

## Supporting Information

# Determining cysteines available for covalent inhibition across the human kinome

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**Table S2.** The PDB structures released with accessible cysteines.

Sub-positions	Kinase	Uniprot	Released PDB id
P-loop-5	MP2K7	O14733	3WZU
	FGFR2	P21802	3R11
	FGFR4	P22455	4R6V
P-loop-7	CHK2	O96017	2YCF 2YCQ 2YIT
P-loop-9	KS6A5	O75582	3KN5
	MK08	P45983	2GMX
	KS6A3	P51812	4D9T 4D9U 4JG6 4JG7 4JG8
	NEK2	P51955	2JAV 2W5A 2W5B 2WQ0 2XK3 2XK4 2XK6 2XK7 2XK8 2XKC 2XKD 2XKE 2XKF 2XNM 2XNN 2XNO 2XNP 4A4A 4AFE
	PLK1	P53350	2OU7 2OWB 2RKU 2YAC 3FC2 3KB7 3THB 4A4L 4A4O 4J52 4J53
	PLK3	Q9H4B4	4B6L
Roof-3	PLK2	Q9NYY3	4I5M 4I5P 4I6B 4I6F 4I6H
	ERBB3	P21860	3KEX 3LMG 4OTW 4RIW 4RIX 4RIY
	Helix-9	CSKP	O14936
TIE2		Q02763	2WQB
KCC2B		Q13554	3BHH
KCC2D		Q13557	2VN9 2WEL
CAMK2G		Q8N4I3	2V7O
M3K14		Q99558	4IDV
KCC2A		Q9UQM7	2VZ6 3SOA
Helix-11	STK25	O00506	2XIK 4NZW
	STK10	O94804	2J7T 4AOT 4BC6 4EQU
	OXSRI	O95747	2VWI
	MP2K2	P36507	1S9I
	MP2K1	Q02750	3DV3 3DY7 3EQB 3EQC 3EQD 3EQF 3EQG 3EQH 3EQI 3MBL 3ORN 3OS3 3PP1 3V01 3VVH 3W8Q 3ZLS 3ZLW 3ZLY 3ZM4 4ARK 4LMN 4MNE 4U7Z 4U81 5BX0
	MKNK2	Q9HBH9	2HW7
	IRAK4	Q9NWX3	2NRU 2NRY 2OIC 2OID 4U9A
	STK24	Q9Y6E0	4QMN 4QMS 4QMV 4QMW 4QO9
Beta4-2	EGFR	P00533	1M17 1XKK 2EB3 2GS7 2ITN 2ITO 2ITP 2ITQ 2ITT 2ITU 2ITV 2ITW 2ITX 2ITY 2ITZ 2J5E 2J5F 2J6M 2J1U 2J1V 2RGP 3BEL 3GT8 3IKA 3LZB 3POZ 3UG2 3VJN 3VJO 3W2O 3W2P 3W2Q 3W2R 3W2S 3W32 3W33 4G5J 4G5P 4HJO 4I22 4I23 4I24 4JQ7 4JQ8 4JR3 4JRV 4LI5 4LLO 4LQM 4LRM 4R55 4RIW 4RIX 4RIY 4RJ4 4RJ5 4RJ6 4RJ7 4RJ8 4WDS 4WKQ 4ZAU 4ZSE 5C8K 5C8M 5C8N 5CAL 5CAN 5CAO 5CAP 5CAQ 5CAS 5CAU 5CAV 5CNN 5CNO 5D41 5EDQ 5EDR 5EM5 5EM6 5EM7 5EM8 5FED 5FEE 5FEQ 5HG7 5HG8 5HG9 5HIB 5HIC
	MELK	Q14680	4BKY 4BKZ 4BL1 4D2P 4D2T 4D2V 4D2W 4UMP 4UMQ 4UMR 4UMT 4UMU 5IH8 5IH9 5IHA 5IHC
	TTBK1	Q5TCY1	4BTJ 4BTK 4BTM 4NFN
Beta4-4	MP2K7	O14733	3WZU
	PK3CA	P42336	3ZIM 4L23 4TV3
	PK3CG	P48736	1E8Z 2A5U 2CHX 2CHZ 3APC 3APF 3CST 3DBS 3DPD 3ENE 3IBE 3L13 3L16 3L17 3L54 3LJ3 3MJW 3ML8 3ML9 3NZS 3NZU 3P2B 3PRE 3PRZ 3PS6 3QAQ 3QAR 3QJZ 3QK0 3R7R 3T8M 3TJP 3TL5 3ZVV 3ZW3 4ANW 4ANX 4AOF 4EZJ 4EZK 4EZL 4F1S 4FAD 4FHJ 4FHK 4FJZ 4FUL 4GB9 4HLE 4HVB 4J6I 4KZC 4PS3 4PS7 4URK 4WWN 4WWP
	ALK	Q9UM73	2XB7 2XBA 2XP2 2YFX 3AOX 3LCS 3LCT 4ANQ 4ANS 4CCB 4CCU 4CD0 4CLI 4CLJ 4CMO 4CMT 4CMU 4CNH 4CTB 4CTC 4DCE 4FNY 4FNZ 4FOB 4FOC 4FOD 4JOA 4MKC 4Z55 5A9U 5AA8 5AA9 5AAA 5AAB 5AAC 5FTO 5FTQ 5IMX 5IUG 5IUH 5IUI 5J7H
Beta4-2	MP2K6	P52564	3FME 3VN9
	MP2K1	Q02750	1S9I 2P55 3DV3 3DY7 3E8N 3EQB 3EQC 3EQD 3EQF 3EQG 3EQH 3EQI 3MBL 3ORN 3OS3 3PP1 3SLS 3V01 3V04 3VVH 3W8Q 3WIG 3ZLS 3ZLW 3ZLX 3ZLY 3ZM4 4AN2 4AN3 4AN9 4ANB 4ARK 4LMN 4MNE 4U7Z 4U80 4U81 5BX0
	RN5A	Q05823	4QAU 4QAV
Hinge-1	FGFR4	P22455	4QQ5 4QQC 4QRC 4R6V 4TYI 4TYJ 4UXQ 4XCU
	TTK	P33981	2X9E 2ZMD 3GFW 3H9F 3HMN 3HMO 3HMP 3VQU 3W1F 3WZJ 3WZK 4BHZ 4BIO 4BI1 4BI2 4C4E 4C4F 4C4G 4C4H 4C4I 4C4J 4JS8 4JT3 4O6L 4ZEG 5AP0 5AP1 5AP2 5AP3 5AP4 5AP5 5EH0 5EHY 5EI2 5EI6 5EI8
	MAPK2	P49137	1NXX 1NY3 2JBO 2JBP 2P3G 2PZY 3A2C 3FPM 3FYJ 3FYK 3GOK 3KAO 3KC3 3KGA 3M2W 3M42 3R2B 3R2Y 3R30 3WI6
	MAPK3	Q16644	3FHR 3FXW 3R1N 3SHE
Hinge-2	PLK4	O00444	3COK 4JXF 4YUR
	CHK1	O14757	1NVQ 1NVR 1NVS 1ZLT 1ZYS 2AYP 2BR1 2BRB 2BRG 2BRH 2BRM 2BRN 2BRO 2C3J 2C3K 2C3L 2CGU 2CGV 2CGW 2CGX 2E9N 2E9O 2E9P 2E9U 2E9V 2GDO 2GHG 2HOG 2HXL 2HXQ 2HY0 2QHM 2QHN 2ROU 2WMQ 2WMR 2WMS 2WMT 2WMU 2WMV 2WMW 2WMX 2X8D 2X8E 2X8I 2XEY 2XEZ 2XFO 2YDI 2YDJ 2YDK 2YER 2YEX 2YM3 2YM4 2YM5 2YM6 2YM7 2YM8 2YWP 3NLB 3OT3 3OT8 3PA3 3PA4 3PA5 3TKH 3TKI 3U9N 4F5M 4F5N 4FSQ 4FSR 4FST 4FSU 4FSW 4FSY 4FSZ 4FT0 4FT3 4FT5 4FT7 4FT9 4FTA 4FTC 4FTI 4FTJ 4FTK 4FTL 4FTM 4FTN 4FTO 4FTQ 4FTR 4FTT 4FTU 4GH2 4HYH 4HYI 4JIK 4QYE 4QYF 4QYG 4QYH 4RVK 4RVL 4RVM 5DLS 5F4N
	IKKB	O14920	4KIK
	GAK	O14976	4C57 4C58 4C59
	ULK1	O75385	4WNO 4WNP 5CI7
	ERN1	O75460	3P23 4U6R 4Y29 4YZC 4YZD 4Z7H
	STK10	O94804	2J7T 4AOT 4BC6 4EQU 5AJQ
	M4K4	O95819	4OBO 4OBP 4OBQ 4RVT 4U40 4U41 4U42 4U43 4U44 4U45 4ZK5 5DI1
	RAF1	P04049	3OMV
	CSF1R	P07333	2I0V 2I0Y 2I1M 3BEA 3DPK 3KRJ 3KRL 3LCD 3LCO 4HW7 4R7H 4R7I

	KIT	P10721	1PKG 1T46 3G0E 3G0F 4HVS
	BRAF	P15056	1UWH 1UWJ 2FB8 3C4C 3D4Q 3IDP 3IIS 3OG7 3PPJ 3PPK 3PRF 3PRI 3PSB 3PSD 3Q4C 3Q96 3SKC 3TV4 3TV6 4DBN 4E26 4E4X 4EHE 4EHG 4FC0 4FK3 4G9C 4G9R 4H58 4JVG 4KSP 4KSQ 4MBJ 4MNF 4PP7 4R5Y 4W05 4XV1 4XV2 4XV3 4XV9 4YHT 5C9C 5CSW 5CSX 5CT7 5FD2 5HI2 5HID 5HIE
	VGFR1	P17948	3HNG
	E2AK2	P19525	2A19
	WEE1	P30291	1X8B 2IN6 2IO6 2Z2W 3BI6 3BIZ 3CQE 3CR0
	VGFR2	P35968	1Y6A 1Y6B 1YWN 2OH4 2P2H 2P2I 2QU5 2QU6 2RL5 2XIR 3B8Q 3B8R 3BE2 3C7Q 3CJF 3CJG 3CP9 3CPB 3CPC 3DTW 3EFL 3EWH 3U6J 3VHE 3VHK 3VID 3VNT 3VO3 3WZD 3WZE 4AG8 4AGC 4AGD 4ASD 4ASE 5EW3
	CDK9	P50750	3BLQ 3BLR 3LQ5 3MIA 3MY1 3TN8 3TNH 4BCF 4BCG 4BCH 4BCI 4BCJ 4IMY 4OGR
	NEK2	P51955	2JAV 2W5A 2W5B 2WQO 2XK3 2XK4 2XK6 2XK7 2XK8 2XKC 2XKD 2XKE 2XKF 2XNM 2XNN 2XNO 2XNP 4A4X 4AFE
	PLK1	P53350	2OU7 2OWB 2RKU 2YAC 3FC2 3KB7 3THB 4A4L 4A4O 4J52 4J53
	CDKL1	Q00532	4AGU
	CDK5	Q00535	1UNG 1UNH 1UNL 4AU8
	FAK1	Q05397	1MP8 2ETM 2IJM 3BZ3 4EBV 4EBW 4GU6 4GU9 4I4E 4I4F 4K8A 4K9Y 4KAB 4KAO 4Q9S
	RN5A	Q05823	4OAU 4OAV
	M3K12	Q12852	5CEO 5CEP
	STK3	Q13188	4LGD
	MELK	Q14680	4BKY 4BKZ 4BL1 4D2P 4D2T 4D2V 4D2W 4UMP 4UMQ 4UMR 4UMT 4UMU 5IH8 5IH9 5IHA 5IHC
	STK11	Q15831	2WTK
	AAK1	Q2M2I8	4WSQ 5L4Q
	KSR2	Q6VAB6	2Y4I
	PTK1	Q8IYN9	3PXK
	NEK1	Q96PY6	4B9D
	SLK	Q9H2G2	2J51 2JFL 2UV2 4USF
	PLK3	Q9H4B4	4B6L
	BMP2K	Q9NSY1	4W9W 4W9X 5I3O 5I3R 5IKW
	PLK2	Q9NYY3	4I5M 4I5P 4I6B 4I6F 4I6H
	E2AK3	Q9NZJ5	4G31 4G34 4M7I 4X7H 4X7J 4X7K 4X7L 4X7N 4X7O
	TBK1	Q9UHD2	4EUT 4EUU 4IM0 4IM2 4IM3 4IW0 4IW1 4IWP 4IWX
	TNIK	Q9UKE5	2X7F
Hinge-3	CSF1R	P07333	2IOV 2IOY 2I1M 3BEA 3DPK 3KRJ 3KRL 3LCD 3LCO
	KIT	P10721	1PKG 1T46 3G0E 3G0F 4HVS
	RON	Q04912	3PLS
Front-2	MP2K7	O14733	3WZU
	EGFR	P00533	1M17 1XKK 2EB3 2GS7 2ITN 2ITO 2ITP 2ITQ 2ITT 2ITU 2ITV 2ITW 2ITX 2ITY 2ITZ 2J5F 2J6M 2JIU 2RGP 3BEL 3GT8 3KA 3LZB 3POZ 3UG2 3VJN 3VJO 3W2O 3W2P 3W2Q 3W2R 3W2S 3W32 3W33 4G5I 4G5P 4HJO 4I22 4I23 4I24 4JQ7 4JQ8 4JR3 4JRV 4LI5 4LLO 4LQM 4LRM 4R5S 4RIW 4RIX 4RIY 4RJ4 4RJ5 4RJ6 4RJ7 4RJ8 4WDS 4ZAU 4ZSE 5C8K 5C8M 5C8N 5CAL 5CAN 5CAO 5CAP 5CAQ 5CAS 5CAU 5CAV 5CNN 5CNO 5D41 5EDQ 5EDR 5EM5 5EM6 5EM7 5EM8 5FED 5FEE 5FEQ 5HG7 5HG8 5HG9 5HIB 5HIC
	ERBB2	P04626	3PPO 3RCD
	BMX	P51813	3SXR 3SXS
	JAK3	P52333	1YVJ 3LXK 3LXL 3PJC 3ZC6 3ZEP 4HVD 4HVG 4HVH 4HVI 4I6Q 4QPS 4QT1 4RIO 4VOG 4Z16
	BTK	Q06187	3GEN 3K54 3OCS 3OCT 3PIX 3PIY 3PIZ 3PJ2 3PJ3 4OT5 4OT6 4OTQ 4OTR 4RFY 4RFZ 4RGO 4RX5 4YHF 4Z3V 4ZLY 4ZLZ 5BPY 5BQ0 5FBN 5FBO
	ITK	Q08881	1SM2 1SNU 3MIY 3MJ1 3MJ2 3QGW 3QGY 3T9T 3V5J 3V5L 3V8T 3V8W 4HCT 4HCU 4HCV 4KIO 4L7S 4M0Y 4M0Z 4M12 4M13 4M14 4M15 4MF0 4MF1 4PP9 4PPA 4PPB 4PPC 4PPN 4QD6
ERBB4	Q15303	2R4B 3BBT	
Front-3	MAPK8	A114K2	2XRW 4G1W 4HYS 4HYU 4IZY
	MK08	P45983	2GMX 2NO3 3ELJ 3V3V 4AWI 4E73 4L7F 4QTD
	MK10	P53779	1JNK 1PMQ 1PMV 2O0U 2O2U 2P33 2ZDU 3CGF 3CGO 3DA6 3G90 3G9L 3G9N 3OXI 3OY1 3RTP 3TTI 3TTJ 3V6R 3V6S 4KKE 4KKH 4U79 4W4V 4W4W 4W4X 4W4Y 4WHZ
Catalytic-2	CSF1R	P07333	3LCO 4HW7 4R7H 4R7I
	KIT	P10721	1T46 3G0F 4HVS
	FGFR1	P11362	1AGW 1FGI 2FGI 3C4F 3GQI 3GQL 3JS2 3RHX 3TTO 3WJ6 4F64 4F65 4NK9 4NKA 4NKS 4UWB 4UWC 4WUN 4ZSA 5A46 5A4C 5AM7 5B7V 5EW8
	VGFR1	P17948	3HNG
	FGFR2	P21802	2PZR 3B2T 3RI1 4J95 4J97 4J99
	FGFR4	P22455	4QQ5 4QQC 4QRC 4R6V 4TYI 4TYJ 4UXQ
	FGFR3	P22607	4K33
	VGFR2	P35968	1Y6A 1YWN 2OH4 2P2H 2P2I 2QU6 2RL5 2XIR 3B8Q 3B8R 3BE2 3CP9 3CPB 3CPC 3DTW 3EFL 3EWH 3U6J 3VHE 3VHK 3VID 3VNT 3VO3 3WZD 3WZE 4AG8 4ASD 4ASE 5EW3
	JAK3	P52333	4HVD 4HVH 4HVI 4I6Q 4QPS 4QT1 4Z16
	FAK2	Q14289	3ET7 3FZP 3FZR 3FZS 3FZT 3H3C 4H1J 4H1M
Catalytic-9	ABL1	P00519	2F4J 2G2I 2H24 2V7A 3UE4 4WA9
	NTRK1	P04629	4AOJ 4PMM 4PMS 4PMT
	INSR	P06213	1IR3 2Z8C 3BU5 4IBM
	FES	P07332	3BKB 3CD3
	IGF1R	P08069	1K3A 2ZM3 3F5P 3I81 3LVP 3NW6 3NW7 3O23
	MET	P08581	1R0P 2RFS 2WD1 2WGI 3A4P 3C1X 3CCN 3CD8 3DKC 3DKF 3I5N 3Q6W 3QTI 3R7O 3RHK 3VW8 3ZBX 3ZCS 3ZCL 3ZXZ 3ZZE 4AOI 4AP7 4DEG 4DEH 4DEI 4EEV 4GG5 4GG7 4IWD 4KNB 4MXC 4XMO 4XYF
	ROS1	P08922	4UXL

	ABL2	P42684	2XYN 3GVU 3HMI
	BMX	P51813	3SXS
	LIMK1	P53667	3S95
	LIMK2	P53671	4TPT
	BTK	Q06187	4NWM 4OT5 4OT6 4OTF 4OTQ 4OTR 4RFY 4RFZ 4RGO
	DDR1	Q08345	4CKR
	ITK	Q08881	15M2 15NU 3MIY 3MJ1 3MJ2 3T9T 3V5L 4L7S 4M0Y 4M0Z 4M12 4M13 4M14 4M15 4MF1 4PP9 4PPA 4PPC 4PQN
	MERTK	Q12866	3TCP 4M3Q 4MH7 4MHA
	NTRK2	Q16620	4AT3 4AT4 4AT5
	ALK	Q9UM73	2XB7 2XBA 2XP2 2YFX 3LCS 3LCT 4ANQ 4ANS 4CCB 4CCU 4CD0 4CLI 4CLJ 4CMO 4CMT 4CMU 4CNH 4CTB 4CTC 4FOB 4FOC 4FOD 4JOA 4MKC
DFG-3	MP2K7	O14733	3WZU
	GAK	O14976	4C57 4C58 4C59
	M3K7	O43318	2EVA 2YIY 4GS6 4L3P 4L52 4L53 4O91 5JGA 5JGB 5JGD
	CDKL5	O76039	4BGQ
	KIT	P10721	1PKG 1T46 3G0E 3G0F 4HVS
	VGFR1	P17948	3HNG
	MK03	P27361	2Z0Q 4QTB
	MK01	P28482	1PME 1TVO 1WZY 2OJG 2OJI 2OJJ 2Y9Q 3I5Z 3I60 3TEI 3W55 4FMQ 4FUX 4FV1 4FV2 4FV3 4FV4 4FV5 4FV6 4FV7 4FV8 4FV9 4G6N 4G6O 4H3P 4H3Q 4I25 4NIF 4O6E 4QP1 4QP2 4QP3 4QP4 4QP6 4QP7 4QP8 4QP9 4QPA 4QTA 4QTE 4XJ0 4ZZM 4ZZN 4ZZO 5AX3 5BUE 5BUI 5BUJ 5BVD 5BVE 5BVF 5K4I 5LCJ 5LCK
	VGFR2	P35968	1Y6A 1Y6B 1YWN 2OH4 2P2H 2P2I 2QU5 2QU6 2RL5 2XIR 3B8Q 3B8R 3BE2 3C7Q 3CJG 3CP9 3CPB 3CPC 3DTW 3EFL 3EWH 3U6J 3VHE 3VHK 3VID 3VNT 3VO3 3WZD 3WZE 4AG8 4AGC 4AGD 4ASD 4ASE 5EW3
	MP2K2	P36507	1S9I
	TGFR1	P36897	5E8X 5E90
	TGFR2	P37173	5E8Y 5E91 5E92
	MP2K4	P45985	3ALN 3ALO
	GSK3B	P49841	1H8F 1J1B 1J1C 1O9U 1PYX 1Q3D 1Q3W 1Q41 1Q4L 1Q5K 1R0E 1UV5 2JLD 2O5K 2OW3 3DU8 3F7Z 3F88 3GB2 3I4B 3L1S 3M1S 3PUP 3Q3B 3SAY 3SD0 3ZDI 3ZRK 3ZRL 3ZRM 4ACC 4ACD 4ACG 4ACH 4AFJ 4B7T 4DIT 4IQ6 4J1R 4J71 4NMO 4NM3 4NM5 4NM7 5F94 5F95 5HLN 5HLP
	KS6A3	P51812	4D9T 4D9U 4JG6 4JG7 4JG8
	MP2K6	P52564	3FME 3VN9
	CDKL1	Q00532	4AGU
	MP2K1	Q02750	1S9J 2P55 3DV3 3DY7 3E8N 3EQB 3EQC 3EQD 3EQF 3EQG 3EQH 3EQI 3MBL 3ORN 3OS3 3PP1 3SL5 3V01 3V04 3VVH 3W8Q 3WIG 3ZLS 3ZLW 3ZLX 3ZLY 3ZM4 4AN2 4AN3 4AN9 4ANB 4ARK 4LMN 4MNE 4U7Z 4U80 4U81 5BX0
	PRP4B	Q13523	4IFC 4IIR 4IJP
	FLT3	P36888	1RJB 4RT7 4XUF
	AAK1	Q2M2I8	4WSQ 5L4Q
	CDKL3	Q8IVW4	3ZDU
	CDKL2	Q92772	4AAA 4BBM
	M3K14	Q99558	4DN5 4IDT 4IDV
	MNK1	Q9BUB5	2HW6
	MKNK2	Q9HBH9	2HW7
BMP2K	Q9NSY1	4W9W 4W9X 5I3O 5I3R 5IKW	
MLTK	Q9NYL2	5HES	
DFG-4	KS6B1	P23443	3WF7 3WF8 3WF9
	RPS6KB1	Q72721	4L3J 4L3L 4L46

Note: Red color shows the structure with the covalent interaction between the cysteine and ligand.

**Table S3.** The list of kinases with available cysteines across the human structural kinome as shown in Figure 7b.

<b>Regions</b>	<b>Kinases</b>
P-loop	ACVR2A CHK2 FGFR2 FGFR4 CSNK1G1 CSNK1G3 RPS6KA3 RPS6KA5 MET MAP2K7 NEK2 PLK1 PLK2 PLK3 SRC VRK1 ZAP70
Roof of pocket	MAP2K7
Front pocket	BMX BTK CASK EGFR ERBB2 ERBB4 ITK JAK3 MAPK8 MAPK10 MAP2K7 RNASEL STK11
DFG-3	AAK1 BMP2K CDKL1 CDKL2 CDKL3 CDKL5 FLT3 GAK GSK3B KIT RPS6KA3 MAP3K14 MAP3K7 MAPK1 MAPK3 MNK1 MKNK2 MLTK MAP2K1 MAP2K2 MAP2K4 MAP2K6 MAP2K7 PRPF4B TGFBR2 FLT1 KDR
Catalytic-2	CSF1R FAK2 FGFR1 FGFR2 FGFR3 FGFR4 JAK3 KIT FLT1 KDR

**Table S4.** The list of kinases with available cysteines for the kinases without PDB released as shown in Figure 7c.

<b>Regions</b>	<b>Kinases</b>
P-loop	CSNK1G2 CRIK Erk3 FGFR1 FGFR3 FGR IRAK1 LIMK1 MAP3K1 MSK2 NEK10 PAN3 ROR1 RSK1 RSK3 RSK4 SgK069 SgK223 SuRTK106 TNK1 VACAMKL YES
Roof of pocket	
Front pocket	BLK EphB3 TEC TXK MAST3 MAST2 MAST1 MAST4 Trio TSSK3 ATM SMG1 ADCK4 ADCK5 RIOK2 SgK493 BMPR2 MISR2 PINK1 Obscn JNK2 PFTAIRES1 SPEG
DFG-3	CDKL4 Erk7 FLT4 Fused GSK3A MAP2K3 MAP2K5 MAPKAPK5 TNIK NLK Obscn PDGFRa PDGFRb PKD1 PKD2 PKD3 RSK3 RSK4 SPEG SuRTK106
Catalytic-2	FLT4 PDGFRa PDGFRb FLT3 FER FES ANPa STK6 CDKL1 CDKL4

**Table S5.** Covalent kinase inhibitor dataset.

Ligand name	Cysteine site	UniprotKB ID of Kinase as targets	PMID
CDDO-Me	Activation-loop	O14920	16998237
Nimbolide	Activation-loop	O15111 O14920	20829362
Compound3	Catalytic-2	P10721	21322567
Cl-Radicicol; A	DFG-3	P35916 P35968 P36888 P09619	10695671
Radicicol; A	DFG-3	P35916 P35968 P36888 P09619	10695671
L-783290	DFG-3	Q02750	10695671
Chloromethyl	DFG-3	P49841	14561081; 19747834
KB-283641	DFG-3	P49841	14561081; 19747834
Chloromethyl	DFG-3	P49841	14561081; 19747834
E6201	DFG-3	Q02750 P36507	24448821
FR265082	DFG-3	P28482 Q02750 P35968 P16234 P35916 P36888 P17948	17194451; 10695671; 19821461
5Z-7-Oxozeaenol	DFG-3	O14733 Q02750 P28482 O43318 P35916 P35968 P36888 P09619	25529738; 17194451; 17676571; 23272696
Hypothemycin	DFG-3	P28482 Q388M1 Q02750 P35968 P16234 P35916 P36888 P17948 P10721 P51955 P27361 Q15139 Q8IW41 P49841	18571434; 23853713; 17194451; 19821461; 16537514
10753475-10	Front pocket	P00533	10753475
10753475-13	Front pocket	P00533	10753475
10753475-21	Front pocket	P00533	10753475
10753475-22	Front pocket	P00533	10753475
10753475-24	Front pocket	P00533	10753475
10753475-26	Front pocket	P00533	10753475
10753475-27	Front pocket	P00533	10753475
10753475-7	Front pocket	P00533	10753475
CHEMBL31588	Front pocket	P00533	10753475
CHEMBL283201	Front pocket	P00533	10753475
CHEMBL27685	Front pocket	P00533	10753475
CHEMBL280757	Front pocket	P00533	10753475
CHEMBL31369	Front pocket	P00533	10753475
CHEMBL27688	Front pocket	P00533	10753475
CHEMBL31326	Front pocket	P00533	10753475
CHEMBL32079	Front pocket	P00533	10753475
AGN-PC-09QDFK	Front pocket	P00533	10753475
CHEMBL31419	Front pocket	P00533	10753475
CHEMBL31373	Front pocket	P00533	10753475
CHEMBL31815	Front pocket	P00533	10753475
neratinib	Front pocket	P00533 P04626	22037378; 15173008
ibrutinib	Front pocket	Q06187	17154430
Tube716	Front pocket	Q06187	17154430
US8476284-5	Front pocket	Q06187	17154430
US8476284-41	Front pocket	Q06187	17154430
US8476284-42	Front pocket	Q06187	17154430
US8497277-9	Front pocket	Q06187	17154430
US8476284-9	Front pocket	Q06187	17154430
US8476284-39	Front pocket	Q06187	17154430
US8476284-38	Front pocket	Q06187	17154430
US8497277-15	Front pocket	Q06187	17154430
SCHEMBL1613911	Front pocket	Q06187	17154430
FR264744	Front pocket	P28482	17194451
pelitinib	Front pocket	P00533	17416531;
PF00299804	Front pocket	P00533 P04626 Q15303	18089823
Canertinib	Front pocket	P00533 P04626 Q15303	18089823; 18667312;

		P52333 P51451 P51813 Q06187 Q08881	10753475
PD168393	Front_pocket	P00533 P04626 Q15303 P52333 P51451 P51813 Q06187	18667312
WZ4002	Front_pocket	Q06187 P51451 P00533 Q15303 Q08881	20033049
afatinib	Front_pocket	P00533 P04626	20550212; 22037378; 18408761
PCI33380	Front_pocket	Q06187	20615965
Btk-inhibitor-4	Front_pocket	P51813 Q06187 P51451 P00533 P04626 P52333 P42680	20615965; 17154430
poziotinib	Front_pocket	P00533 P04626 Q15303	21306821
JNK-IN-1	Front_pocket	P45983 P45984 P53779	22284361
JNK-IN-2	Front_pocket	P45983 P45984 P53779	22284361
JNK-IN-4	Front_pocket	P45983 P45984 P53779	22284361
JNK-IN-5	Front_pocket	P45983 P45984 P53779	22284361
JNK-IN-7	Front_pocket	P45983 P45984 P53779	22284361
JNK-IN-8	Front_pocket	P45983 P45984 P53779	22284361
JNK-IN-9	Front_pocket	P53779	22284361
JNK-IN-10	Front_pocket	P53779	22284361
JNK-IN-11	Front_pocket	P45983 P45984 P53779	22284361
JNK-IN-12	Front_pocket	P45983 P45984 P53779	22284361
spebrutinib	Front_pocket	Q06187	22612424
CNX-774	Front_pocket	Q06187	22621397
G5K	Front_pocket	Q08881	23098091
CHEMBL2179816	Front_pocket	Q08881	23098091
CHEMBL2179804	Front_pocket	Q08881	23098091
IAQ	Front_pocket	Q08881	23098091
18R	Front_pocket	Q08881	23098091
CNX-1351	Front_pocket	P42336	23360348
CNX-1220	Front_pocket	P42336	23360348
BMX-IN-1	Front_pocket	P51813	23594111
rociletinib	Front_pocket	P00533	24065731
QL47	Front_pocket	Q06187	24556163
Compound31	Front_pocket	P51813 Q06187 P51451 P42680	24915291
Compound38	Front_pocket	P51813 Q06187 P51451 P00533 P04626 Q15303 P42680	24915291
37Q	Front_pocket	P52333	25552479
PRN694	Front_pocket	P51813 Q06187 P51451 Q08881 P52333 P42680	25593320
naquotinib	Front_pocket	P00533	26508839
ONO-4059	Front_pocket	Q06187	26542378
osimertinib	Front_pocket	P00533	27071706
olmutinib	Front_pocket	P51813 Q06187 P51451 P00533 Q08881 P52333 P42680	27090981
nazartinib	Front_pocket	P00533	27433829
FIIN-3	Front_pocket	P22455 P00533	25776529
BLU9931	Hing-1	P22455	25776529
CMK	P-loop	P51812 Q15418	15919995
FIIN-1	P-loop	P11362 P21802 P22607 P22455	20338520
CHEMBL1802381	P-loop	P51955	21627121
CHEMBL1802870	P-loop	P51955	21627121
CHEMBL1802387	P-loop	P51955	21627121
CHEMBL1802382	P-loop	P51955	21627121
CHEMBL1802383	P-loop	P51955	21627121
CHEMBL1802384	P-loop	P51955	21627121



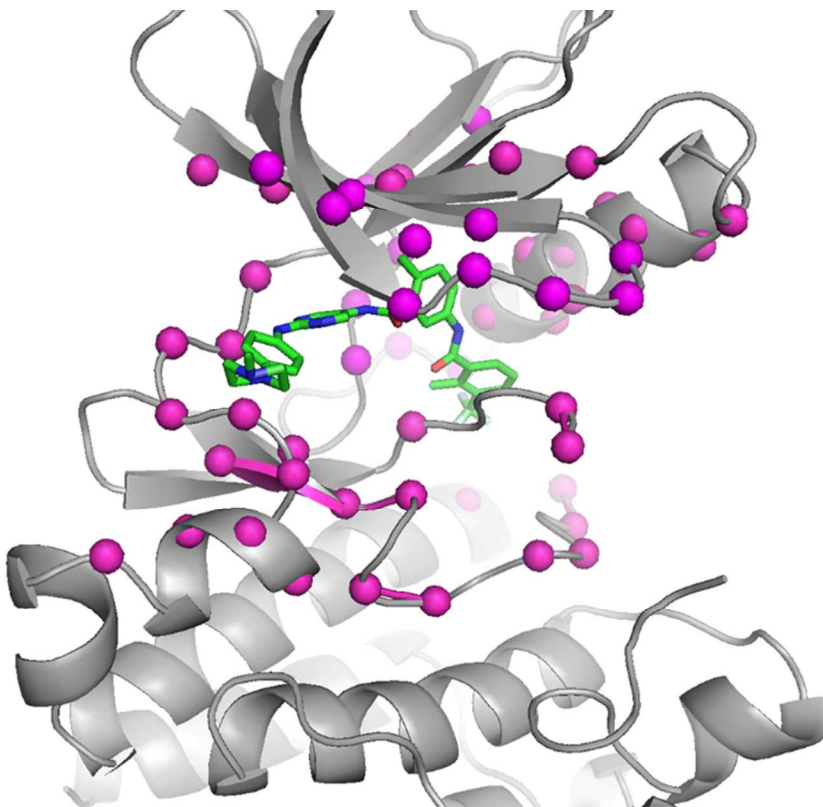
21627121-12	P-loop	P51955	21627121
CHEMBL1802388	P-loop	P51955	21627121
CHEMBL1802869	P-loop	P51955	21627121
CHEMBL1802872	P-loop	P51955	21627121
RCI16	P-loop	P51812	22466421
RCI14	P-loop	P51812	22466421
FMK	P-loop	P51812 Q15418	22466421; 22806944; 15919995
23540679-4	P-loop	P51812 P51955 P53350	23540679
SCHEMBL1907851	P-loop	P51812 P51955	23540679
SCHEMBL12675979	P-loop	P51812 P51955 P53350	23540679
SCHEMBL12675980	P-loop	P51812 P51955 P53350	23540679
SCHEMBL1904658	P-loop	P51812 P51955 P53350	23540679
SCHEMBL14682587	P-loop	P51812 P51955 P53350	23540679
1LB	P-loop	P51812	23540679
SCHEMBL1905217	P-loop	P51812 P51955 P53350	23540679
SCHEMBL12676021	P-loop	P51812 P51955 P53350	23540679
ZINC00018730	P-loop	P51812 P51955 P53350	23540679
23540679-3	P-loop	P51812 P51955 P53350	23540679
23540679-5	P-loop	P51812	23540679
23540679-10	P-loop	P51812 P53350	23540679
1LE	P-loop	P51812	23540679
1LC	P-loop	P51812	23540679
O37	P-loop	P22455	25776529
23225637-2	Extended_front- pocket	Q16539	23225637
Bio-THZ1	Remote_Cys	P50613	25043025
THZ1	Remote_Cys	P50613 Q9NYV4	25043025
TX1-85-1	Roof	P21860	26094118; 25326665
TX2-121-1	Roof	P21860	26094118; 25326665

**Table S6.** The sequence alignment of the kinases with the available cysteines in five different regions across the human kinome.

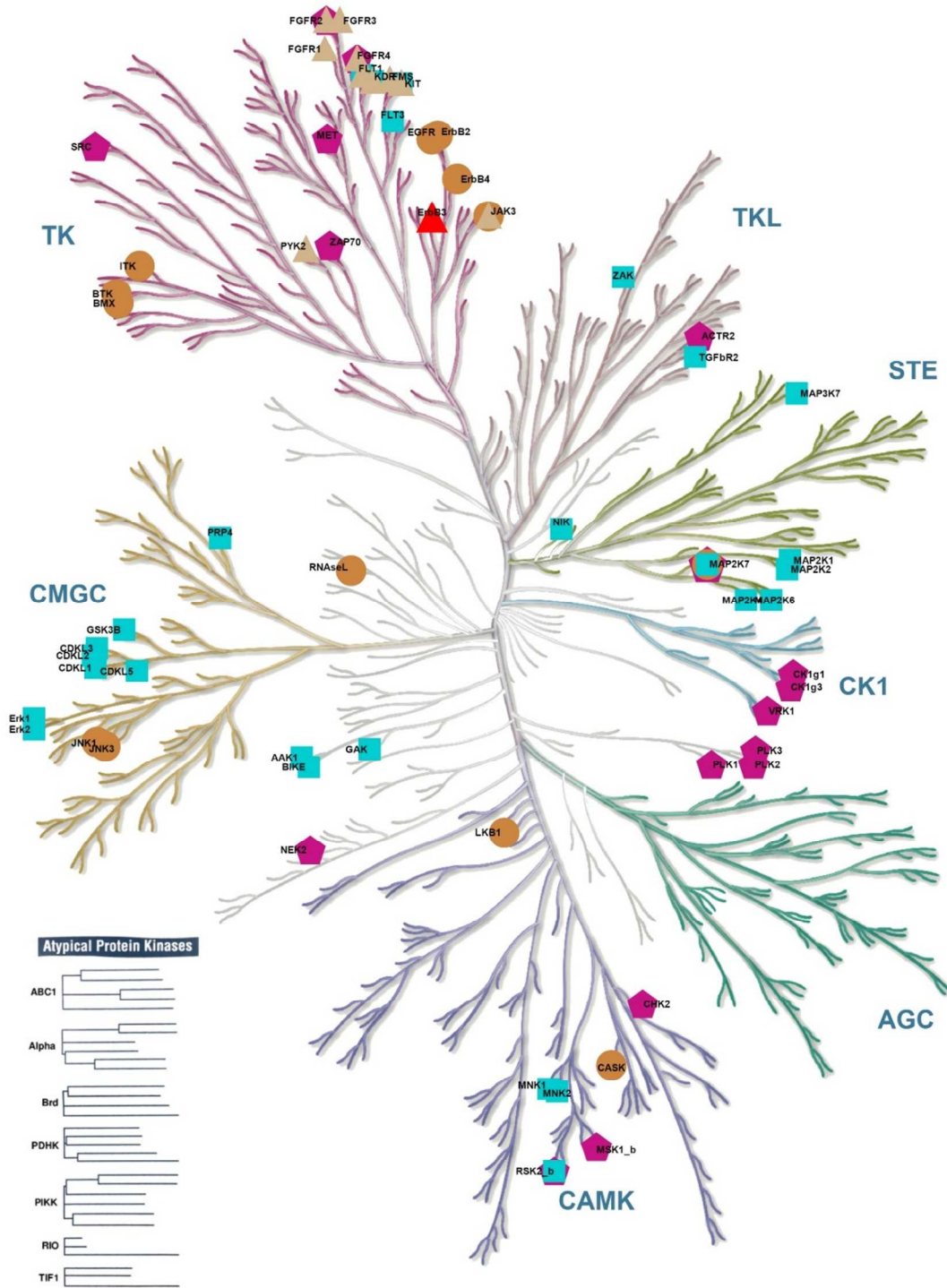
<b>Region: P-loop</b>		Obscn	PE-----LL-----PC
ZAP70	GCG--N-FG--SV	MAP2K7	C-----AE-----KL
MET	GRG--H-FG--CV	JNK2	N-----LC-----QV
FGFR1	GEG--C-FG--QV	JNK1	N-----LC-----QV
FGFR2	GEG--C-FG--QV	JNK3	N-----LC-----QV
FGFR3	GEG--C-FG--QV	PFTAIRE1	D-----LC-----QY
TNK1	GSG--C-FG--VV	SPEG	RE-----LL-----CG
FGR	GTG--C-FG--DV	<b>Region: DFG-3</b>	
SRC	GQG--C-FG--EV	FLT4	C
YES	GQG--C-FG--EV	FLT1	C
ROR1	GEC--A-FG--KI	KDR	C
FGFR4	GEG--C-FG--QV	PDGFRa	C
CR1K	GCG--H-FA--EV	PDGFRb	C
PLK1	GKG--G-FA--KC	KIT	C
PLK2	GKG--G-FA--KC	FLT3	C
PLK3	GKG--G-FA--RC	Obscn	C
RSK42	GVG--S-YS--VC	SPEG	C
RSK32	GVG--S-YS--VC	Fused	C
RSK12	GVG--S-YS--EC	MAPKAPK5	C
RSK22	GVG--S-YS--VC	RSK4	C
MSK12	GEG--S-FS--IC	RSK3	C
MSK22	GQG--S-FS--VC	RSK1	C
CHK2	GSG--A-CG--EV	RSK2	C
VACAMKL	KTE--E-FC--EI	PKD2	C
CK1g2	GCG--N-FG--EL	PKD1	C
CK1g1	GCG--N-FG--EL	PKD3	C
CK1g3	GCG--N-FG--EL	MNK2	C
VRK1	GQG--G-FG--CI	GAK	C
PAN3	NFG--Y-IT--SC	AAK1	C
ACTR2	ARG--R-FG--CV	BIKE	C
ACTR2B	ARG--R-FG--CV	PRP4	C
SgK223	GDA--I-YY--CA	GSK3A	C
Erk3	GCG--G-NG--LV	GSK3B	C
MAP2K7	GSG--T-CG--QV	NIK	C
SuRTK106	CSG--S-CG--PI	MAP2K1	C
SgK069	GQG--C-YG--RV	MAP2K2	C
IRAK1	GEG--G-FG--CV	MAP2K7	C
LIMK1	GKG--C-FG--QA	MAP2K4	C
NEK10	GSG--A-FG--CV	MAP2K3	C
NEK2	GTG--S-YG--RC	MAP2K6	C
MAP3K1	GLG--A-FS--SC	SuRTK106	C
<b>Region: roof of pocket</b>		MNK1	C
ErbB3	VCI	TAK1	C
<b>Region: front pocket</b>		ZAK	C
JAK3	GCL-----R-----DF	Erk7	C
EGFR	GCL-----L-----DY	NLK	C
ErbB2	GCL-----L-----DH	Erk1	C
BLK	GCL-----L-----DF	Erk2	C
EphB3	CAL-----D-----SF	CDKL5	C
ErbB4	GCL-----L-----EY	CDKL1	C
BMX	GCL-----L-----NY	CDKL4	C
BTK	GCL-----L-----NY	CDKL2	C
ITK	GCL-----S-----DY	CDKL3	C
TEC	GCL-----L-----NF	MAP2K5	C
		<b>Region: Catalytic-3</b>	
		JAK3	C

TXK	GCL-----L-----NY	PYK2	C
MAST3	GDC-----A-----TL	FGFR1	C
MAST2	GDC-----A-----TL	FGFR2	C
MAST1	GDC-----A-----TL	FGFR3	C
MAST4	GDC-----A-----TL	FLT4	C
Trio	GRL-----L-----DC	FLT1	C
TSSK3	GDV-----F-----DC	KDR	C
CASK	ADL-----C-----FE	PDGFRa	C
ATM	QPVFRYFCMEKFLDPAIW	PDGFRb	C
SMG1	PNLLAKELWSSCTTPDEW	KIT	C
ADCK4	VPL-----DQC	FMS	C
ADCK5	CKV-----NDV	FLT3	C
RIOK2	-----YPL---CQI	FGFR4	C
NME7a	-----DAI---CEW	FER	C
SgK493	-----DLGSCVRE---	FES	C
RNAseL	C---LDVHRG-----	ANPa	C
BMPR2	-----GSLCKY	STLK6	C
MISR2	-----GSLCHY	CDKL1	C
PINK1	-----CTL---	CDKL4	C

**Figure S1.** Accessible cysteines at the different locations presented on a reference binding site (pdb id 3byu).



**Figure S2.** The high resolution figure for the kinases with available cysteines across the human structural kinome as shown in Figure 7b.



**Figure S3.** The high resolution figure for the kinases with available cysteines for all kinases without PDB released as shown in Figure 7c.

