

Supplementary Figure 1. MerTK and Axl activation loops are conserved in their sequences.

Sequence alignment of Axl and MerTK kinase domains, generated with UniProtKB sequences P30530 and Q12866, using the program ALINE [36]. The secondary structure of apo-MerTK PDB entry 7AB0 is superimposed on top of the sequences. Secondary structure elements are labelled according to Fabbro et al. [8]; with α -helices depicted as tubes, β -strands as arrows, 310 helices as spirals and disordered regions as dashed lines. The position of DFG-motif, APE-motif and A-loop are indicated, variant residues are highlighted in red.

Supplementary Figure 2. Binding analysis for MerTK by surface plasmon resonance.

Sensorgrams are presented for gilteritinib (A, B), LDC1267 (C, D), merestinib (E, F) and EX172 (G, H) for binding to dephosphorylated MerTK (A, C, E, G) and autophosphorylated MerTK (B, D, F, H).

Supplementary Figure 3. Disorder of the activation loop in MerTK crystal structures.

(A) The superposition of all MerTK PDB entries and apo structure 7AB0 highlights the conformational conformity of the kinase domain and the general absence of the A-loop. Sequences of all residues included in the coordinates were extracted and aligned, with A-loop residues 736-770 depicted in (B). (B) PDB ID and model chain are indicated. For clarity a reference sequence of MerTK was added at the bottom of the alignment, and the location of DFG-motif, APE-motif and A-loop highlighted.

Supplementary Table 1. Details and refinement statistics of the crystal structures presented.

Values in parentheses are for the highest-resolution shell.

PDB entry	7AB1	7AB2	7AAX	7AAY	7AAZ	7AB0
MerTK construct	GSHM_E571-V864, K591R/K693R/K702R/K856R	GSHM_E571-V864, K591R/K693R/K702R/K856R	GSHM_E571-V864, K591R/K693R/K702R/K856R	GSHM_E571-V864, Δ M659-Q662	GS_E571-V864	GSHM_E571-V864, K591R/K693R/K702R/K856R
ligand	gilteritinib	UNC2025	LDC1267	merestinib	EX172	apo
Complex formation	soak	soak	co-cryst.	co-cryst.	co-cryst.	N/A
Data Collection						
Beamline	DLS i03	DLS i04	DLS i03	DLS i02	DLS i03	DLS i04
Date	2020-01-23	2020-02-07	2016-07-22	2016-08-02	2017-08-11	2019-12-05
Detector	Eiger 16M	Eiger 16M	PILATUS3 6M	PILATUS 6M-F	PILATUS3 6M	Eiger 16M
Wavelength (Å)	0.976254	0.979499	0.97623	0.97949	0.97627	0.97950
AutoPROC / STARANISO						
Space group	C 2 2 21	C 2 2 21	C 2 2 21	C 2 2 21	P 43 21 2	C 2 2 21
Cell: a b c (Å)	93.3 94.1 70.7	91.9 92.0 71.6	92.7 92.8 71.0	93.1 131.0 54.2	78.6 78.6 137.5	91.6 91.6 71.6
Cell: α β γ (°)	90.0 90.0 90.0	90.0 90.0 90.0	90.0 90.0 90.0	90.0 90.0 90.0	90.0 90.0 90.0	90.0 90.0 90.0
Resolution (Å)	46.66-1.93 (2.05-1.93)	48.14-1.78 (1.96-1.78)	65.59-1.76 (1.89-1.76)	46.56-1.86 (2.08-1.86)	68.25-1.86 (1.97-1.86)	48.04-1.74 (1.98-1.74)
Rmeas (%)	12.5 (126.9)	4.0 (118.1)	4.2 (81.1)	11.8 (91.0)	13.8 (227.8)	5.5 (98.4)
Reflections, total	100656 (4179)	119488 (5299)	139432 (4651)	120285 (3353)	403632 (18945)	114741 (5092)
Reflections, unique	18953 (949)	18168 (908)	23363 (1169)	19081 (954)	32643 (1634)	17430 (872)
Mean(I)/sd(I)	9.8 (1.5)	21.0 (1.5)	19.0 (1.5)	10.6 (1.4)	13.1 (1.4)	16.3 (1.7)
Completeness, ellipsoidal (%)	88.3 (56.3)	93.8 (64.0)	89.1 (42.9)	93.8 (63.6)	95.7 (59.4)	93.2 (67.3)
Multiplicity	5.3 (4.4)	6.6 (5.8)	6.0 (4.0)	6.3 (3.5)	12.4 (11.6)	6.6 (5.8)
CC(1/2) (%)	99.6 (80.8)	100.0 (63.5)	100.0 (70.2)	99.8 (58.2)	99.9 (53.8)	100.0 (70.9)
Model						
Structure Determination	molecular replacement	molecular replacement	molecular replacement	molecular replacement	molecular replacement	molecular replacement
molecules / AU	1	1	1	1	1	1
REFMAC5						
Rwork (%) / Rfree (%)	23.4 / 29.8	19.3 / 25.0	19.9 / 25.3	19.4 / 22.4	18.8 / 21.9	20.7 / 24.7

B value (\AA^2), protein	55.0	49.7	48.5	37.1	40.5	43.0
B value (\AA^2), ligand	65.3	82.6	46.9	28.9	30.6	NA
B value (\AA^2), water	51.8	48.0	46.5	34.6	44.5	44.0
B value (\AA^2), solvent	72.1	65.5	46.7	33.0	40.8	45.2
N° of atoms, protein	2075	2138	2154	2162	2279	2147
N° of atoms, ligand	40	35	41	41	43	NA
N° of atoms, water	54	89	87	117	132	132
N° of atoms, solvent	8	12	3	3	14	5
rmsd bond lengths (\AA)	0.012	0.013	0.012	0.009	0.012	0.009
rmsd bond angles ($^\circ$)	1.54	1.52	1.50	1.30	1.47	1.32
MOL Probity [37]						
Ramachandran favored (%)	95.5	97.0	97.0	97.4	97.6	98.5
Ramachandran outliers (%)	1.1	0.0	0.0	0.0	0.4	0.0

Supplementary Table 2. Biochemical inhibition of 395 human kinases by EX172.

Inhibition was determined at a compound concentration of 0.1 μ M (ThermoFisher SelectScreen Kinase Profiling Services). The table is sorted by mean inhibition.

Kinase Name	Mean Inhibition (%)	Molecular Target
MERTK (cMER)	101	c-mer Proto-Oncogene Tyrosine Kinase
MERTK (cMER)	98	c-mer Proto-Oncogene Tyrosine Kinase
AXL	97	AXL Receptor Tyrosine Kinase
CHEK2 (CHK2)	55	Checkpoint Kinase 2
NTRK1 (TRKA)	32	Neurotrophic Receptor Tyrosine Kinase Type 1
TYRO3 (RSE)	31	TYRO3 Protein Tyrosine Kinase
MST4	29	Mammalian STE20-like Protein Kinase 4
STK38L (NDR2)	28	Serine/Threonine Kinase 38 like
MAP2K4 (MEK4)	28	Mitogen-Activated Protein Kinase Kinase 4
SGKL (SGK3)	24	Serum/glucocorticoid Regulated Kinase 3
MAPK9 (JNK2)	22	Mitogen Activated Protein Kinase 9
CAMKK1 (CAMKKA)	21	Calmodulin Dependent Kinase Kinase Alpha
MAP2K1 (MEK1)	21	Mitogen Activated Protein Kinase Kinase 1
RPS6KA2 (RSK3)	21	Ribosomal Protein S6 Kinase polypeptide 2
PKN2 (PRK2)	20	Protein Kinase C Related Kinase 2
MELK	20	Maternal Embryonic Leucine Zipper Kinase
NLK	18	Nemo-like Kinase
CDK17/cyclin Y	18	PCTAIRE Protein Kinase 2
DNA-PK	18	DNA-dependent Protein Kinase
SNF1LK2	17	SNF1-like Kinase 2
PRKCG (PKC gamma)	17	Protein Kinase C gamma
LATS1	17	LATS, large tumor suppressor, homolog 1 (Drosophila)
AMPK (A1/B2/G3)	16	AMP-activated Protein Kinase?
FLT3	15	fms-Related Tyrosine Kinase 3
RPS6KB2 (p70S6Kb)	15	Ribosomal Protein S6 Kinase, 70kDa, polypeptide 2
STK22D (TSSK1)	14	Testis-specific Serine Kinase 1B
PRKCA (PKC alpha)	14	Protein Kinase C alpha
ZAP70	14	Zeta Chain Associated Protein Kinase
STK17B (DRAK2)	14	Serine/Threonine Kinase 17b
SRC	13	v-src sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog
MAP4K1 (HPK1)	13	Mitogen-Activated Protein Kinase Kinase Kinase Kinase 1
STK24 (MST3)	13	Serine/Threonine Kinase 24 (STE20 homolog, yeast)
ACVR1B (ALK4)	13	Activin A Receptor type IB
MAPK10 (JNK3)	13	Mitogen-activated protein kinase 10
MAP2K1 (MEK1)	13	Mitogen Activated Protein Kinase Kinase 1
TAOK2 (TAO1)	12	TAO Kinase 2
CDC42 BPG (MRCKG)	12	CDC42 Binding Protein Kinase gamma (DMPK-like)
CDC42 BPA (MRCKA)	12	CDC42 Binding Protein Kinase alpha (DMPK-like)
STK38 (NDR)	12	Serine/Threonine kinase 38
PAK3	12	p21 (CDKN1A)-activated Kinase 3
CSNK2A1 (CK2 alpha 1)	12	Casein Kinase 2, alpha 1 polypeptide
IRAK3	12	Interleukin-1 Receptor-Associated Kinase 3
DAPK2	12	Death-Associated Protein Kinase 2
TBK1	12	TANK-binding Kinase 1
PRKCE (PKC epsilon)	11	Protein Kinase C epsilon
MAP2K2 (MEK2)	11	Mitogen-Activated Protein Kinase Kinase 2
LYN B	11	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog
STK25 (YSK1)	11	Serine/Threonine Kinase 25 (STE20 homolog, yeast)
PRKCN (PKD3)	11	Protein Kinase D3
CSNK1G1 (CK1 gamma 1)	11	Casein Kinase 1 gamma 1
PIK3CG (p110 gamma)	11	Phosphoinositide 3 Kinase Gamma (PI3K Gamma)
VRK2	11	Vaccinia Related Kinase 2
EPHA4	11	EPH Receptor A4
PHKG1	11	Phosphorylase Kinase, gamma 1 (muscle)
IKBKE (IKK epsilon)	11	I Kappa B Kinase Epsilon

SRMS (Srm)	11	Src-related Kinase Lacking C-terminal Regulatory Tyrosine and N-terminal Myristylation Sites
CDK7/cyclin H/MNAT1	11	Cyclin Dependent Kinase 6:Cyclin H:MNAT1
DYRK1A	11	Dual Specificity Tyrosine Phosphorylation Regulated Kinase 1A
SIK3	11	SIK Family Kinase 3
SBK1	10	SH3-Binding Domain Kinase 1
MAPK14 (p38 alpha) Direct	10	Mitogen-Activated Protein Kinase 14
MAPK7 (ERK5)	10	Mitogen-Activated Protein Kinase 7
NEK6	10	NIMA (never in mitosis gene a)-related kinase 6
PRKCB2 (PKC beta II)	10	Protein Kinase C beta 1
BRAF	10	v-raf Murine Sarcoma Viral Oncogene Homolog B1
RAF1 (cRAF) Y340D Y341D	10	v-raf murine leukemia viral oncogene homolog 1
TAOK3 (JIK)	10	TAO Kinase 3
SGK2	9	Serum/gluocorticoid Regulated Kinase 2
PHKG2	9	Phosphorylase Kinase gamma 2
PKN1 (PRK1)	9	Protein Kinase N1
TEK (Tie2)	9	Tie2 receptor tyrosine kinase
CSNK2A2 (CK2 alpha 2)	9	Casein Kinase 2 alpha prime polypeptide
MUSK	9	Muscle Skeletal Receptor Tyrosine Kinase
CSNK1A1 (CK1 alpha 1)	9	Casein Kinase 1, alpha 1
KDR (VEGFR2)	9	Kinase Insert Domain Receptor
PIK3C2A (PI3K-C2 alpha)	9	PIK3C2A phosphatidylinositol-4-phosphate 3-kinase, catalytic subunit type 2 alpha
MAPK11 (p38 beta)	9	Stress Activated Protein Kinase 2b
CDKL5	9	Cyclin-Dependent Kinase-like 5
DCAMKL1 (DCLK1)	9	Doublecortin-like Kinase 1
CSNK1G2 (CK1 gamma 2)	9	Casein Kinase 1 gamma 2
MAP2K6 (MKK6)	9	Mitogen Activated Protein Kinase Kinase 6
KSR2	9	Kinase Suppressor of Ras 2
PAK1	9	P21 Activated Kinase 1
TTK	8	TTK Protein Kinase
PIK3C2G (PI3K-C2 gamma)	8	Phosphoinositide-3-Kinase, class 2, gamma polypeptide
MAPKAPK3	8	Mitogen-Activated Protein Kinase-Activated Protein Kinase 3
PRKD2 (PKD2)	8	Protein Kinase D2
PRKACG (PRKAC gamma)	8	Protein Kinase, cAMP-dependent, catalytic, gamma
AMPK (A2/B1/G3)	8	AMP-activated Protein Kinase?
PAK2 (PAK65)	8	p21 (CDKN1A)-activated kinase 2
FGFR4	8	Fibroblast Growth Factor Receptor 4
FYN	8	FYN oncogene related to SRC, FGR, YES
INSRR (IRR)	8	Insulin Receptor-Related Receptor
MAP4K3 (GLK)	8	Mitogen-Activated Protein Kinase Kinase Kinase Kinase 3
MAP4K5 (KHS1)	8	Mitogen-Activated Protein Kinase Kinase Kinase Kinase 5
CAMK4 (CaMKIV)	8	Calcium/calmodulin-Dependent Protein Kinase IV
ULK3	8	Unc-51-like kinase 3
CAMK2D (CaMKII delta)	8	Calcium/calmodulin-Dependent Protein Kinase (CaM kinase) II delta
PDK1	8	3-Phosphoinositide Dependent Protein Kinase-1
CDK5 (Inactive)	8	Cyclin Dependent Kinase 5
ROCK2	8	Rho Associated, Coiled Coil Containing Protein Kinase 2
MAPKAPK2	8	MAPK Activated Protein Kinase-2
IRAK1	8	Interleukin-1 Receptor-associated Kinase 1
PRKCQ (PKC theta)	8	Protein Kinase C theta
PAK6	8	p21 Activated Kinase 6
FRK (PTK5)	8	Fyn-related Kinase
TNIK	8	TRAF2 and NCK Interacting Kinase
STK32B (YANK2)	7	Serine/Threonine Kinase 32B
AMPK A2/B1/G1	7	AMP-activated Protein Kinase?
LYN A	7	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog
MARK4	7	MAP/microtubule Affinity-Regulating Kinase 4
CSK	7	C-Src Kinase
PRKG1	7	Protein Kinase, cGMP-dependant, type 1
ROCK1	7	Rho Associated, Coiled Coil Containing Protein Kinase 1
CLK1	7	CDC-like Kinase 1
MASTL	7	Microtubule Associated Serine/threonine kinase like
TNK1	7	Tyrosine Kinase, non-Receptor, 1
TEC	7	Tec protein tyrosine kinase

LATS2	7	LATS, large tumor suppressor, homolog 2 (Drosophila)
ACVRL1 (ALK1)	7	Activin A Receptor Type II-like 1
SLK	7	STE20-like kinase
HIPK4	7	Homeodomain Interacting Protein Kinase 4
HCK	7	Hemopoietic Cell Kinase
RET V804L	7	Ret Proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, Hirschsprung disease)
ULK1	7	Unc-51-like Kinase 1 (C. elegans)
LCK	6	Lymphocyte-Specific Protein Tyrosine Kinase
GRK6	6	G protein-coupled receptor kinase 6
CAMKK2 (CaMKK beta)	6	Calmodulin Dependent Kinase Kinase Beta
RPS6KB1 (p70S6K)	6	P70S6 Kinase
ERN1	6	Endoplasmic Reticulum to Nucleus Signaling 1
CAMK2G (CaMKII gamma)	6	Calcium/calmodulin-Dependent Protein Kinase (CaM kinase) II gamma
MAP4K4 (HGK)	6	Mitogen Activated Protein Kinase Kinase Kinase Kinase 4
PRKG2 (PKG2)	6	Protein Kinase, cGMP-dependent, type II
NEK1	6	NIMA (never in mitosis gene a)-related Kinase 1
ACVR2B	6	Activin A Receptor, type IIB
GSG2 (Haspin)	6	germ cell associated 2 haspin
IGF1R	6	Insulin Like Growth Factor Receptor 1
EGFR (ErbB1)	6	Epidermal Growth Factor Receptor
PRKCZ (PKC zeta)	6	Protein Kinase C zeta
CDK18/cyclin Y	6	PCTAIRE Protein Kinase 3
PEAK1	6	Pseudopodium Enriched Atypical kinase 1
PRKD1 (PKC mu)	6	Protein Kinase D1
CDK2/cyclin O	6	Cyclin Dependent Kinase 2:Cyclin O
TNK2 (ACK)	6	Tyrosine Kinase, non-Receptor, 2
DMPK	6	Dystrophia Myotonica-protein Kinase
RPS6KA4 (MSK2)	6	Ribosomal Protein S6 Kinase polypeptide 4
TGFBR2	6	Transforming Growth Factor - Beta Receptor Type 2
AKT3 (PKB gamma)	6	v-akt murine thymoma viral oncogene homolog 3
MAPK8 (JNK1)	6	Mitogen Activated Protein Kinase 8
GRK5	6	G protein-coupled receptor kinase 5
FGFR3	5	Fibroblast Growth Factor Receptor 3
CAMK1G (CAMKI gamma)	5	Calcium/Calmodulin-dependent Protein Kinase IG
PKMYT1	5	Protein Kinase, Membrane Associated Tyrosine/Threonine 1
PIM1	5	PIM 1 oncogene
CSNK1E (CK1 epsilon)	5	Casein Kinase 1, epsilon
NEK7	5	NIMA (never in mitosis gene a)-Related Kinase 7
PRKACB (PRKAC beta)	5	Protein Kinase, cAMP-dependent, catalytic, beta
AURKA (Aurora A)	5	Aurora Kinase A
AURKC (Aurora C)	5	Aurora Kinase C
CDK9/cyclin T1	5	Cyclin Dependent Kinase 9:Cyclin T
PLK2	5	Polo-like Kinase 2
MAPK13 (p38 delta)	5	Mitogen Activated Protein Kinase 13
CDK8/cyclin C	5	Cyclin Dependent Kinase 8:Cyclin C
TLK2	5	Tousled-like Kinase 2
STK17A (DRAK1)	5	Serine/Threonine Kinase 17a (apoptosis-inducing)
YES1	5	v-yes-1 Yamaguchi Sarcoma Viral Oncogene Homolog 1
DDR2	5	Discoidin Domain Receptor Family Member 2
EPHA5	5	EPH Receptor A5
CSNK1A1L	4	Casein Kinase 1, alpha 1-like
MAPK3 (ERK1)	4	Mitogen Activated Protein Kinase 3
DYRK3	4	Dual Specificity Tyrosine Phosphorylated Regulated Kinase 3
RPS6KA1 (RSK1)	4	MAPK Activated Protein Kinase-1a
MKNK2 (MNK2)	4	MAP Kinase Interacting Serine/Threonine Kinase 2
BMX	4	BMX Non-Receptor Tyrosine Kinase
PDGFRB (PDGFR beta)	4	Platelet Derived Growth Factor Receptor Beta
LIMK1	4	LIM Domain Kinase 1
JAK2 JH1 JH2	4	Janus Kinase 2
AMPK (A1/B1/G2)	4	AMP-activated Protein Kinase?
PI4K2A (PI4K2 alpha)	4	Phosphatidylinositol 4-kinase type 2 alpha
PDK1 Direct	4	3-Phosphoinositide Dependent Protein Kinase-1

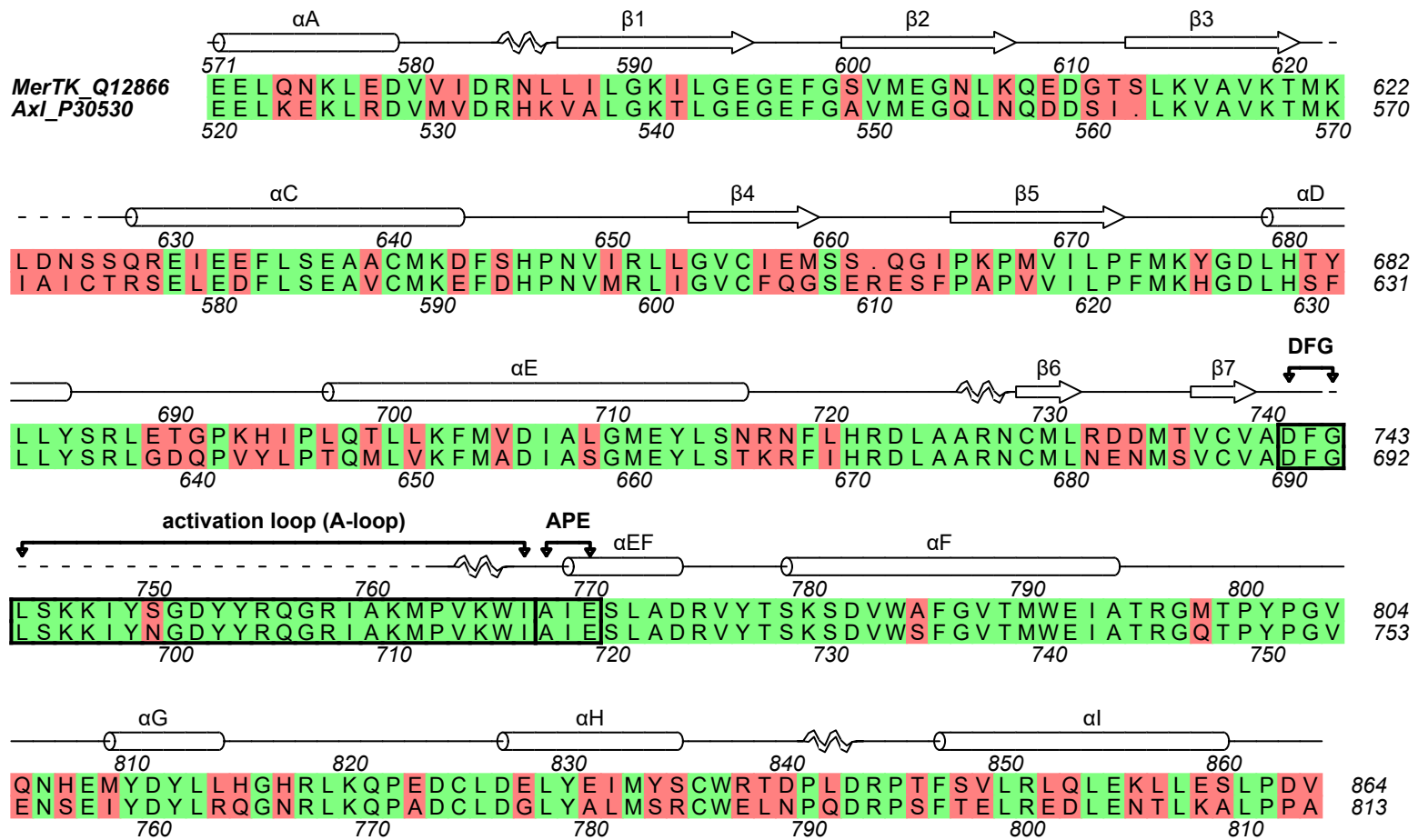
DYRK2	4	Dual Specificity Tyrosine Phosphorylation Regulated Kinase 2
CSF1R (FMS)	4	Colony Stimulating Factor 1 Receptor
BRAF	4	v-raf Murine Sarcoma Viral Oncogene Homolog B1
FLT4 (VEGFR3)	4	Vascular endothelial growth factor receptor 3
NEK8	4	NIMA (never in mitosis gene a)- related Kinase 8
EPHA3	4	EPH Receptor A3
STK23 (MSSK1)	4	Serine/Threonine Kinase 23
CDK2/cyclin A	4	Cyclin Dependent Kinase 2:Cyclin A
GRK7	4	G Protein-coupled Receptor Kinase 7
AMPK (A2/B2/G2)	4	AMP-activated Protein Kinase?
PTK2B (FAK2)	4	PTK2B Protein Tyrosine Kinase 2 beta
MAPK12 (p38 gamma)	4	Mitogen-Activated Protein Kinase 12
MARK3	4	MAP / Microtubule Affinity-Regulating Kinase 3
ACVR2A	4	Activin A Receptor, type IIA
CAMK2B (CaMKII beta)	3	Calcium/calmodulin-Dependent Protein Kinase (CaM kinase) II beta
MYO3B (MYO3 beta)	3	Myosin IIIB
MAPK14 (p38 alpha) Direct	3	Mitogen-Activated Protein Kinase 14
STK3 (MST2)	3	Serine/Threonine Kinase 3 (STE20 homolog, yeast)
STK22B (TSSK2)	3	Testis-specific Serine Kinase 2
PRKX	3	Protein Kinase, X-linked
AAK1	3	AP2 Associated Kinase 1
MAPKAPK2	3	MAPK Activated Protein Kinase-2
CHUK (IKK alpha)	3	I Kappa B Kinase 1
MAP2K6 (MKK6)	3	Mitogen Activated Protein Kinase Kinase 6
FLT1 (VEGFR1)	3	Vascular Endothelial Growth Factor Receptor 1
NEK4	3	NIMA (never in mitosis gene a)- related Kinase 4
CLK2	3	CDC-like kinase 2
PTK6 (Brk)	3	Protein Tyrosine Kinase 6
RPS6KA3 (RSK2)	3	MAPK Activated Protein Kinase-1b
MAP3K7/MAP3K7IP1 (TAK1-TAB1)	3	Mitogen-Activated Protein Kinase Kinase Kinase 7
TGFBR1 (ALK5)	3	Transforming growth factor, beta receptor I
EPHB2	3	EPH Receptor B2
MARK2	3	MAP/microtubule Affinity-Regulating Kinase 2
MARK1 (MARK)	3	MAP/microtubule Affinity-Regulating Kinase 1
TYK2	3	Tyrosine Kinase 2
NEK9	3	NIMA (never in mitosis gene a)- related Kinase 9
ROS1	3	v-ros UR2 Sarcoma Virus Oncogene Homolog 1
PTK2 (FAK)	3	Focal Adhesion Kinase 1
FGFR1 V561M	3	Fibroblast Growth Factor Receptor 1
PDGFRA (PDGFR alpha)	3	Platelet Derived Growth Factor Receptor Alpha
EPHA7	3	EPH Receptor A7
TXK	3	TXK Tyrosine Kinase
HIPK3 (YAK1)	3	Homeodomain-interacting Protein Kinase 3
WEE1	3	WEE1 homolog (S. pombe)
PIM3	2	PIM 3 oncogene
ADRBK1 (GRK2)	2	Adrenergic, Beta Receptor Kinase 1
PAK7 (KIAA1264)	2	p21 Activated Kinase 5
HIPK1 (Myak)	2	Homeodomain Interacting Protein Kinase 1
EPHB1	2	EPH Receptor B1
ICK	2	Lymphocyte-Specific Protein Tyrosine Kinase
DCAMKL2 (DCK2)	2	Doublecortin and CaM Kinase-like 2
CDK5/p35	2	Cyclin Dependent Kinase 5
ERN2	2	Endoplasmic Reticulum to Nucleus signaling 2
MAP4K2 (GCK)	2	Mitogen-Activated Protein Kinase Kinase Kinase Kinase 2
FES (FPS)	2	FES proto-oncogene, tyrosine kinase
IKKB (IKK beta)	2	I Kappa B Kinase 2
ERBB4 (HER4)	2	v-erb-a erythroblastic leukemia viral oncogene homolog 4
FGFR1	2	Fibroblast Growth Factor Receptor 1
SGK (SGK1)	2	Serum Glucocorticoid-regulated Kinase 1
PRKCB1 (PKC beta I)	2	Protein Kinase C beta 1
ABL2 (Arg)	2	v-abl Abelson Murine Leukemia Viral oncogene homolog 2
MAPK9 (JNK2)	2	Mitogen Activated Protein Kinase 9

CDK14 (PFTK1)/cyclin Y	2	PFTAIRE Protein Kinase 1
NEK2	2	NIMA (never in mitosis gene a)-related Kinase 2
GSK3A (GSK3 alpha)	2	Glycogen Synthase Kinase-3 alpha
CDK1/cyclin A2	2	Cyclin-Dependent kinase 1:Cyclin A2
EPHB3	2	EPH Receptor B3
PRKCH (PKC eta)	2	Protein Kinase C eta
MYLK (MLCK)	1	Myosin, Light chain Kinase
DYRK4	1	Dual-Specificity Tyrosine Phosphorylation Regulated kinase 4
HIPK2	1	Homeodomain-interacting Protein Kinase 2
EPHA1	1	EPH Receptor A1
CDC7/DBF4	1	Cell Division Cycle 7 Homolog (<i>S. cerevisiae</i>)
ULK2	1	Unc-51-Like Kinase 2
PASK	1	PAS Domain Containing Serine/threonine Kinase
MAPKAPK5 (PRAK)	1	p38 Regulated Activated Kinase
BTK	1	Bruton agammaglobulinemia Tyrosine Kinase
RPS6KA5 (MSK1)	1	Mitogen and Stress Activated Protein Kinase 1
CDK9 (Inactive)	1	Cyclin-Dependent Kinase 9 (CDC2-related kinase)
CDK11 (Inactive)	1	Cyclin-Dependent Kinase 19
DAPK3 (ZIPK)	1	Death-Associated Protein Kinase 3
CDK1/cyclin B	1	Cyclin Dependent Kinase 1:Cyclin B
SRPK1	1	SFRS Protein Kinase 1
EPHA2	1	EPH Receptor A2
CSNK1D (CK1 delta)	1	Casein Kinase 1 delta
GSK3B (GSK3 beta)	1	Glycogen Synthase Kinase-3 beta
NTRK3 (TRKC)	1	Neurotrophic Tyrosine Kinase, Receptor, type 3
PI4KA (PI4K alpha)	1	Phosphatidylinositol 4-kinase type III alpha
TAOK1	1	TAO kinase 1
CDC42 BPB (MRCKB)	0	CDC42 Binding Protein Kinase beta (DMPK-like)
MLCK (MLCK2)	0	Myosin Light Chain Kinase 3
ZAK	0	Sterile Alpha Motif and Leucine Zipper containing Kinase AZK
BLK	0	B Lymphoid Tyrosine Kinase
FER	0	Fer (fps/fes related) Tyrosine Kinase phosphoprotein NCP94
AMPK A2/B1/G1	0	AMP-activated Protein Kinase?
PAK4	0	P21 Activated Kinase 4
NTRK2 (TRKB)	0	Neurotrophic Receptor Tyrosine Kinase Type 2
AMPK (A1/B1/G3)	0	AMP-activated Protein Kinase?
NIM1K	0	Serine/threonine-protein Kinase NIM1
CLK3	0	CDC-like Kinase 3
CDK9/cyclin K	0	Cyclin-Dependent Kinase 9 (CDC2-related kinase)
AMPK (A2/B1/G2)	0	AMP-activated Protein Kinase?
PLK1	0	Polo-like Kinase 1
RET	0	Ret Proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, Hirschsprung disease)
PI4K2B (PI4K2 beta)	0	Phosphatidylinositol 4 Kinase?
MAPK15 (ERK7)	0	Mitogen-Activated Protein Kinase 15
ALK	0	Anaplastic Lymphoma Kinase
PLK4	0	Polo-like Kinase 4 (<i>Drosophila</i>)
AKT1 (PKB alpha)	0	v-akt murine thymoma viral oncogene homolog 1
SIK1	0	Salt-Inducible kinase 1
INSR	0	Insulin Receptor
TLK1	0	Tousled-like Kinase 1
SYK	0	Spleen tyrosine kinase
MLK4	0	Mixed Lineage Kinase 4
AMPK (A1/B2/G1)	0	AMP-activated Protein Kinase?
MAP3K10 (MLK2)	-1	Mitogen-Activated Protein Kinase Kinase Kinase 10
ABL1	-1	v-abl Abelson Murine Leukemia Viral oncogene homolog 1
GAK	-1	Cyclin G Associated Kinase
CAMK2A (CaMKII alpha)	-1	Calcium/calmodulin-Dependent Protein Kinase (CaM kinase) II, alpha
PIK3CB/PIK3R1 (p110 beta/p85 alpha)	-1	Phosphoinositide 3 Kinase Beta (PI3K Beta)
RIPK2	-1	Receptor-Interacting serine/threonine Kinase 2
MAPK1 (ERK2)	-1	Mitogen Activated Protein Kinase 1
MAP3K11 (MLK3)	-1	Mitogen-Activated Protein Kinase Kinase Kinase 11

LTK (TYK1)	-1	Leukocyte Tyrosine Kinase
FGR	-1	Gardner-Rasheed feline sarcoma viral (v-fgr) oncogene homolog
EPHB4	-1	EPH receptor B4
CLK4	-2	CDC-like Kinase 4
EIF2AK2 (PKR)	-2	Eukaryotic Translation Initiation Factor 2-alpha Kinase 2
AMPK (A2/B2/G3)	-2	AMP-activated Protein Kinase?
MYO3A (MYO3 alpha)	-2	Myosin IIIA
STK33	-2	Serine/Threonine Kinase 33
PLK3	-2	Polo-like Kinase 3
MAP3K14 (NIK)	-2	Mitogen-Activated Protein Kinase Kinase Kinase 14
LRRK2 FL	-2	Leucine-rich Repeat Kinase 2
CDK16 (PCTK1)/cyclin Y	-2	PCTAIRE Protein Kinase 1
MAP3K19 (YSK4)	-2	Yeast Sps1/Ste20-Related Kinase 4 (S. cerevisiae)
EGFR (ErbB1) T790M L858R	-2	Epidermal Growth Factor Receptor
MAPK10 (JNK3)	-2	Mitogen-activated protein kinase 10
CSNK1G3 (CK1 gamma 3)	-2	Casein Kinase 1 gamma 3
BRSK2	-2	BR Serine/Threonine Kinase 2
MAP2K2 (MEK2)	-2	Mitogen-Activated Protein Kinase Kinase 2
NUAK2	-2	NUAK Family, SNF1-like Kinase, 2
MET (cMet)	-2	c-met Tyrosine Kinase (MTK)
BMPR2	-3	Bone Morphogenetic Protein Receptor, type II (Serine/Threonine Kinase)
CDK5/p25	-3	Cyclin Dependent Kinase 5
MAP3K8 (COT)	-3	Mitogen-Activated Protein Kinase Kinase Kinase 8
ADRBK2 (GRK3)	-3	Adrenergic, Beta Receptor kinase 2
CAMK1D (CaMKI delta)	-3	Calcium/calmodulin-Dependent Protein Kinase I delta
SPHK2	-3	Sphingosine Kinase 2
RET V804M	-3	Ret Proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, Hirschsprung disease)
ADCK3	-3	Chaperone, ABC1 activity of bc1 complex homolog (S. pombe)
MAP2K5 (MEK5)	-3	Mitogen-activated Protein Kinase Kinase 5
AMPK (A2/B2/G1)	-3	AMP-activated Protein Kinase?
MAP3K2 (MEKK2)	-3	Mitogen-Activated Protein Kinase Kinase Kinase 2
FRAP1 (mTOR)	-3	FK506 binding protein 12-rapamycin associated protein 1
MAP3K5 (ASK1)	-4	Mitogen-Activated Protein Kinase Kinase Kinase 5
PRKCD (PKC delta)	-4	Protein Kinase C delta
MKNK1 (MNK1)	-4	MAP Kinase Interacting Serine/Threonine Kinase 1
EPHA8	-4	EPH Receptor A8
MYLK2 (skMLCK)	-4	Myosin Light Chain Kinase 2
GRK1	-4	G Protein-coupled Receptor Kinase 1
STK4 (MST1)	-4	Serine/Threonine Kinase 4
CDK2/cyclin A1	-4	Cyclin Dependent Kinase 2:Cyclin A
SRPK2	-5	SFRS Protein Kinase 2
PIK3C2B (PI3K-C2 beta)	-5	Phosphoinositide-3-Kinase, class 2, beta polypeptide
MATK (HYL)	-5	Megakaryocyte-associated Tyrosine Kinase
ITK	-5	IL2 Inducible T Cell Kinase
DDR1	-5	Discoidin Domain Receptor family, member 1
ACVR1 (ALK2)	-5	Activin A Receptor, type I
PIK3C3 (hVPS34)	-5	Phosphoinositide-3-kinase, Class 3
CAMK1 (CaMK1)	-6	Calcium/Calmodulin-Dependent Protein Kinase 1
BMPR1A (ALK3)	-6	Bone Morphogenetic Protein Receptor, type IA
EPHA6	-6	EPH Receptor A6
PRKCI (PKC iota)	-6	Protein Kinase C iota
DYRK1B	-6	Dual-specificity Tyrosine Phosphorylation Regulated Kinase 1B
RIPK3	-6	Receptor-Interacting Serine-Threonine Kinase 3
JAK2	-7	Janus Kinase 2
RPS6KA6 (RSK4)	-7	Ribosomal Protein S6 Kinase polypeptide 6
SPHK1	-7	Sphingosine Kinase 1
STK16 (PKL12)	-7	Serine/Threonine Kinase 16
CHEK1 (CHK1)	-7	Checkpoint Kinase I
MINK1	-7	Misshapen-like Kinase 1
ERBB2 (HER2)	-7	Erythroblastic leukemia viral oncogene homolog 2 Erythroblastic leukemia viral oncogene homolog 2
TESK1	-7	Testis-Specific Kinase 1

MAP3K9 (MLK1)	-8	Mitogen-Activated Protein Kinase Kinase Kinase 9
FGFR2	-8	Fibroblast Growth Factor Receptor 2
BRSK1 (SAD1)	-8	BR Serine/threonine Kinase 1
GRK4	-8	G Protein-coupled Receptor Kinase 4
AKT2 (PKB beta)	-8	v-akt murine thymoma viral oncogene homolog 2
LIMK2	-8	LIM domain Kinase 2
PRKACA (PKA)	-8	Protein Kinase, cAMP-dependent, catalytic, alpha
LRRK2	-9	Leucine-rich Repeat Kinase 2
IRAK4	-9	Interleukin-1 Receptor-Associated Kinase 4
STK32C (YANK3)	-9	Serine/Threonine Kinase 32C
DAPK1	-9	Death-Associated Protein Kinase 1
JAK3	-10	Janus Kinase 3
JAK1	-10	Janus Kinase 1
STK39 (STLK3)	-10	Serine Threonine Kinase 39 (STE20/SPS1 homolog, yeast)
MAP3K3 (MEKK3)	-10	Mitogen-Activated Protein Kinase Kinase Kinase 3
WNK2	-10	WNK lysine deficient Protein Kinase 2
CDK3/cyclin E1	-10	Cyclin Dependent Kinase 3:Cyclin E1
PIK3CA/PIK3R1 (p110 alpha/p85 alpha)	-11	Phosphoinositide-3-kinase, catalytic, alpha Polypeptide:phosphoinositide-3-kinase, regulatory subunit 1 (alpha) Complex
MST1R (RON)	-11	Macrophage Stimulating 1 Receptor (c-met-related tyrosine kinase)
PI4KB (PI4K beta)	-13	Phosphatidylinositol 4-kinase type III beta
CASK	-13	Calcium/calmodulin-dependent Serine Protein Kinase
KIT	-13	cKIT
AURKB (Aurora B)	-13	Aurora Kinase B
PIK3CD/PIK3R1 (p110 delta/p85 alpha)	-15	Phosphoinositide 3 Kinase Delta (PI3K Delta)
FYN A	-15	FYN oncogene related to SRC, FGR, YES
CDK2/cyclin E1	-17	Cyclin Dependent Kinase 2:Cyclin E
MYLK4	-17	Myosin Light Chain Kinase Family, member 4
NUAK1 (ARK5)	-17	AMPK-Related Protein Kinase 5
WNK3	-18	WNK lysine deficient Protein Kinase 3
HUNK	-19	Hormonally Upregulated Neu-associated Kinase
PIM2	-19	PIM 2 oncogene
EEF2K	-21	Eukaryotic Elongation Factor 2 Kinase

Supplementary Figure 1



Supplementary Figure 2

