Supplementary Methods

Cells and Cell culture

MCF-10A-derived cells were maintained in DMEM/F12 (Thermo Scientific, South Logan, Utah) supplemented with 5% horse serum (Invitrogen), 20 ng/ml EGF (Peprotech), 10 μg/ml insulin (Sigma), 100 ng/ml cholera toxin (Sigma), 0.5 μg/ml hydrocortisone (Sigma), 100 units/ml penicillin and 100 μg/ml streptomycin. BT474 cells were grown in Dulbecco modified Eagle medium/nutrient mixture/F-12 supplemented with 10% fetal bovine serum (FBS). SKBR3 cells were maintained in modified McCoy 5α, containing 1.5 mM l-glutamine, 2200 mg/l sodium bicarbonate, and 10% FBS. MDA MB361 were cultured in L15 supplemented with 10% FBS. All other cells were cultured at Roswell Park Memorial Institute supplemented with 10% FBS, 100 units/ml penicillin, and 100 μg/ml streptomycin. Cells were frozen at early passages and used for less than 4 weeks in continuous culture.

Generation of lentiviruses expressing wild-type c-MET or MET-T1010I

We designed and GeneArt synthesized constructs expressing Flag epitope-tagged full-length human MET or MET-T1010I. The gene cassette was transferred into a lentiviral vector, pLVX-tdTomato-N1 (Clontech, Mountain View, CA). The lentiviruses were used for transduction of HCC1954 or MCF-10A cells. To ensure that most of the cells were infected with one aimed gene-carrying virus, we optimized conditions to achieve ~20-30% transduction efficiency in the titration assay. Then, we experimented with 3-4 times more cells than the infecting viral particles. After selection with puromycin, the cells expressing Flag-tagged WT MET or MET-T1010I were used for studies.

Migration or migration inhibition assays

Cell migration assays or inhibition assays were performed with 24-well BD BioCoat migration chambers with 8.0-micron polycarbonate filters (BD Biosciences, CA). Briefly, cells were starved in serum-free medium with or without tepotinib at different doses for overnight. A total of 5×10^4 cells in 0.6 ml of serum-free medium were inoculated into the upper chamber, and 0.75 ml of serum-free medium containing HGF (50 ng/ml) and fibronectin (5 μg/ml) was added to the lower chamber. For migration inhibition assays, the cells were treated with tepotinib with the doses as indicated in serum free medium overnight. The cells were collected and seeded in the chamber. The drug or vehicle was added to both the upper and lower chambers. The cells were allowed to pass through the filter at 37°C, 5% CO2, for 22 hours. Non-migration cells on the upper surface of the filter were removed by wiping with a cotton swab. The cells that penetrated through the Matrigel's pores to the filter's underside were stained with 0.25% crystal violet in 20% methanol for 30 minutes. Migrated cells were photographed and counted in 10 random fields.

Cell growth and morphogenesis assays

Cell growth and morphogenesis assays were performed in three-dimensional (3D) culture in Matrigel as previously described [25, 28]. Briefly, 4×10^3 cells were resuspended in low FBS (2.5%) medium supplemented with 20 ng/ml HGF containing 2% growth factor reduced Matrigel (Corning, Glendale, AZ) and seeded onto Matrigel matrix in eight-well chamber slides (BD Bioscience), with or without treatment as indicated. Medium with or without drug was replaced every 3 days. Photographs of representative fields were taken as indicated. Acini were photographed and counted in 10 randomly chosen fields. Total number and area of acini were quantitatively analyzed using AlphaView SA software (Cell Biosciences) and expressed as means ± standard deviation (SD), representing three independent experiments.

Western blot analyses

Western blot analysis was performed as described previously [28]. Briefly, after washing with cold PBS, the cultured cells were lysed in ice-cold lysis buffer [1 % Triton X-100, 50 mM HEPES, pH 7.4, 150 mM NaCl, 1.5 mM $MgCl_2$, 1 mM EGTA, 100 mM NaF, 10 mM Na pyrophosphate, 1 mM Na_3VO_4, 10 % glycerol, protease inhibitor cocktail (Roche Applied Science), and phosphatase inhibitors, PhosSTOP (Roche Applied Science)]. Quantitative analysis of the bands was performed using AlphaView SA software. The antibodies utilized are listed in Table S2. Quantitative analysis of the bands was performed with AlphaView SA software.

Pathway sore analysis

RPPA data from snap-frozen tumor samples were further analyzed for pathway sores based on a panel of pathways published previously [34]. These pathways were predefined based on a PubMed literature search of review and original articles describing the various pathways in detail. These pathways include epithelial-mesenchymal transition (EMT), Apoptosis, Cell cycle, Core reactive, DNA damage response, PI3K-AKT, TSC-mTOR, and Immune Signature. The pathway score was calculated by summing the relative protein levels of all positive regulatory components minus that of negative regulatory components in a particular pathway. The t-test was used for two groups. P values less than 0.05 were considered statistically significant.

Phospho-receptor tyrosine kinase (p-RTK) an d phosphor-protein kinase (p-PK) ar rays

Phosphorylation of 49 human RTKs and 42 PKs in MCF10A cells transduced with WT MET or MET-T1010I was assessed using the human phospho-RTK Array kit and the human phosphor-PK kit (R&D Systems, Minneapolis, MN) following the manufacturer's directions. Briefly, cells were serum-starved overnight, followed by stimulation with recombinant human HGF (40 ng/ml) for 30 minutes. Cell lysates were prepared. Extracted protein concentration was quantified, and 300

μg total protein lysate was added to each array. Signals were detected following the manufacturer's directions. Quantitative analysis was performed with AlphaView SA software.

Establishment of human HGF-MET paired breast cancer spontaneous metastasis mouse model

All animal studies were carried out under Animal Care and Use Form-approved protocols. The hHGF Tg/SCID mice were bred in a room specifically for SCID mice. After testing serum human HGF, 6-week-old female mice were used for experiments. The HCC1954 cells transduced with empty vector (control), WT MET, or MET-T1010I were implanted orthotopically into the mammary fat pad of each mouse (5×10^6 in 150 μL of phosphate-buffered saline). Xenograft tumor growth was measured with a caliper every other day. Tumor volume was calculated with the formula $V = lw^2/2$. When the size reached approximately 1000 mm^3, the xenografts were resected (survival surgery protocol) under anesthesia with isoflurane (1.5%, 0.5 L/min O_2). The mice were closely monitored postoperatively. When exhibiting abnormal health conditions, or aged 40 weeks, the mice were sacrificed with CO_2. The main organs, including lung, liver and brain, were subjected to double-blind histopathological analysis by a veterinary pathologist.

Human samples

Blood samples from breast cancer patients and healthy volunteers, along with clinical data, were obtained under protocols approved by the institutional review board at the University of Texas MD Anderson Cancer Center. Patients and tumor characteristics were collected by chart review [36]. The Institutional Review Board of MD Anderson approved the laboratory study. After the collection of whole blood, it was left undisturbed at room temperature for 30 minutes. The samples were then centrifuged at 1000-2000 x g for 10 minutes in a refrigerated centrifuge. Serum samples

from patients and similar-aged healthy women were stored at -80°C until further analysis for HGF and cytokines.

Cytokine and chemokine chip detection

In total, 60 serum cytokines (Table S3) were measured using the kits the Bio-Plex Pro™ Human Chemokine Panel 40-plex, Bio-Plex Pro Human Cytokine Group I, and Bio-Plex Pro Human Cytokine Group II (Bio-Rad Laboratories, Inc., CA) according to the manufacturer's instructions. Fluorescence detection FI values were obtained using Luminex MAGPIX System and the data were analyzed using the Bioplex Manager software following the manufacturer's instructions.

Statistical analyses

One-way ANOVA was used for multiple groups, and the *t*-test was used for two groups

using Prism 10 (GraphPad Software, La Jolla, CA). RPPA data were analyzed as previously described [32,33], followed by further analysis with one-way ANOVA to compare different groups. Data were expressed as mean ± SD. P values less than 0.05 were considered statistically significant. The data from migration assays, cell growth and inhibition assays were analyzed with one-way ANOVA for multiple groups, and the *t*-test was used for two groups. All other statistical tests were performed using Prism (GraphPad Software, La Jolla, CA)

Supplementary Table 1. shRNA Sequences

shRNA	Clone ID	Mature Antisense Sequence
shMET_1	V3LHS_642482	TTCTTGCCATCATTGTCCA
shMET_2	V3LHS_642486	AGAATGACATTCTGGATGG
shMET_3	V3LHS_642481	TGATATTGAGACAACACCA
shMET_4	V3LHS_642487	ATTCTTGTGTGAAAAGTCT
shMET_5	V3LHS_646098	TTAATTGCATGATTTATCA
shMET_6	V3LHS_381508	TAAACACTTCCTTCTTTGT
shRNA-NS	Non-silencing shRNA	

Supplementary Table 2. Antibodies used for RPPA and Western blot

Antibody Name	Company	Validation Status
14-3-3-zeta	Santa Cruz1	Valid*
4E-BP1	CST2	Valid
4E-BP1_pS65	CST	Valid
4E-BP1_pT37_T46	CST	Valid
53BP1	CST	Valid
AceCS1	CST	Valid
ACC1	Epitomics/Abcam3	Caution**
ACC_pS79	CST	Valid
ACSL1	CST	Valid
ADAR1	Abcam	Valid
Akt	CST	Valid
Akt_pS473	CST	Valid
Akt_pT308	CST	Valid
Akt1	CST	Valid
Akt1_pS473	CST	Valid
Akt2	CST	Valid
Akt2_pS474	CST	Caution
ALKBH5	Abcam	Valid
D-a-Tubulin	Abcam	Valid
Ambra1_pS52	Millipore4	Caution
AMPKa	CST	Caution
AMPKa_pT172	CST	Caution
AR	CST	Valid
Annexin-I	BD Biosciences5	Valid
A-Raf	CST	Valid
A-Raf_pS299	MyBioSource6	Caution
ARID1A	Sigma-Aldrich	Caution
ASNS	Sigma-Aldrich	Valid
Atg4B	CST	Caution
Atg5	CST	Caution
Atg7	CST	Valid
ATM	CST	Valid
ATM_pS1981	CST	Valid
ATP5A	Abcam	Caution
ATP5H	Invitrogen7	Valid
ACLY_pS455	CST	Valid
ATR	CST	Valid
ATR_pS428	Abcam	Caution
ATRX	Abcam	Caution

Aurora-A	CST	Caution
Aurora-ABC_pT288_pT232_pT198	CST	Caution
Aurora-B	Invitrogen	Valid
Axl	CST	Valid
B7-H3	CST	Caution
B7-H4	CST	Caution
Bad_pS112	CST	Valid
Bak	Epitomics/Abcam	Caution
BAP1	Santa Cruz	Valid
Bax	CST	Valid
Bcl2	CST	Caution
Bcl2A1	Abnova[8]	Valid
Bcl-xL	CST	Valid
Beclin	ThermoFisher[9]	Caution
b-Actin	CST	Caution
b-Catenin	CST	Valid
b-Catenin_pT41_S45	CST	Valid
Bid	CST	Caution
Bim	CST	Valid
B-Raf	CST	Caution
B-Raf_pS445	CST	Valid
BRCA1	Millipore	Caution
BRD4	CST	Valid
c-Abl	CST	Valid
c-Abl_pY412	CST	Caution
Cadherin-6	CST	Caution
Calnexin	CST	Valid
Caspase-3-cleaved	CST	Caution
Caspase-7-cleaved	CST	Caution
Caspase-8-cleaved	CST	Caution
Caveolin-1	CST	Valid
CD134	CST	Valid
CD171	Biolegend[10]	Valid
CD2	Santa Cruz	Caution
CD20	Invitrogen	Caution
CD26	Abcam	Valid
CD4	Abcam	Valid
CD44	CST	Caution
CD45	DAKO	Valid
CD68	R&D Systems[11]	Caution
cdc2_pY15	CST	Caution

cdc25C	CST	Valid
Cdc6	CST	Valid
CDK1_pT14	Abcam	Caution
CDK9	CST	Valid
CDT1	CST	Valid
CENP-A	CST	Valid
CHD1L	CST	Valid
Chk1	CST	Caution
Chk1_pS296	Abcam	Valid
Chk1_pS345	CST	Caution
Chk2	CST	Valid
Chk2_pT68	CST	Caution
c-IAP2	CST	Caution
c-Jun_pS73	CST	Valid
c-Kit	Abcam	Valid
Claudin-7	Millipore Sigma	Valid
c-Met_pY1234_Y1235	CST	Valid
c-Myc	Santa Cruz	Caution
COG3	ProteinTech12	Valid
Collagen-VI	Santa Cruz	Valid
Connexin-43	CST	Caution
Coup-TFII	CST	Caution
Cox-IV	CST	Valid
Cox2	CST	Valid
CRABP2	Novus Biologicals13	Valid
C-Raf_pS338	CST	Valid
Creb	CST	Caution
Creb_pS133	CST	Caution
Csk	CST	Caution
CtIP	CST	Valid
Cyclin-B1	Epitomics/Abcam	Valid
Cyclin-D1	Millipore Sigma	Caution
Cyclin-D3	CST	Valid
Cyclin-E1	CST	Valid
Cyclophilin-F	Abcam	Valid
DAPK1_pS308	GeneTex	Caution
DDB-1	CST	Valid
DDR1	CST	Valid
DDR1_pY513	Millipore Sigma	Caution
DNA-Ligase-IV	CST	Caution
DNA-POLG	CST	Valid

DNMT1	CST	Valid
DRP1	CST	Valid
DUSP4	CST	Valid
DUSP6	Abcam	Caution
Dvl3	CST	Valid
DYRK1B	CST	Caution
E2F1	CST	Valid
E-Cadherin	GeneTex14	Valid
eEF2	CST	Caution
eEF2K	CST	Valid
EGFR	CST	Valid
EGFR_pY1173	Epitomics/Abcam	Valid
eIF4E	CST	Valid
eIF4E_pS209	Abcam	Valid
eIF4G	CST	Caution
Elk1_pS383	CST	Caution
Enolase-1	CST	Valid
Enolase-2	CST	Valid
ENY2	GeneTex	Caution
EphA2	CST	Valid
EphA2_pY588	CST	Caution
EphA2_pS897	CST	Caution
EMA	DAKO15	Caution
HER2_pY1248	R&D Systems	Valid
HER3_pY1289	CST	Caution
HER3	Santa Cruz	Valid
ERCC1	CST	Caution
ERCC5	Proteintech	Caution
Erk5	CST	Valid
BMK1-Erk5_pT218_Y220	Millipore	Valid
ERRalpha	CST	Valid
ER-a	CST	Valid
ER-a_pS118	Epitomics/Abcam	Valid
Ets-1	Bethyl16	Valid
EVI1	CST	Valid
Ezh2	CST	Valid
FABP5	Proteintech	Caution
FAK	CST	Caution
FAK_pY397	CST	Valid
FASN	CST	Valid
FGF-basic	Peprotech17	Caution

FGFR1	CST	Valid
FGFR2	CST	Valid
Fibronectin	Epitomics/Abcam	Valid
Folate-Binding-Protein	Abcam	Valid
Folliculin	CST	Valid
FOXM1	CST	Valid
FoxO3	CST	Valid
FoxO3a_pS318_S321	Biorbyt	Caution
FRS2-alpha_pY196	Invitrogen	Valid
FTO	Abcam	Valid
G6PD	CST	Valid
Gab2	CST	Valid
GAPDH	Invitrogen	Caution
GATA3	BD Biosciences	Valid
GATA6	CST	Valid
GCLC	Proteintech	Caution
GCLM	Invitrogen	Valid
GCN5L2	CST	Valid
GGPS1	Santa Cruz	Valid
Gli1	CST	Caution
Gli3	Abcam	Valid
Glucocorticoid-Receptor	CST	Valid
Glutamate-D1-2	Novus	Valid
Glutaminase	Abcam	Caution
Gys	CST	Valid
Gys_pS641	CST	Valid
Granzyme-B	CST	Valid
GRB2	CST	Valid
GRB7	Abcam	Valid
Grp75	CST	Caution
GSK-3a-b	Santa Cruz	Valid
GSK-3a-b_pS21_S9	CST	Valid
GSK-3B	CST	Caution
TSC1	CST	Valid
HER2	Lab Vision18	Valid
Heregulin	CST	Valid
HES1	CST	Valid
Hexokinase-I	CST	Caution
Hexokinase-II	Abcam	Valid
Hif-1-alpha	CST	Caution
H2AX_pS139	CST	Caution

H2AX_pS140	Abcam	Caution
U-Histone-H2B	CST	Caution
Histone-H3	Abcam	Valid
DM-Histone-H3	Millipore	Valid
Histone-H3_pS10	CST	Valid
HMHA1	ProteinTech	Valid
HNRNPK	CST	Valid
HSP27	CST	Caution
HSP27_pS82	CST	Valid
HSP60	CST	Valid
TRAP1	BD Biosciences	Valid
IDO	CST	Caution
IGFRb	CST	Caution
IGF1R_pY1135_Y1136	CST	Valid
IGFBP2	CST	Valid
IGFBP3	BD Biosciences	Valid
IL-6	CST	Caution
INPP4b	CST	Caution
IR-b	CST	Caution
IRF-1	CST	Valid
IRF-3	CST	Valid
IRS1	Millipore	Valid
IRS2	CST	Caution
JAB1	Santa Cruz	Caution
Jagged1	Abcam	Valid
Jak2	CST	Valid
JNK_pT183_Y185	CST	Caution
KAP1	Abcam	Valid
KEAP1	CST	Valid
LAD1	Atlas/Sigma-Aldrich	Valid
Lasu1	Bethyl	Valid
LC3A-B	CST	Caution
Lck	CST	Valid
LCN2	CST	Valid
LDHA	CST	Caution
LRP6_pS1490	CST	Valid
Lyn	CST	Valid
MACC1	CST	Valid
Mcl-1	CST	Valid
MDM2_pS166	Abcam	Valid
MEK1	Epitomics/Abcam	Valid

MEK1_pS217_S221	CST	Valid
MERIT40	CST	Caution
MERIT40_pS29	CST	Valid
Merlin	Novus	Caution
METTL3	Abcam	Valid
Midkine	Invitrogen	Valid
MIF	CST	Valid
MIG6	CST	Valid
MITF	CST	Valid
Mitofusin-1	CST	Valid
Mitofusin-2	CST	Valid
MLH1	CST	Valid
MLKL	CST	Valid
MMP14	Abcam	Valid
Mnk1	CST	Valid
MCT4	Millipore	Valid
MRAP	GeneTex	Valid
MSH2	CST	Caution
MSH6	sdix/Novus	Caution
MSI2	Abcam	Caution
MTCO1	Abcam	Valid
mTOR	CST	Valid
mTOR_pS2448	CST	Caution
MYH11	GeneTex	Caution
Myosin-IIa	CST	Caution
Myosin-IIa_pS1943	CST	Valid
Myt1	CST	Caution
N-Cadherin	CST	Valid
NDRG1_pT346	CST	Valid
NF-kB-p65_pS536	CST	Caution
Notch1	CST	Valid
Notch1-cleaved	CST	Valid
Notch3	Santa Cruz	Caution
NQO1	CST	Valid
N-Ras	Santa Cruz	Valid
NRF2	CST	Caution
Oct-4	CST	Caution
p21	Invitrogen	Caution
p27_pT198	Abcam	Valid
p27-Kip1	Abcam	Caution
p38-a	CST	Valid

p38-MAPK	CST	Valid
p38-MAPK_pT180_Y182	CST	Valid
p44-42-MAPK	CST	Valid
MAPK_pT202_Y204	CST	Caution
p53	CST	Caution
p70-S6K1	Epitomics/Abcam	Valid
p70-S6K_pT389	CST	Valid
p73	Abcam	Valid
PAI-1	BD Biosciences	Valid
PAICS	Sigma-Aldrich	Caution
PAK1	CST	Valid
PAK_pT423_T402	CST	Caution
PAK4	Invitrogen	Valid
PAK_pS474_S602_S560	CST	Valid
PAR	Trevigen	Caution
PARG	CST	Caution
DJ1	Abcam	Valid
PARP	CST	Valid
PAX6	CST	Valid
PAX8	Novus Biologicals	Caution
Paxillin	CST	Caution
P-Cadherin	CST	Caution
PCNA	CST	Caution
PD-1	GeneTex	Valid
Pdcd4	Rockland19	Caution
PDHK1	CST	Caution
PDK1	CST	Valid
PDK1_pS241	CST	Valid
PD-L1	CST	r = 0.88
PEA-15	CST	Valid
PEA-15_pS116	MyBioSource20	Valid
PERK	CST	Valid
PGM1	Abcam	Valid
PHGDH	CST	Caution
PHLPP	Proteintech	Valid
PI3K-p110-a	CST	Caution
PI3K-p85	Millipore	Caution
PIP4K2A	CST	Valid
PIP4K2B	CST	Valid
PKA-a	CST	Valid
PKC-b-II_pS660	CST	Valid

PKCa	CST	Valid
PKC-a-b-II_pT638_T641	CST	Valid
PKC-delta_pS664	Millipore	Valid
PKM2	CST	Caution
PLC-gamma1	CST	Valid
PLC-gamma1_pS1248	CST	Valid
PLC-gamma2_pY759	GeneTex	Valid
PLK1	CST	Caution
PMS2	Abcam	Valid
PRAS40	Invitrogen	Caution
PRAS40_pT246	Invitrogen	Valid
PRC1_pT481	Aviva Systems Biology21	Caution
PREX1	Abcam	Valid
PRMT1	CST	Valid
PRMT5	Abcam	Valid
PR	abcam	Valid
PTEN	CST	Valid
PTPN12	Abcam	Valid
Puma	CST	Caution
PYGB	Sigma-Aldrich	Valid
PYGM	Novus/Abnova	Caution
Pyk2_pY402	CST	Caution
PDHA1	CST	Valid
Rab11	CST	Caution
Rab11FIP1	CST	Valid
Rab25	CST	Valid
Cdc42	CST	Caution
Rad17_pS645	CST	Valid
Rad23A	CST	Caution
Rad50	CST	Valid
Rad51	Millipore	Caution
C-Raf	Millipore	Caution
Raptor	CST	Valid
Rb	CST	Red_Blob
Rb_pS807_S811	CST	Valid
RBM15	Novus	Valid
Rheb	R&D Systems	Caution
Rictor	CST	Caution
Rictor_pT1135	CST	Valid
RIP	CST	Caution
RPA32	CST	Valid

RPA32_pS4_S8	Bethyl	Caution
RRM2	Life Technologies22	Caution
RSK1	CST	Valid
p90RSK_pT573	Invitrogen	Caution
RSK	CST	Caution
S100A4	CST	Valid
S6	CST	Valid
S6_pS235_S236	CST	Valid
S6_pS240_S244	CST	Valid
SCD	Santa Cruz	Valid
SDHA	CST	Valid
SFRP1	CST	Valid
SGK1	CST	Valid
SGK3	CST	Valid
Shc_pY317	Bioss	Caution
SHP2	CST	Valid
SHP-2_pY542	CST	Caution
SIRP-alpha	Abcam	Valid
SLC1A5	Sigma-Aldrich	Caution
Slfn11	Santa Cruz	Valid
Smac	CST	Red_Blob
Smad1	Epitomics/Abcam	Valid
Smad3	Epitomics/Abcam	Valid
Smad4	CST	Valid
Snail	CST	Red_Blob
SOD1	CST	Valid
SOD2	CST	Valid
Sox17	Abcam	Valid
Sox2	CST	Valid
Sox7	Novus Biologicals	Valid
Src	CST	Valid
Src_pY527	CST	Valid
Src_pY416	CST	Valid
Stat1_pY701	CST	Valid
Stat3	CST	Caution
Stat3_pY705	Fisher	Caution
Stat5a	Epitomics/Abcam	Valid
Stathmin-1	Epitomics/Abcam	Valid
STING	CST	Valid
Syk	Santa Cruz	Valid
Synaptophysin	CST	Caution

Tau	Millipore	Caution
TAZ	CST	Valid
ZEB1	CST	Valid
TEAD	CST	Caution
TFAM	CST	Valid
TIGAR	Epitomics/Abcam	Valid
TFRC	Novus	Valid
Transglutaminase	Lab Vision/Fisher	Valid
TRIM24	G-Biosciences23	Caution
TRIM25	Abcam	Caution
TRIP13	Invitrogen	Valid
TROP2	Abcam	Valid
TTF1	Epitomics/Abcam	Valid
Tuberin	Epitomics/Abcam	Valid
Tuberin_pT1462	Abcam	Valid
TUFM	Invitrogen	Valid
FN14	CST	Caution
Twist	Santa Cruz	Caution
UBAC1	Sigma-Aldrich	Valid
UGT1A	Santa Cruz	Valid
ULK1_pS757	CST	Caution
VASP	CST	Valid
Vav1	CST	Caution
VEGFR-2	CST	Valid
VEGFR2_pY1175	CST	Caution
VHL	CST	Caution
VHL-EPPK1	BD Biosciences	Caution
Vinculin	Sigma-Aldrich	Valid
Wee1	CST	Caution
Wee1_pS642	CST	Caution
WIPI1	CST	Caution
WIPI2	CST	Caution
WTAP	Abcam	Valid
XBP-1	Santa Cruz	Caution
XIAP	CST	Caution
XPA	Santa Cruz	Valid
XPF	CST	Caution
XRCC1	Invitrogen	Caution
YAP_pS127	CST	Valid
YAP	Santa Cruz	Caution
YB1_pS102	CST	Valid

YES1	CST	Valid
YTHDF2	Abcam	Valid
YTHDF3	Abcam	Caution
ZAP-70	CST	Valid

* RPPA and WB correlation > 0.7

** RPPA and WB correlation < 0.7

1Santa Cruz (Santa Cruz, CA)

2Cell Sigaling Technology (Danvers, MA)

3Abcam (Waltham, MA)

4MilliporeSigma (Burlington, MA)

5BD Biosciences (San Jose, CA)

6MyBioSource (San Diego, CA)

7Invitrogen (Carlsbad, CA)

8Abnova (Taipei, Taiwan)

9ThermoFisher (Sugar Land, TX)

10BioLegend (San Diego, CA)

11R&D Systems (Minneapolis, MN)

12ProteinTech (Rosemont, IL)

13Novus Biologicals (Centennial, CO)

14GeneTex (Irvine , CA)

15DAKO (Carpinteria, CA)

16Bethyl (Montgomery, TX)

17Peprotech(Rocky Hill, NJ)

18Lab Vision (Fremont, CA)

19Rockland (Limerick, PA)

20MyBioSource (San Diego, CA)

21Aviva Systems Biology (San Diego, CA)

22Life Technologies (Carlsbad, CA)

23G-Biosciences (St. Louis, MO)

Supplementary Table 3. Human Cytokines/Chemokines

Cytokines	Chemokines	
Group 1	6Ckine / CCL21	BCA-1 / CXCL13
IL-1Rα	CTACK / CCL27	ENA-78 / CXCL5
IL-5	Eotaxin / CCL11	Eotaxin-2 / CCL24
IL-7	Eotaxin-3 / CCL26	Fractalkine / CXC3CL1
IL-9	GCP-2 / CXCL6	GM-CSF
IL-12	Gro-α / CXCL1	Gro-β / CXCL2
IL-13	I-309 / CCL1	IFN-γ
IL-15	IL-1β	IL-2
IL-17A	IL-4	IL-6
FGF	IL-8 / CXCL8	IL-10
CGF	IL-16	IP-10 / CXCL10
PDGF	I-TAC / CXCL11	MCP-1 / CCL2
RNATES	MCP-2 / CCL8	MCP-3 / CCL7
VEGF	MCP-4 / CCL13	MDC / CCL22
	MIF	MIG / CXCL9
Group 2	MIP-1α / CCL3	MIP-1δ / CCL15
IL-2Rα	MIP-3α / CCL20	MIP-3β / CCL19
IL-18	MPIF-1 / CCL23	SCYB16 / CXCL16
IFN-α2	SDF-1 α+β / CXCL12	TARC / CCL17
LIF	TECK / CCL25	TNF-α
β-NGF		
SCF		
TRAIL		

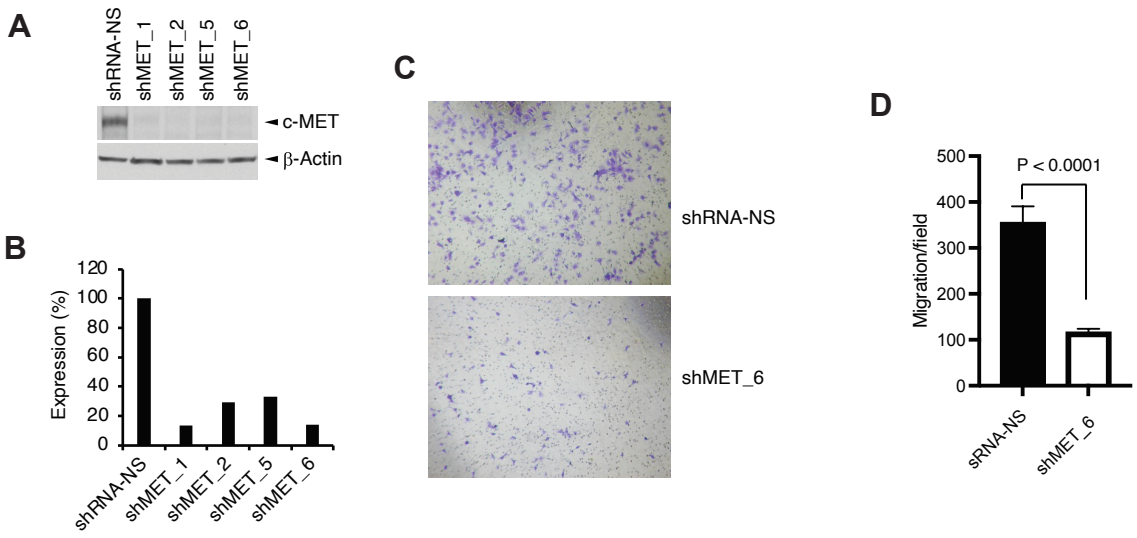


Fig. S1. Knockdown of c-MET reduces HGF-induced cell migration. c-MET was silenced by specific shRNAs in HCC1954 cells. The puromycin-resistant stable colonies were pooled together and named shMET. A pool of cells infected with the lentivirus containing a non-effective vector (shRNA-NS) was selected and used as the control. Western blot analyses were used to confirm the reduction in c-MET expression (**A**). The density of the bands was quantitatively analyzed (**B**). Cell migration assays were tested (**C**). Data were analyzed using *t*-test analysis of variance and are reported as the mean ± SD of triplicates (**D**)

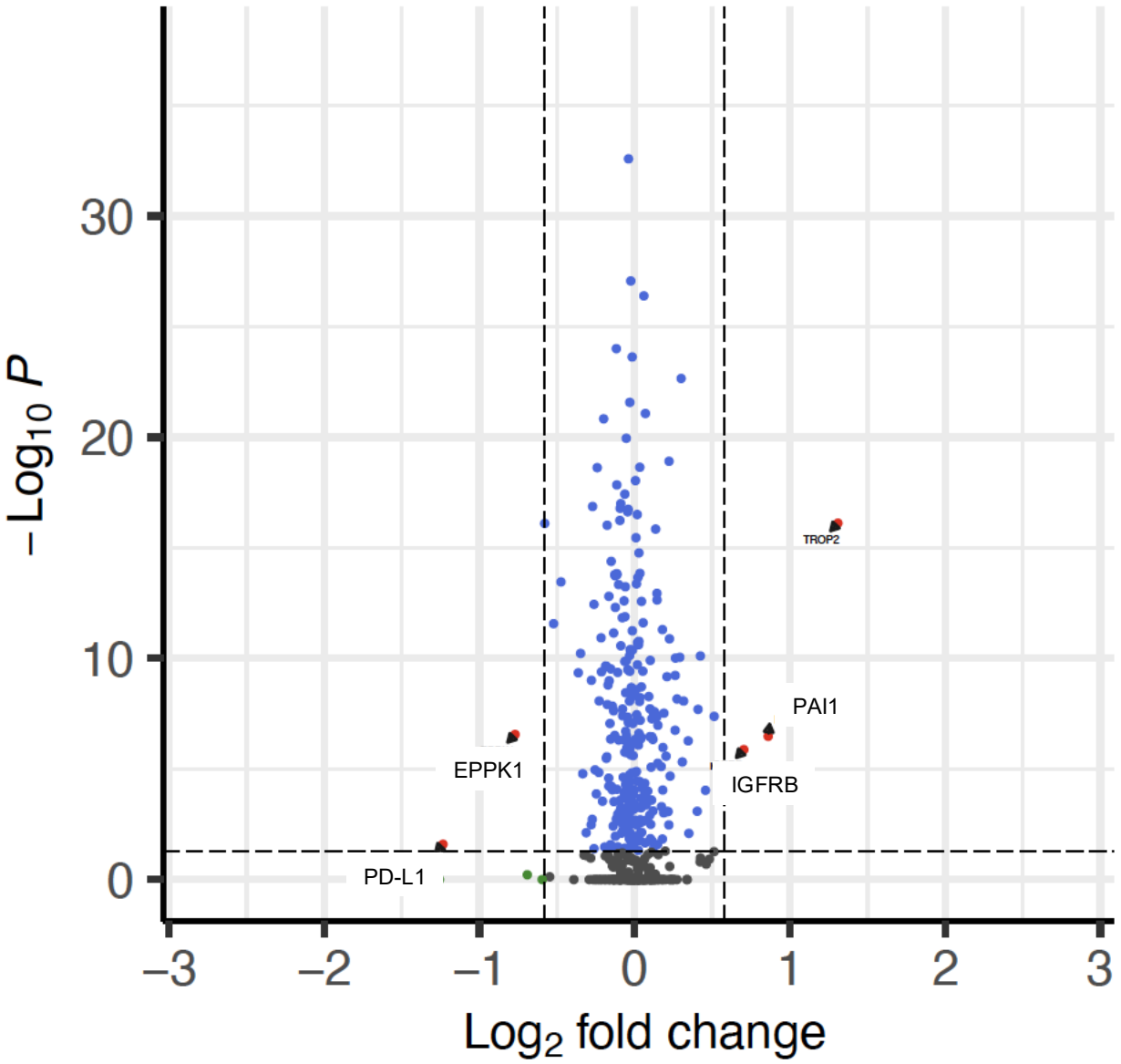


Fig. S2. Volcano plot of comparison WT MET vs. Vector. RPPA data from WT MET overexpression tumor samples were further analyzed. volcano plot shows the significant proteins identified for the comparison WT MET vs.Vector. Y-axis represents negative log10-transformed Bonferroni-adjusted ANOVA's p values. Black: not significant; Green: log2FC is >0.58 or <-0.58 but not significant; Blue: significant but log2FC is <0.58 or >-0.58; Red: significant and log2FC is >0.58 or <-0.58.

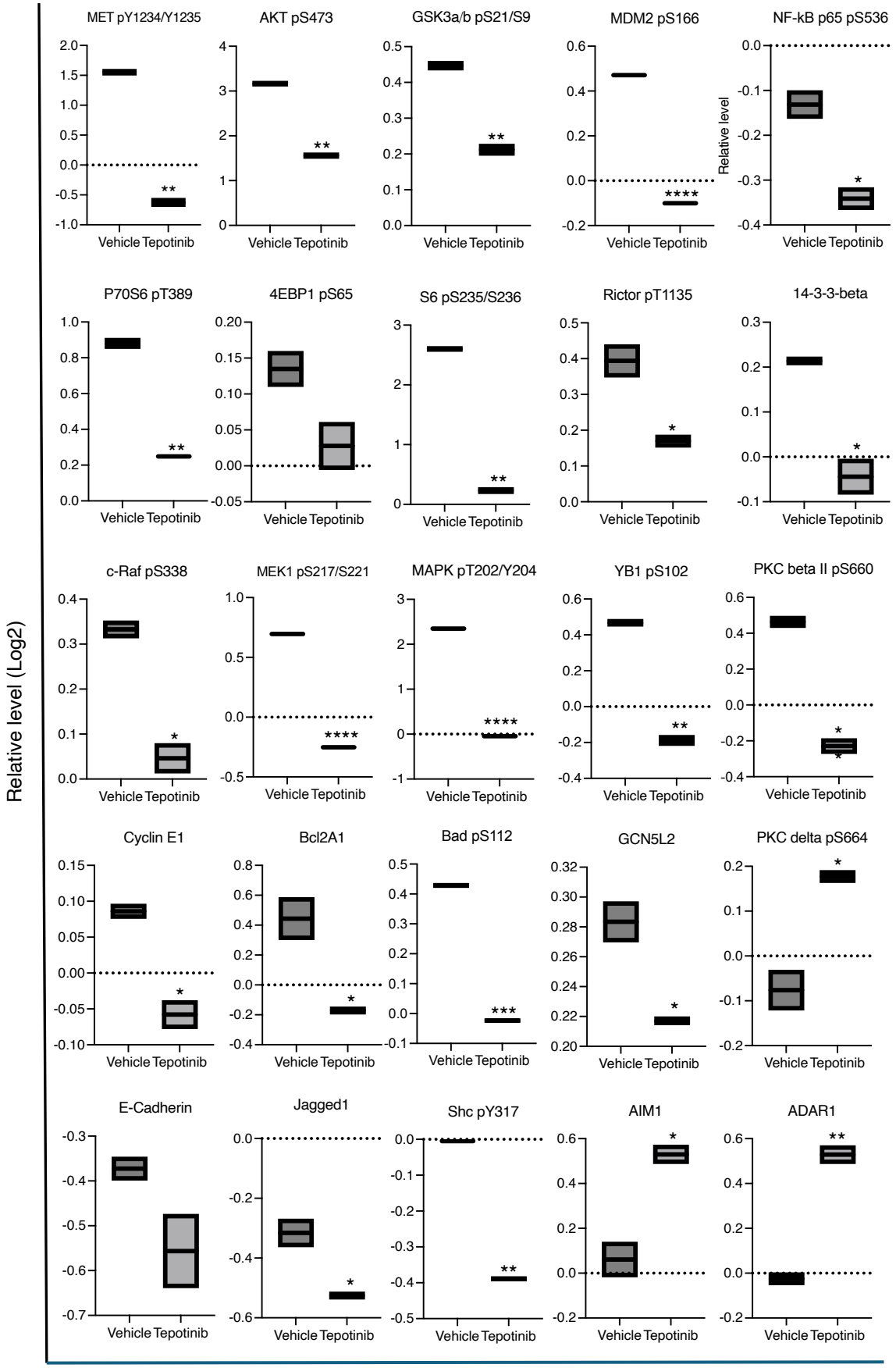


Fig. S3. MET inhibitor blocked oncogenic pathways induced by HGF in MET-T1010I transduced cells. RPPA data from MET-T1010I transduced cells treated with tepotinib or vehicle were further quantitatively analyzed. The data were expressed as mean ± SD (*, P < 0.05; **, P < 0.01; ***, P < 0.001; ****, P < 0.0001 vs. vehicle, *t*-test).

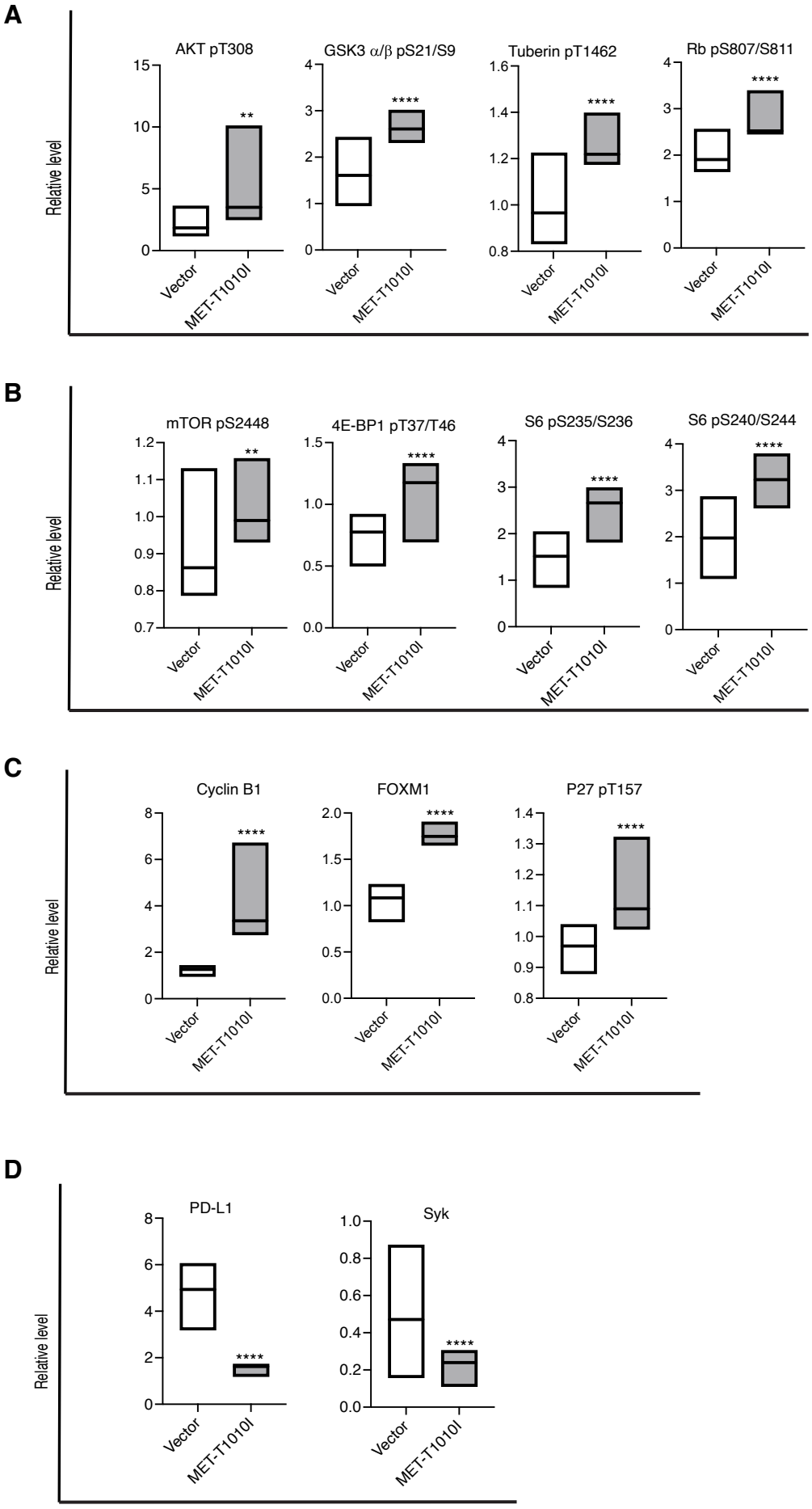
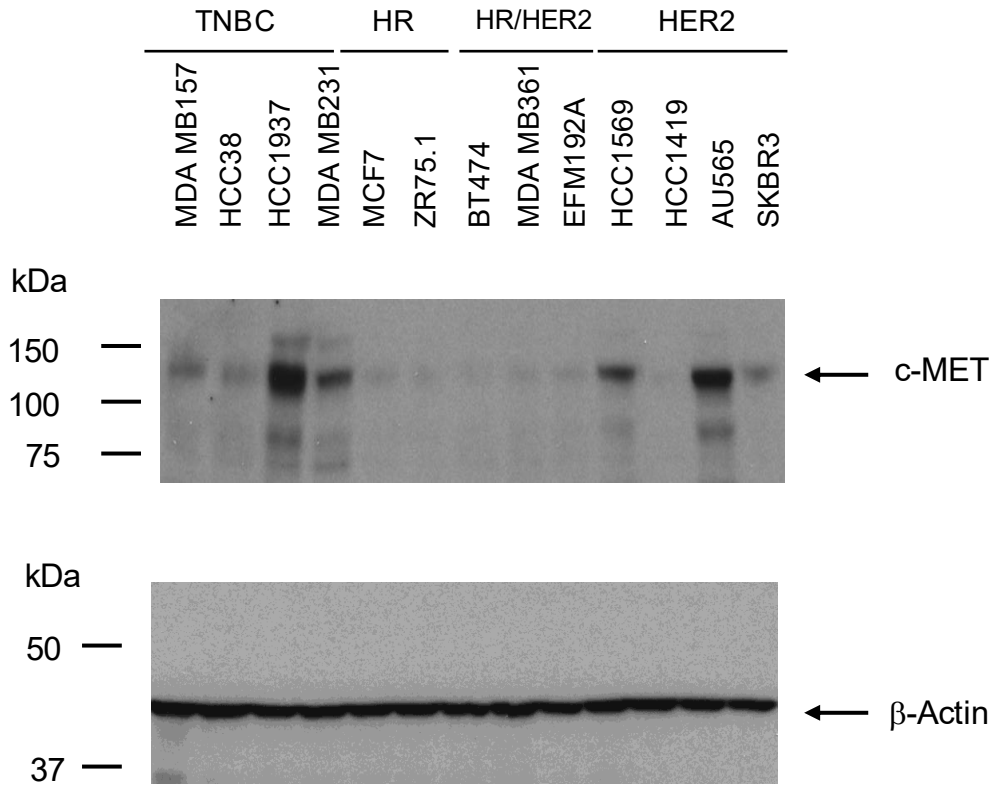


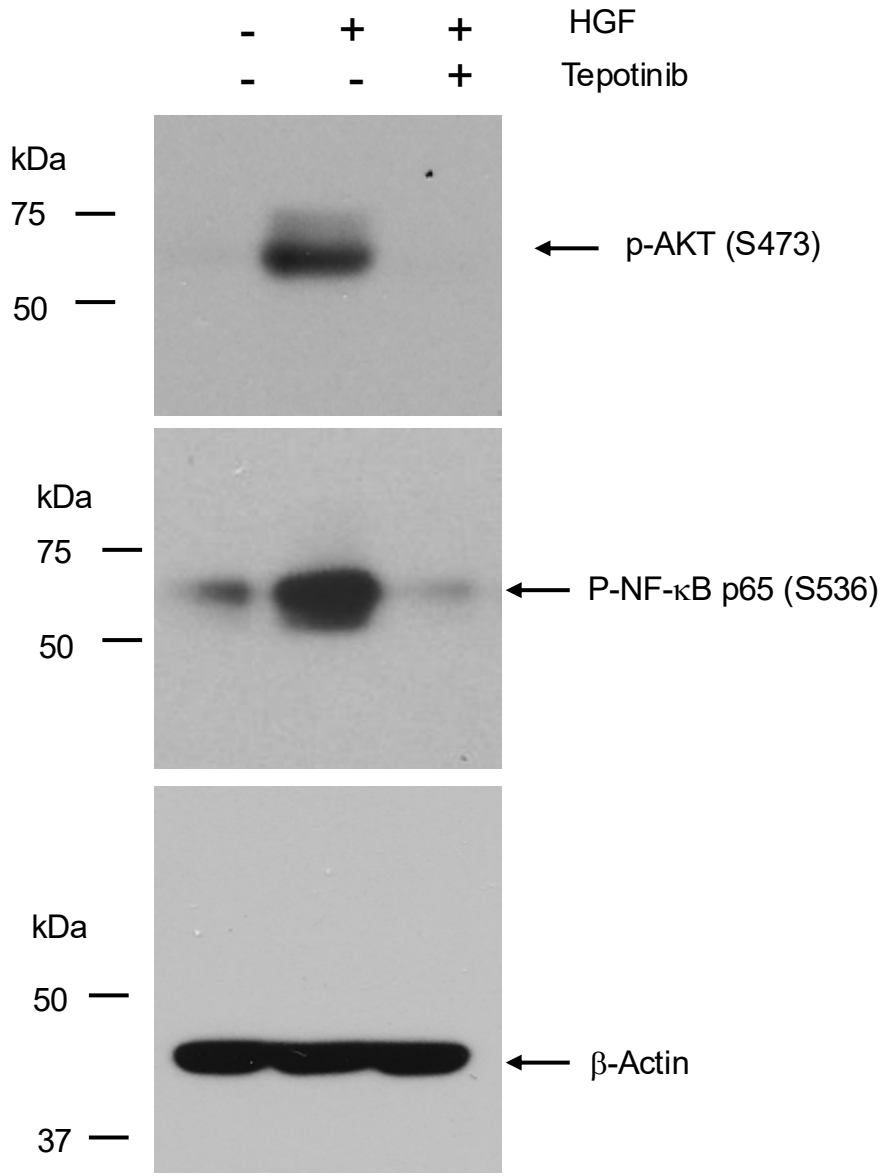
Fig. S4. Effects of MET-T1010I expression on HGF-induced signaling pathways. **A**. PI3K-AKT pathway. **B**. mTOR pathway. **C**. Cell cycle signaling. **D**. Immune signature. Quantitative analysis of the RPPA data from snap tumors were expressed as mean ± SD (**, $P < 0.01$; ****, $P < 0.0001$ vs. vector, t-test).

Fig. S5. Uncropped image of blots

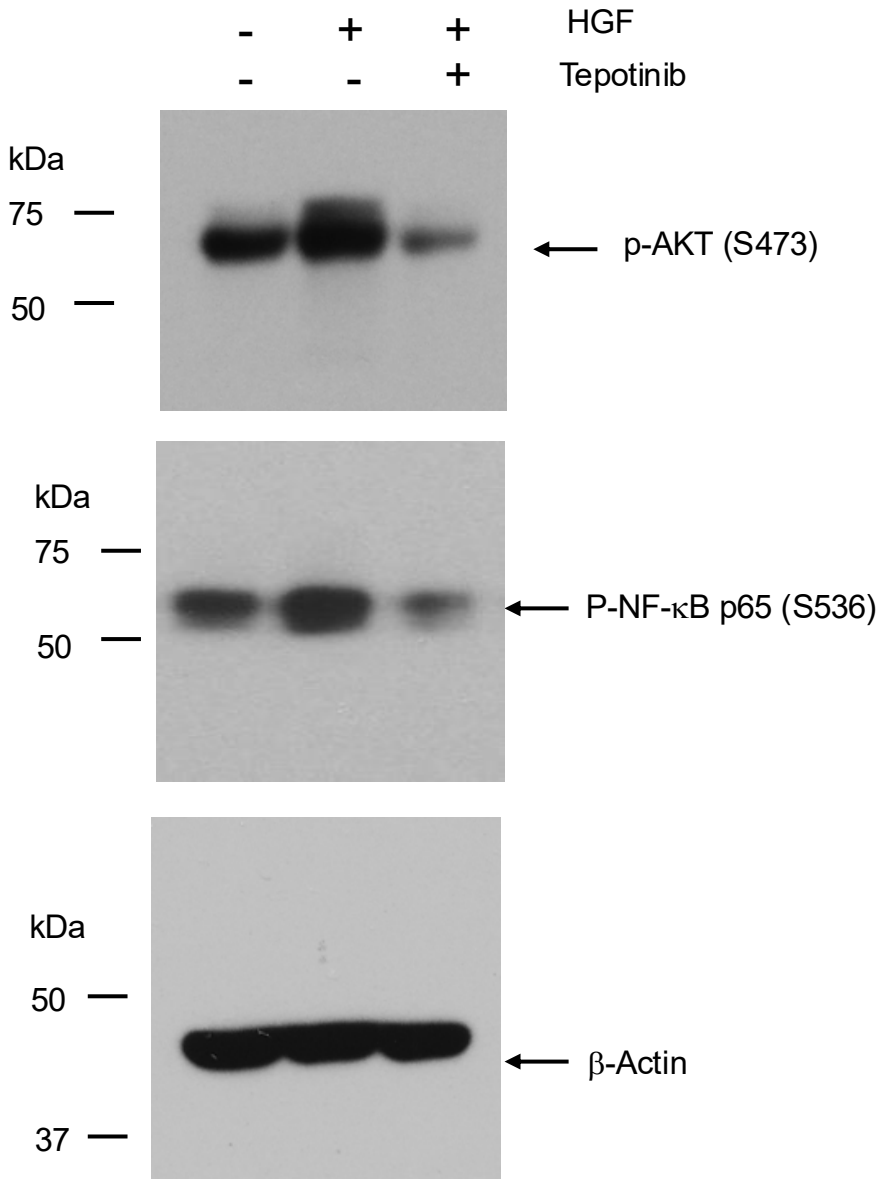
For Fig. 1A



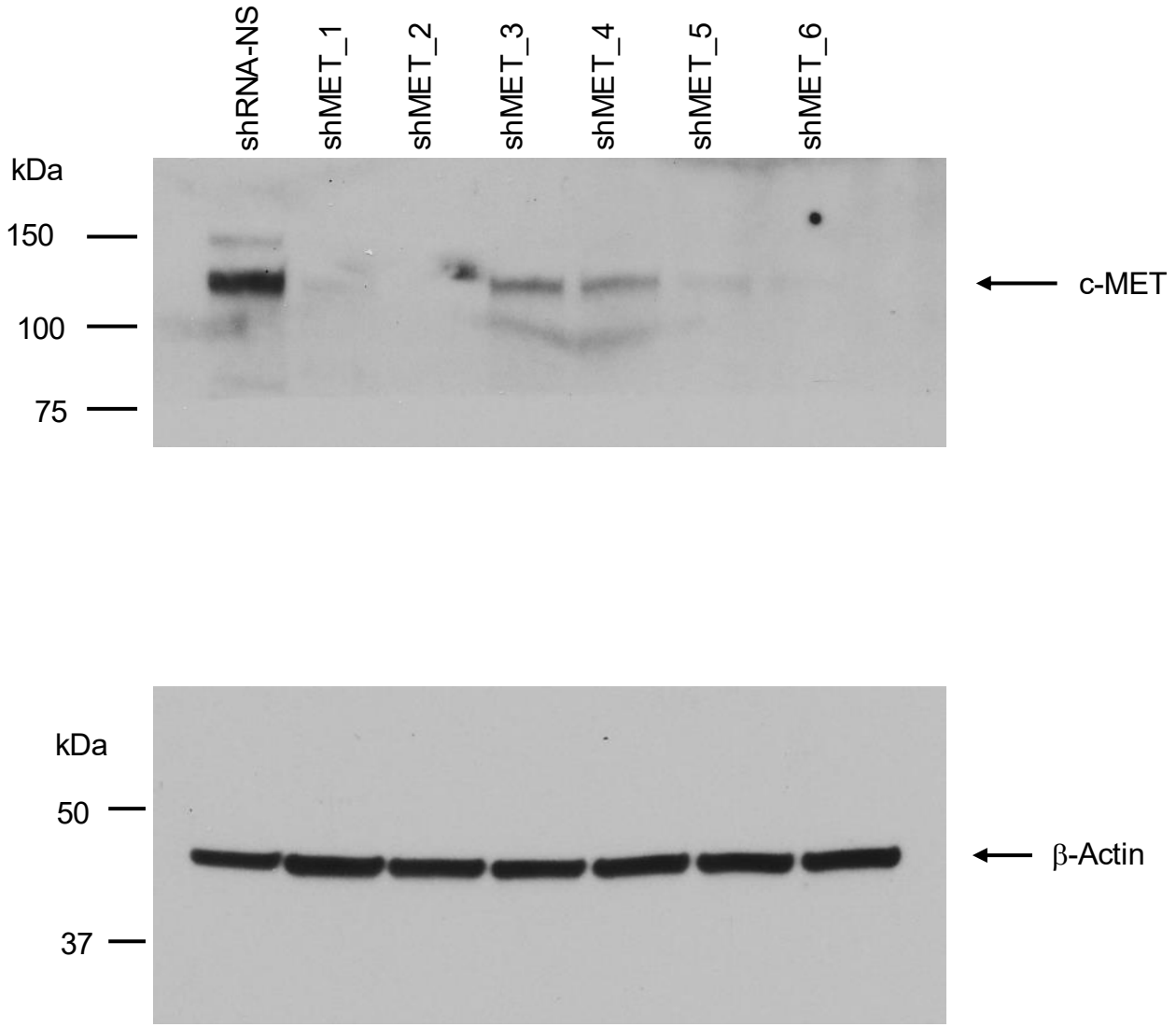
For Fig. 1E



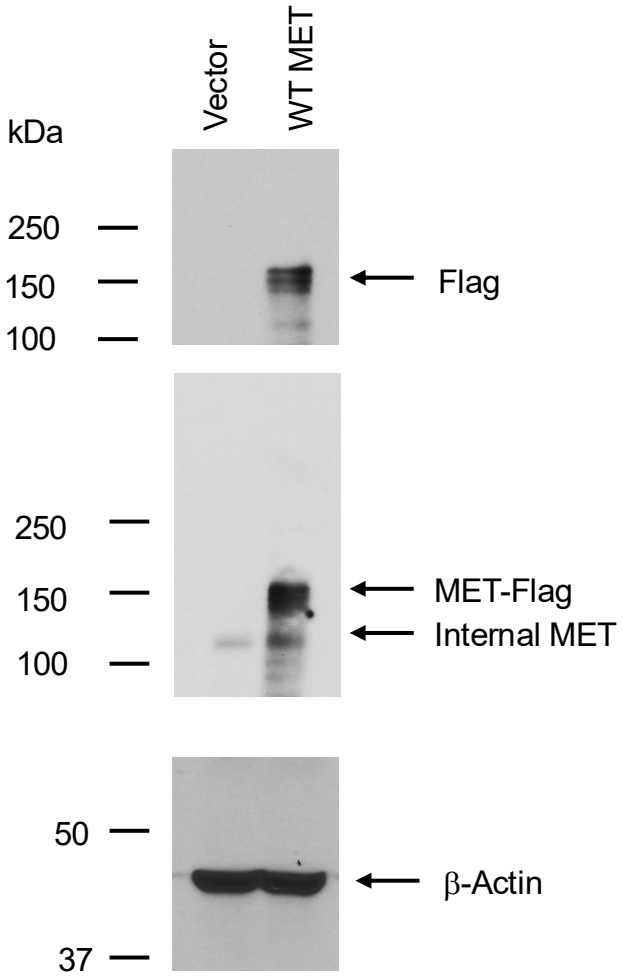
For Fig. 1H



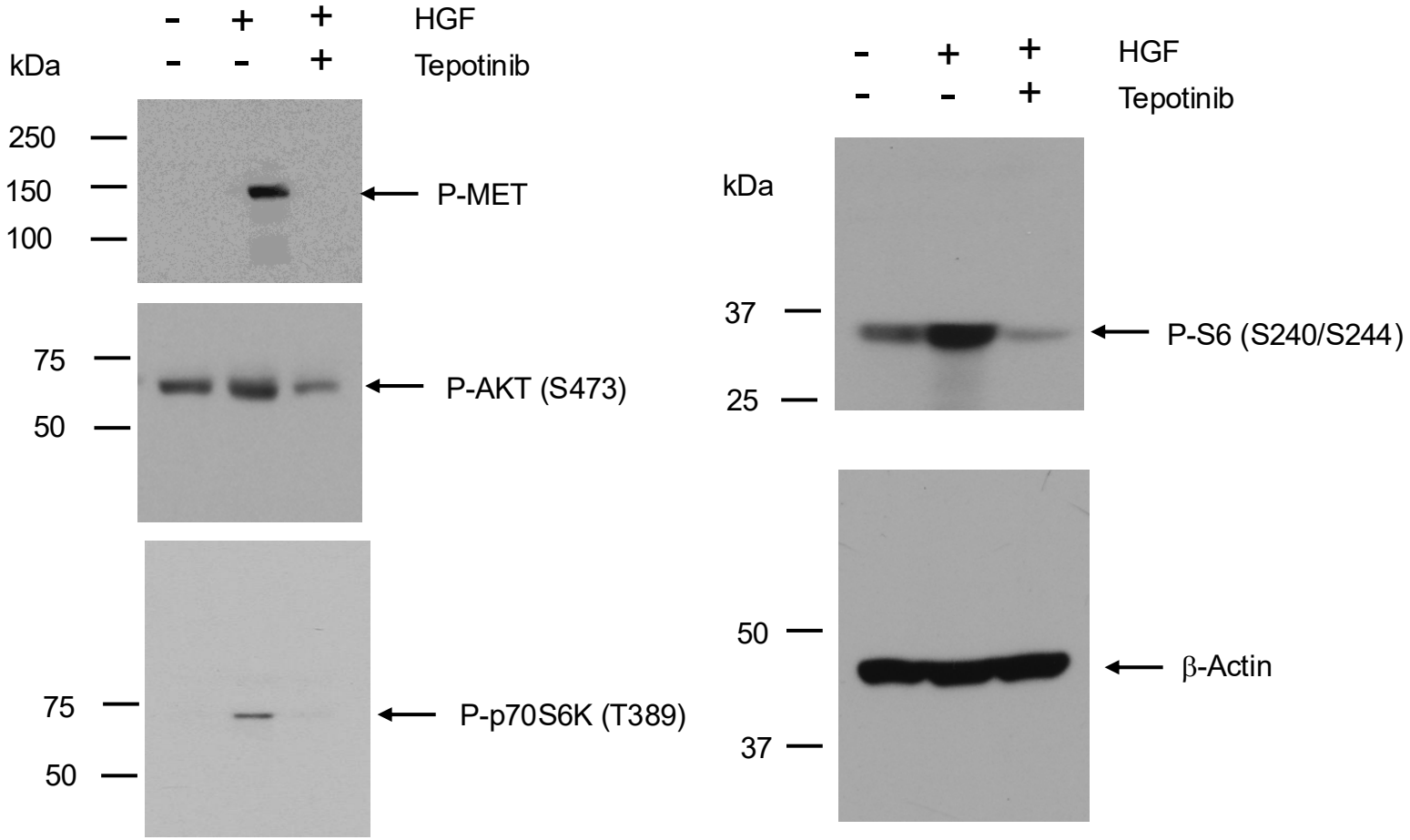
For Fig. 1I



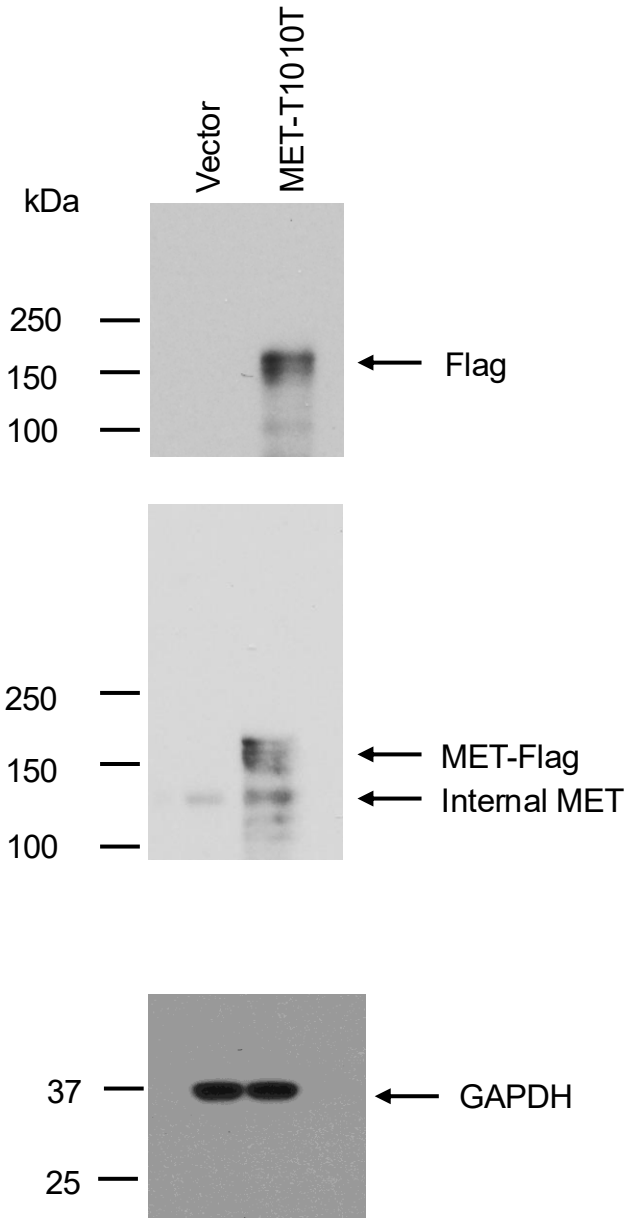
For Fig. 2C



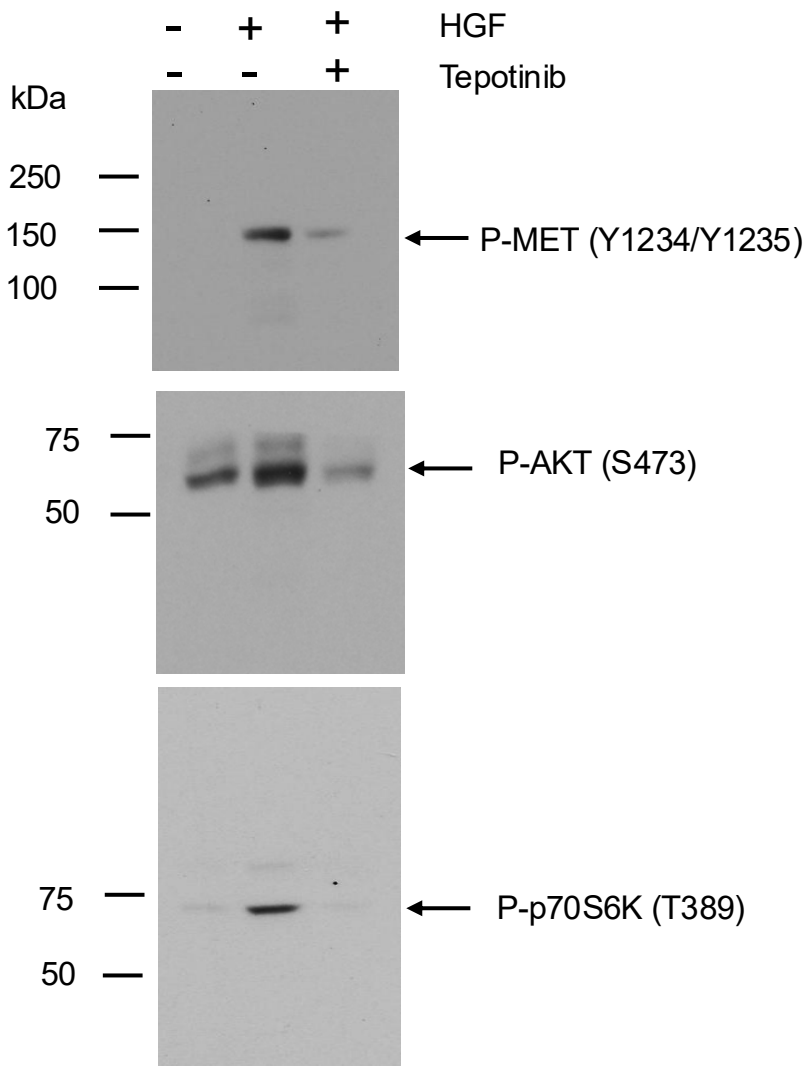
For Fig. 2N

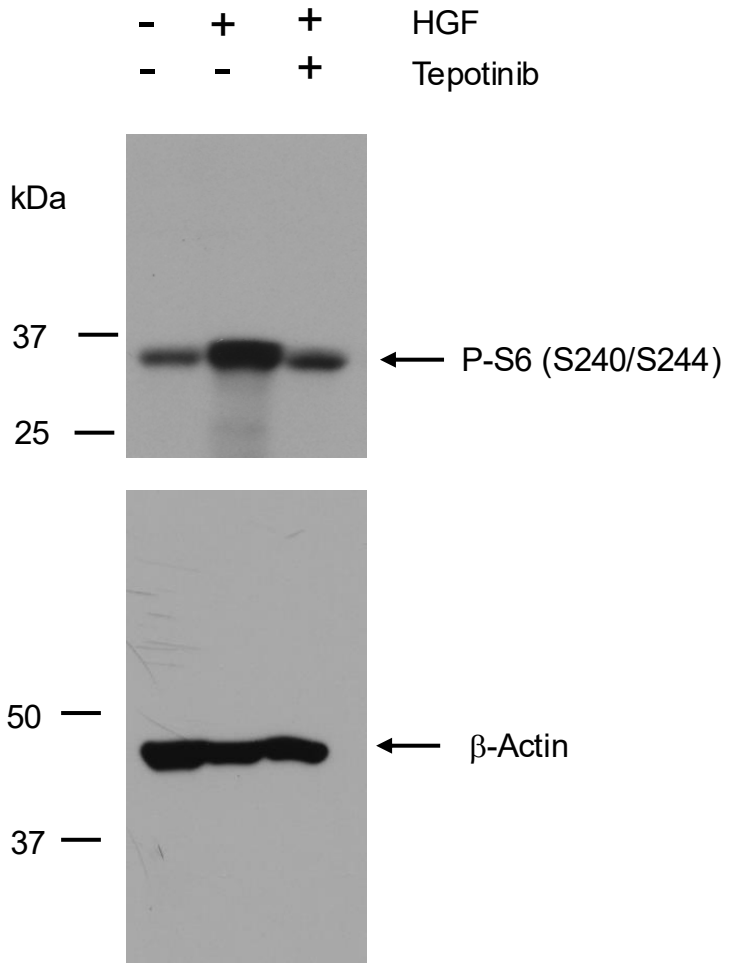


For Fig. 4C

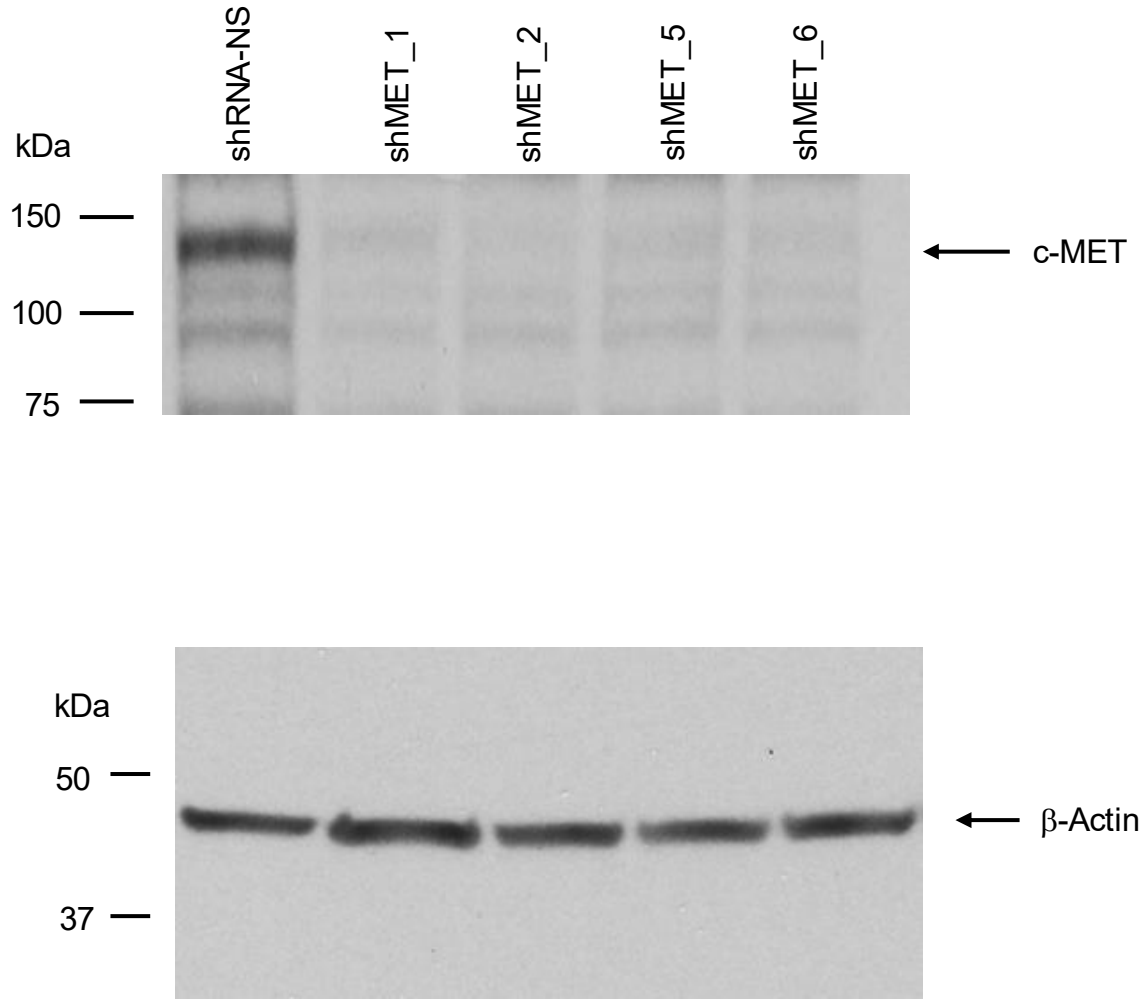


For Fig. 4M





For Fig. S1A


shRNA-NS
shMET_1
shMET_2
shMET_5
shMET_6
kDa
150
100
75
c-MET
kDa
50
37
β-Actin