

Table S1 The 520 cancer-related genes included in the OncoScreen Plus panel

ABL1	CDK4	ESR2	ICOSLG	MSH6	POLE	SMO
ABL2	CDK6	EWSR1	ID3	MST1	POM121L12	SNCAIP
ACVR1	CDK8	EZH2	IDH1	MST1R	PPM1D	SOCS1
ACVR1B	CDKN1A	FAM175A	IDH2	MTOR	PPP2R1A	SOX2
ADGRA2	CDKN1B	FAM46C	IFNGR1	MUTYH	PPP2R2A	SOX9
AKT1	CDKN1C	FANCA	IGF1	MYC	PPP6C	SOX10
AKT2	CDKN2A	FANCC	IGF1R	MYCL	PRDM1	SOX17
AKT3	CDKN2B	FANCD2	IGF2	MYCN	PREX2	SPEN
ALK	CDKN2C	FANCE	IKBKE	MYD88	PRKAR1A	SPOP
ALOX12B	CEBPA	FANCF	IKZF1	MYOD1	PRKC1	SPTA1
AMER1	CENPA	FANCG	IL10	NBN	PRKDC	SRC
ANKRD11	CHD1	FANCI	IL7R	NCOA3	PRSS8	SRSF2
APC	CHD2	FANCL	INHBA	NCOR1	PTCH1	STAG2
APCDD1	CHD4	FANCM	INHBA	NEB	PTEN	STAT3
AR	CHEK1	FAS	INPP4A	NEGR1	PTK2	STAT4
ARAF	CHEK2	FAT1	INPP4B	NF1	PTPN11	STAT5A
ARFRP1	CHUK	FAT3	INSR	NF2	PTPRD	STAT5B
ARID1A	CIC	FBXW7	IRF2	NFE2L2	PTPRS	STK11
ARID1B	CRBN	FCGR2B	IRF4	NFKB1A	PTPRT	STK40
ARID2	CREBBP	FGF10	IRS1	NKX2-1	QK1	SUFU
ARID5B	CRKL	FGF12	IRS2	NKX3-1	RAB35	SUZ12
ASXL1	CRLF2	FGF23	JAK1	NOTCH1	RAC1	SYK
ASXL2	CSF1R	FGF6	JAK2	NOTCH2	RAD21	TACC3
ATF1	CSF3R	FGF7	JAK3	NOTCH3	RAD50	TAF1
ATM	CTCF	FGFR14	JUN	NOTCH4	RAD51	TBX3
ATR	CTLA4	FGFR1	KAT5A	NPM1	RAD51B	TCF3
ATRX	CTNNA1	FGFR2	KDM5A	NRAS	RAD51C	TCF7L2
AURKA	CTNNB1	FGFR3	KDM5C	NR4A3	RAD51D	TERC
AURKB	CUL3	FOXA1	KDM6A	NRG1	RAD52	TERT
AXIN1	CUL4A	FOXL2	KDR	NSD1	RAD54L	TET1
AXIN2	CUL4B	FRS2	KEAP1	NTHL1	RAF1	TET2
AXL	CXCR4	FYN	KEL	NTRK1	RANBP2	TGFBR1
B2M	CYCLD	GABRA6	KIT	NTRK2	RARA	TGFBR2
BACH1	CYP17A1	GATA4	KLF4	NTRK3	RASA1	TIPARP
BAP1	DAXX	GATA6	KLHL6	NUP93	RB1	TMEM127
BARD1	DCUN1D1	GID4	KMT2A	PAK1	RBM10	TMPRSS5
BBC3	DDR2	GNA13	KMT2C	PAK3	RECQL4	TNFAIP3
BCL2	DICER1	GPS2	KMT2D	PAK7	REL	TNFRSF14
BCL10	DIS3	GREM1	KRAS	PALB2	RET	TNFSF11
BCL2L1	DNAJB1	GRM3	LATS1	PARK2	RFWD2	TOP1
BCL2L11	DNMT1	GSK3B	LATS2	PARP1	RHEB	TOP2A
BCL2L2	DNMT3A	GSTM1	LMO1	PARP2	RHOA	TP53
BCL6	DNMT3B	GSTT1	LRP1B	PARP3	RICTOR	TRAF2
BCOR	DOT1L	H3F3A	LYN	PARP4	RIT1	TRAF7
BCORL1	E2F3	H3F3B	LZTR1	PAX5	RNF43	TRRAP
BCR	EED	HDAC1	MAG12	PBRM1	ROS1	TSC1
BLM	EGFL7	HDAC2	MALT1	PDCD1	RPA1	TSC2
BMPR1A	EGFR	HDAC4	MAP2K1	PDCD1LG2	RPS6KA4	TSHR
BRAF	EIF1AX	HGF	MAP2K2	PDFRA	RPS6KB2	U2AF1
BRCA1	EIF4A2	HIST1H1C	MAP2K4	PDGFRB	RPTOR	VEGFA
BRCA2	EIF4E	HIST1H2BD	MAP3K1	PDK1	RUNX1	VEGFB
BRD4	ELOC	HIST1H3A	MAP3K13	PGR	RUNX1T1	VEGFC
BRIP1	EMSY	HIST1H3B	MAP3K14	PHOX2B	RYBP	VHL
BTG1	EP300	HIST1H3C	MAP3K3	PIK3CA	SDHA	VTCN1
BTK	EPCAM	HIST1H3D	MAPK1	PIK3CB	SDHAF2	WISP3
CALR	EPHA2	HIST1H3E	MAX	PIK3C2B	SDHB	WRN
CARD11	EPHA3	HIST1H3F	MCL1	PIK3C2G	SDHC	WT1
CASP8	EPHA5	HIST1H3G	MDM2	PIK3C3	SDHD	XIAP
CBFB	EPHA7	HIST1H3H	MDM4	PIK3CD	SETD2	XPO1
CBL	EPHB1	HIST1H3I	MED12	PIK3CG	SF3B1	XRCC2
CCND1	ERBB2	HIST1H3J	MEF2B	PIK3R1	SH2B3	XRCC3
CCND2	ERBB3	HIST2H3C	MEN1	PIK3R2	SH2D1A	YAP1
CCND3	ERBB4	HIST2H3D	MET	PIK3R3	SHQ1	YES1
CCNE1	ERBB5	HIST3H3	MGA	PIM1	SLIT2	ZBTB2
CD274	ERCC1	HLA-A	MITF	PLCG2	SLX4	ZFH3
CD276	ERCC2	HNF1A	MLH1	PLK2	SMAD2	ZNF217
CD79A	ERCC3	HNF1B	MLH3	PMAIP1	SMAD3	ZNF703
CD79B	ERCC4	HOXB13	MPL	PMS1	SMAD4	ZNRF3
CDC73	ERCC5	HRAS	MRE11A	PMS2	SMARCA4	ZRSR2
CDH1	ERG	HSD3B1	MSH2	PNRC1	SMARCB1	
CDK12	ERRF1	HSP90AA1	MSH3	POLD1	SMARCD1	

Table S2 The 168 cancer-related genes included in the OncoScreen Plus panel

AKT1	CDK6	FAT3	JAK1	NBN	PTPRT	TGFBR2
ALK	CDKN1A	FBXW7	JAK2	NF1	RAD50	TP53
APC	CDKN1B	FGF19	KDM5A	NOTCH1	RAD51B	TP63
AR	CDKN2A	FGF3	KDM6A	NRAS	RAD51C	TRIM58
ARID1A	CHEK1	FGF4	KDR	NRG1	RAD51D	TRPC5
ATM	CHEK2	FGFR1	IGF1	NTRK1	RAD54L	U2AF1
ATR	CREBBP	FGFR2	IGF1R	NTRK2	RAF1	UGT1A1
B2M	CSMD3	FGFR3	KEAP1	NTRK3	RARA	VEGFA
BARD1	CTNNB1	FLT1	KIT	PAK5	RB1	VEGFB
BCL2L11	CYP2A6	FLT3	KMT2D	PALB2	RBM10	VEGFC
BCOR	DIS3	FLT4	KRAS	PARP1	RET	VHL
BLM	DNMT3A	GATA2	LRP1B	PDGFRA	RNF43	YES1
BRAF	DPYD	GATA3	MAP2K1	PDGFRB	ROS1	
BRCA1	EGFR	GRIN2A	MAP3K13	PIK3C2G	RUNX1	
BRCA2	EMSY	H3F3C	MAX	PIK3C3	SETD2	
BRINP3	EP300	HGF	MCL1	PIK3CA	SMAD4	
BRIP1	EPHA3	HIST1H1C	MEN1	PIK3CG	SMARCA4	
CARD11	EPHA5	HIST1H3B	MET	PIK3R1	SOX2	
CASP8	EPHA7	HIST1H3G	MRE11	PMS2	SOX9	
CBL	EPHB1	HRAS	MSH2	POLD1	SPOP	
CCND1	ERBB2	IDH1	MSH6	POLE	SPTA1	
CCNE1	ERBB3	IDH2	MTOR	POM121L12	SRC	
CD274	ERBB4	IGF2	MUTYH	PPP2R1A	STAG2	
CD74	ESR1	IKZF1	MYC	PRKDC	STK11	
CDH18	FANCA	IL7R	MYCN	PTEN	TBX3	
CDK4	FANCI	INHBA	NAV3	PTPRD	TERT	

Table S3 The eight cancer-related genes included in the OncoScreen Plus panel

EGFR
 ALK
 BRAF
 ERBB2
 KRAS
 MET
 RET
 ROS1

Table S4 Clinicopathologic features of *HER2* TMD mutation V659E in lung adenocarcinomas

No.	Onset Age, y	Gender	Smoking status	Histologic subtype	Stage	Baseline ECOG-PS	TMD Protein Alteration	ERBB2/ <i>HER2</i> alteration	Abundance
1	48	F	Positive history	Adenocarcinoma	IVa	1	V659E	c.1976_1977delTTinsAA	32.50%
2	68	M	Never-smoker	Adenocarcinoma+Neuroendocrinal differentiation	IVa	1	V659E	c.1976_1977inv	1.84%
3	53	M	Never-smoker	Adenocarcinoma	IVa	NR	V659E	c.1976_1978inv	86.90%
4	69	F	Positive history	Adenocarcinoma	IVc	1	V659E	c.1976_1979inv	17.20%
5	60	M	Never-smoker	Adenocarcinoma	IVc	0	V659E	c.1976_1980inv	22.84%
6	65	F	Positive history	Adenocarcinoma	IVb	2	V659E	c.1976_1977delinsAG	26.54%
7	72	M	Never-smoker	Adenocarcinoma	IVa	1	V659E	c.1976_1977delinsAG	1.16%
8	75	M	Never-smoker	Adenocarcinoma	IVa	NR	V659E	c.1976_1977inv	11.38%
9	75	F	Never-smoker	Adenocarcinoma	IVa	NR	V659E	c.1976_1978inv	41.60%
10	69	M	Never-smoker	Adenocarcinoma	IV	NR	V659E	c.1976_1979inv	28.50%
11	70	M	Positive history	Adenocarcinoma	IA	0	V659E	c.1976_1977delinsAG	11.61%
12	44	F		Adenocarcinoma	NR	NR	V659E	c.1976_1977delinsAG	
13	69	F	Never-smoker	Adenocarcinoma	IA	NR	V659E	c.1976_1977inv	
14	55	F	Never-smoker	Adenocarcinoma	IA	NR	V659E	c.1976_1978inv	
15	45	M	NR	Adenocarcinoma	IVb	NR	V659E	c.1976_1977delinsAG	
16	67	F	NR	Adenocarcinoma	IVa	NR	V659E	c.1976_1977delinsAG	

Table S5 The ΔG value of molecules non-covalent binding with *HER2* kinase.

Ligand	VDWAALS (kcal/mol)	EEL (kcal/mol)	EGB (kcal/mol)	ESURF (kcal/mol)	ΔG (kcal/mol)
Lapatinib	-76.16	17.98	9.91	-8.85	-57.12
Afatinib	-61.45	-65.53	74.82	-7.55	-59.71
Pyrotinib	-74.22	-7.9	25.4	-9.19	-65.92