

Supplemental materials

Supplemental Figure 1. Antibody map of the tyrosine kinase array used in Figure 1B, adapted from the RayBio Human RTK Phosphorylation Antibody Array protocol.

Supplemental Figure 2. Antibody map of the growth factor array used in Figure 2C, adapted from the RayBio Human Growth Factor Antibody Array protocol.

Supplemental Figure 3. EGFR expression levels of the different cell lines used in this study and the relationship between PRL-3, PTP1B and hyperphosphorylated EGFR. **(A)** Expression levels of EGFR protein in the various human cancer cell lines used. GAPDH, loading control. **(B)** PRL-3 overexpression results in PTP1B downregulation in A2780 ovarian cancer cells. GAPDH, loading control. **(C)** Representative immunoblots of MDA-MB-468-vec and MDA-MB-468-PRL-3 cells starved in 0.5% FBS medium overnight containing 0.1% DMSO, 1 μ M AG-1478 (AG), 2 μ M erlotinib (erlo.) or 100 nM cetuximab (CTX) for 24 h before lysis. The loss of p-ERK1/2 signals served as a positive control for EGFR inhibition. GAPDH, loading control. Bottom, bar charts reflecting band densities normalized to total EGFR (for p-EGFR) and GAPDH (for PTP1B). *Solid bars*, MDA-MB-468-vec; *hollow bars*, MDA-MB-468-PRL-3. **(D)** MDA-MB-468-vec and MDA-MB-468-PRL-3 cells were transiently transfected (18 h) with either empty vector (VC) or FLAG-PTP1B constructs and analyzed for EGFR phosphorylation. GAPDH, loading control. **(E)** MDA-MB-468-PRL-3 cells transiently transfected (72 h) with non-specific siRNA (si-scr) or PTP1B-targeting siRNA (si-PTP1B) were analyzed for EGFR phosphorylation. GAPDH, loading control. Numbers below selected immunoblots reflect band densities normalized to both EGFR and GAPDH (for p-EGFR) or GAPDH (for PTP1B).

Supplemental Figure 4. The inhibition of A431-vec or A431-PRL-3 cell growth after 48 h exposure to DMSO (0.1%), PP2 (5 μ M), perifosine (1 μ M), or U0126 (10 μ M) in 0.5% FBS medium. Cell growth was measured using an MTT assay and normalized to A431-vec DMSO-treated cells (mean $\pm$ SD, n = 3, unpaired t-test; * p < 0.05).

Supplemental Figure 5. PRL-3 is expressed at higher levels in gefitinib-sensitive NSCLC cell lines

2 compared to gefitinib-resistant NSCLC cell lines ($n = 27$; t -test, $p = 0.020$).

Supplemental Table 1. Quantitation of duplicate spots on the RTK phospho-activation array using

4 densitometry.

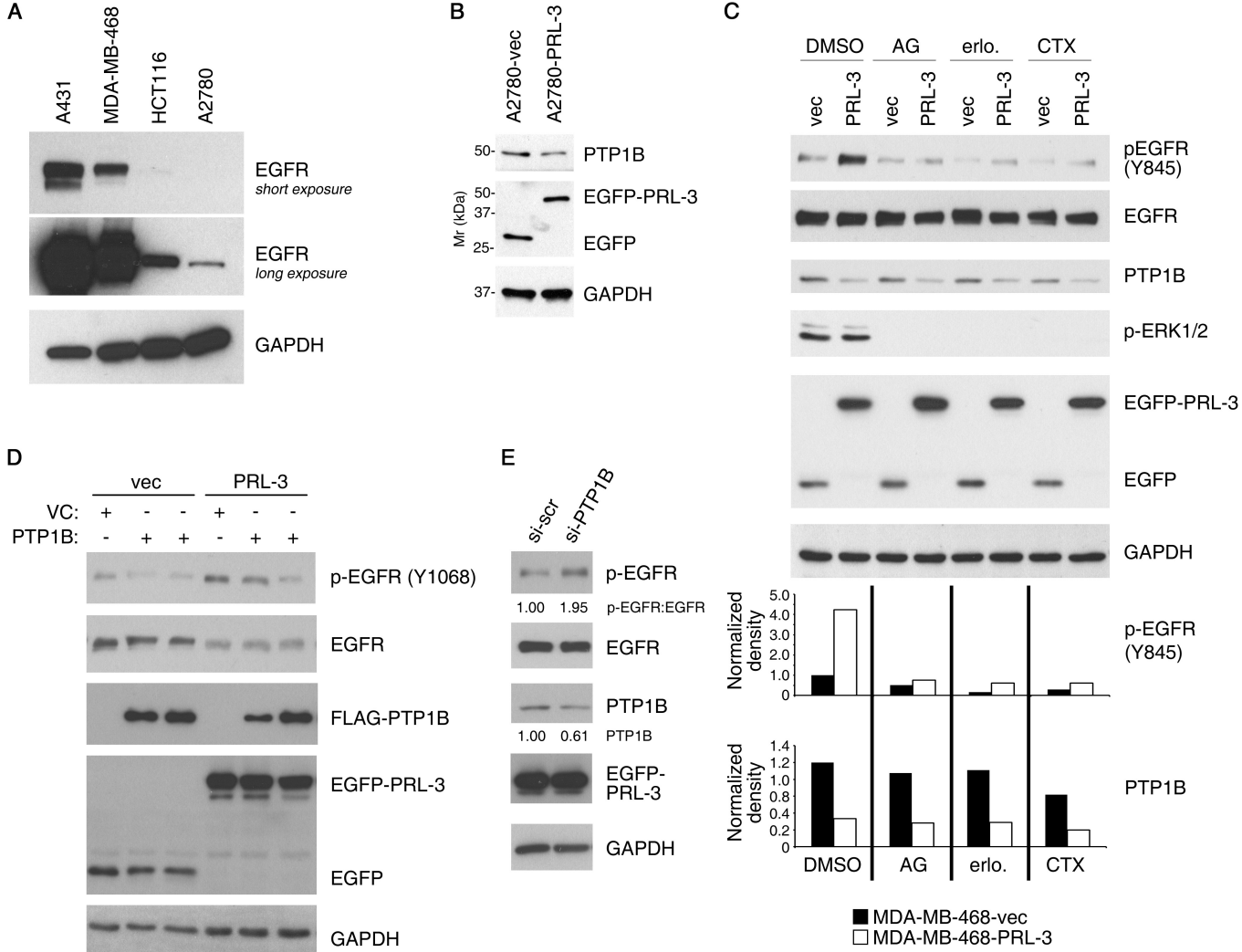
6

	A	B	C	D	E	F	G	H	I	J	K	L
1	POS 1	POS 1	POS 2	POS 2	POS3	POS3	ABL1	ABL1	ACK1	ACK1	ALK	ALK
2	NEG	NEG	NEG	NEG	Axl	Axl	Blk	Blk	BMX	BMX	Btk	Btk
3	Csk	Csk	Dtk	Dtk	EGFR	EGFR	EphA1	EphA1	EphA2	EphA2	EphA3	EphA3
4	EphA4	EphA4	EphA5	EphA5	EphA6	EphA6	EphA7	EphA7	EphA8	EphA8	EphB1	EphB1
5	EphB2	EphB2	EphB3	EphB3	EphB4	EphB4	EphB6	EphB6	ErbB2	ErbB2	ErbB3	ErbB3
6	ErbB4	ErbB4	FAK	FAK	FER	FER	FGFR1	FGFR1	FGFR2	FGFR2	FGFR2 (α isoform)	FGFR2 (α isoform)
7	Fgr	Fgr	FRK	FRK	Fyn	Fyn	Hck	Hck	HGFR	HGFR	IGF-I R	IGF-I R
8	Insulin R	Insulin R	Itk	Itk	JAK1	JAK1	JAK2	JAK2	JAK3	JAK3	LCK	LCK
9	LTK	LTK	Lyn	Lyn	MATK	MATK	M-CSFR	M-CSFR	MUSK	MUSK	NGFR	NGFR
10	PDGFR-α	PDGFR-α	PDGFR-β	PDGFR-β	PYK2	PYK2	RET	RET	ROR1	ROR1	ROR2	ROR2
11	ROS	ROS	RYK	RYK	SCFR	SCFR	SRMS	SRMS	SYK	SYK	Tec	Tec
12	Tie-1	Tie-1	Tie-2	Tie-2	TNK1	TNK1	TRKB	TRKB	TXK	TXK	NEG	NEG
13	Tyk2	Tyk2	TYRO10	TYRO10	VEGFR2	VEGFR2	VEGFR3	VEGFR3	ZAP70	ZAP70	POS2	POS2

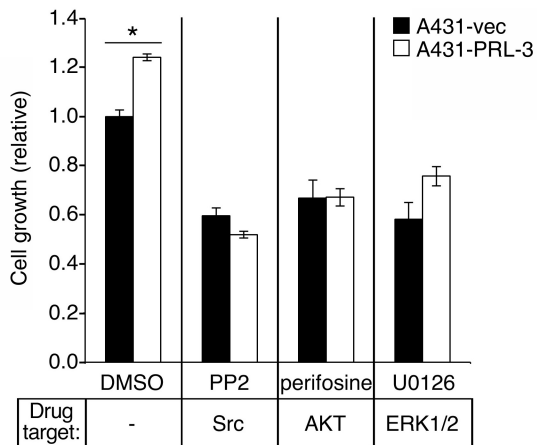
Supplemental Figure 1

	A	B	C	D	E	F	G	H	I	J	K	L
1	POS	POS	NEG	NEG	AR	bFGF	b-NGF	EGF	EGF R	FGF-4	FGF-6	FGF-7
2	POS	POS	NEG	NEG	AR	bFGF	b-NGF	EGF	EGF R	FGF-4	FGF-6	FGF-7
3	GCSF	GDNF	GM-CSF	HB-EGF	HGF	IGFBP-1	IGFBP-2	IGFBP-3	IGFBP-4	IGFBP-6	IGF-I	IGF-I SR
4	GCSF	GDNF	GM-CSF	HB-EGF	HGF	IGFBP-1	IGFBP-2	IGFBP-3	IGFBP-4	IGFBP-6	IGF-I	IGF-I SR
5	IGF-II	M-CSF	M-CSF R	NT-3	NT-4	PDGF R α	PDGF R β	PDGF-AA	PDGF-AB	PDGF-BB	PIGF	SCF
6	IGF-II	M-CSF	M-CSF R	NT-3	NT-4	PDGF R α	PDGF R β	PDGF-AA	PDGF-AB	PDGF-BB	PIGF	SCF
7	SCF R	TGF- α	TGF- β	TGF- β 2	TGF- β 3	VEGF	VEGF R2	VEGF R3	VEGF-D	BLANK	BLANK	POS
8	SCF R	TGF- α	TGF- β	TGF- β 2	TGF- β 3	VEGF	VEGF R2	VEGF R3	VEGF-D	BLANK	BLANK	POS

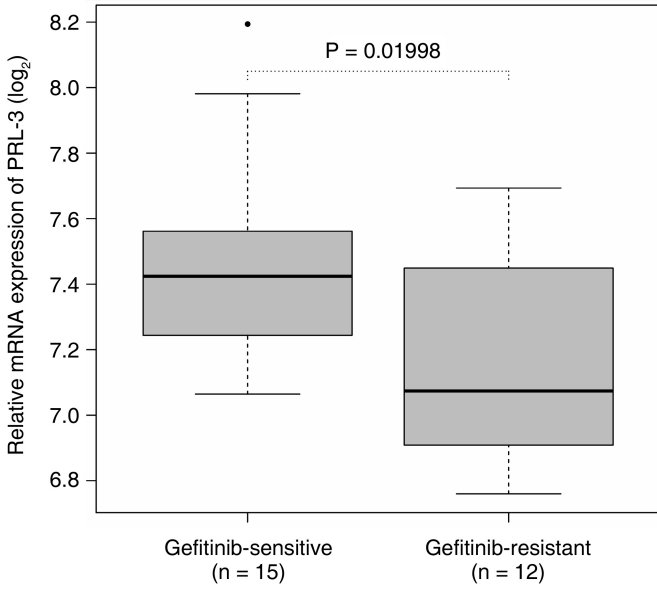
Supplemental Figure 2



Supplemental Figure 3



Supplemental Figure 4



Supplemental Figure 5

Supplemental Table 1

RTK	A431-vec		A431-PRL-3		Fold change
	Average Density (OD/mm ²)	Std Deviation	Average Density (OD/mm ²)	Std Deviation	
ABL1	0.064	0.018	0.116	0.018	1.81
ACK1	0.217	0.006	0.346	0.027	1.59
ALK	0.040	0.000	0.095	0.017	2.38
Axl	0.169	0.000	0.617	0.045	3.65
Blk	0.012	0.001	0.025	0.001	
BMX	0.521	0.010	0.696	0.016	1.34
Btk	0.033	0.003	0.062	0.011	
Csk	0.011	0.018	0.022	0.002	
Dtk	0.031	0.009	0.069	0.010	
EGFR	1.414	0.001	3.346	0.060	2.37
EphA1	0.045	0.002	0.081	0.023	1.80
EphA2	0.010	0.018	0.027	0.000	
EphA3	0.081	0.019	0.134	0.008	1.65
EphA4	0.007	0.002	0.006	0.004	0.86
EphA5	0.012	0.013	0.033	0.010	
EphA6	0.005	0.003	0.027	0.004	
EphA7	0.002	0.003	0.012	0.003	
EphA8	0.039	0.000	0.063	0.000	
EphB1	0.042	0.001	0.058	0.003	1.38
EphB2	0.067	0.001	0.056	0.004	0.84
EphB3	0.043	0.011	0.061	0.007	1.42
EphB4	0.006	0.012	0.021	0.001	
EphB6	0.003	0.000	0.011	0.000	
ErbB2	0.053	0.001	0.196	0.007	3.70
ErbB3	0.175	0.001	0.199	0.014	1.14
ErbB4	0.024	0.001	0.017	0.000	
FAK	0.033	0.003	0.044	0.002	
FER	0.060	0.002	0.073	0.004	1.22
FGFR1	0.022	0.004	0.024	0.010	
FGFR2	0.328	0.012	0.403	0.002	1.23
FGFR2 α	0.065	0.003	0.082	0.016	1.26
Fgr	0.219	0.004	0.193	0.005	0.88
FRK	0.041	0.002	0.049	0.001	1.20
Fyn	0.027	0.011	0.033	0.001	
Hck	0.598	0.002	0.775	0.059	1.30
HGFR	0.851	0.014	1.043	0.021	1.23
IGF-I R	0.192	0.118	0.227	0.018	1.18
Insulin R	0.018	0.002	0.013	0.011	
Itk	0.090	0.002	0.098	0.001	1.09
JAK1	0.047	0.007	0.060	0.010	1.28
JAK2	0.808	0.003	0.850	0.052	1.05
JAK3	0.078	0.002	0.097	0.001	1.24
LCK	0.013	0.094	0.025	0.001	
LTK	0.049	0.006	0.048	0.003	0.98
Lyn	0.327	0.003	0.257	0.003	0.79
MATK	0.118	0.007	0.126	0.016	1.07
M-CSFR	0.017	0.038	0.020	0.003	
MUSK	0.037	0.007	0.047	0.000	
NGFR	0.025	0.001	0.035	0.003	
PDGFR- α	0.008	0.002	0.010	0.006	
PDGFR- β	0.028	0.005	0.027	0.003	
PYK2	0.020	0.005	0.028	0.001	
RET	0.033	0.004	0.033	0.012	
ROR1	0.003	0.001	0.002	0.001	
ROR2	0.045	0.004	0.043	0.005	0.96
ROS	0.037	0.004	0.039	0.001	
RYK	0.016	0.005	0.014	0.004	
SCFR	0.037	0.004	0.033	0.002	
SRMS	0.305	0.005	0.291	0.043	0.95
SYK	0.029	0.003	0.020	0.003	
Tec	0.030	0.020	0.018	0.004	
Tie-1	0.033	0.014	0.023	0.000	
Tie-2	0.102	0.002	0.073	0.002	0.72
TNK1	0.184	0.005	0.196	0.001	1.07
TRKB	0.082	0.013	0.068	0.016	0.83
TXK	0.644	0.012	0.527	0.035	0.82
Tyk2	0.042	0.001	0.029	0.006	
TYRO10	0.011	0.004	0.001	0.002	
VEGFR2	0.025	0.001	0.020	0.004	
VEGFR3	0.046	0.000	0.039	0.004	
ZAP70	0.109	0.005	0.068	0.015	0.62

Note: Shaded RTKs indicate those who were censored from the results due to average densities being equal or lower than that of the negative control (i.e. ≤ 0.040 OD/mm²).