activation	positive	Multiple
TIMD4	3	Priming and activation	positive	Multiple
SLAMF7	3	Priming and activation	positive	Multiple
SLAMF6	3	Priming and activation	positive	Multiple
SLAMF1	3	Priming and activation	positive	Multiple
SLAMF9	3	Priming and activation	positive	Multiple
SLAMF8	3	Priming and activation	positive	Multiple
CD2	3	Priming and activation	positive	Multiple
CD48	3	Priming and activation	positive	Multiple
CD58	3	Priming and activation	positive	Multiple
CD226	3	Priming and activation	positive	Multiple
ICOS	3	Priming and activation	positive	Multiple
ICOSLG	3	Priming and activation	positive	Multiple
KLRK1	3	Priming and activation	positive	Multiple
MICA	3	Priming and activation	positive	Multiple
MICB	3	Priming and activation	positive	Multiple
RAET1E	3	Priming and activation	positive	Multiple
RAET1G	3	Priming and activation	positive	Multiple
CRTAM	3	Priming and activation	positive	Multiple
CADM1	3	Priming and activation	positive	Multiple
CTLA4	3	Priming and activation	negative	Multiple
PDCD1	3	Priming and activation	negative	Multiple
PDCD1LG2	3	Priming and activation	negative	Multiple
CD274	3	Priming and activation	negative	Multiple
CD160	3	Priming and activation	negative	Multiple
TNFRSF14	3	Priming and activation	negative	Multiple
BTLA	3	Priming and activation	negative	Multiple
VSIR	3	Priming and activation	negative	Multiple
LAIR1	3	Priming and activation	negative	Multiple
HAVCR1	3	Priming and activation	negative	Multiple
HAVCR2	3	Priming and activation	negative	Multiple
LGALS9	3	Priming and activation	negative	Multiple

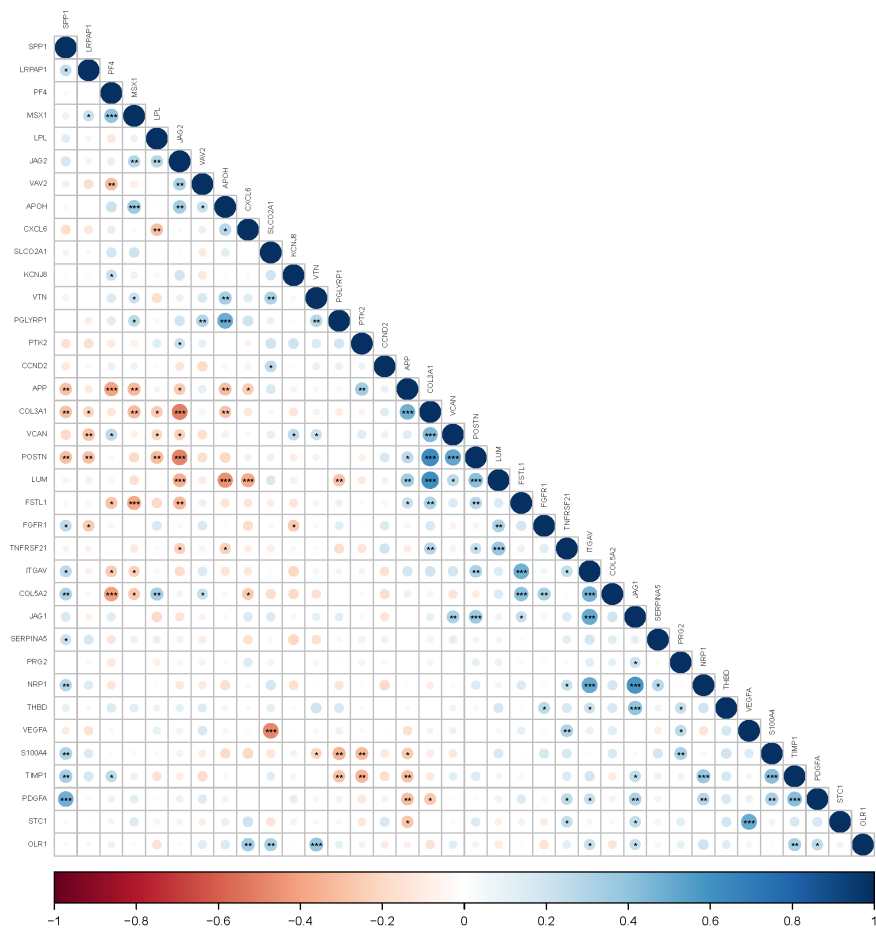
TIMD4	3	Priming and activation	negative	Multiple
CD244	3	Priming and activation	negative	Multiple
CD48	3	Priming and activation	negative	Multiple
TIGIT	3	Priming and activation	negative	Multiple
NECTIN3	3	Priming and activation	negative	Multiple
LAG3	3	Priming and activation	negative	Multiple
IL2	3	Priming and activation	positive	Multiple
IL12A	3	Priming and activation	positive	Multiple
IL12B	3	Priming and activation	positive	Multiple
CXCR5	4	immune cell recruitment	positive	B cell
CXCL13	4	immune cell recruitment	positive	B cell
CCL24	4	immune cell recruitment	positive	Basophil
CCL26	4	immune cell recruitment	positive	Basophil
CCL19	4	immune cell recruitment	positive	CD4 T cell
CX3CL1	4	immune cell recruitment	positive	CD4 T cell
CXCL16	4	immune cell recruitment	positive	CD4 T cell
CCR5	4	immune cell recruitment	positive	CD8 T cell
CXCR3	4	immune cell recruitment	positive	CD8 T cell
CXCL10	4	immune cell recruitment	positive	CD8 T cell
CXCL9	4	immune cell recruitment	positive	CD8 T cell
CCL20	4	immune cell recruitment	positive	CD8 T cell
CXCL11	4	immune cell recruitment	positive	CD8 T cell
CX3CL1	4	immune cell recruitment	positive	CD8 T cell
CXCL16	4	immune cell recruitment	positive	CD8 T cell
CCR7	4	immune cell recruitment	positive	Dendritic cell
CCL3	4	immune cell recruitment	positive	Dendritic cell
CCL4	4	immune cell recruitment	positive	Dendritic cell
CCL5	4	immune cell recruitment	positive	Dendritic cell
CCL21	4	immune cell recruitment	positive	Dendritic cell
CCL11	4	immune cell recruitment	positive	Eosinophil
CCL24	4	immune cell recruitment	positive	Eosinophil
CCL26	4	immune cell recruitment	positive	Eosinophil
CSF1	4	immune cell recruitment	positive	Macrophage
CCL2	4	immune cell recruitment	positive	Macrophage
CCL3	4	immune cell recruitment	positive	Macrophage
CCL4	4	immune cell recruitment	positive	Macrophage
CCL5	4	immune cell recruitment	positive	Macrophage
CXCR2	4	immune cell recruitment	positive	MDSC
CXCL5	4	immune cell recruitment	positive	MDSC
CCL2	4	immune cell recruitment	positive	Monocyte
CCL7	4	immune cell recruitment	positive	Monocyte
CX3CL1	4	immune cell recruitment	positive	Monocyte
CXCL1	4	immune cell recruitment	positive	Neutrophil
CXCL2	4	immune cell recruitment	positive	Neutrophil

CXCL3	4	immune cell recruitment	positive	Neutrophil
CXCL8	4	immune cell recruitment	positive	Neutrophil
CXCL6	4	immune cell recruitment	positive	Neutrophil
CXCL5	4	immune cell recruitment	positive	Neutrophil
CXCR3	4	immune cell recruitment	positive	NK cell
CXCL10	4	immune cell recruitment	positive	NK cell
CXCL9	4	immune cell recruitment	positive	NK cell
CCL3	4	immune cell recruitment	positive	NK cell
CCL4	4	immune cell recruitment	positive	NK cell
CCL5	4	immune cell recruitment	positive	NK cell
CXCL11	4	immune cell recruitment	positive	NK cell
CX3CL1	4	immune cell recruitment	positive	NK cell
CXCR5	4	immune cell recruitment	positive	T cell
CCR7	4	immune cell recruitment	positive	T cell
CXCL9	4	immune cell recruitment	positive	T cell
CCL3	4	immune cell recruitment	positive	T cell
CCL4	4	immune cell recruitment	positive	T cell
CCL5	4	immune cell recruitment	positive	T cell
CCL19	4	immune cell recruitment	positive	T cell
CCL21	4	immune cell recruitment	positive	T cell
CX3CL1	4	immune cell recruitment	positive	T cell
CXCL13	4	immune cell recruitment	positive	T cell
CXCR3	4	immune cell recruitment	positive	TH1 cell
CXCL10	4	immune cell recruitment	positive	TH1 cell
CXCL9	4	immune cell recruitment	positive	TH1 cell
CXCL11	4	immune cell recruitment	positive	TH1 cell
CCR6	4	immune cell recruitment	positive	TH17 cell
CCL20	4	immune cell recruitment	positive	TH17 cell
CXCL12	4	immune cell recruitment	positive	TH17 cell
CXCR4	4	immune cell recruitment	positive	TH17 cell
CCL1	4	immune cell recruitment	positive	Th2 cell
CCL17	4	immune cell recruitment	positive	Th2 cell
CCL22	4	immune cell recruitment	positive	Th2 cell
CCR6	4	immune cell recruitment	positive	TH22 cell
CCL20	4	immune cell recruitment	positive	TH22 cell
CCR4	4	immune cell recruitment	positive	Treg cell
CCR10	4	immune cell recruitment	positive	Treg cell
CCL1	4	immune cell recruitment	positive	Treg cell
CCL17	4	immune cell recruitment	positive	Treg cell
CCL22	4	immune cell recruitment	positive	Treg cell
CCL28	4	immune cell recruitment	positive	Treg cell
STAT1	5	infiltration of immune cells into tumours	positive	T cell

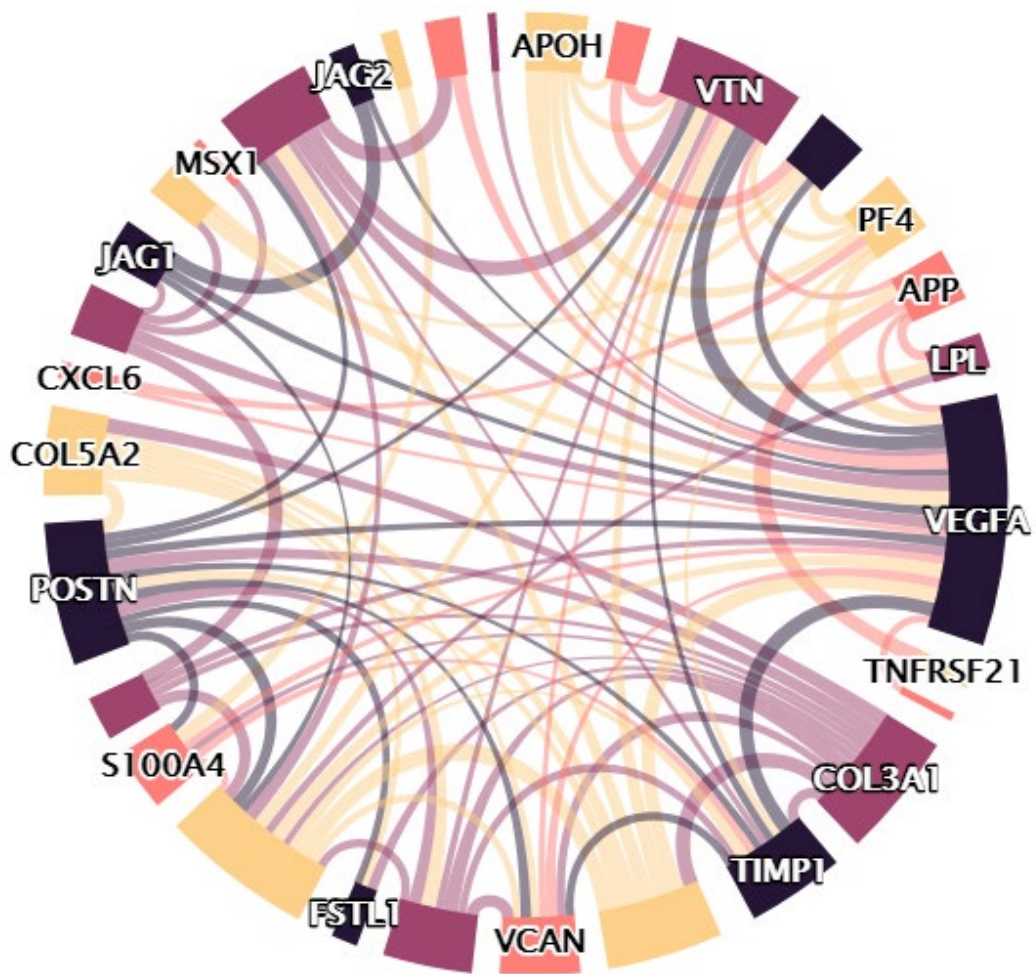
IRF5	5	infiltration of immune cells into tumours	positive	T cell
KLF2	5	infiltration of immune cells into tumours	positive	T cell
ITGB2	5	infiltration of immune cells into tumours	positive	T cell
ICAM1	5	infiltration of immune cells into tumours	negative	T cell
EZH2	5	infiltration of immune cells into tumours	negative	T cell
DNMT1	5	infiltration of immune cells into tumours	negative	T cell
VEGFA	5	infiltration of immune cells into tumours	negative	T cell
EDNRB	5	infiltration of immune cells into tumours	negative	T cell
CD28	6	Recognition of cancer cells by T cells	positive	Multiple
ICOS	6	Recognition of cancer cells by T cells	positive	Multiple
ICOSLG	6	Recognition of cancer cells by T cells	positive	Multiple
TNFRSF9	6	Recognition of cancer cells by T cells	positive	Multiple
TNFSF9	6	Recognition of cancer cells by T cells	positive	Multiple
CD27	6	Recognition of cancer cells by T cells	positive	Multiple
CD70	6	Recognition of cancer cells by T cells	positive	Multiple
TNFRSF4	6	Recognition of cancer cells by T cells	positive	Multiple
TNFSF4	6	Recognition of cancer cells by T cells	positive	Multiple
TNFSF14	6	Recognition of cancer cells by T cells	positive	Multiple
CD40	6	Recognition of cancer cells by T cells	positive	Multiple
CD40LG	6	Recognition of cancer cells by T cells	positive	Multiple
HLAA	6	Recognition of cancer cells by T cells	positive	Multiple
B2M	6	Recognition of cancer cells by T cells	positive	Multiple

TAP1	6	Recognition of cancer cells by T cells	positive	Multiple
BIRC5	6	Recognition of cancer cells by T cells	positive	Multiple
MDM2	6	Recognition of cancer cells by T cells	positive	Multiple
MAGEA4	6	Recognition of cancer cells by T cells	positive	Multiple
TP53	6	Recognition of cancer cells by T cells	positive	Multiple
PDCD1	6	Recognition of cancer cells by T cells	negative	Multiple
PDCD1LG2	6	Recognition of cancer cells by T cells	negative	Multiple
CD274	6	Recognition of cancer cells by T cells	negative	Multiple
CTLA4	6	Recognition of cancer cells by T cells	negative	Multiple
BTLA	6	Recognition of cancer cells by T cells	negative	Multiple
VTCN1	6	Recognition of cancer cells by T cells	negative	Multiple
IFNG	7	Killing of cancer cells	positive	Multiple
GZMB	7	Killing of cancer cells	positive	Multiple
PRF1	7	Killing of cancer cells	positive	Multiple
PDCD1	7	Killing of cancer cells	negative	Multiple
SMC3	7	Killing of cancer cells	negative	Multiple
VTCN1	7	Killing of cancer cells	negative	Multiple
HAVCR2	7	Killing of cancer cells	negative	Multiple
MICA	7	Killing of cancer cells	negative	Multiple
MICB	7	Killing of cancer cells	negative	Multiple
BTLA	7	Killing of cancer cells	negative	Multiple
VSIR	7	Killing of cancer cells	negative	Multiple
LAG3	7	Killing of cancer cells	negative	Multiple
IDO1	7	Killing of cancer cells	negative	Multiple
IDO2	7	Killing of cancer cells	negative	Multiple
ARG1	7	Killing of cancer cells	negative	Multiple
ARG2	7	Killing of cancer cells	negative	Multiple
NOS1	7	Killing of cancer cells	negative	Multiple
NOS2	7	Killing of cancer cells	negative	Multiple
NOS3	7	Killing of cancer cells	negative	Multiple
TGFB1	7	Killing of cancer cells	negative	Multiple
IL10	7	Killing of cancer cells	negative	Multiple
CCL28	7	Killing of cancer cells	negative	Multiple

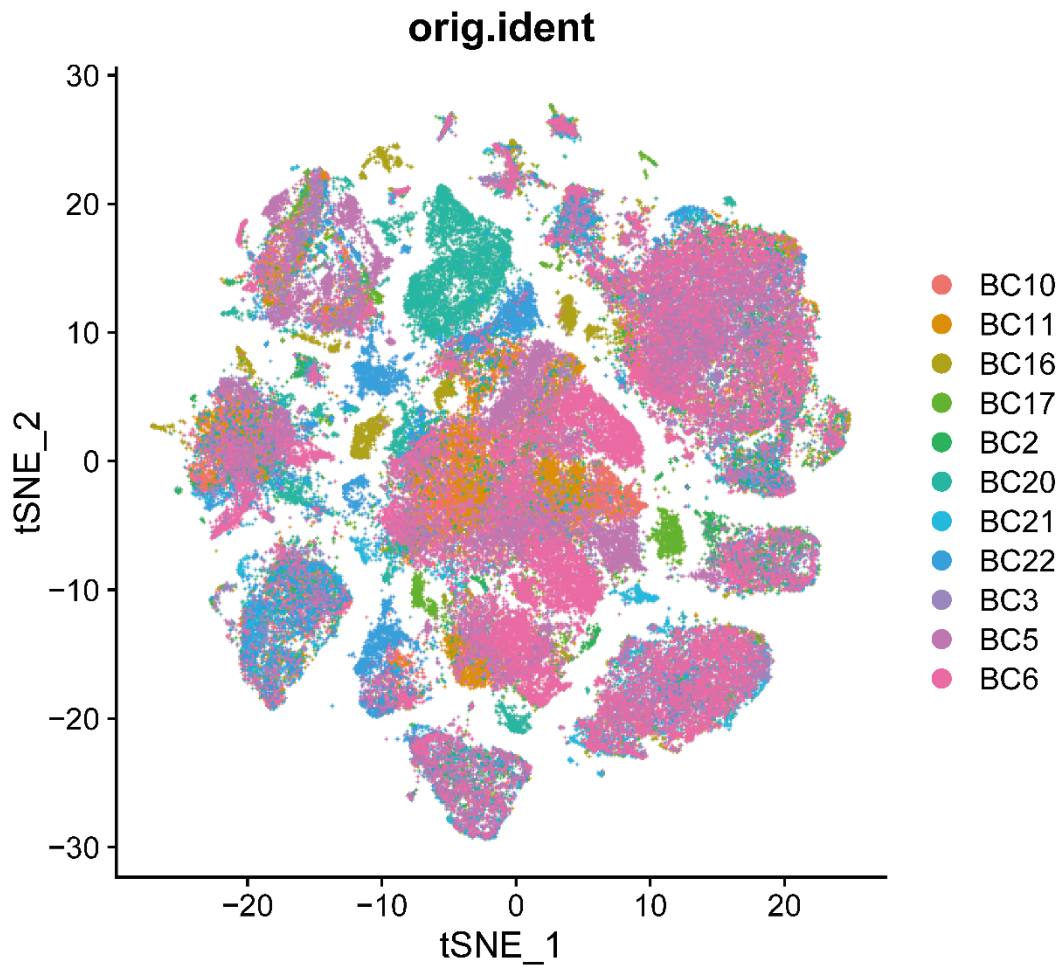
CXCL12	7	Killing of cancer cells	negative	Multiple
CCL2	7	Killing of cancer cells	negative	Multiple
CXCL8	7	Killing of cancer cells	negative	Multiple



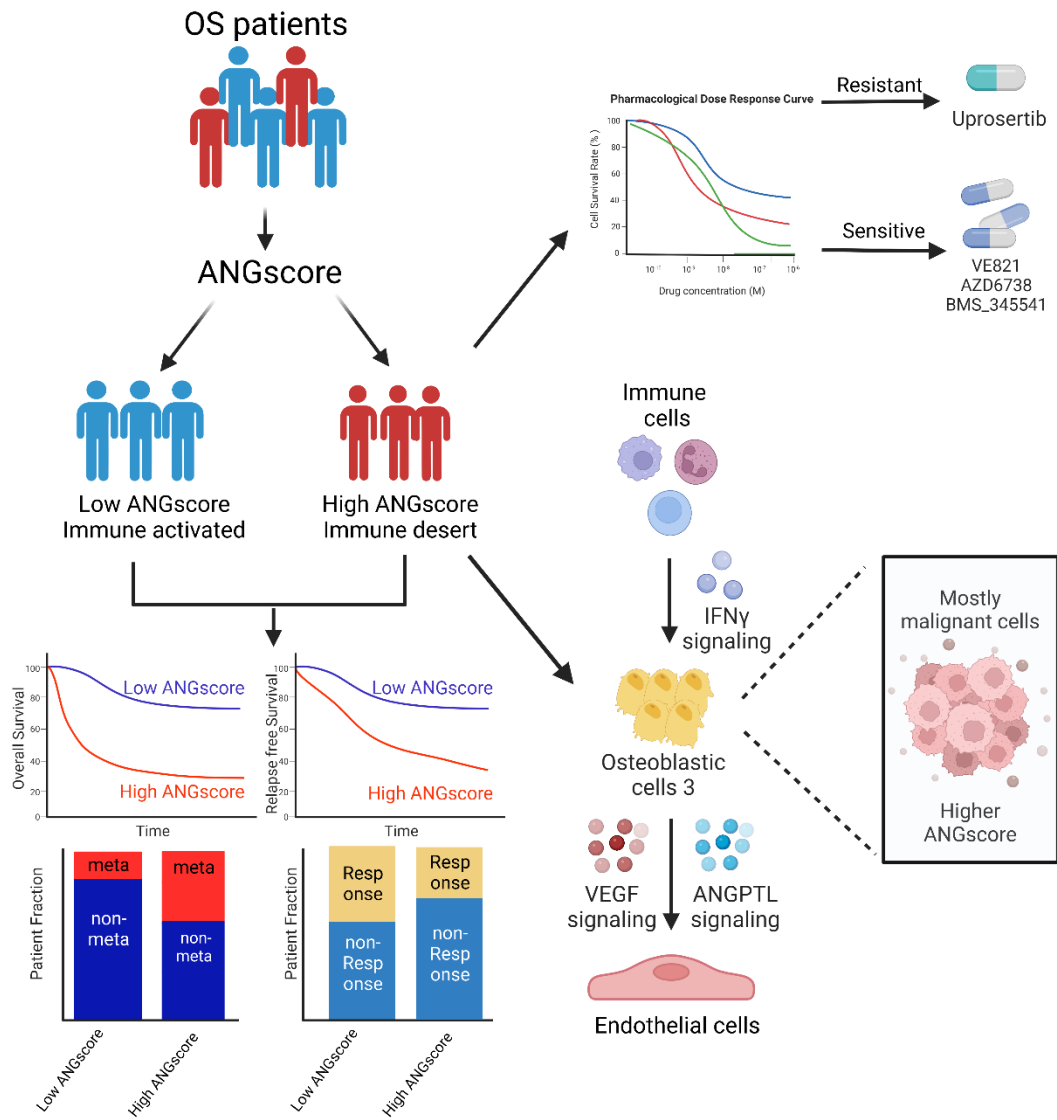
Supplementary Figure 1. Correlation of angiogenesis genes in TARGET-OS database.



Supplementary Figure 2. Interaction of angiogenesis genes in the TARGET-OS database.



Supplementary Figure 3. The t-SNE plot showing the batch effect after correction by harmony algorithm.



Supplementary Figure 4. The mechanism figure of the study. (Created with Biorender.com)