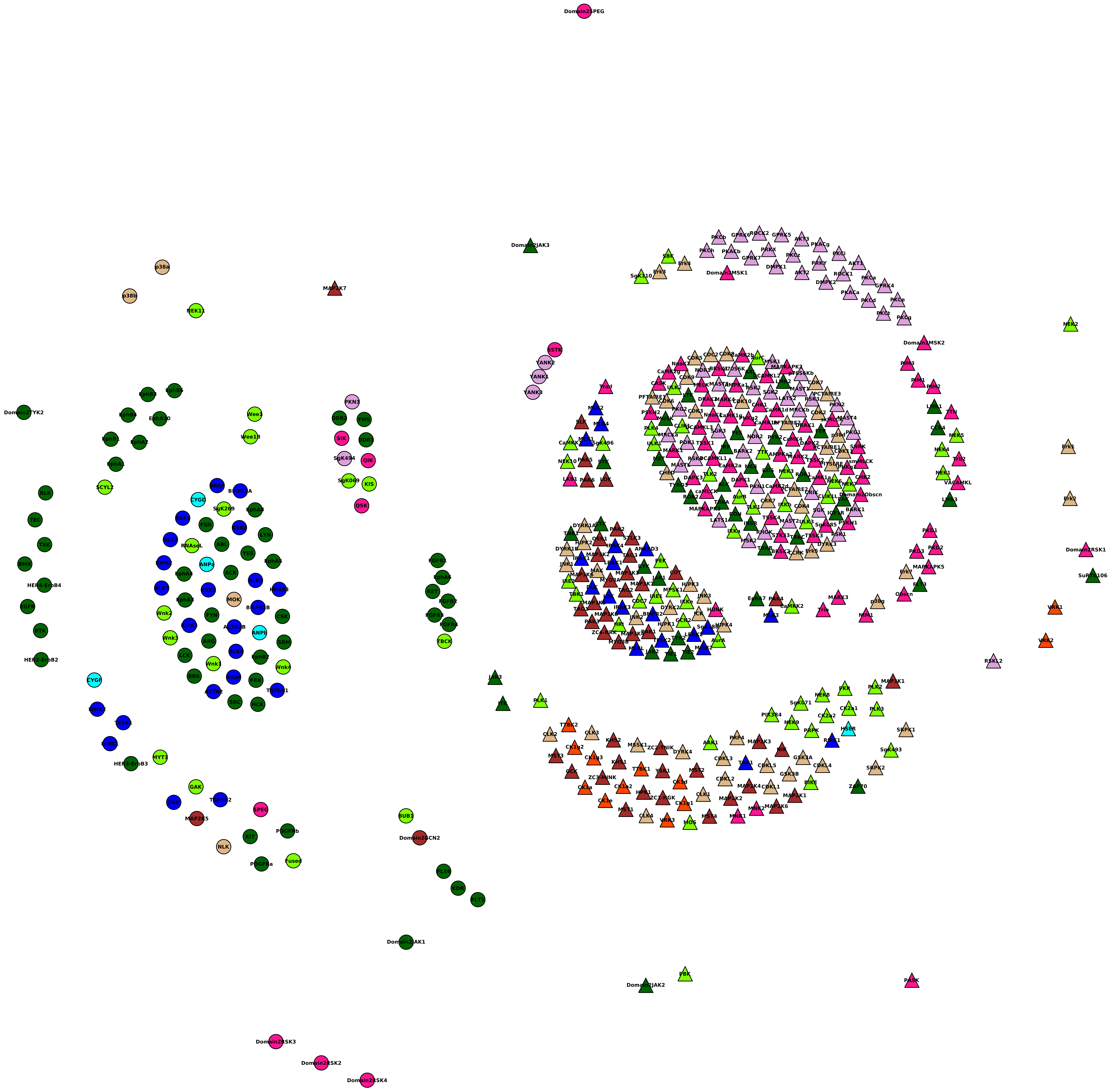

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Domain2JAK3
MAP3K7
p38a
p38b
NEK11
Domain2TYK2
EphB3
EphB6
EphB4
EphA10
EphB1
EphA2
EphA1
SCYL2
Wee1
Wee1B
PKN3
DDR2
FMS
SIK
DDR1
SgK494
QIK
SgK069
KIS
QSK
BLK
TEC
TXK
BMX
HER4-ErbB4
EGFR
ITK
HER2-ErbB2
CYGF
LMR2
TESK1
LIMK1
HER3-ErbB3
MYT1
GAK
TESK2
ZAK
MAP2K5
SPEG
NLK
KIT
PDGFRb
PDGFRa
Fused
BUB1
Domain2GCN2
FLT4
KDR
FLT1
Domain2JAK1
Domain2JAK2
PBK
Domain2RSK3
Domain2RSK2
Domain2RSK4
FGFR1
EphA5
RET
FGFR2
FGFR3
FGFR4
TBCK
PLK1
YANK2
YANK1
YANK3
SSTK
Domain2MSK1
Domain2MSK2
NEK2
Erk3
Erk2
Domain2RSK1
SuRTK106
VRK1
VRK2
RSKL2
PASK
MARK3
Trib
NIM1
p38g
SRPK1
SRPK2
SgK493
ZAP70
SgK110
SBK
Erk4
Erk5
CYGD
ANPa
ANPb
MOK
Wnk1
Wnk2
Wnk3
Wnk4

Supporting Information

Kinase selectivity potential for inhibitors targeting the ATP binding site: A network analysis

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Contents

1 Strategies to design selective type I inhibitors

Effective strategies for the design of selective type I inhibitors mainly consist of targeting sequence variability at a given position of the ATP binding site or exploiting a cavity of variable size in different kinases [1, 2, 3].

Gatekeeper. Although the hydrophobic pocket (H-pocket) is not occupied by ATP (main text, Figure 1, Top), it is exploited by many kinase inhibitors. The size of this pocket is mainly determined by a residue called gatekeeper [1, 2, 3, 4, 5] (position 17 in main text, Figure 1, Middle). The gatekeeper residue is not conserved and its amino acid distribution is shown in Figure S2. About three-quarters of kinases have a bulky side chain at position 17 (methionine, leucine, or phenylalanine), and thus a relatively small H-pocket. Kinases with gatekeeper of small side chain present a relatively large H-pocket, and are targeted by structurally diverse classes of inhibitors, including pyridinylimdazoles [6], pyrazolopyrimidines [7], purines [8], quinazolines [9] and phenylaminopyrimidines [10]. The size difference of the H-pocket is often utilized to gain selectivity [1].

Threonine is the gatekeeper in 19% of the kinases. Its hydroxyl group can act as both hydrogen bond donor and acceptor, and this property can be responsible for the selectivity of these kinases with respect to those with an apolar side chain. Strikingly, Dasatinib (**3** of Figure S1) [11], which is active on 65 of about 300 kinases ($K_d < 3$ μM is used as threshold throughout this work), has a strong preference for those with threonine as gatekeeper, as 57 of the 65 kinases have threonine at position 17. In contrast, only one of the 11 kinases with valine at position 17 is inhibited by Dasatinib which shows that not only size but also the hydrogen bonding ability are important for selectivity. Similar observations can be also made for EKB-569 [12] and Imatinib [13] (**4** and **5** of Figure S1). The latter is a type II inhibitor and a hydrogen bond with gatekeeper further improves its selectivity for the Abl tyrosine kinase over others.

A striking example of selective kinases are those with glutamine as gatekeeper.

Four of them are in the set tested by Karaman and coworkers [14]. They are inhibited on average by only 2 of the 38 compounds, which is much less than the average of about 10 active compounds for the kinases with a gatekeeper different than glutamine.

Covalent bond with cysteine. A covalent bond with the sulfhydryl group of cysteine around the ATP binding site is another strategy to improve selectivity. Interesting examples include compounds with adenine derived scaffold [15], which make use of a cysteine at the glycine rich loop (Position 9, main text, Figure 1), and compounds with quinazoline scaffold [16], which utilize a cysteine at the entrance pocket (Position 24, main text, Figure 1). Selectivity can be achieved because only 11 kinases possess cysteine at positions 9 or 24. Two EGFR inhibitors (CI-1033 and EKB-569, **2** and **4** of Figure S1) were developed using this strategy, and are under clinical development [17, 18]. Both of them utilize the cysteine at position 24 of EGFR [12, 19]. Among nine kinases with a cysteine at position 24 tested by Karaman et al., 8 and 6 of them are inhibited by CI-1033 and EKB-569 [14], respectively. Both compounds are active for 13-15% of about 300 kinases and the selectivity of EGFR over other kinases without cysteine at position 24 is about 500 (CI-1033) and 13 (EKB-569) folds. Apart from these two positions, in principle cysteine at other positions of the ATP binding site can be also utilized to improve selectivity [15], e.g., the position near DFG motif (Position 33, main text, Figure 1) and about 10% of the kinases have cysteine at this position.

Position 24. Position 24 is also non-conserved. Residues at this position include aspartate, serine, glutamate and asparagine and their distributions are 32%, 26%, 16%, and 9%, respectively. It is possible to exploit this residue variability, i.e., different hydrogen bonding abilities, for designing selective inhibitors. Examples include a triazolopyrimidine derivative (**6** of Figure S1) [20] which is 167 times more selective for cyclin-dependent kinase 2 (CDK2) over glycogen synthase kinase 3β (GSK-3β). Such selectivity is important in the design of CDK2 inhibitors because CDK2 and GSK-3β often share similarities in their small-molecule inhi-

bition profiles [3, 21]. The structural analysis shows that position 24 is aspartate for CDK2 and threonine for GSK-3β. This difference influences the interaction with the sulfonamide group of compound **6**, which is the main reason for the factor of 167 in selectivity [20]. In another case, position 24 is asparagine for fibroblast growth factor receptors (FGFR) and fetal liver kinase-1 (Flk-1), so that the negatively charged propionic acid group of compound **7** can act as acceptor for a hydrogen bond with this asparagine, leading to the selectivity for FGFR and Flk-1 over CDK2 [3, 22]. Another example (compound **8**) can be found in the design of selectivity of c-Jun N-terminal kinases 3 (JNK3) over p38α [23].

Hinge loop. As mentioned in the main text, VX-745 is an example of very selective type I inhibitor against a kinase with DFG-out conformation. Only 10 kinases are inhibited by VX-745 among about 300 kinases [14]. Moreover, the binding affinity for its primary target (i.e., p38α) is more than 250 times higher than for the other kinases (apart from p38β). Besides the utilization of the selectivity of the threonine gatekeeper, a second strategy is used by exploring an interesting peptide flip phenomenon [24]. The residue at position 21 is a glycine which allows the backbone of the preceding methionine to rotate by 180 degrees to become a hydrogen bond donor instead of the usual hydrogen bond acceptor. This conformational change is predicted to be energetically more favorable in p38α when the position 21 is glycine compared with mutants where this glycine is mutated to a bulkier residue [24]. About 10% of kinases have this feature (energetically favorable backbone flip) based on structural and sequence alignment as described in the previous section.

Another selectivity feature at the hinge loop is observed in three kinases encoded by pim genes (PIM-1,PIM-2, and PIM-3), which have an unusual proline at position 20 and thus lack a backbone hydrogen bond donor as compared with other kinases.

Adenine binding pocket. Although the adenine binding pocket (A-pocket) is highly conserved, some kinases have specific features in this pocket that can be used to design selective inhibitors [3]. Kinases in the AGC group, including protein kinases A, B, and C, as well as Rho-associated coiled-coiled kinase (ROCK), have

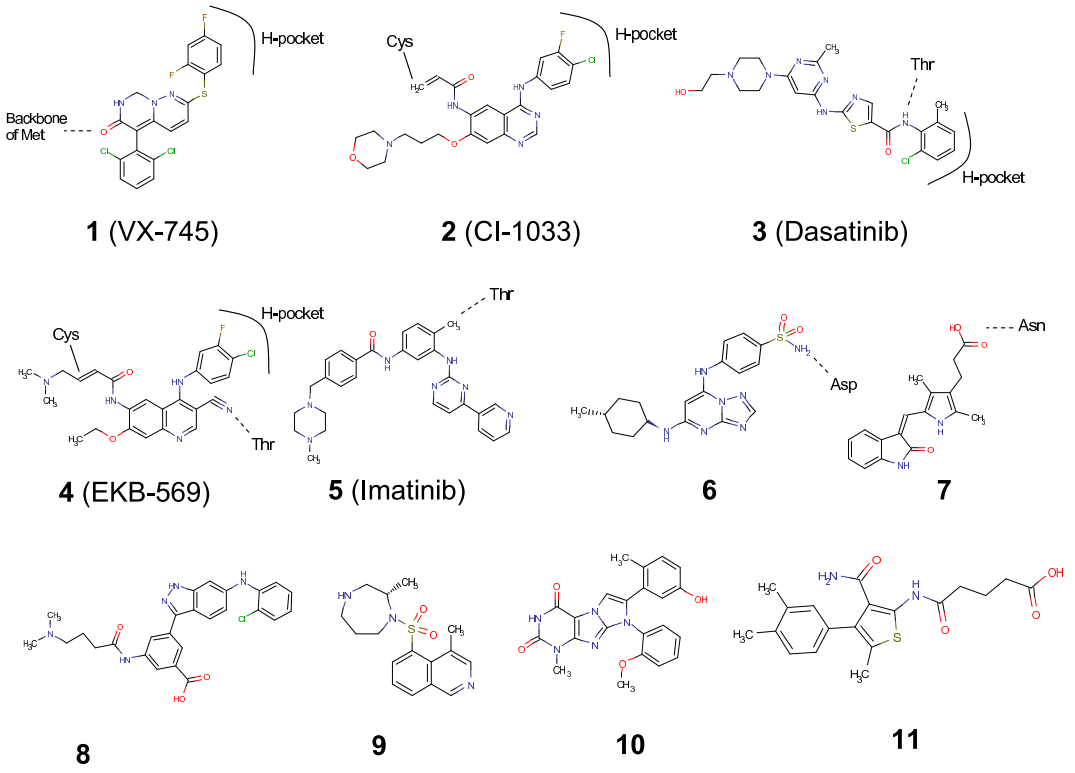

Figure S1: Structural formula and numbering of the inhibitors mentioned in the text. Compounds 1-9 refer to selective inhibitors of protein kinases disclosed in the literature. Interactions with the kinase are emphasized: covalent bonds (solid lines), hydrogen bonds (dashed lines), apolar interaction with the hydrophobic pocket (solid arc). Compounds 10 and 11 are two EphB4 inhibitors reported recently [29].

an hydrophobic motif (HM motif) [3, 25, 26]. The HM motif has a characteristic phenylalanine positioned on a C-terminal chain, which folds back into the catalytic cleft, significantly contributes the contacts with ATP, and changes the size of A-pocket. This feature can be used to design inhibitors, e.g., compound **9** for ROCK [3].

Position 10 is alanine in 92% of the kinases. For the remaining 8% of kinases, this position is bulkier, e.g., valine for casein kinase II [27, 28]. Thus such bulkier side chain makes the A-pocket smaller than that of the large majority of protein kinases [28].

2 Structures of 24 inhibitors used to plot Fig. 5

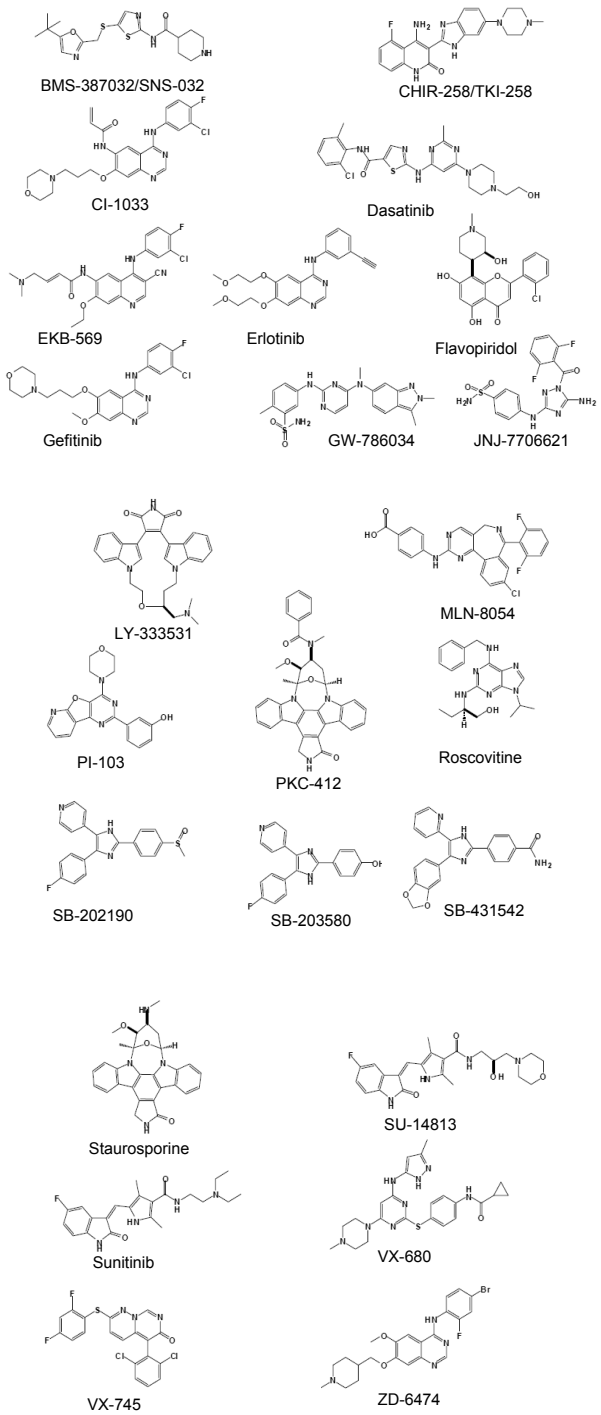

Figure S2: Structures of 24 inhibitors used to plot Fig. 5 [14]

3 Figures of kinase selectivity potential network using different weighting factors

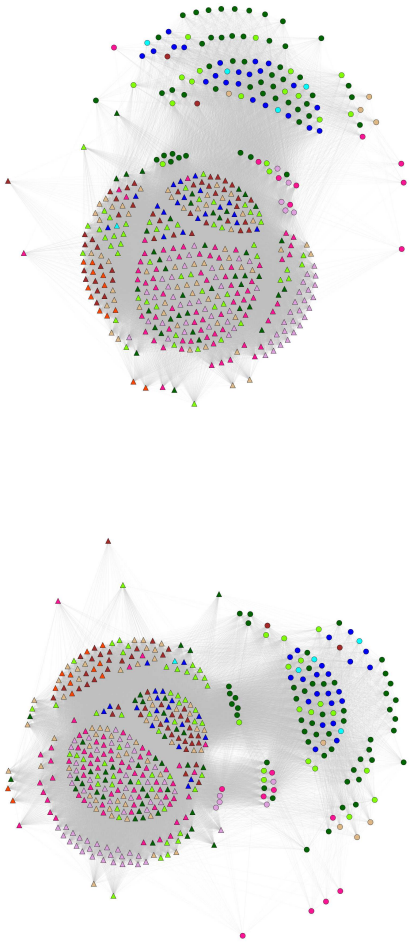

Figure S3: Figures of kinase selectivity potential network using different weighting factors. Pairs of protein kinases (nodes) are considered to have similar selectivity features (i.e., are connected by an edge) if they have less than three bits difference in the 9-bit fingerprint. (Top) Edges with 0-, 1-, and 2-bit difference are weighted equally. (Bottom) Edges are weighted with 3, 2, and 1 for 0-, 1-, and 2-bit difference, respectively.

4 PDB codes and names of 116 kinases

1A06 CaMK1a_CAMK

1AD5 HCK_TK

1ATP PKACa_AGC

1B6C TGFbR1_TKL

1BI7 CDK6_CMGC

1BYG CSK_TK

1CKI CK1d_CK1

1CM8 p38g_CMGC

1ERK Erk2_CMGC

1F3M PAK1_STE

1FGK FGFR1_TK

1FMK SRC_TK

1FPU ABL_TK

1FVR TIE2_TK

1GJO FGFR2_TK

1GZK AKT2_AGC

1H1W PDK1_AGC

1H4L CDK5_CMGC

1HCK CDK2_CMGC

1I09 GSK3B_CMGC

1IA8 CHK1_CAMK

1IG1 DAPK1_CAMK

1IRK INSR_TK

1JNK JNK3_CMGC

1JWH CK2a1_Other

1K2P BTK_TK

1KWP MAPKAPK2_CAMK

1LUF MUSK_TK

1M14 EGFR_TK

1MP8 FAK_TK

1MQB EphA2_TK

1MUO AurA_Other

1OMW BARK1_AGC

1PKG KIT_TK

1R0P MET_TK

1RJB FLT3_TK

1S9I MAP2K2_STE

1S9J MAP2K1_STE

1SM2 ITK_TK

1T4H Wnk1_Other

1TKI TTN_CAMK

1U46 ACK_TK

1U5Q TAO2_STE

1UA2 CDK7_CMGC

1UKH JNK1_CMGC

1UWH BRAF_TKL

1VR2 KDR_TK

1VZO MSK1_AGC

1WBP SRPK1_CMGC

1WFC p38a_CMGC

1X8B Wee1_Other

1XJD PKCt_AGC

1XWS PIM1_CAMK

1YVJ JAK3_TK

1Z57 CLK1_CMGC

1ZMU MARK2_CAMK

1ZRZ PKCi_AGC

1ZWS DAPK2_CAMK

2AC3 MNK2_CAMK

2ACX GPRK6_AGC

2B7A JAK2_TK

2BUJ MPSK1_Other

2BVA PAK4_STE

2C30 PAK6_STE

2C47 CK1g2_CK1

2CHL CK1g3_CK1

2CL1 NEK2_Other

2CLQ MAP3K5_STE

2CMW CK1g1_CK1

2CN5 CHK2_CAMK

2DQ7 FYN_TK

2DYL MAP2K7_STE

2ETR ROCK1_AGC

2EU9 CLK3_CMGC

2EVA TAK1_TKL

2F2U ROCK2_AGC

2F57 PAK5_STE

2GSF EphA3_TK

2H6D AMPKa2_CAMK

2HEL EphA4_TK

2HW6 MNK1_CAMK

2I0E PKCb_AGC

2I1M FMS_TK

2I6L Erk3_CMGC

2IVS RET_TK

2IWI PIM2_CAMK

2J51 SLK_STE

2J7T LOK_STE

2J90 DAPK3_CAMK

2JAM CaMK1g_CAMK

2JC6 CaMK1d_CAMK

2JII VRK3_CK1

2NRU IRAK4_TKL

2OWB PLK1_Other

2P0C MER_TK

2PHK PHKg1_CAMK

2QLU ACTR2B_TKL

2QNJ MARK3_CAMK

2R2P EphA5_TK

2REI EphA7_TK

2V62 VRK2_CK1

2V7O CaMK2g_CAMK

2VD5 DMPK1_AGC

2VN9 CaMK2d_CAMK

2Z7Q RSK3_AGC

3BBT HER4-ErbB4_TK

3BHH CaMK2b_CAMK

3BKB FES_TK

3C0G CASK_CAMK

3CC6 PYK2_TK

3CEK TTK_Other

3CKW MST3_STE

3COI p38d_CMGC

3COK PLK4_Other

3COM MST1_STE

3LCK LCK_TK

5 Names of kinases of category 4

ARG_TK

ALK2_TKL

ALK4_TKL

ACTR2_TKL

ACTR2B_TKL

ALK1_TKL

AKT1_AGC

BMPR1A_TKL

BMPR2_TKL

BRAF_TKL

BRSK1_CAMK

CaMK1a_CAMK

CK1a2_CK1

EphA1_TK

EphA2_TK

EphA3_TK

EphA4_TK

EphA5_TK

EphA6_TK

EphB1_TK

EphB2_TK

EphB3_TK

EphB4_TK

HER2-ErbB2_TK

HER4-ErbB4_TK

Erk1_CMGC

FLT1_TK

FLT3_TK

FRK_TK

FYN_TK

GAK_Other

GSK3A_CMGC

IGF1R_TK

LATS1_AGC

LIMK1_TKL

LIMK2_TKL

LKB1_CAMK

MAP3K4_STE

p38a_CMGC

p38b_CMGC

p38g_CMGC

PDGFRb_TK

PDK1_AGC

PKN1_AGC

RAF1_TKL

RET_TK

ROS_TK

RSK1_AGC

SgK085_CAMK

SRM_TK

SRPK1_CMGC

SYK_TK

TESK1_TKL

TGFbR1_TKL

TGFbR2_TKL

TIE1_TK

HH498_TKL

TRKA_TK

TYRO3_TK

Wee1_Other

YANK2_AGC

YSK1_STE

ZAP70_TK

6 Sequence of the 36 residues of the ATP binding site

LGSGGFGSVAKIRLLILERPEPVQ-DLF–DKENLIDFG PIM1_CAMK

LGSGGFGTVAKIRLLVLERPEPAQ-DLF–DKENLIDFG PIM3_CAMK

LGKGGFGTVAKIRLLVLERPLPAQ-DLF–DKENLIDFG PIM2_CAMK

IGVGSYSECAKITLLVTELM–RGGELLD-DKSNLCDFG Domain2RSK3_CAMK

IGEGSFGKAVKVQYIVMDYC–EGGDLFK-DKQNFGDFG NEK1_Other

LSKGGFAKCAKVGFVVLELC–RRRSLLE-DKGNFGDFG PLK1_Other

LGSGSFGTVVKVKFIITEYC–EGRDLDD-DKKNFGDFG NEK11_Other

LGVGTFGKVAKIKLMVMEYV–SGGELFD-DKENLADFG AMPKa2_CAMK

IGQGASGTVAKVNFVVMEYL–AGGSLTD-DKDNLTDFG PAK2_STE

IGQGASGTVAKVNYVVMEYL–AGGSLTD-DKDNLTDFG PAK1_STE

IGQGASGTVAKVNYVVMEYL–AGGSLTD-DKDNLTDFG PAK3_STE

IGKGSYGVVAKVKLMVFELV–NQGPVME-DKSNLADFG CaMKK2_Other

KARGRFGVVVKMSLLIAESC–GNRELLC-DKDNLVDFG Domain2SPEG_CAMK

LGKGSFGIVAKIHLLVMELC–EDGELKE-DKENMTDFG STK33_CAMK

IGRGRFSIVAKITLLILELM–DDGRLLD-DKENLIDLE Trad_CAMK

IGRGSYGVVAKERIFVMEFC–EGGDLNQ-DKDNLADFG CLIK1_Other

VGHGAFAVVAKVALLVMEYC–NGGDLAD-DKQNLADFG ULK2_Other

LGRGRFSVVAKVGLLVLEMA–DQGRLLD-DKENLADFG Trio_CAMK

IPRGAFGKVAKAELLFMEAG–EGGSVLE-DKSNVVDFG COT_STE

IGKGNFAKVAKVKLLVMEYA–SGGEVFD-DKENLADFG MARK1_CAMK

IGKGNFAKVAKVKLLVMEYA–SAGEVFD-DQENLADFG MARK4_CAMK

IGKGNFAKVAKVKLLIMEYA–SGGKVFD-DKENLADFG MARK3_CAMK

IGKGNFAKVAKVKLLVMEYA–SGGEVFD-DKENLADFG MARK2_CAMK

LGKGQTGLVAKLKLLVLEHV–SGGELFD-DKENLADFG BRSK2_CAMK

LGKGQTGLVAKLKLLVLEHV–SGGELFD-DKENLADFG BRSK1_CAMK

IGSGNFSQVAKIRLLVMEYA–GGGELFG-DKENFGDFG NIM1_CAMK

IGKGAFSVVAKVRLLVFDLV–TGGELFE-DKENLADFG CaMK2b_CAMK

IGEGTYSKVAKIQVLVMELA–EGGDVFD-DKENLTDFG TSSK3_CAMK

LGKGAFSVVAKVRLLIFDLV–TGGELFE-DKENLADFG CaMK2a_CAMK

LGKGAFSVVAKVRLLVFDLV–TGGELFE-DKENLADFG CaMK2g_CAMK

LGKGAFSVVAKVRLLVFDLV–TGGELFE-DKENLADFG CaMK2d_CAMK

IGEGSFGRAAKVAFIVMEYC–DGGDLMQ-DKKNFGDFG NEK3_Other

LGRGEFGIVMKLHLMIFEFI–SGLDIFE-DRENIIEFG TTN_CAMK

LGEGSYGKVAKIQLMVMEYC–VCGMQEM-DKGNLSDLG LKB1_CAMK

LGRGGFSEVAKVKLTVLEYC–EGNDLDF-DKGNLTDFG TLK1_Other

LGRGGFSEVAKVKLTVLEYC–EGNDLDF-DKGNLTDFG TLK2_Other

LGEGSYAKVAKIKTIVMELA–VQGDLLE-DKDNLSDFS TSSK1_CAMK

LGKGGFARCAKVRFIFLELC–SRKSLAH-DKGNFGDFG PLK3_Other

LGEGSFAKVAKTQLLVMELC–PGGNLMH-DKENLIDFG HUNK_CAMK

LGEGGFSYVAKLRLLLLPFF–KRGTLWN-DKTNLMDLG MPSK1_Other

IGDGNFAVVAKVLLLVMELV–KGGDLFD-DKENLGDFG DCAMKL1_CAMK

LGEGAYAKVAKLELLVFEKL–QGGSILA-DKENLCDFD MNK1_CAMK

IGKGAYGVVAKVKLLVFDLL–RKGPVME-DKSNLADFG CaMKK1_Other

IGEGSYSKVAKVHVYIVMEA–AATDLLQ-DKENLTDFG SSTK_CAMK

IGDGNFAVVAKIMLLVMELV–KGGDLFD-DKENLGDFG DCAMKL2_CAMK

IADTSEGGIAKVTFFVCVTL–CEQTLEA-DQQNLADFD RNAseL_Other

LGKGSYAKVAKIKTIIMELG–VQGDLLE-DKENLSDFG TSSK2_CAMK

LGRGAFGEAVKIAYIELEYC–NGGNLYD-DKLNFGDYG NEK9_Other

LGSGACGEVAKIKIIVLELM–EGGELFD-DKENLTDFG CHK2_CAMK

LGVGTFGKVAKIKLMVMEYV–SGGELFD-DKENLADFG AMPKa1_CAMK

LGSGSYGRVAKQTLFAQEYA–PCGDLSG-DKDNLGDLG SgK110_Other

LGKGTYGIVAKVQYIFMEQV–PGGSLSA-DKDNLSDFG MAP3K5_STE

IGRGAFGEVAKVQLMVMEYM–PGGDLVN-DKDNLADFG ROCK1_AGC

IGTGSYGRCVKVRYIVMEYC–EGGDLAS-DKANFGDFG NEK2_Other

IGRGVFGFVAKTGLLILELC–SSEELLD-DKSNLCDFG Obscn_CAMK

IGVGSYSVCAKITLVVTELM–KGGELLD-DKSNLCDFG Domain2RSK2_CAMK

IGHGSYGSVAKINFIILELA–QGGDVLE-DKENLSDFG TSSK4_CAMK

IGDGNFAVVAKVKLLILEYV–QGGDLFD-DKENLADFG DCAMKL3_CAMK

VGRGAFGIVIKIEYIAMEYA–PGGTLAE-DKQNLGDFG NEK8_Other

LGRGVSSVVAKIQLLVFDLM–KRGELFD-DKENLTDFG PHKg1_CAMK

LGSGQFAIVAKITLLILELV–SGGELFD-DKENMIDFG DAPK3_CAMK

LGKGTYGKVAKKVFFAQEYA–PAGDLFD-DKENLADFG SBK_Other

VGSGTYGDVAKVAYICMEYC–GGGSLQD-DKANLADFG KHS1_STE

IGSGATAVVAKVSYLVMKLL–SGGSVLD-DKGNLADFG OSR1_STE

IGSGATAVVAKVTYLVMKLL–SGGSMLD-DKGNLADFG STLK3_STE

LGKGTYGKVAKISIIIMEYA–SKGELYD-DKENLADFG NuaK1_CAMK

IGVGSYSVCAKITLLVTDLM–KGGELLD-DKSNLCDFG Domain2RSK4_CAMK

IGTGGFAKVAKCQLMVLEYC–PGGELFD-DKENLIDFG MELK_CAMK

IGKGPFSVVAKVELMVFEFM–DGADLCF-DKHCLGGFG CASK_CAMK

LGSGAFSEVAKVALLAMELV–TGGELFD-DKENLSDFG CaMK1b_CAMK

IGVGSYSVCAKITLLVMELM–RGGELLD-DKSNLCDFG Domain2RSK1_CAMK

IGKGNFAVVAKIRLLVTEYA–SGGEIFD-DKENLADFG QSK_CAMK

LGKGTYGKVAKIAIIVMEYA–SRGDLYD-DKENLADFG NuaK2_CAMK

LGQGRYGRVAKTAYFLTEPV–LHGDLMA-DKENLTDFG SgK069_Other

IGRGAFGEVAKVQLMVMEYM–PGGDLVN-DKDNLADFG ROCK2_AGC

IGQGAFGKAVKVAFIVMEYC–DGGDLMK-DKQNFGDFG NEK5_Other

LGSGQFAVVAKITLLILELV–AGGELFD-DKENMIDFG DAPK1_CAMK

IGRGVSSVVAKITLLVFDLM–RKGELFD-DKENLSDFG PHKg2_CAMK

LGGGTYGEVAKVAYICMEFC–GAGSLQD-DKANLADFG HPK1_STE

VGRGSYGVVAKIHLFVMDFC–DGGDMNE-DKDNLADFG CLIK1L_Other

IKTEEFCEITKLQLIFLELA–TGREVFD-NKENVSDFH VACAMKL_CAMK

LGRGHFACGAKVRLLILELG–DGGDMFD-DKENVTDFG SNRK_CAMK

IGTGSFSRVAKVQLMVMELA–TGGELFD-NKENLTDFG PSKH2_CAMK

IGRGSFSRVAKIQLMVMELA–TGGELFD-DKENLTDFG PSKH1_CAMK

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LGKGNFAVVAKIKLLVTEYA–KNGEIFD-DKENLADFG QIK_CAMK

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LGTGAFSEVAKVALLIMQLV–SGGELFD-DKENLSDFG CaMK1a_CAMK

VGKGSYGEVVKVTYIVMGFC–EGGDLYR-DKQNFGDLG NEK4_Other

LGKGGFAKCAKVQFILLEYC–SRRSMAH-DKGNFGDFG PLK2_Other

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VASGGFSQVAKVSIIVMEFM–ANGSLEK-DKGNLSDFG SgK288_TKL

LGQGAFGRVAKVQYIFMEYM–PGGSIKD-DKANLGDFG MAP3K2_STE

IGEGQYGKVAKVRYIFMEYC–DEGTLEE-DKANFGDFG MAP3K4_STE

LGQGATANVAKVKLLIMEFC–PCGSLYT-DKGNMTDFG TBK1_Other

IGLGAFSSCAKIRMLFIEWM–AGGSVAH-DKANLADFG MAP3K1_STE

LGQGATASVAKVKLLVMEYC–SSGSLLS-DKGNMTDFG IKKe_Other

LGTGGFGNVAKVKALAMEYC–SGGDLRK-DKENVIDLG IKKa_Other

LGTGGFGNVAKVAALAMEYC–QGGDLRK-DKENVIDLG IKKb_Other

LGDGAFGKVAKVKLIMIEFC–PGGAVDA-DKGNLADFG LOK_STE

IGKGTYGKVAKVRFLVLELC–SGGSVTD-DKNNLVDFG MYO3A_STE

LGDGAFGKVAKVKLILIEFC–AGGAVDA-DKGNLADFG SLK_STE

IGKGTYGKVAKVKFLVLELC–NGGSVTE-DKNNLVDFG MYO3B_STE

LGEGAYGEVAKVKFLFLEYC–SGGELFD-DKENLSDFG CHK1_CAMK

LGEGAFAQVVKMKFLVGELY–SYGTLLN-DKDNIIDLG BUB1_Other

LGEGLFGEVAKVKLIIMELY–PYGELGH-DARNLGDFG PYK2_TK

LAEGGFAIVAKVGYILMDFC–RGGQVVN-DKENLCDFG AAK1_Other

IGAGEFGEVAKIRLIITEYM–ENGALDK-DARNLSDFG EphA2_TK

LGHGAFGEVAKVRCILLELM–SGGDMKS-DARNLGDFG LTK_TK

LAEGGFSTVAKIVGILMEYC–RAGQVVN-DKENLCDFG BIKE_Other

LGGGRFGQVAKIQLLVMEYV–DGGELFD-DKENLIDFG SgK085_CAMK

LGEDRFGKVAKVCLMIFSYC–SHGDLHE-DARNLSDLG ROR2_TK

LGECAFGKIAKVCLMLFEYI–NQGDLHE-DARNLSDLG ROR1_TK

LGKGTYGVVAKVRYIFMEEV–PGGSLSS-DKDNLSDFG MAP3K6_STE

IGAGEFGEVAKIHLIITEFM–ENGSLDS-DARNLSDFG EphB2_TK

IGAGEFGEVAKIRLIITEFM–ENGALDS-DARNLSDFG EphB1_TK

IGAGEFGEVAKIRLILTEFM–ENCALDS-DARNLSDFG EphB3_TK

IGAGEFGEVAKIRLILTEFM–ENGALDS-DARNLSDFG EphB4_TK

LGKGNFGEVAKVKLIIMELV–SGGDFLT-DARNLSDFG FER_TK

LGKLVYNALWKVRYIVVDIL–SGVSLAA-VSSNLTDYS Domain2GCN2_STE

IGRGHFGCVAKLSLVVLPYM–KHGDLRN-DARNMADFG MET_TK

IGQGRWGRVARVLFIITSFC–KGRTLHS-DKKNFTDFG KSR1_TKL

LGSGCFGVVAKLRLMVMELA–PLGSLHA-DARNQADFG TNK1_TK

LGGGRFGQVAKIQLLVMEYV–DGGELFD-DKENLIDFG caMLCK_CAMK

VGKGRYGEVAKLGFLITHYH–EHGSLYD-DKRNLADLG ALK1_TKL

LGEGEFGAVAKMRLVILPFM–KHGDLHS-DARNMADFG AXL_TK

HGDGSFGSVAKISLLVMELA–SKGSLDR-DKHNLADYG LRRK2_TKL

LGSGNFGTVAKVRMLVMEMA–ELGPLNK-DARNLSDFG SYK_TK

IGKGHFGVVAKLALVLLPYM–CHGDLLQ-DARNMADFG RON_TK

MGEGGFGVVAKVELLVYVYM–PNGSLLD-DKANLSDFG IRAK4_TKL

LGFGTGVNVAKVGYLAMEYG–GEKSLND-DKSNVCDVG PBK_Other

ICSGSCGPIIKVQLMVLEDV–AQGDLLG-DARNLCGLG SuRTK106_TK

LGLGVNGKVAKVCIIIMECM–EGGELFS-DKENLTDFG MAPKAPK3_CAMK

LGEGAHARVAKLELLVFEKM–RGGSILS-DKENLCDFD MNK2_CAMK

LGGGKFGAVAKIQLLFMEYI–EGGELFE-DKENLIDFG skMLCK_CAMK

LGSGAFGKVAKVNLIITEYC–FYGDLVN-DARNLCDFG PDGFRa_TK

LGSGAFGQVAKVNLIITEYC–RYGDLVD-DARNLCDFG PDGFRb_TK

LGEGEFGKVAKIKLLIVEYA–KYGSLRG-DARNLSDFG RET_TK

LGEGCFGQVAKINLVIVECA–AKGNLRE-DARNLADFG FGFR4_TK

LGEGCFGQVAKINLVIVEYA–SKGNLRE-DARNLADFG FGFR1_TK

IGRGNFGEVAKVRLIVMELV–QGGDFLT-DARNLSDFG FES_TK

AGDAVYYTAAKKENVITREV–PCLTVAD-DRENLQGFG SgK269_Other

LGSGAFGEVAKLKQIILELM–EGGDLLT-DARNLGDFG ROS_TK

LGEGCFGQVAKINLVIVEYA–SKGNLRE-DARNLADFG FGFR2_TK

LGEGCFGQVAKINLVLVEYA–AKGNLRE-DARNLADFG FGFR3_TK

IGEGEFGAVAKVRLIVMEHV–SKGNLVN-DARNLSDFG CTK_TK

IGIGGFGKVAKIALLVMEFA–RGGPLNR-DKSNLTDFG MLK1_TKL

IGSGQFGLVAKVQLLVFEFM–EHGCLSD-DARNLSDFG ITK_TK

LGSGLFGVVAKVQLIVTEFM–ERGCLLN-DARNLSDFG TEC_TK

LGTGQFGVVAKVQLIITEYM–ANGCLLN-DARNLSDFG BTK_TK

LGEGQFGEVAKIHLMITEYM–ENGDLNQ-DARNLADFG DDR2_TK

IGSGWFGKVVKLQCLIMEFC–QLGDLKR-DARNLGDYG LMR3_TK

VKQGAEARVKRAPVLYMEEI–EG-SVTVRDTSNLIDFG PRPK_Other

LGAGAFGKVAKVNLVITEYC–CYGDLLN-DARNLCDFG KIT_TK

LGSGQFGEVAKVRLIVTEYM–ARGCLLD-DRANLADFG BLK_TK

LGDGSFGVVAKIRLMVTELA–PLGSLLD-DARNLGDFG ACK_TK

LGQGCFGEVAKVQLIVTEYM–SKGSLLD-DRANLADFG SRC_TK

LGQGCFGEVAKVPLIVTEFM–SKGSLLD-DRANLADFG YES_TK

IGIGGFGKVAKIALLVMEYA–AGGPLSR-DKNNLTDFG MLK3_TKL

LGSGAFGTVAKSRLLVTQLM–PYGCLLD-DARNLTDFG HER2-ErbB2_TK

LGSGVFGTVCKVRLLVTQYL–PLGSLLD-NARNLADFG HER3-ErbB3_TK

MTAHGKYQIAKTRFIVTEYC–PRGSLQD-SKSNVTDYG ANPb_RGC

LGEGQFGEVAKIRLMITDYM–ENGDLNQ-DARNLADFG DDR1_TK

LGKSEFGEVLKVRLMVLEYV–DLGDLKQ-DARNLSALG CCK4_TK

KARGRFGCVAKLQFLITAFH–EKGSLSD-DKKNLADFG ACTR2_TKL

KARGRFGCVAKLQFLITAFH–DKGSLTD-DKKNLADFG ACTR2B_TKL

LGNGQFGEVAKVQLIVTEYM–NKGSLLD-DRANLADFG FYN_TK

IGVGGFGKVAKIALLVMEYA–RGGALSR-DKINLTDFG MLK2_TKL

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LGSGAFGTVAKVRLLVTQLM–PHGCLLE-DARNLTDFG HER4-ErbB4_TK

LGEGHFGKVAKVKYLIMEFL–PSGSLKE-DARNLGDFG JAK1_TK

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IGRGRYGAVAKARFLVMEYY–PNGSLCK-DNRNLSDFG BMPR2_TKL

LGRGAFGKVAKVNLVIVEYC–KYGNLSN-DARNLCDFG FLT1_TK

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LGKGNFGSVAKVKYLIMEYL–PYGSLRD-DARNLGDFG JAK2_TK

LGRGSFKTVACVRFLVTELM–TSGTLKT-DKDNFGDLG Wnk2_Other

LGRGAFKTVACVRFLVTELM–TSGTLKT-DKDNFGDLG Wnk3_Other

IGRGSFKTVACVRFLVTELM–TSGTLKT-DKDNFGDLG Wnk4_Other

IGRGSFKTVACVRFLVTELM–TSGTLKT-DKDNFGDLG Wnk1_Other

LGEGEFGSVAKIRLVILPFM–KYGDLHT-DARNMADFG MER_TK

LGKGFFGQAMMLKFLLTEYI–EGGTLKD-DNHNLADFG LIMK2_TKL

LGKGCFGQAMMLKFFITEYI–KGGTLRG-DNHNLADFG LIMK1_TKL

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LGYGAFGKVAKVNLVIVEFC–KYGNLSN-DARNLCDFG FLT4_TK

LGQGSFSVCAKVNLLVLELL–RGGELLE-DKENLIDFG Domain2MSK2_CAMK

LGHGSFTKIAKVLLMVQEFV–HLGAIDM-NSRKLSDPG Domain2JAK3_TK

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IGAGGFGQVAKIELLVLEFA–RGGALNR-DKSNLTDFG MLK4_TKL

LGVGGFGRVAKVKLMLLEAC–LGGELWS-DKENIVDFG PKG2_AGC

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LGSGAFGKVAKVNLLIFEYC–CYGDLLN-DARNLCDFG FLT3_TK

IGEGSTGIVAKVEMVLMEFL–QGGALTD-DKDSLSDFG PAK6_STE

IGEGSTGIVAKVEMVVMEFL–EGGALTD-DKDSLSDFG PAK4_STE

LGRGKFAVVAKINLLVLEYA–AGGEIFD-DKQNLVDFG DRAK1_CAMK

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IGEGSTGIVAKVDMVVMEFL–EGGALTD-DKDSLSDFG PAK5_STE

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IGKGRFGEVAKLGFLVSDYH–EHGSLFD-DKKNLADLG ALK4_TKL

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LGEGAFGKVAKVKFMVFEYM–KHGDLNK-DARNLGDFG TRKC_TK

LGEGAFGKVAKVKFMVFEYM–KHGDLNK-DARNLGDFG TRKB_TK

LGQGSFGMVAKVRLVIMELM–TRGDLKS-DARNMGDFG IGF1R_TK

LGGGQYGEVAKVQLIVTEYM–PYGNLLD-DARNLADFG ARG_TK

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LGQGSFGMVAKVRLVIMELM–TRGDLKS-DARNMGDFG IRR_TK

VGAGEFGEVAKIRLIVTEYM–ENGSLDS-DARNLSDFG EphA3_TK

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LGRGKFAVVAKINLLILEYA–AGGEIFS-DKQNLVDFG DRAK2_CAMK

VGSGAQGAVAKITFILMEFC–AQGQLYE-DKPNLSDFG DLK_TKL

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IGVGEFGEVAKIHLIITEYM–ENGSLDA-DARNLSDFG EphA4_TK

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IGEGNFGQVAKINLLAIEYA–PHGNLLD-DARNLADFG TIE2_TK

IGSGDSGEVAKIRLIVTEYM–ENGSLDT-DARNLSDFG EphA8_TK

IGEGAFGRVAKVKLLLFEYM–AYGDLNE-DARNLADFG MUSK_TK

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VGKGRFAEVAKLQFLITAFH–AKGNLQE-DNSNLCDFG TGFbR2_TKL

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LGIGAFGEVAKVKLFVMDYI–PGGDMMS-DKDNLTDFG LATS2_AGC
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LGSGYFGEVAKLALIITELM–AKGSLLE-DARNLGDFG BRK_TK
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VGNGTYGQVAKATYLVMEFC–GAGSVTD-DKQNLVDFG ZC2-TNIK_STE
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IGRGAFGEVAKTALLVMDYY–VGGDLLT-DKDNLADFG MRCKb_AGC
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LGKGKFGNVAKLRLLILEYA–PRGELYK-DKENLADFG AurB_Other
LGTGAFSEVAKVALLVMQLV–SGGELFD-DKENLSDFG CaMK1d_CAMK
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LGKGAFGAVAKVRYIQMEYC–EKSTLRD-DKVNFGDFG GCN2_Other

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LGKGTFGKVAKTSLFVMEYV–NGGELFF-DKENMTDFG AKT3_AGC

LGEGSYGSVAKVKYIVMEYC–GAGSVSD-DKGNLADFG MST1_STE

LGEGSYGSVAKVKYIVMEYC–GAGSVSD-DKGNLADFG MST2_STE

VGTGTFGRVAKIRLMLMEYV–PGGELFS-DKENLTDFG PRKX_AGC

ISNGAYGAVAKVGMMVMEYV–EGGDCAT-DKDNLTDFG MAST1_AGC

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IGKGSFGKVAKVGLFVLDFV–NGGELFF-DKENLTDFG SGK3_AGC

IGKGNYGKVAKVGLFVLDYV–NGGELFF-DKENLTDFG SGK2_AGC

LGEGYFGEVAKIRLIVTELM–RKGNLQA-DARNLADFG SRM_TK

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LGKGTYGIVAKVQYIFMEQV–PGGSLSA-DKDNLSDFG MAP3K7_STE

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LGQGGSGTVAKVALFALELA–PLSSLNT-DKDNLSDYG LRRK1_TKL

LGEGSFSICAKVKLLVMELL–NGGELFE-DKENLIDFG Domain2MSK1_CAMK

VQDPATGGTMKSSGPHLNLL–TPARLPS-DHGNLTYFG RSKL2_AGC

MGTGTFGRVAKIRLMLMEYV–PGGELFS-DKENLTDFG PRKY_AGC

LGRGSFGEVAKVPLIFMELL–EGGSLGQ-DKDNLCDFG NIK_STE

SGPSQHLDSAKAEGVVSEHC–TRGSLQD-RKRNITDHG CYGD_RGC

MGSGYTKAVAKLQLTTITEL–GA-PVEM-DRRQVTDLD SgK493_Other

CGSNGLPLTSKCQYVVVAEH–CERSLED-ASHNLAKFG TBCK_Other

VGSGAYGSVAKIGLLVMPFM–QT-DLQKIDKGNALDFG p38d_CMGC

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LGDGTYGSVAKVKLFIFEYM–KE-NLYQLDKENLADFG ICK_CMGC

IGEGAYGMVAKIGIIVQDLM–ET-DLYKLDKSNLCDFG Erk1_CMGC

IGEGAYGMVAKIGIIVQDLM–ET-DLYKLDKSNLCDFG Erk2_CMGC

IGEGTYGVVAKVSLLIFEFL–SM-DLKKYDKQNLADFG CDC2_CMGC

IGNGSFGVVAKVRLLVLDYV–PE-TVYRVDKQNLCDFG GSK3B_CMGC

IGNGSFGVVAKVRLLVLEYV–PE-TVYRVDKQNLCDFG GSK3A_CMGC

LGSGAFGFVVKIKVLVMEKH–GS-GLDLFDKENVIDFG PASK_CAMK

IGSGGSSKVAKIRLMVMECG–NI-DLNSWDKANLIDFG TTK_Other

IGSGSFGDIAKPTIMVMELL–GP-SLEDLDKDNLIDFG CK1d_CK1

IGSGSFGDIAKPSIMVMELL–GP-SLEDLDKDNLIDFG CK1e_CK1

VGSGAYGAVAKIGLLVMPFM–GT-DLGKLDKGNALDFG p38g_CMGC

LNPGALGVNVKSVYLVMEFN–EL-SFQEVNKSNIQDLS SgK071_Other

IGSGAQGIVAKISLLVMELM–DA-NLCQVDKSNVLDFG JNK2_CMGC

VGSGAYGSVAKIGLLVTHLM–GA-DLNNIDKSNALDFG p38a_CMGC

IGSGAQGIVAKISLLVMELM–DA-NLCQVDKSNVLDFG JNK3_CMGC

IGSGAQGIVAKIGLIVMELM–DA-NLCQVDKSNVLDFG JNK1_CMGC

LGRGKYSEVVKIKLLVFEYI–NN-TDFKQDKHNMIDWG CK2a2_Other

LGRGKYSEVVKITLLVFEHV–NN-TDFKQDKHNMIDWG CK2a1_Other

TGQGVFSNVAKLRLLVFEPL–SM-NLREVDKDNLCDFG PRP4_CMGC

LGCGGNGLVAKVKVIVQEYM–ET-DLANVDKANFGDFG Erk3_CMGC

LGEGSYATVAKVLLFVFEYM–HT-DLAQYDKQNLADFG PFTAIRE2_CMGC

LGQGAYGIVAKISLLVFEFM–DT-DLNAVDKSNLCDFG Erk7_CMGC

LEPLEGDHVVKNQIVFFERS–YG-DMHSFDKRKIESLE Trb2_CAMK

IGSGSFGDVAKPHMLVMDLL–GP-SLEDLDKDNLIDFG CK1a2_CK1

IGSGSFGDIAKPHILVMDLL–GP-SLEDLDKDNLIDFG CK1a_CK1

IGEGTFSEVAKLMLLICELM–DM-NIYELDKENLGDFG MOK_CMGC

LGEGTYATVAKVTLLVFEYL–DK-DLKQYDKQNLADFG PCTAIRE2_CMGC

LGEGTYATVAKVTLLVFEYL–DK-DLKQYDKQNLADFG PCTAIRE1_CMGC

LGWGHFSTVAKVQLMVLEVL–GH-QLLKWDKENLADLG MSSK1_CMGC

IGEGSFGRVAKVHMVVTDYA–EG-ELFQIDKQNLCDFG Fused_Other

LGWGHFSTVAKVQLMVFEVL–GH-HLLKWDKENLADLG SRPK1_CMGC

LGWGHFSTVAKVQLMVFEVL–GH-HLLKWDKENLADLG SRPK2_CMGC

IGKGSFGQVAKIHMMTFELL–SM-NLYELDKENLIDFG DYRK2_CMGC

IGKGSFGQVAKIHMMAFELL–SI-DLYELDKENLIDFG DYRK3_CMGC

IGKGSFGQVAKVHMITFELL–GI-NLYELDKENVIDFG DYRK4_CMGC

LGRGTFGQVAKVRALVFEML–EQ-NLYDFDKENMIDFG HIPK2_CMGC

LGRGTFGQVAKVRSLVFEML–EQ-NLYDFDKENMIDFG HIPK1_CMGC

LGRGTFGQVAKVRALVFEML–EQ-NLYDFDKENMIDFG HIPK3_CMGC

VGEGSYGTVAKVNLLVFEFI–DH-TVLDEDKENLCDFG CDKL3_CMGC

IGVGAYGTVAKVRLLVFEHV–DQ-DLRTYDKENLADFG CDK4_CMGC

VGEGSYGMVAKVNLLVFEFV–DH-TILDDDKENLCDFG CDKL2_CMGC

LGEGSYATVAKVLLLVFEYV–HT-DLCQYDKQNLADFG PFTAIRE1_CMGC

IGEGTYGTVAKVRLLVFEFC–DQ-DLKKYDKQNLADFG CDK5_CMGC

LGEGQFATVAKIGLLVFDFM–ET-DLEVIDKNNLADFG CDK7_CMGC

TGEGSYGVVAKVNLLVFEYC–DH-TLLNEDKENLCDFG CDKL4_CMGC

IGQGTFGEVAKVNLLVFDFC–EH-DLAGLDKANLADFG CDK9_CMGC

IGEGSYGVVAKVNLLVFEYC–DH-TVLHEDKENLCDFG CDKL1_CMGC

LGEGTFGRVAKVQMISFELL–GL-STFDFDKENLVDFG CLK2_CMGC

LGEGTFGKVAKVLMIAFELL–GK-NTFEFDKENLADFG CLK3_CMGC

LGEGAFGKVAKVQMIVFELL–GL-STYDFDKENLVDFG CLK1_CMGC

IGNGAYGVVAKIAIVVLDLM–ES-DLHQIDKSNLGDFG Erk5_CMGC

IGKGSFGQVAKVHLLVFEML–SY-NLYDLDKENLVDFG DYRK1A_CMGC

IGKGSFGQVAKHDTLVFELL–SY-NLYDLDKENLVDFG DYRK1B_CMGC

IGEGAYGKVAKVRLLVFEHV–DQ-DLTTYDKQNLADFG CDK6_CMGC

LGKGTFGEVAKIRFLVFELL–EQ-NLFEFDKENMIDFG HIPK4_CMGC

IGRGAFSYLAKLYFIVTELC–TE-ELLERDKENLCDFG SPEG_CAMK

IGEGAHGIVAKVQLLAFEFM–LS-DLAEVDKANLADFG CCRK_CMGC

IGSGGFGLIVKPLFMVMERL–GI-DLQKIDKANLADYG VRK2_CK1

LGSGSSASVAKVTLVPSRCL–LL-ELLDVDKRNLIDFG KIS_Other

IGGGGFGEIAKCRFVVMQLQ–GR-NLADLDKSNALDFG TTBK2_CK1

IGGGGFGEIAKCRFVVMQLQ–GR-NLADLDKSNALDFG TTBK1_CK1

IGQGGFGCIVKPKYMIMDRF–GS-DLQKIDKSNLVDYG VRK1_CK1

IGTGSFGTVAKLLFIITQWC–EGSSLYH-DKNNFGDFG ARAF_TKL

IGSGSFGTVAKLLFIVTQWC–EGSSLYK-DKNNFGDFG RAF1_TKL

LGRGAYGVVAKVTFICMELM–DT-SLDKFDKSNLCDFG MAP2K3_STE

LAEGGFAFVAKVQFLLTELC–KG-QLVEFDKENLCDFG GAK_Other

VGSGAYGSVAKIGLLVTTLM–GA-DLNNIDKSNALDFG p38b_CMGC

VAKGSFGTVAKHSLIMCSYC–ST-DLYSLDKENLTDFG SgK494_AGC

IGRGAYGSVAKVQFICMELM–ST-SFDKFDKSNLCDFG MAP2K4_STE

LGRGAYGVVAKVTFICMELM–DT-SLDKFDKSNLCDFG MAP2K6_STE

MGSGTCGQVAKVQCIAMELM–GT-CAEKLDKSNLCDFG MAP2K7_STE

IGSGSFGTVAKLLFIVTQWC–EGSSLYH-DKNNFGDFG BRAF_TKL

LGSGQFGVVAKVNLVVMEKL–HG-DMLEMDKENLCDFG PKD2_CAMK

LGSGQFGIVAKVNLVVMEKL–HG-DMLEMDKENLCDFG PKD1_CAMK

LGSGQFGIVAKVNLVVMEKL–HG-DMLEMDKENLCDFG PKD3_CAMK

IGYGAFGVVAKLSAVVTELM–QS-DLHKIDKGNLCDFG NLK_CMGC

LGFGVNGLVAKVKVIVQEYM–ET-DLARLDKANFGDFG Erk4_CMGC

IGCGNFGELAKPQVMVLELL–GP-SLEDLDKENLIDFG CK1g3_CK1

IGCGNFGELAKPQVMVLELL–GP-SLEDLDKENLIDFG CK1g2_CK1

IGCGNFGELAKPQVMVLELL–GP-SLEDLDKENLIDFG CK1g1_CK1

LGHGSYGEVAKVRLLQTELC–GP-SLQQHDKANFGDFG MYT1_Other

IGEGTYGVVAKVKLLVFEFL–HQ-DLKKFDKQNLADFG CDK2_CMGC

IGEGTYGVVAKVRLLVFEFL–SQ-DLKKYDKQNLADFG CDK3_CMGC

IEEGTYGVVAKVTVIVMNYV–EH-DLKSLDKSNLGDFG PITSLRE_CMGC

LGRGAGGTFAKLRYIALELC–RA-SLQEYDKGNLSDFG IRE2_Other

VGRGTYGHVAKIALLLFDYA–EH-DLWHIDKANLADMG CDK11_CMGC

VGRGTYGHVAKISLLLFDYA–EH-DLWHIDKANLADMG CDK8_CMGC

IGEGTYGIVAKVELLVMGYC–EQ-DLASLDKSNLADFG CDK10_CMGC

VGEGAYGVVAKVELLVFEYV–EK-NMLELDKENLCDFG CDKL5_CMGC

LGKGGYGRVAKVGYIQMQLC–EL-SLWDWDKRNFGDFG HRI_Other

GGNGLAWKIAKLTVFCTEPV–FASLANV-NTENIMGFD SCYL2_Other

IGEGTYGQVAKINMLVFEYM–DH-DLMGLDKSNLADFG CHED_CMGC

IGEGTYGQVAKVNMLVFEYM–DH-DLMGLDKSNLADFG CRK7_CMGC

LGHGAEGTIAKIRYIAIELC–AA-TLQEYDKHNLSDFG IRE1_Other

LGEGAFGKVAKVQMIVFELL–GL-STYDFDKENLVDFG CLK4_CMGC

MGFGVHQDKSKPTCLVLPSL–GR-SLQSANTENFAGYG VRK3_CK1

LGRGQYGVVAKVDLAVLLIM–ER-LHRDLDKKNLTDLG SgK496_Other

LGSGAFGCVAKVRYIVMELI–EGAPLGE-DTNNMTDFG NEK10_Other

LGGGRFGELAHVRLIVTEYM–SHGALDG-GARHLSGFG EphA10_TK

LGAGGFGSVAKVRVIIMEFG–GNVTLHQ-DKANLSDFG MOS_Other

LGRGTRTHIIKVYLIMVEEV–EGGPLDL-NCKNLSDPG Domain2JAK1_TK

IGEGEFGEVAKLHLIITEFM–ENAALDA-DARNLSDFG EphA1_TK

LGQGTRTNVVKAFVMVTEYV–EHGPLDV-NCRNLSDPG Domain2TYK2_TK

LGRGGFGVVAKVRYIQMQLC–RKENLKD-DKSNFGDFG PEK_Other

IGEGTFSSVAKVKYIAMPYL–EHESFLD-DKSNLVDFG CDC7_Other

7 Fingerprint and cluster number of each kinase

Fingerprints ID group kinase_name cluster_ID

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1 0 0 0 0 0 0 0 0 0 3 AGC BARK1 1

1 0 0 0 0 0 0 0 0 0 4 AGC BARK2 1

1 0 0 0 0 0 0 0 0 0 5 AGC CRIK 1

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1 0 0 0 0 0 0 0 1 28 AGC PKACg 4

1 0 0 0 0 0 0 0 1 29 AGC PKCa 4

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1 0 0 0 0 0 0 0 1 32 AGC PKCe 4

1 0 0 0 0 0 0 0 1 33 AGC PKCg 4

1 0 0 0 0 0 0 0 1 34 AGC PKCh 4

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1 0 0 0 0 3 0 0 0 226 Other CaMKK2 6

1 0 0 0 0 3 0 0 0 241 Other NEK10 6

1 0 0 0 0 3 0 0 0 268 Other SgK496 6

1 0 0 0 0 3 0 0 0 294 STE LOK 6

1 0 0 0 0 3 0 0 0 321 STE PAK4 6

1 0 0 0 0 3 0 0 0 322 STE PAK5 6

1 0 0 0 0 3 0 0 0 323 STE PAK6 6

1 0 0 0 0 3 0 0 0 324 STE SLK 6

1 0 0 0 0 3 0 0 0 360 TK EphA7 6

1 0 0 0 0 3 0 0 0 414 TK SYK 6

1 0 0 0 0 3 0 0 0 453 TKL MLK1 6

1 0 0 0 0 3 0 0 0 454 TKL MLK2 6

1 0 0 0 0 3 0 0 0 455 TKL MLK3 6

1 0 0 0 0 3 0 0 0 456 TKL MLK4 6

0 1 0 0 0 1 0 0 0 198 CMGC MOK 7

0 1 0 0 0 1 0 0 0 260 Other RNAseL 7

0 1 0 0 0 1 0 0 0 266 Other SgK269 7

0 1 0 0 0 1 0 0 0 279 Other Wnk1 7

0 1 0 0 0 1 0 0 0 280 Other Wnk2 7

0 1 0 0 0 1 0 0 0 281 Other Wnk3 7

0 1 0 0 0 1 0 0 0 282 Other Wnk4 7

0 1 0 0 0 1 0 0 0 283 RGC ANPa 7

0 1 0 0 0 1 0 0 0 284 RGC ANPb 7

0 1 0 0 0 1 0 0 0 285 RGC CYGD 7

0 1 0 0 0 1 0 0 0 334 TK ABL 7

0 1 0 0 0 1 0 0 0 335 TK ACK 7

0 1 0 0 0 1 0 0 0 337 TK ARG 7

0 1 0 0 0 1 0 0 0 341 TK BRK 7

0 1 0 0 0 1 0 0 0 344 TK CSK 7

0 1 0 0 0 1 0 0 0 356 TK EphA3 7

0 1 0 0 0 1 0 0 0 357 TK EphA4 7

0 1 0 0 0 1 0 0 0 358 TK EphA5 7

0 1 0 0 0 1 0 0 0 361 TK EphA8 7

0 1 0 0 0 1 0 0 0 363 TK EphB2 7

0 1 0 0 0 1 0 0 0 374 TK FGR 7

0 1 0 0 0 1 0 0 0 379 TK FRK 7

0 1 0 0 0 1 0 0 0 380 TK FYN 7

0 1 0 0 0 1 0 0 0 381 TK HCK 7

0 1 0 0 0 1 0 0 0 394 TK LCK 7

0 1 0 0 0 1 0 0 0 399 TK LYN 7

0 1 0 0 0 1 0 0 0 412 TK SRC 7

0 1 0 0 0 1 0 0 0 413 TK SRM 7

0 1 0 0 0 1 0 0 0 426 TK YES 7

0 1 0 0 0 1 0 0 0 428 TKL ACTR2 7

0 1 0 0 0 1 0 0 0 429 TKL ACTR2B 7

0 1 0 0 0 1 0 0 0 430 TKL ALK1 7

0 1 0 0 0 1 0 0 0 431 TKL ALK2 7

0 1 0 0 0 1 0 0 0 432 TKL ALK4 7

0 1 0 0 0 1 0 0 0 433 TKL ALK7 7

0 1 0 0 0 1 0 0 0 435 TKL ARAF 7

0 1 0 0 0 1 0 0 0 436 TKL BMPR1A 7

0 1 0 0 0 1 0 0 0 437 TKL BMPR1B 7

0 1 0 0 0 1 0 0 0 439 TKL BRAF 7

0 1 0 0 0 1 0 0 0 441 TKL HH498 7

0 1 0 0 0 1 0 0 0 445 TKL KSR1 7

0 1 0 0 0 1 0 0 0 446 TKL KSR2 7

0 1 0 0 0 1 0 0 0 458 TKL RAF1 7

0 1 0 0 0 1 0 0 0 460 TKL RIPK2 7

0 1 0 0 0 1 0 0 0 461 TKL RIPK3 7

0 1 0 0 0 1 0 0 0 466 TKL TGFbR1 7

0 1 0 0 0 0 0 0 0 42 AGC PKN3 8

0 1 0 0 0 0 0 0 0 56 AGC SgK494 8

0 1 0 0 0 0 0 0 0 121 CAMK QIK 8

0 1 0 0 0 0 0 0 0 122 CAMK QSK 8

0 1 0 0 0 0 0 0 0 123 CAMK SIK 8

0 1 0 0 0 0 0 0 0 236 Other KIS 8

0 1 0 0 0 0 0 0 0 263 Other SgK069 8

0 1 0 0 0 0 0 0 0 346 TK DDR1 8

0 1 0 0 0 0 0 0 0 347 TK DDR2 8

0 1 0 0 0 0 0 0 0 378 TK FMS 8

0 1 0 0 0 3 0 0 0 262 Other SCYL2 9

0 1 0 0 0 3 0 0 0 353 TK EphA1 9

0 1 0 0 0 3 0 0 0 354 TK EphA10 9

0 1 0 0 0 3 0 0 0 355 TK EphA2 9

0 1 0 0 0 3 0 0 0 362 TK EphB1 9

0 1 0 0 0 3 0 0 0 364 TK EphB3 9

0 1 0 0 0 3 0 0 0 365 TK EphB4 9

0 1 0 0 0 3 0 0 0 366 TK EphB6 9

0 1 0 1 0 1 0 0 0 339 TK BLK 10

0 1 0 1 0 1 0 0 0 340 TK BMX 10

0 1 0 1 0 1 0 0 0 342 TK BTK 10

0 1 0 1 0 1 0 0 0 352 TK EGFR 10

0 1 0 1 0 1 0 0 0 382 TK HER2-ErbB2 10

0 1 0 1 0 1 0 0 0 384 TK HER4-ErbB4 10

0 1 0 1 0 1 0 0 0 416 TK TEC 10

0 1 0 1 0 1 0 0 0 423 TK TXK 10

0 0 0 0 0 1 0 0 0 269 Other TBCK 11

0 0 0 0 0 1 0 0 0 359 TK EphA6 11

0 0 0 0 0 1 0 0 0 370 TK FGFR1 11

0 0 0 0 0 1 0 0 0 371 TK FGFR2 11

0 0 0 0 0 1 0 0 0 372 TK FGFR3 11

0 0 0 0 0 1 0 0 0 373 TK FGFR4 11

0 0 0 0 0 1 0 0 0 406 TK RET 11

0 1 0 0 1 0 0 0 0 125 CAMK SPEG 12

0 1 0 0 1 0 0 0 0 200 CMGC NLK 12

0 1 0 0 1 0 0 0 0 227 Other Fused 12

0 1 0 0 1 0 0 0 0 393 TK KIT 12

0 1 0 0 1 0 0 0 0 403 TK PDGFRa 12

0 1 0 0 1 0 0 0 0 404 TK PDGFRb 12

0 1 0 0 0 1 1 0 0 239 Other MYT1 -

1 0 0 0 0 2 0 1 0 52 AGC RSKL2 -

0 0 0 0 0 0 0 0 0 57 AGC YANK1 -

0 0 0 0 0 0 0 0 0 58 AGC YANK2 -

0 0 0 0 0 0 0 0 0 59 AGC YANK3 -

1 0 1 0 0 0 0 0 0 86 CAMK Domain2MSK1 -

1 0 1 0 0 0 0 0 0 87 CAMK Domain2MSK2 -

1 0 1 0 1 0 0 0 0 89 CAMK Domain2RSK1 -

0 1 1 0 1 0 0 0 0 90 CAMK Domain2RSK2 -

0 1 1 0 1 0 0 0 0 91 CAMK Domain2RSK3 -

0 1 1 0 1 0 0 0 0 92 CAMK Domain2RSK4 -

0 0 0 0 0 0 1 1 0 93 CAMK Domain2SPEG -

1 0 0 0 1 0 0 0 0 98 CAMK MAPKAPK5 -

1 0 0 0 0 2 0 0 0 101 CAMK MARK3 -

1 0 0 0 0 0 1 0 0 106 CAMK NIM1 -

1 0 0 0 1 0 0 0 0 109 CAMK Obscn -

1 0 0 0 0 3 1 1 0 110 CAMK PASK -

1 0 0 0 0 0 2 0 0 113 CAMK PIM1 -

1 0 0 0 0 0 2 0 0 114 CAMK PIM2 -

1 0 0 0 0 0 2 0 0 115 CAMK PIM3 -

1 0 0 0 1 0 0 0 0 116 CAMK PKD1 -

1 0 0 0 1 0 0 0 0 117 CAMK PKD2 -

1 0 0 0 1 0 0 0 0 118 CAMK PKD3 -

0 0 0 0 0 0 0 0 0 126 CAMK SSTK -

1 0 0 0 0 0 0 1 0 133 CAMK TTN -

1 0 0 0 0 2 0 0 0 134 CAMK Trad -

1 0 0 0 0 0 0 1 0 135 CAMK Trb2 -

1 0 0 0 0 2 0 0 0 136 CAMK Trio -

1 0 0 0 0 0 0 1 0 137 CAMK VACAMKL -

1 0 0 0 0 0 1 1 0 150 CK1 VRK1 -

1 0 0 0 0 0 1 1 0 151 CK1 VRK2 -

1 2 0 0 1 0 0 0 0 181 CMGC Erk1 -

1 2 0 0 1 0 0 0 0 182 CMGC Erk2 -

1 2 0 0 0 0 0 0 0 183 CMGC Erk3 -

1 2 0 0 0 0 0 0 0 184 CMGC Erk4 -

1 0 0 0 1 0 0 0 0 186 CMGC Erk7 -

1 0 0 0 0 3 1 0 0 208 CMGC SRPK1 -

1 0 0 0 0 3 1 0 0 209 CMGC SRPK2 -

0 1 0 0 0 0 1 0 0 210 CMGC p38a -

0 1 0 0 0 0 1 0 0 211 CMGC p38b -

1 0 0 0 0 0 1 0 0 213 CMGC p38g -

0 0 0 0 0 1 0 1 0 219 Other BUB1 -

1 0 0 0 0 1 0 1 0 221 Other CK2a1 -

1 0 0 0 0 1 0 1 0 222 Other CK2a2 -

0 1 0 0 1 1 0 0 0 228 Other GAK -

1 0 0 0 0 0 0 1 0 240 Other NEK1 -

0 1 0 0 0 0 0 1 0 242 Other NEK11 -

1 0 1 0 0 0 0 1 0 243 Other NEK2 -

1 0 0 0 0 0 0 1 0 245 Other NEK4 -

1 0 0 0 0 0 0 1 0 246 Other NEK5 -

1 0 0 0 0 1 0 1 0 249 Other NEK8 -

1 0 0 0 0 1 0 1 0 250 Other NEK9 -

1 0 0 0 1 1 1 0 0 251 Other PBK -

1 0 0 0 0 1 0 1 0 253 Other PIK3R4 -

1 0 0 0 0 1 0 1 0 254 Other PKR -

1 0 1 0 0 1 0 0 0 255 Other PLK1 -

1 0 1 0 0 1 0 0 0 256 Other PLK2 -

1 0 1 0 0 1 0 0 0 257 Other PLK3 -

1 0 0 0 0 1 0 1 0 259 Other PRPK -

1 2 0 0 0 0 0 0 0 261 Other SBK -

1 0 0 0 0 1 0 1 0 264 Other SgK071 -

1 2 0 0 0 0 0 0 0 265 Other SgK110 -

1 0 0 0 0 3 1 0 0 267 Other SgK493 -

0 2 0 0 0 1 0 0 0 277 Other Wee1 -

0 2 0 0 0 1 0 0 0 278 Other Wee1B -

0 1 0 0 0 1 0 1 0 286 RGC CYGF -

1 0 0 0 0 1 0 1 0 287 RGC HSER -

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0 1 0 0 1 1 0 0 0 299 STE MAP2K5 -

1 0 0 1 1 1 1 0 0 301 STE MAP2K7 -

1 0 1 0 0 1 0 0 0 302 STE MAP3K1 -

1 0 0 0 0 0 0 1 0 343 TK CCK4 -

0 0 0 0 0 3 0 1 0 348 TK Domain2JAK1 -

1 2 0 0 0 1 0 1 0 349 TK Domain2JAK2 -

1 2 0 0 0 3 0 0 0 350 TK Domain2JAK3 -

0 1 0 0 0 3 0 1 0 351 TK Domain2TYK2 -

0 0 0 0 1 1 0 0 0 375 TK FLT1 -

1 0 0 0 1 0 0 0 0 376 TK FLT3 -

0 0 0 0 1 1 0 0 0 377 TK FLT4 -

0 1 0 0 0 1 0 1 0 383 TK HER3-ErbB3 -

1 0 0 1 0 1 0 0 0 388 TK ITK -

1 0 0 1 0 1 0 0 0 391 TK JAK3 -

0 0 0 0 1 1 0 0 0 392 TK KDR -

1 0 0 0 0 0 0 1 0 395 TK LMR1 -

1 0 0 0 0 0 0 1 0 397 TK LMR3 -

1 0 0 0 1 0 0 1 0 415 TK SuRTK106 -

1 0 0 0 0 3 1 0 0 427 TK ZAP70 -

0 1 0 0 0 1 0 1 0 447 TKL LIMK1 -

0 1 0 0 0 1 0 1 0 448 TKL LIMK2 -

1 0 0 0 0 1 0 1 0 459 TKL RIPK1 -

0 1 0 0 0 1 0 1 0 464 TKL TESK1 -

0 1 0 0 1 1 0 0 0 467 TKL TGFbR2 -

0 1 0 0 1 1 0 0 0 468 TKL ZAK -

8 85 kinases tested for selectivity

ATP Concentration Groupings For Screening Assays

5μM	20μM	50μM
ΔPH-PKBα (S473D)	Aurora B	ΔPH-PKBß (S474D)
CK2α	CaMKKß	AMPK
DYRK3	CDK2/cyclin A	BRSK2
EF2K	CHK1	BTK
EPH-B3	CHK2	CaMK1
ERK1	CK1δ	DYRK1a
ERK8	CSK	DYRK2
GSK3ß	FGF-R1	EPH-A2
HER4	GCK	IKKε
HIPK2	IR-HIS	LCK
IGF1R	IRAK4	MAPK2/ERK2
IKKß	JNK1α1	MAPKAP-K1a/RSK1
IRR	JNK2	MAPKAP-K1b/RSK2
MARK3	LKB1	MELK
MKK1	MAPKAP-K2	MINK1
p38γ MAPK	MLK1	MNK1
p38δ MAPK	MLK3	MNK2α
PAK4	MSK1	NEK2a
PIM2	MST2	NEK6
PKCζ	MST4	p38α MAPK
PLK1	NUAK1	PhKγ1
PRK2	p38ß MAPK	PKD1
	PAK5	smMLCK
	PAK6	Src
	PDK1	SRPK-1
	PIM1	TBK1
	PIM3	
	PKA	
	PKCα	
	PRAK	
	ROCKII	
	S6K1 (T412E)	
	SGK1	
	SYK	
	TTK	
	VEG-FR	
	YES1	

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