

**Table S1: dT-HESC 2hr Post-Infection Array Analysis with Fold Changes Compared to Mock Infection and Annotated Functions.** Proteins with z-score ratios greater than 1.0 (red) or less than -1.0 (blue) were considered significant.

Target Protein Name	Phospho Site (Human)	Full Target Protein Name	Fold Ch. GB112	Fold Ch. GB411	Fold Ch. GB590	Fold Ch. GB653	Function as summarized from the Uniprot Database ( <a href="http://www.uniprot.com">www.uniprot.com</a> )	Phospho Site Information (Kinexus PhosphoNET Database)
4E-BP1	T45	Eukaryotic translation initiation factor 4E binding protein 1 (PHAS1)	0.2	0.1	1.2	-0.2	Repressor of translation initiation that regulates EIF4E activity by preventing its assembly into the eIF4F complex: hypophosphorylated form binds to EIF4E, leading to repress translation. In contrast, hyperphosphorylated form dissociates from EIF4E, leading to initiation of translation. Mediates the regulation of protein translation by hormones, growth factors and other stimuli that signal through MAPK and mTORC1 pathways.	Release of its inhibition toward EIF4E. T45 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1), FRAP1 (mTOR), p38a MAPK (MAPK14).
A6r	Y309	Twinfilin-2	-0.7	-0.7	-0.9	-1.1	Actin-binding protein involved in motile and morphological processes. Inhibits actin polymerization, likely by sequestering G-actin. By capping the barbed ends of filaments, it also regulates motility. Seems to play an important role in clathrin-mediated endocytosis and distribution of endocytic organelles.	No data available.
ABL1	Pan-specific	Abelson proto-oncogene-encoded protein-tyrosine kinase	2.0	1.1	2.0	1.2	Non-receptor tyrosine-protein kinase that plays a role in many key processes linked to cell growth and survival such as cytoskeleton remodeling in response to extracellular stimuli, cell motility and adhesion, receptor endocytosis, autophagy, DNA damage response and apoptosis. Pathogens can hijack ABL1 kinase signaling to reorganize the host actin cytoskeleton for entry, facilitating intracellular movement and host cell exit.	NA
ABL1	Y264	Abelson proto-oncogene-encoded protein-tyrosine kinase	1.1	0.6	0.9	0.3	see above	Predicted to be inhibitory for phosphotransferase activity.
ACK1	Pan-specific	Activated CDC42 kinase 1 (TNK2)	2.7	1.0	2.0	2.0	Non-receptor tyrosine-protein and serine/threonine-protein kinase that is implicated in cell spreading and migration, cell survival, cell growth and proliferation. Transduces extracellular signals to cytosolic and nuclear effectors. Implicated in trafficking and clathrin-mediated endocytosis through binding to EGFR and clathrin. Regulates ligand-induced degradation of EGFR, thereby contributing to the accumulation of EGFR at the limiting membrane of early endosomes. Downstream effector of CDC42 which mediates CDC42-dependent cell migration.	NA
ACTA1	Pan-specific	ACTA1 (Alpha-actin)	0.7	1.4	2.2	2.1	Actins are highly conserved proteins that are involved in various types of cell motility and are ubiquitously expressed in all eukaryotic cells.	NA
ACTB	Y294	Actin, cytoplasmic 1 (Beta-actin)	1.1	0.8	0.5	-0.1	Actins are highly conserved proteins that are involved in various types of cell motility and are ubiquitously expressed in all eukaryotic cells.	No data available.

Adducin a/g	S726	Adducin alpha, gamma (ADD 1/3)	-0.1	0.6	-0.8	-1.0	Membrane-cytoskeleton-associated protein that promotes the assembly of the spectrin-actin network. Plays a role in actin filament capping. Binds to calmodulin.	Phosphorylated by PKACA, PKAc, PKCz.
AKT1 (PKBa)	Pan-specific	RAC-alpha serine/threonine-protein kinase	0.4	1.0	-0.4	-0.2	Serine/threonine-protein kinase which regulates many processes including metabolism, proliferation, cell survival, growth and angiogenesis. This is mediated through serine and/or threonine phosphorylation of a range of downstream substrates. Over 100 substrate candidates have been reported.	NA
AKT2 (PKBb)	Pan-specific	RAC-beta serine/threonine-protein kinase	1.5	1.1	1.6	1.6	Serine/threonine-protein kinase which regulates many processes including metabolism, proliferation, cell survival, growth and angiogenesis. This is mediated through serine and/or threonine phosphorylation of a range of downstream substrates. Over 100 substrate candidates have been reported.	NA
Akt1 (PKBa)	Y474	RAC-alpha serine/threonine-protein kinase	0.2	-0.1	1.0	0.5	AKT1 is one of 3 closely related serine/threonine-protein kinases (AKT1, AKT2 and AKT3) called the AKT kinase, and which regulate many processes including metabolism, proliferation, cell survival, growth and angiogenesis. This is mediated through serine and/or threonine phosphorylation of a range of downstream substrates.	Stimulates phosphotransferase activity.
ALK	Pan-specific	Anaplastic lymphoma kinase	-0.4	0.9	-1.1	-1.2	Neuronal receptor tyrosine kinase that is essentially and transiently expressed in specific regions of the central and peripheral nervous systems and plays an important role in the genesis and differentiation of the nervous system.	NA
AMPKa2	S377	5'-AMP-activated protein kinase catalytic subunit alpha-2 (PRKAA2)	0.1	-0.2	1.4	0.8	Catalytic subunit of AMPK, an energy sensor protein kinase that plays a key role in regulating cellular energy metabolism. In response to reduction of intracellular ATP levels, AMPK activates energy-producing pathways and inhibits energy-consuming processes. Also acts as a regulator of cellular polarity by remodeling the actin cytoskeleton and activating myosin.	No data available. Other sites are phosphorylated by LKB1 (STK11).
ANXA2	Y238	Annexin A2	0.8	1.4	1.7	1.6	Calcium-regulated membrane-binding protein whose affinity for calcium is greatly enhanced by anionic phospholipids. May be involved in heat-stress response.	No data available.
APP	T743	Amyloid beta A4 protein	0.8	0.9	1.6	0.8	Functions as a cell surface receptor and performs physiological functions on the surface of neurons relevant to neurite growth, neuronal adhesion and axonogenesis. Involved in cell mobility and transcription regulation through protein-protein interactions.	T743 is phosphorylated by CDK1 (CDC2), GSK3b, JNK1 (MAPK8), JNK2 (MAPK9), JNK3 (MAPK10).
A-Raf (RafA)	Pan-specific	A-Raf proto-oncogene serine/threonine-protein kinase	1.3	1.1	1.3	1.0	Involved in the transduction of mitogenic signals from the cell membrane to the nucleus. May also regulate TOR signaling.	NA

Arrestin b	S412	Arrestin beta 1 (ARRB1)	-0.6	0.5	-1.0	-1.3	Functions in regulating agonist-mediated GPCR signaling by mediating both receptor desensitization and resensitization processes. Targets many receptors for internalization by acting as an endocytic adapter (CLASPs, clathrin-associated sorting proteins) and recruiting the GPRCs to the adapter protein 2 complex 2 (AP-2) in clathrin-coated pits (CCPs). Can also play a role in MAPK, AKT and NFkB signaling.	S412 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1).
ASK1	Pan-specific	Apoptosis signal regulating protein-serine kinase 1 (MAP3K5)	3.1	0.8	1.4	1.6	Serine/threonine kinase which acts as an essential component of the MAPK pathway in response to changes in the environment to determine cell fates such as differentiation and survival. Regulates apoptosis through mitochondria-dependent caspase activation, and is required for the innate immune response. Mediates signal transduction of various stressors such as oxidative stress as receptor-mediated inflammatory signals (i.e. TNF and LPS). Acts as an upstream activator of the MKK/JNK and p38 MAPK signal transduction cascades through the phosphorylation and activation of MAP2Ks (MAP2K4/SEK1, MAP2K3/MKK3, MAP2K6/MKK6 and MAP2K7/MKK7).	NA
ATM	Pan-specific	Ataxia telangiectasia mutated	1.7	-0.2	-0.3	0.1	Serine/threonine protein kinase which activates checkpoint signaling upon double strand breaks (DSBs), apoptosis, and genotoxic stresses (i.e. UV light), thereby acting as a DNA damage sensor. Also involved in signal transduction and cell cycle control. May function as a tumor suppressor. Necessary for activation of ABL1 and SAPK.	NA
ATR	Pan-specific	Ataxia telangiectasia and Rad3 related	1.2	-0.6	-0.1	0.0	Serine/threonine protein kinase which activates checkpoint signaling upon genotoxic stresses (ionizing radiation, UV light, DNA replication stalling), thereby acting as a DNA damage sensor. Phosphorylates BRCA1, CHEK1, MCM2, RAD17, RPA2, SMC1 and p53/TP53, which collectively inhibit DNA replication and mitosis and promote DNA repair, recombination and apoptosis.	NA
ATR	S435+S436	Ataxia telangiectasia and Rad3 related	0.2	-0.3	0.9	1.4	see above	Stimulates phosphotransferase activity.
AurKA (Aurora A)	Pan-specific	Aurora Kinase A (serine/threonine protein kinase 6), (AIK, STK15)	1.1	-0.3	0.3	-0.3	Mitotic serine/threonine kinase that contributes to the regulation of cell cycle progression at several stages of mitosis. Also regulates the p53/TP53 pathway by phosphorylating and stabilizing p53/TP53.	NA
BAK	Pan-specific	Bcl2 homologous antagonist/killer (BCK2L7)	1.2	-0.5	1.5	1.8	In the presence of an appropriate stimulus, accelerates programmed cell death by binding to, and antagonizing the anti-apoptotic action of BCL2.	NA
BCR	Y177	Breakpoint cluster region protein	1.1	0.3	1.3	1.3	GTPase-activating protein for RAC1 and CDC42. Promotes the exchange of RAC or CDC42-bound GDP by GTP, thereby activating them. Displays serine/threonine kinase activity.	Induces interaction with Gab2, Grb2 and SOS1, and inhibits interaction with Hck. Y177 is phosphorylated by Abl1, Bcr, Fes, Fyn, Hck, Lyn.

Bmx	Pan-specific	Bone marrow X protein-tyrosine kinase (Etk)	0.6	0.0	1.1	1.2	Non-receptor tyrosine kinase that contributes to the regulation of actin reorganization, cell migration, cell proliferation and survival, cell adhesion, and apoptosis. Participates in signal transduction stimulated by growth factor receptors, cytokine receptors, G-protein coupled receptors, antigen receptors and integrins.	NA
B-Raf (RafB)	S446+S447	RafB proto-oncogene-encoded protein-serine kinase	0.4	0.8	1.3	0.3	Protein kinase involved in the transduction of mitogenic signals from the cell membrane to the nucleus. Contributes to MAPK signaling via phosphorylation of MAP2K1.	Stimulates phosphotransferase activity and induces interaction with H-Ras-1. S446 is phosphorylated by PAK1, PKACa (PRKACA).
B-Raf (RafB)	S729	RafB proto-oncogene-encoded protein-serine kinase	0.1	0.4	0.7	1.2	see above	Stimulates phosphotransferase activity and regulates cell differentiation, cell growth, and molecular association with 14-3-3b.
BRCA1	S1423	Breast cancer type 1 susceptibility protein	0.2	0.0	1.0	1.1	E3 ubiquitin-protein ligase that specifically mediates the formation of 'Lys-6'-linked polyubiquitin chains and plays a central role in DNA repair by facilitating cellular responses to DNA damage.	Phosphorylated by ATM and ATR.
BRSK1	T189	BR serine/threonine-protein kinase 1	0.2	-0.3	0.3	1.2	Serine/threonine-protein kinase that plays a key role in polarization of neurons and centrosome duplication. Phosphorylates CDC25B, CDC25C, MAPT/TAU, RIMS1, TUBG1, TUBG2 and WEE1. Involved in the UV-induced DNA damage checkpoint response through inhibition of CDK1, CDC25B and CDC25C and by activating WEE1.	No data available. Other sites are phosphorylated by BRSK1, LKB1.
BTK	Pan-specific	Bruton's agammaglobulinemia tyrosine kinase	2.3	0.2	0.8	1.3	Non-receptor tyrosine kinase that regulates apoptosis and is required for B lymphocyte development, differentiation and signaling. After BCR engagement and activation, phosphorylates PLCG2, igniting the downstream signaling pathway through calcium mobilization, followed by activation of PKC family members.	NA
Caldesmon	S789	Caldesmon	1.9	2.3	3.7	3.8	Actin- and myosin-binding protein implicated in the regulation of actomyosin interactions in smooth muscle and nonmuscle cells (could act as a bridge between myosin and actin filaments). Stimulates actin binding of tropomyosin which increases the stabilization of actin filament structure.	S789 is phosphorylated by CDK1 (CDC2), CDK6, ERK1 (MAPK3), ERK2 (MAPK1), p38a MAPK (MAPK14), PKCa (PRKCA).
CaMK1a	T177	Calcium/calmodulin-dependent protein-serine kinase 1 alpha (CaMKI)	1.1	0.0	0.5	-0.1	Calcium/calmodulin-dependent protein kinase that operates in the calcium-triggered CaMKK-CaMK1 signaling cascade and, upon calcium influx, regulates transcription activators activity, cell cycle, hormone production, cell differentiation, actin filament organization and neurite outgrowth.	Stimulates phosphotransferase activity. T177 is phosphorylated by CAMKK1.
Catenin a	S641	Catenin (cadherin-associated protein) alpha (CTNNA1)	0.1	0.2	1.3	2.1	Associates with the cytoplasmic domain of a variety of cadherins. The association of catenins to cadherins produces a complex which is linked to the actin filament network, and which seems to be of primary importance for cadherins cell-adhesion properties. Can associate with both E- and N-cadherins.	No data available.

Catenin b	Pan-specific	Catenin (cadherin-associated protein) beta 1 (CTNNB1)	0.0	2.1	-0.2	0.2	Key downstream component of the canonical Wnt signaling pathway. In the absence of Wnt, forms a complex with AXIN1, AXIN2, APC, CSNK1A1 and GSK3B that promotes phosphorylation and ubiquitination of CTNNB1 via BTRC and its subsequent degradation by the proteasome. In the presence of Wnt, it is not ubiquitinated and accumulates in the nucleus, where it acts as a coactivator for TFs of the TCF/LEF family to activate Wnt responsive genes. Involved in the regulation of cell adhesion.	NA
Catenin b	S33	Catenin (cadherin-associated protein) beta 1 (CTNNB1)	0.1	-0.6	1.1	1.9	see above	Inhibits transcriptional activity and induces binding to CBLL1. S33 is phosphorylated by CDK2, GSK3a, GSK3b, IKKa (CHUK).
Caveolin 1	Y14	Caveolin 1 (CAV1)	0.3	-0.2	1.0	1.7	May act as a scaffolding protein within caveolar membranes. Interacts directly with G-protein alpha subunits and can functionally regulate their activity. Involved in the costimulatory signal essential for T-cell receptor (TCR)-mediated T-cell activation. Its binding to DPP4 induces T-cell proliferation and NF-kappa-B activation in a T-cell receptor/CD3-dependent manner. Recruits CTNNB1 to caveolar membranes and may regulate CTNNB1-mediated signaling through the Wnt pathway. Negatively regulates TGF $\beta$ 1-mediated activation of SMAD2/3 by mediating the internalization of TGFBR1 from membrane rafts leading to its subsequent degradation.	Y14 is phosphorylated by Fyn, InsR, Src.
CDK1	Pan-specific	Cyclin-dependent protein-serine kinase 1 (CDC2)	1.2	0.7	1.3	1.4	Plays a key role in the control of the eukaryotic cell cycle by modulating the centrosome cycle and mitotic onset; promotes G2-M transition, and regulates G1 progress and G1-S transition via association with multiple interphase cyclins. Required for entry into S-phase and mitosis.	NA
CDK1	T161	Cyclin-dependent protein-serine kinase 1 (CDC2)	-0.1	-0.5	0.6	1.0	see above	Stimulates phosphotransferase activity and protein interaction. Phosphorylation regulates cell cycle progression, cell growth and molecular association. T161 is phosphorylated by CDK7.
CDK1	Pan-specific	Cyclin-dependent protein-serine kinase 1 (CDC2)	-0.7	0.8	-1.0	-1.1	see above	NA
CDK1/2	Y15	Cyclin-dependent protein-serine kinase 1/2 (CDC2)	0.6	0.5	2.3	2.1	see above	Inhibits phosphotransferase activity, and regulates cell cycle progression and apoptosis. Y15 is phosphorylated by CDK1 (CDC2), Chk1 (CHEK1), MYT1 (PKMYT1), Src, Wee1.
CDK1/2	Y15	Cyclin-dependent protein-serine kinase 1/2 (CDC2)	0.4	0.0	2.1	1.5	see above	Inhibits phosphotransferase activity, and regulates cell cycle progression and apoptosis. Y15 is phosphorylated by CDK1 (CDC2), Chk1 (CHEK1), MYT1 (PKMYT1), Src, Wee1.

CDK1/2	T161	Cyclin-dependent protein-serine kinase 1/2 (CDC2)	0.3	0.0	1.9	1.7	see above	Stimulates phosphotransferase activity and protein interaction. Phosphorylation regulates cell cycle progression, cell growth and molecular association. T161 is phosphorylated by CDK7.
CDK10	T196	Cyclin-dependent protein-serine kinase 10 (PISSLRE)	0.5	-0.2	0.6	1.5	Cyclin-dependent kinase that phosphorylates the transcription factor ETS2 (in vitro) and positively controls its proteasomal degradation (in cells).	Stimulates phosphotransferase activity.
CDK2	Pan-specific	Cyclin-dependent protein-serine kinase 2	1.7	0.8	1.5	2.0	Serine/threonine-protein kinase involved in the control of the cell cycle; essential for meiosis, but dispensable for mitosis. Phosphorylates CTNNB1, USP37, p53/TP53, NPM1, CDK7, RB1, BRCA2, MYC, NPAT, EZH2. Triggers duplication of centrosomes and DNA. Acts at the G1-S transition to promote the E2F transcriptional program and the initiation of DNA synthesis, and modulates G2 progression; controls the timing of entry into mitosis/meiosis by controlling the activation of cyclin B/CDK1 by phosphorylation. Orchestrates the balance between cellular proliferation, cell death, and DNA repair.	NA
CDK2	Pan-specific	Cyclin-dependent protein-serine kinase 2	1.7	0.0	1.7	1.6	see above	NA
CDK2	T160	Cyclin-dependent protein-serine kinase 2	0.0	-0.3	-0.8	-1.3	see above	Stimulates phosphotransferase activity, and regulates cell cycle progression, chromatin organization and protein conformation. T160 is phosphorylated by CCRK (CDK20), CDK2, CDK7, ERK1 (MAPK3), ERK2 (MAPK1).
CDK4	Pan-specific	Cyclin-dependent protein-serine kinase 4	1.4	0.4	2.2	2.8	Ser/Thr-kinase component of cyclin D-CDK4 (DC) complexes that phosphorylate and inhibit members of the retinoblastoma (RB) protein family including RB1 and regulate the cell-cycle during G1/S transition. Phosphorylation of RB1 allows dissociation of the transcription factor E2F from the RB/E2F complexes and the subsequent transcription of E2F target genes which are responsible for the progression through the G1 phase.	NA
CDK4	T172	Cyclin-dependent protein-serine kinase 4	-0.1	-0.3	0.5	1.1	see above	Stimulates phosphotransferase activity. T172 is phosphorylated by CDK7.

CDK5	Pan-specific	Cyclin-dependent protein-serine kinase 5	1.6	-0.1	1.2	1.9	Proline-directed serine/threonine-protein kinase essential for neuronal cell cycle arrest and differentiation and may be involved in apoptotic cell death in neuronal diseases. Interacts with D1 and D3-type G1 cyclins. Phosphorylates SRC, NOS3, VIM/vimentin, p35/CDK5R1, MEF2A, SIPA1L1, SH3GLB1, PXN, PAK1, MCAM/MUC18, SEPT5, SYN1, DNMT1, AMPH, SYNJ1, CDK16, RAC1, RHOA, CDC42, TONEBP/NFAT5, MAPT/TAU, MAP1B, histone H1, p53/TP53, HDAC1, APEX1, PTK2/FAK1, huntingtin/HTT, ATM, MAP2, NEFH and NEFM. Regulates several neuronal development and physiological processes.	NA
CDK7	Pan-specific	Cyclin-dependent protein-serine kinase 7	1.5	0.1	1.3	2.1	Serine/threonine kinase involved in cell cycle control and in RNA polymerase II-mediated RNA transcription. Required for both activation and complex formation of CDK1/cyclin-B during G2-M transition, and for activation of CDK2/cyclins during G1-S transition. CDK7 is the catalytic subunit of the CDK-activating kinase (CAK) complex. Upon DNA damage, triggers p53/TP53 activation (phosphorylation), allowing cell cycle arrest and recovery or apoptosis.	NA
CDK9	Pan-specific	Cyclin-dependent protein-serine kinase 9	1.1	0.1	0.3	1.3	Protein kinase involved in the regulation of transcription, cotranscriptional histone modification, and mRNA processing and export. Member of the CDK9/cyclin-T complex (aka P-TEFb), which facilitates the transition from abortive to productive elongation by phosphorylating RNA polymerase II (RNAP II). Regulates cytokine inducible transcription networks by facilitating promoter recognition of target transcription factors (e.g. TNF-inducible RELA/p65 activation and IL-6-inducible STAT3 signaling). Promotes RNA synthesis for cell growth and differentiation. The CDK9/cyclin-K complex is required for genome integrity maintenance, by promoting cell cycle recovery from replication arrest and limiting ss-DNA in response to replication stress.	NA
CHK1	Pan-specific	Checkpoint protein-serine kinase 1 (CHEK1)	1.7	0.2	1.3	2.3	Serine/threonine-protein kinase which is required for checkpoint-mediated cell cycle arrest and activation of DNA repair in response to the presence of DNA damage or unreplicated DNA. May also negatively regulate cell cycle progression during unperturbed cell cycles.	NA
CHK1	S280	Checkpoint protein-serine kinase 1 (CHEK1)	0.3	-0.5	1.6	1.4	see above	Inhibits phosphotransferase activity. Phosphorylation regulates cell cycle progression, intracellular location, protein degradation by promoting mono and/or diubiquitination and molecular association. S280 is phosphorylated by Akt1 (PKBa).
CHK1	Pan-specific	Checkpoint protein-serine kinase 1 (CHEK1)	2.1	-0.1	1.5	2.2	see above	NA



CHK1	S280	Checkpoint protein-serine kinase 1 (CHEK1)	0.4	-0.1	0.9	2.7	see above	Inhibits phosphotransferase activity. Phosphorylation regulates cell cycle progression, intracellular location, protein degradation by promoting mono and/or diubiquitination and molecular association. S280 is phosphorylated by Akt1 (PKBa).
CHK2	Pan-specific	Checkpoint protein-serine kinase 2 (CHEK2)	1.6	0.5	1.6	2.2	Serine/threonine-protein kinase which is required for checkpoint-mediated cell cycle arrest, activation of DNA repair and apoptosis in response to the presence of DNA double-strand breaks. May also negatively regulate cell cycle progression during unperturbed cell cycles.	na
CHK2	T68	Checkpoint protein-serine kinase 2 (CHEK2)	-0.6	-1.1	-0.2	-0.5	see above	Stimulates phosphotransferase activity, and induces interactions with Chk2 (homodimerization), MDC1, NBS1 and Plk1. T68 is phosphorylated by ATM, ATR, Chk2 (CHEK2), DNAPK (PRKDC), Plk1 (PLK), TTK, ZAK (MLTK).
CREB1	S133	cAMP response element binding protein 1	2.0	-0.9	-0.5	-0.4	Phosphorylation-dependent transcription factor that stimulates transcription upon binding to the DNA cAMP response element (CRE). Transcription activation is enhanced by the TORC coactivators which act independently of Ser-133 phosphorylation. Involved in different cellular processes including the synchronization of circadian rhythmicity and the differentiation of adipose cells.	Stimulates transcriptional activity. S133 is phosphorylated by Akt1 (PKBa), Btk, CaMK1a, CaMK2a, CaMK4, DYRK3, MAPKAPK2, MSK1 (RPS6KA5), MSK2 (RPS6KA4), PKACa (PRKACA), PKCa (PRKCA), PKCe (PRKCE), PKD1 (PRKCM), RSK1 (RPS6KA2), RSK2 (RPS6KA3), RSK3 (RPS6KA1), SGK1, TSSK4, VRK1.
Crystallin aB	S19	Crystallin alpha B (heat-shock 20 kDa like-protein) (HspB5; CRYA2; CRYAB)	0.3	0.6	-0.9	-1.0	Has chaperone-like activity, preventing aggregation of various proteins under a wide range of stress conditions.	Regulates conformation, intracellular location, protein degradation, and molecular association.
CSF1R	Pan-specific	Macrophage colony-stimulating factor 1 receptor (Fms)	-0.5	-1.3	-1.1	-1.1	Tyrosine-protein kinase that acts as cell-surface receptor for CSF1 and IL34 and aids in the regulation of survival, proliferation and differentiation of hematopoietic precursor cells (i.e. macrophages and monocytes). Promotes the release of proinflammatory chemokines in response to IL34 and CSF1. Regulates osteoclast proliferation and differentiation, bone resorption, and bone and tooth development. Required for normal male and female fertility, and for normal development of milk ducts and acinar structures in the mammary gland during pregnancy.	NA
CSF1R	Pan-specific	Macrophage colony-stimulating factor 1 receptor (Fms)	-0.8	-1.3	-1.3	-1.1	see above	NA



CSF1R	Y699	Macrophage colony-stimulating factor 1 receptor (Fms)	-0.3	-0.2	-0.9	-1.2	see above	Induces binding to PIK3CB and Grb2. Y699 is phosphorylated by CSF1R.
CSK	Pan-specific	C-terminus of Src tyrosine kinase	-0.2	2.5	0.8	1.3	Non-receptor tyrosine-protein kinase that plays an important role in the regulation of cell growth, differentiation, migration and immune response. Phosphorylates Src-family kinases (SFKs) including LCK, SRC, HCK, FYN, LYN or YES1.	NA
CSK	Pan-specific	C-terminus of Src tyrosine kinase	0.4	0.5	1.7	2.0	see above	NA
Cyclin B1	Pan-specific	Cyclin B1 (CCNB1)	2.0	0.6	2.2	2.3	Essential for the control of the cell cycle at the G2/M (mitosis) transition.	NA
Cyclin E1	Pan-specific	Cyclin E1 (CCNE1)	2.1	0.4	1.5	1.5	Essential for the control of the cell cycle at the G1/S (start) transition.	NA
EFNB2	Y316	EPH-related receptor tyrosine kinase ligand 5	0.6	0.9	1.7	0.6	Cell surface transmembrane ligand for Eph receptors, a family of receptor tyrosine kinases which are crucial for migration, repulsion and adhesion during neuronal, vascular and epithelial development. Also binds Eph receptors residing on adjacent cells, leading to contact-dependent bidirectional signaling into neighboring cells.	No data available.
EGFR	T693	Epidermal growth factor receptor-tyrosine kinase (ErbB1)	0.7	2.1	6.6	5.5	Receptor tyrosine kinase binding ligands of the EGF family and activating several signaling cascades to convert extracellular cues into appropriate cellular responses. Known ligands: EGF, TGFA/TGF-alpha, amphiregulin, epigen/EPGN, BTC/betacellulin, epiregulin/EREG and HBEGF/heparin-binding EGF. Ligand binding triggers receptor homo- and/or heterodimerization and autophosphorylation on key cytoplasmic residues. The phosphorylated receptor recruits adapter proteins like GRB2 which activate downstream signaling cascades. Activates at least 4 major pathways including the RAS-RAF-MEK-ERK, PI3 kinase-AKT, PLCgamma-PKC and STATs modules. May also activate the NF-kappa-B signaling.	Inhibits phosphotransferase activity. T693 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1), p38a MAPK (MAPK14), PRKD1.
EGFR	Pan-specific	Epidermal growth factor receptor-tyrosine kinase (ErbB1)	-0.3	-1.1	1.1	1.0	see above	NA
EGFR	Pan-specific	Epidermal growth factor receptor-tyrosine kinase (ErbB1)	0.0	-1.1	-0.7	-0.6	see above	NA
EGFR	Pan-specific	Epidermal growth factor receptor-tyrosine kinase (ErbB1)	-0.3	-1.4	-1.2	-1.2	see above	NA

EGFR	Y1069	Epidermal growth factor receptor-tyrosine kinase (ErbB1)	0.6	0.1	0.7	1.6	see above	Stimulates phosphotransferase activity. Phosphorylation induces protein ubiquitination and degradation, and regulates molecular association. Y1069 is phosphorylated by EGFR.
eIF4E	S209	Eukaryotic translation initiation factor 4 (mRNA cap binding protein)	0.0	1.6	0.1	0.1	Recognizes and binds the 7-methylguanosine-containing mRNA cap during an early step in the initiation of protein synthesis and facilitates ribosome binding by inducing the unwinding of the mRNAs secondary structures. Component of the CYFIP1-EIF4E-FMR1 complex which binds to the mRNA cap and mediates translational repression.	Increases the affinity of this protein for the 7-methylguanosine-containing mRNA cap, although another report describes inhibition of interaction with RNA. S209 is phosphorylated by MNK1 (MKNK1), PKCa (PRKCA).
eIF4E	S209	Eukaryotic translation initiation factor 4 (mRNA cap binding protein)	-0.5	1.4	-1.0	-1.2	see above	see above
EphA3	Y779	Ephrin type-A receptor 3 protein-tyrosine kinase	-0.3	0.1	-0.3	-1.2	Receptor tyrosine kinase which binds promiscuously membrane-bound ephrin family ligands residing on adjacent cells, leading to contact-dependent bidirectional signaling into neighboring cells.	Stimulates phosphotransferase activity. Phosphorylation regulates cell adhesion, cytoskeletal reorganization, and molecular association.
ER-alpha	S104	Estrogen receptor alpha (ESR1)	0.6	0.1	0.9	2.0	Nuclear hormone receptor. The steroid hormones and their receptors are involved in the regulation of eukaryotic gene expression and affect cellular proliferation and differentiation in target tissues. Ligand-dependent nuclear transactivation involves either direct homodimer binding to a palindromic estrogen response element (ERE) sequence or association with other DNA-binding transcription factors, such as AP-1/c-Jun, c-Fos, ATF-2, Sp1 and Sp3, to mediate ERE-independent signaling. Decreases NF-kappa-B DNA-binding activity and transcription from the IL6 promoter and displaces RELA/p65 and associated coregulators from the promoter. Recruited to the NF-kappa-B response element of the CCL2 and IL8 promoters and can displace CREBBP.	Stimulates transcriptional activity and regulates molecular association, including inducing interactions with NCoA2, SRC-3 and Src. S104 is phosphorylated by BARK2 (GRK3, ADRBK2), CDK2, ERK1 (MAPK3), ERK2 (MAPK1), GSK3b.
ErbB2 (HER2)	Y1248	ErbB2 (Neu) receptor-tyrosine kinase	1.6	0.7	-0.4	0.0	Protein tyrosine kinase that is part of several cell surface receptor complexes but needs a coreceptor for ligand binding. Essential component of a neuregulin-receptor complex. GP30 is a potential ligand. Regulates outgrowth and stabilization of peripheral microtubules (MTs). Upon ERBB2 activation, the MEMO1-RHOA-DIAPH1 signaling pathway elicits the phosphorylation and inhibition of GSK3B at cell membrane. This prevents the phosphorylation of APC and CLASP2, allowing its association with the cell membrane. Membrane-bound APC allows the localization of MACF1 to the cell membrane, which is required for microtubule capture and stabilization.	Stimulates phosphotransferase activity. Phosphorylation regulates cell motility, cytoskeletal reorganization, transcription, intracellular location and molecular association. Y1248 is phosphorylated by ErbB2.
ErbB2 (HER2)	Y735	ErbB2 (Neu) receptor-tyrosine kinase	1.5	0.2	0.8	0.9	see above	No data available.

ErbB2 (HER2)	Pan-specific	ErbB2 (Neu) receptor-tyrosine kinase	1.1	0.4	1.1	0.6	see above	NA
ERBB2IP	Y1104	Protein LAP2 (Erbin)	1.6	0.5	0.3	0.4	Acts as an adapter for the receptor ERBB2. By binding the unphosphorylated 'Tyr-1248' of receptor ERBB2, it may contribute to stabilize this unphosphorylated state. Inhibits NOD2-dependent NF-kappa-B signaling and proinflammatory cytokine secretion.	No data available.
ErbB3 (HER3)	Pan-specific	Tyrosine kinase-type cell surface receptor HER3	1.4	0.5	0.4	0.6	Tyrosine-protein kinase that plays an essential role as cell surface receptor for neuregulins. Binds to neuregulin-1 (NRG1) and is activated by it; ligand-binding increases phosphorylation on tyrosine residues and promotes its association with the p85 subunit of phosphatidylinositol 3-kinase.	NA
ErbB3 (HER3)	Y1328	Tyrosine kinase-type cell surface receptor HER3	1.1	0.3	2.1	1.0	see above	No data available for this site - other sites regulate interaction with other proteins and molecular association.
ERK1 (MAPK3)	Pan-specific	Extracellular regulated protein-serine kinase 1 (p44 MAP kinase)	3.3	1.5	0.4	0.4	Serine/threonine kinase; major effector of the MAPK/ERK cascade. Depending on the cellular context, this cascade mediates diverse biological functions such as cell growth, adhesion, survival and differentiation through the regulation of transcription, translation, cytoskeletal rearrangements. Also plays a role in initiation and regulation of meiosis, mitosis, and postmitotic functions in differentiated cells by phosphorylating a number of transcription factors. Participates in a signaling cascade initiated by activated KIT and KITLG/SCF.	NA
ERK1 (MAPK3)	Pan-specific	Extracellular regulated protein-serine kinase 1 (p44 MAP kinase)	2.7	0.8	0.4	0.5	see above	NA
ERK1 (MAPK3)	T207	Extracellular regulated protein-serine kinase 1 (p44 MAP kinase)	0.1	0.3	2.0	0.6	see above	Inhibits phosphotransferase activity. T207 is phosphorylated by ERK1 (MAPK3).

ERK1 (MAPK3)	Y204+T207	Extracellular regulated protein-serine kinase 1 (p44 MAP kinase)	-0.3	-0.5	1.2	0.0	see above	Stimulates phosphotransferase activity and regulates cell growth, cell motility, cytoskeletal reorganization, transcription, protein conformation, intracellular location, protein degradation, and molecular association. Y204 is phosphorylated by the following protein kinases in vitro: ERK1 (MAPK3), JAK2, Lck, MEK1 (MAP2K1), MEK2 (MAP2K2).
Ezrin	Y354	Cytovillin 2	0.4	-0.2	0.8	1.6	Involved in connections of major cytoskeletal structures to the plasma membrane. In epithelial cells, required for the formation of microvilli and membrane ruffles on the apical pole. Along with PLEKHG6, required for normal macropinocytosis.	Y354 is phosphorylated by EGFR.
FAK (PTK2)	S910	Focal adhesion protein-tyrosine kinase	0.8	1.9	1.9	1.2	Non-receptor tyrosine kinase that regulates cell migration, adhesion, spreading, reorganization of the actin cytoskeleton, formation and disassembly of focal adhesions and cell protrusions, cell cycle progression, cell proliferation and apoptosis. Required for early embryonic development, placenta development, embryonic angiogenesis, normal cardiomyocyte migration and proliferation, and normal heart development. Regulates axon growth and neuronal cell migration, axon branching and synapse formation; required for normal development of the nervous system. Plays a role in osteogenesis and differentiation of osteoblasts. Functions in signaling downstream of integrins, growth factor receptors, GPCRs, EPHA2, netrin receptors and LDL receptors. Forms multisubunit signaling complexes with SRC and SRC family members, leading to SRC activation and the creation of binding sites for scaffold proteins, effectors and substrates. Promotes activation of PI3K-AKT1 signaling, the MAPK pathway and RAC1. Promotes activation of GEFs and GAPs to regulate activity of Rho family GTPases. Recruits MDM2 to P53/TP53 in the nucleus, and phosphorylates ACTN1, ARHGEF7, GRB7, RET and WASL. Promotes phosphorylation of PXN, STAT1, BCAR1, GIT2, SHC1, BMX and PIK3R1.	Phosphorylation regulates cell adhesion, cell growth, and cytoskeletal reorganization. S910 is phosphorylated by CDK5, ERK1 (MAPK3), ERK2 (MAPK1).

FAK (PTK2)	Y397	Focal adhesion protein-tyrosine kinase	0.1	-0.4	0.9	1.7	see above	Stimulates phosphotransferase activity and induces interaction with Src and other Src family kinases, Bmx, PIK3R1, RASA1 and SHC1, and this leads to phosphorylation at Y576, Y577 and additional tyrosine phosphosites. Phosphorylation regulates apoptosis, cell adhesion, cell differentiation, cell growth, cell motility, cytoskeletal reorganization, endocytosis, transcription, alters intracellular location, protein degradation and molecular associations. Y397 is phosphorylated by FAK (PTK2), Fgr, Met, Src.
FAK (PTK2)	Pan-specific	Focal adhesion protein-tyrosine kinase	0.6	0.1	1.0	1.4	see above	NA
FAK (PTK2)	Y576+Y577	Focal adhesion protein-tyrosine kinase	0.4	-0.2	0.3	1.1	see above	Stimulates phosphotransferase activity. Phosphorylation regulates cell adhesion, cell differentiation, cytoskeletal reorganization, transcription, and alters intracellular location. Y576 is phosphorylated by FAK (PTK2), Fgr, Met, Src.
FAK (PTK2)	Y576+Y577	Focal adhesion protein-tyrosine kinase	0.2	-0.1	0.5	1.1	see above	Stimulates phosphotransferase activity. Phosphorylation regulates cell adhesion, cell differentiation, cytoskeletal reorganization, and transcription. Y577 is phosphorylated by FAK (PTK2), Fer, Met, Src.
FKHR	S256	Forkhead box protein O1 (FOXO1A)	0.5	0.0	1.1	2.1	Transcription factor that is the main target of insulin signaling and regulates metabolic homeostasis in response to oxidative stress. Binds to the insulin response element (IRE). Important regulator of cell death acting downstream of CDK1, PKB/AKT1 and SKT4/MST1.	Inhibits transcription by preventing nuclear import, regulates protein degradation and molecular association; phosphorylation induces interaction with 14-3-3 beta, SKP2, and inhibits interaction with DNA. S256 is phosphorylated by Akt1 (PKBa), Akt3 (PKBg).

FKHR	S319	Forkhead box protein O1 (FOXO1A)	0.6	-0.2	0.5	1.2	see above	Phosphorylation decreases rate of nuclear exclusion It also creates the pSer-Xaa-Xaa-Ser recognition motif for CK1, allowing it to phosphorylate Ser-322, and regulates apoptosis and transcription. S319 is phosphorylated by Akt1 (PKBa), Akt3 (PKBg), SGK1.
FOS	Pan-specific	Fos-c FBJ murine osteosarcoma oncoprotein-related transcription factor	0.6	0.7	1.5	2.2	Nuclear phosphoprotein which forms a complex with the JUN/AP-1 transcription factor. On TGF-beta activation, forms a multimeric SMAD3/SMAD4/JUN/FOS complex at the AP1/SMAD-binding site to regulate TGF-beta signaling. Has an important role in signal transduction, cell proliferation and differentiation. Aids in regulation of cells involved in skeletal development, and, in growing cells, activates phospholipid synthesis, possibly via CDS1 and PI4K2A.	NA
FRS2	Y348	Fibroblast growth factor receptor substrate 2	-0.6	-1.3	-1.5	-1.7	Adapter protein that links activated FGR and NGF receptors to downstream pathways. Aids in activation of MAPKs and phosphorylation of PIK3R1, the regulatory subunit of PI3K, in response to ligand-mediated activation of FGFR1. Modulates signaling via SHC1 by competing for a common binding site on NTRK1.	No data available.
FYN	Pan-specific	Fyn proto-oncogene-encoded protein-tyrosine kinase	1.0	1.0	2.7	3.1	Non-receptor tyrosine kinase that plays a role in many biological processes including regulation of cell growth and survival, cell adhesion, integrin-mediated signaling, cytoskeletal remodeling, cell motility, immune response and axon guidance. Following activation by PKA, FYN associates with PTK2/FAK1, allowing PTK2/FAK1 phosphorylation, activation and targeting to focal adhesions. Involved in the regulation of cell adhesion and motility through phosphorylation of beta and delta-catenin (CTNNB1, CTNND1). Regulates cytoskeletal remodeling by phosphorylating WAS, MAP2, and MAPT. Promotes cell survival by phosphorylating AGAP2/PIKE-A and preventing its apoptotic cleavage.	NA
GCK	Pan-specific	Germinal centre protein-serine kinase	1.2	-0.2	0.7	1.3	Serine/threonine kinase; acts as a MAP4K and is an upstream activator of the SAP/JNK signaling pathway and, to a lesser extent, the p38 MAPKs pathway. Required for the efficient activation of JNKs by TRAF6-dependent stimuli, including PAMPs such as polyinosine-polycytidine (poly(IC)), lipopolysaccharides (LPS), lipid A, peptidoglycan (PGN), or bacterial flagellin. IL-1 and engagement of CD40 also stimulate MAP4K2-mediated JNKs activation. Enhances activation of MAP3K1, MAP3K10/MLK2 and MAP3K11/MLK3. May play a role in the regulation of vesicle targeting/fusion.	NA
GFAP	S8	Glial fibrillary acidic protein	-0.1	92.5	109.4	150.3	GFAP, a class-III intermediate filament, is a cell-specific marker that, during the development of the central nervous system, distinguishes astrocytes from other glial cells.	S8 is phosphorylated by PKACa (PRKACA), PKCa (PRKCA).

GRK2 (BARK1)	S670	G protein-coupled receptor-serine kinase 2 ( ADRBK1)	-0.6	0.3	-0.9	-1.2	Specifically phosphorylates the agonist-occupied form of the beta-adrenergic and closely related receptors, probably inducing a desensitization of them. Key regulator of LPAR1 signaling. Competes with RALA for binding to LPAR1 thus affecting the signaling properties of the receptor. Desensitizes LPAR1 and LPAR2 in a phosphorylation-independent manner.	Inhibits phosphotransferase activity. Phosphorylation regulates cell cycle progression, cell growth, protein degradation, and molecular association. S670 is phosphorylated by ERK1 (MAPK3).
HSP90a/b	Pan-specific	Heat shock 90 kDa protein alpha/beta	0.8	0.0	0.8	1.9	Molecular chaperone that promotes the maturation, structural maintenance and proper regulation of specific target proteins involved in cell cycle control and signal transduction. Binds bacterial LPS and mediates LPS-induced inflammatory response, including TNF secretion by monocytes.	NA
ICK	Y156+T157	Intestinal cell (MAK-like) kinase	-1.3	-1.4	-1.5	-1.2	Required for ciliogenesis.	Stimulates phosphotransferase activity. T157 is phosphorylated by CCRK (CDK20).
IkBb	Pan-specific	Inhibitor of NF-kappa-B beta (thyroid receptor interacting protein 9)	1.0	-0.2	0.6	1.4	Inhibits the activity of dimeric NF-kappa-B/REL complexes by trapping REL dimers in the cytoplasm through masking of their nuclear localization signals. On cellular stimulation by immune and proinflammatory responses, becomes phosphorylated promoting ubiquitination and degradation, enabling the dimeric RELA to translocate to the nucleus and activate transcription.	NA
IKKa	Pan-specific	Inhibitor of NF-kappa-B protein-serine kinase alpha (CHUK, IkbKA)	0.3	0.3	0.2	1.3	Serine kinase that plays an essential role in the NF-kappa-B signaling pathway which is activated by multiple stimuli such as inflammatory cytokines, bacterial or viral products, DNA damages or other cellular stresses. Acts as part of the canonical IKK complex in the conventional pathway of NF-kappa-B activation and phosphorylates inhibitors of NF-kappa-B on serine residues.	NA
IKKa	Pan-specific	Inhibitor of NF-kappa-B protein-serine kinase alpha (CHUK, IkbKA)	1.0	0.3	0.7	1.2	see above	NA
InsR (IR)	Y999	Insulin receptor beta chain	-1.4	-1.6	-1.4	-1.3	Receptor tyrosine kinase which mediates the pleiotropic actions of insulin. Binding of insulin leads to phosphorylation of several intracellular substrates, including, insulin receptor substrates (IRS1, 2, 3, 4), SHC, GAB1, CBL and other signaling intermediates. Each of these phosphorylated proteins serve as docking proteins for other signaling proteins that contain Src-homology-2 domains (SH2 domain) that specifically recognize different phosphotyrosine residues, including the p85 regulatory subunit of PI3K and SHP2. Phosphorylation of IRSs proteins lead to the activation of the PI3K-AKT/PKB pathway, which is responsible for most of the metabolic actions of insulin, and the Ras-MAPK pathway, which regulates expression of some genes and cooperates with the PI3K pathway to control cell growth and differentiation.	Stimulates phosphotransferase activity and induces interaction with IRS1 and Shc1 (via their PTB/PID domains), STAT5B and SOCS3. Phosphorylation regulates cell cycle progression, receptor internalization, and molecular association. Y999 is phosphorylated by InsR.
InsR (IR)	Y1189	Insulin receptor beta chain	-1.0	-1.1	-0.9	-0.8	see above	Stimulates phosphotransferase activity, receptor internalization and induces interaction with SOCS1, IRS2 and PTP1B. Y1189 is phosphorylated by InsR.



IR/IGF1R	Y1189/Y1190	Insulin receptor / Insulin-like growth factor 1 receptor (INSR)	-0.7	-1.2	-0.8	-1.0	see above (InsR/IR are alternate names)	Stimulates phosphotransferase activity, receptor internalization and induces interaction with SOCS1, IRS2 and PTP1B. Y1189 and Y1190 are phosphorylated by InsR.
IRAK1	Pan-specific	Interleukin 1 receptor-associated kinase 1 (Pelle-like protein kinase)	0.8	0.1	1.6	1.8	Serine/threonine-protein kinase that plays a critical role in initiating innate immune response against foreign pathogens. Involved in Toll-like receptor (TLR) and IL-1R signaling pathways.	NA
IRAK4	T345+S346	Interleukin 1 receptor-associated kinase 4	0.5	0.4	1.5	1.7	Serine/threonine-protein kinase that plays a critical role in initiating innate immune response against foreign pathogens. Involved in Toll-like receptor (TLR) and IL-1R signaling pathways.	Stimulates phosphotransferase activity. T345 and S346 are phosphorylated by IRAK4.
IRS1	S639	Insulin receptor substrate 1	-1.4	-1.5	-1.2	-1.2	May mediate the control of various cellular processes by insulin. When phosphorylated by the insulin receptor binds specifically to various cellular proteins containing SH2 domains such as PI3K p85 subunit or GRB2.	Regulates intracellular location and inhibition of tyrosine phosphorylation. S639 is phosphorylated by BARK1 (GRK2; ADRBK1), ERK2 (MAPK1), FRAP1 (mTOR), p70S6K (RPS6KB1), ROCK1, ROCK2.
IRS1	S312	Insulin receptor substrate 1	-0.6	-1.0	0.2	0.9	see above	Regulates apoptosis, alters intracellular location, protein degradation, regulates molecular association, and inhibits interaction with IKK-alpha, IKK-beta. S312 is phosphorylated by CK2a1 (CSNK2A1), ERK1 (MAPK3), ERK2 (MAPK1), IKKa (CHUK), IKKb (IKBKINASE), JNK1 (MAPK8), p70S6K (RPS6KB1), PKCa (PRKCA), PKCz (PRKCZ).
ITSN2	Y968	Intersectin-2	-0.8	-0.7	-1.0	-0.4	Adapter protein that may provide indirect link between the endocytic membrane traffic and the actin assembly machinery. May regulate the formation and maturation of clathrin-coated vesicles (CCPs). Involved in endocytosis of integrin beta-1 (ITGB1) and transferrin receptor (TFR).	No data available.
JAK1	Pan-specific	Janus protein-tyrosine kinase 1	-1.7	-1.8	-1.8	-1.8	Tyrosine kinase of the non-receptor type, involved in the IFN-alpha/beta/gamma signal pathway. Involved in IL-2 receptor signaling.	NA
JAK1	Y1034	Janus protein-tyrosine kinase 1	-1.6	-1.6	-1.6	-1.5	see above	Stimulates phosphotransferase activity.

JAK2	Pan-specific	Janus protein-tyrosine kinase 2	-1.7	-1.6	-1.6	-1.8	Non-receptor tyrosine kinase involved in various processes such as cell growth, development, differentiation or histone modifications. Mediates essential signaling events in both innate and adaptive immunity. In the cytoplasm, plays a pivotal role in signal transduction via its association with type I receptors such as growth hormone (GHR), prolactin (PRLR), leptin (LEPR), erythropoietin (EPOR), thrombopoietin (THPO); or type II receptors including IFN-alpha, IFN-beta, IFN-gamma and multiple interleukins.	NA
JAK2	Y1007+Y1008	Janus protein-tyrosine kinase 2	0.0	0.9	-0.9	-1.0	see above	Stimulates phosphotransferase activity. Y1007 is phosphorylated by JAK2, PYK2 (PTK2B). Y1008 is phosphorylated by Abl1, JAK2, PYK2 (PTK2B).
JAK3	Y980+Y981	Janus protein-tyrosine kinase 3	1.3	-0.4	-0.1	0.3	Non-receptor tyrosine kinase involved in various processes such as cell growth, development, or differentiation. Mediates essential signaling events in both innate and adaptive immunity and plays a crucial role in hematopoiesis during T-cells development. In the cytoplasm, plays a pivotal role in signal transduction via its association with type I receptors sharing the common subunit gamma such as IL2R, IL4R, IL7R, IL9R, IL15R and IL21R.	Stimulates phosphotransferase activity. Y980 and Y981 are phosphorylated by JAK3.
JNK1	Pan-specific	Jun N-terminus protein-serine kinase (stress-activated protein kinase (SAPK)) 1 (SAPKγ, MAPK8)	3.7	-0.1	0.0	0.2	Serine/threonine-protein kinase involved in various processes such as cell proliferation, differentiation, migration, transformation and programmed cell death. Extracellular stimuli such as proinflammatory cytokines or physical stress stimulate the stress-activated protein kinase/c-Jun N-terminal kinase (SAP/JNK) signaling pathway. Activated by MAP2K4/MKK4 and MAP2K7/MKK7. Phosphorylates a number of transcription factors, primarily components of AP-1 such as JUN, JDP2 and ATF2.	NA
JUN	S73	Jun proto-oncogene-encoded AP1 transcription factor (c-Jun)	0.3	0.6	-1.0	-1.1	Transcription factor that recognizes and binds to the enhancer heptamer motif 5'-TGA[CG]TCA-3'. Promotes activity of NR5A1 when phosphorylated by HIPK3 leading to increased steroidogenic gene expression upon cAMP signaling pathway stimulation.	Stimulates transcriptional activity. S73 is phosphorylated by CDK1 (CDC2), CDK3, CK2a1 (CSNK2A1), ERK1 (MAPK3), ERK2 (MAPK1), JNK1 (MAPK8), JNK2 (MAPK9), JNK3 (MAPK10), PIK3 (CNK), VRK1.
JUN	Y170	Jun proto-oncogene-encoded AP1 transcription factor (c-Jun)	0.5	0.4	1.9	2.7	see above	Y170 is phosphorylated by Abl1.
KIT	Y936	*Mast/stem cell growth factor receptor Kit	14.5	30.8	26.7	18.1	Tyrosine-protein kinase that acts as cell-surface receptor for the cytokine KITLG/SCF, leading to regulation of cell survival and proliferation, hematopoiesis, stem cell maintenance, gametogenesis, mast cell development, migration and function, and in melanogenesis. Phosphorylates PIK3R1, PLCG1, SH2B2/APS and CBL. Activates the AKT1 signaling pathway by phosphorylation of PIK3R1, the regulatory subunit of PI3K. Activated KIT also signals via GRB2 and activation of RAS, RAF1 and ERK1/2 MAPKs. Promotes activation of STAT family members STAT1, STAT3, STAT5A and STAT5B.	Stimulates phosphotransferase activity and induces interaction with Grb2 and Grb7. Phosphorylation also induces receptor internalization and protein degradation. Y936 is phosphorylated by Kit.

KIT	Y703	*Mast/stem cell growth factor receptor Kit	-0.5	0.2	-1.0	-1.1	see above	Induces interaction with Grb2. Y703 is phosphorylated by Kit.
KIT	Y730	*Mast/stem cell growth factor receptor Kit	-0.2	0.4	-0.9	-1.2	see above	No data available.
KSR1	S404	Protein-serine kinase suppressor of Ras 1	-0.8	-1.0	-0.8	-0.4	Scaffolding protein that is part of a multiprotein signaling complex. Promotes phosphorylation of Raf family members and activation of downstream MAPKs. Promotes activation of MAPK1 and/or MAPK3 in response to EGF and to cAMP.	S404 is phosphorylated by MARK3, NM23 (NME1), TAK1 (MAP3K7).
LATS1	S909	Large tumor suppressor 1 protein-serine kinase (WARTS)	0.3	0.2	0.3	1.6	Negative regulator of YAP1 in the Hippo signaling pathway that plays a pivotal role in organ size control and tumor suppression by restricting proliferation and promoting apoptosis. In this cascade, STK3/MST2 and STK4/MST1 complex with regulatory protein SAV1, leading to phosphorylation/activation of LATS1/2 in complex with its regulatory protein MOB1, which phosphorylates and inactivates YAP1 and WWTR1/TAZ.	Stimulates phosphotransferase activity. S909 is phosphorylated by MST2 (CLIK1; STK3).
LCK	Pan-specific	Lymphocyte-specific protein-tyrosine kinase	1.3	0.3	1.8	1.9	Non-receptor tyrosine kinase that plays an essential role in the selection and maturation of developing T-cells in the thymus and in the function of mature T-cells. Plays a key role in T-cell antigen receptor (TCR)-linked signal transduction pathways.	NA
LCK	Y505	Lymphocyte-specific protein-tyrosine kinase	0.2	0.3	1.2	0.8	see above	Inhibits phosphotransferase activity, and regulates cell growth and molecular association, including inducing interaction with Lck. Y505 is phosphorylated by the following protein kinases in vitro: CSK, Lck
LCK	Y192	Lymphocyte-specific protein-tyrosine kinase	-0.3	0.5	-1.0	-1.2	see above	Inhibits phosphotransferase activity. Phosphorylation regulates molecular association.
LCK	S158	Lymphocyte-specific protein-tyrosine kinase	-0.3	0.3	-0.9	-1.2	see above	No data available.
LIMK1	T508	LIM domain kinase 1	-1.1	-1.3	-1.0	-0.6	Serine/threonine kinase that plays an essential role in the regulation of actin filament dynamics. Acts downstream of several Rho family GTPase signal transduction pathways. Activated by upstream kinases including ROCK1, PAK1 and PAK4. LIMK1 subsequently phosphorylates and inactivates the actin binding/depolymerizing factors cofilin-1/CFL1, cofilin-2/CFL2 and destrin/DSTN, thereby preventing the cleavage of F-actin, and stabilizing the actin cytoskeleton.	Stimulates phosphotransferase activity and induced interaction with NISCH. T508 is phosphorylated by MRCKa (PK428), PAK1, PAK4, ROCK1.
LKB1	Pan-specific	Serine/threonine-protein kinase 11 (STK11)	-1.0	-1.4	-1.5	-1.3	Tumor suppressor serine/threonine-protein kinase that controls the activity of AMPK family members, thereby playing a role in various processes such as cell metabolism, cell polarity, apoptosis and DNA damage response.	NA

LKB1	S428	Serine/threonine-protein kinase 11 (STK11)	0.0	-0.8	0.3	1.2	see above	Stimulates phosphotransferase activity. Phosphorylation regulates cell growth, intracellular location and molecular association, including inducing interaction with STRAD and exportin 1. S428 is phosphorylated by DNAPK (PRKDC), LKB1 (STK11), MSK1 (RPS6KA5), p70S6K (RPS6KB1), PKACa (PRKACA), PKCz (PRKCZ), RSK1 (RPS6KA2).
LTK	Y672	Leukocyte tyrosine kinase receptor	0.3	0.5	0.3	1.0	Receptor with a tyrosine kinase activity. The exact function is not known but may promote cell growth and survival. Signaling appears to involve the PI3 kinase pathway.	No data available.
LYN	Y508	Yes-related protein-tyrosine kinase	1.5	0.9	1.9	0.4	Non-receptor tyrosine kinase that transmits signals from cell surface receptors and plays an important role in the regulation of innate and adaptive immune responses, hematopoiesis, responses to growth factors and cytokines, integrin signaling, but also responses to DNA damage and genotoxic agents. Functions primarily as negative regulator, but also as an activator in certain circumstances. Required for both the initiation and termination of the B-cell response, and aids in regulation of B-cell differentiation, proliferation, survival and apoptosis. It is also important for immune self-tolerance.	Inhibits phosphotransferase activity. Y508 is phosphorylated by CSK, CTK (MATK).
LYN	Pan-specific	Yes-related protein-tyrosine kinase	0.6	0.8	1.3	0.7	see above	NA
MAPKAPK2	Pan-specific	Mitogen-activated protein kinase-activated protein kinase 2	1.2	1.1	2.2	1.3	Stress-activated serine/threonine-protein kinase involved in cytokine production, endocytosis, reorganization of the cytoskeleton, cell migration, cell cycle control, chromatin remodeling, DNA damage response and transcriptional regulation. Following stress, it is phosphorylated and activated by MAPK p38-alpha/MAPK14, leading to phosphorylation of substrates.	NA
MAPKAPK2	T222	Mitogen-activated protein kinase-activated protein kinase 2	0.6	1.1	1.7	1.1	see above	Stimulates phosphotransferase activity. T222 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1), p38a MAPK (MAPK14).
MAPKAPK2	T334	Mitogen-activated protein kinase-activated protein kinase 2	-0.3	0.4	-0.8	-1.1	see above	Stimulates phosphotransferase activity. T334 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1), p38a MAPK (MAPK14).

MAPKAPK5	T186	MAP kinase-activated protein kinase 5 (PRAK)	0.4	1.2	0.3	-0.1	Serine/threonine kinase involved in mTORC1 signaling and post-transcriptional regulation. Phosphorylates FOXO3, ERK3/MAPK6, ERK4/MAPK4, HSP27/HSPB1, p53/TP53 and RHEB. Acts as a tumor suppressor by mediating Ras-induced senescence and phosphorylating p53/TP53. Involved in post-transcriptional regulation of MYC by phosphorylating FOXO3. This leads to FOXO3 nuclear localization, enabling expression of miR-34b and miR-34c (post-transcriptional regulators of MYC that bind to the 3'UTR of MYC transcript and prevent translation). Negatively regulates mTORC1 via RHEB phosphorylation.	Predicted to be stimulatory for phosphotransferase activity.
MARK1	T215	MAP/microtubule affinity-regulating protein-serine kinase 1	1.1	0.5	1.0	0.6	Serine/threonine-protein kinase involved in cell polarity and microtubule dynamics regulation.	Stimulates phosphotransferase activity. T215 is phosphorylated by LKB1 (STK11), TAO1 (TAOK1/MAP3K16).
MDM2	S166	Double minute 2	-0.2	0.7	1.4	0.3	E3 ubiquitin-protein ligase that mediates ubiquitination of p53/TP53, leading to its degradation by the proteasome. Inhibits p53/TP53- and p73/TP73-mediated cell cycle arrest and apoptosis by binding its transcriptional activation domain.	S166 is phosphorylated by Akt1 (PKBa), DAPK3 (ZIPK), MAPKAPK2, Pim1, RSK1 (RPS6KA2).
MEK1	Pan-specific	MAPK/ERK protein-serine kinase 1 (MKK1, MAP2K1)	1.5	1.4	1.1	0.5	Dual specificity kinase which acts as an essential component of the MAPK signal transduction pathway. Binding of extracellular ligands such as growth factors, cytokines and hormones to their cell-surface receptors activates RAS and initiates RAF1 activation. RAF1 activates the MAP2K1/MEK1 and MAP2K2/MEK2. Both MAP2K1/MEK1 and MAP2K2/MEK2 phosphorylate and activate MAPK3/ERK1 and MAPK1/ERK2. Depending on the cellular context, this pathway mediates diverse biological functions such as cell growth, adhesion, survival and differentiation, predominantly through the regulation of transcription, metabolism and cytoskeletal rearrangements.	NA
MEK1	Pan-specific	MAPK/ERK protein-serine kinase 1 (MKK1, MAP2K1)	0.7	1.1	1.1	0.6	see above	NA
MEK1	T292	MAPK/ERK protein-serine kinase 1 (MKK1, MAP2K1)	-0.5	0.8	-1.0	-1.3	see above	Phosphorylation increases molecular association with ERK2 and Raf1, but reduces interaction with ERK1 and phosphorylation of S298 by PAK isoforms. It promotes dephosphorylation of the activating residues S218 and S222. T292 is phosphorylated by CDK1 (CDC2), ERK1 (MAPK3), ERK2 (MAPK1), MEKK1 (MAP3K1).

MEK1	S298	MAPK/ERK protein-serine kinase 1 (MKK1, MAP2K1)	-0.6	0.4	-1.1	-1.3	see above	Stimulates phosphotransferase activity. Phosphorylation regulates cell growth and molecular association. MAPK1/ERK2 phosphorylation of Thr-292 in response to cellular adhesion leads to inhibition of S298 phosphorylation by PAK. S298 is phosphorylated by MEK1 (MAP2K1), PAK1, PAK2, PAK3.
MEK1	T386	MAPK/ERK protein-serine kinase 1 (MKK1, MAP2K1)	-0.5	0.1	-0.8	-1.2	see above	Phosphorylation induces interaction with ERK2 and regulates intracellular location. T386 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1).
MEK1	T386	MAPK/ERK protein-serine kinase 1 (MKK1, MAP2K1)	-0.7	0.0	-1.0	-1.3	see above	Phosphorylation induces interaction with ERK2 and regulates intracellular location. T386 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1).
MEK2	T394	MAPK/ERK protein-serine kinase 2 (MKK2, MAP2K2)	1.1	1.5	-0.3	-0.9	Upstream component of the MAPK pathway. Activates the ERK1 and ERK2 MAPKs.	No data available.
MEK2	T394	MAPK/ERK protein-serine kinase 2 (MKK2, MAP2K2) (mouse)	-0.5	1.6	-0.9	-1.3	see above	No data available.
MEK3	Pan-specific	MAPK/ERK protein-serine kinase 3 beta isoform (MKK3 beta, MAP2K3)	2.3	1.7	2.6	2.8	Dual specificity kinase. Is activated by cytokines and environmental stress in vivo. Phosphorylates and activates the MAPK p38. Part of a signaling cascade that begins with the activation of the adrenergic receptor ADRA1B and leads to the activation of MAPK14.	NA
MEK3/6	S218/S207	MAPK/ERK protein-serine kinase 3 beta isoform (MKK3 beta, MAP2K3)	0.5	0.7	2.1	-0.1	Dual specificity kinase. Is activated by cytokines and environmental stress in vivo. Phosphorylates and activates the MAPK p38. Part of a signaling cascade that begins with the activation of the adrenergic receptor ADRA1B and leads to the activation of MAPK14.	Stimulates phosphotransferase activity and regulates transcription. S218 and S207 are phosphorylated by ASK1 (MAP3K5), COT (MAP3K8), MEKK3 (MAP3K3), MKK3 (MAP2K3, MEK3), MLK3 (MAP3K11).
MEK4	Pan-specific	MAPK/ERK protein-serine kinase 4 (MKK4, MAP2K4)	1.6	1.9	3.3	3.2	Dual specificity protein kinase which acts as an essential component of the MAPK signal transduction pathway. With MAP2K7/MKK7, is one of the only known kinases to directly activate the MAPK8/JNK1, MAPK9/JNK2 and MAPK10/JNK3.	NA
MEK5	Pan-specific	MAPK/ERK protein-serine kinase 5 (MKK5, MAP2K5)	1.6	1.2	2.1	1.9	Acts as a scaffold for the formation of a ternary MAP3K2/MAP3K3-MAP3K5-MAPK7 signaling complex. Activation of this pathway appears to play a critical role in protecting cells from stress-induced apoptosis, neuronal survival and cardiac development and angiogenesis.	NA

MEK5	S311	MAPK/ERK protein-serine kinase 5 (MKK5, MAP2K5)	1.4	0.8	0.6	0.6	see above	Stimulates phosphotransferase activity and inhibits interaction with ERK5. S311 is phosphorylated by MEKK2 (MAP3K2).
MEK5	Pan-specific	MAPK/ERK protein-serine kinase 5 (MKK5, MAP2K5)	1.3	0.8	1.1	1.2	see above	NA
MEKK1	Pan-specific	MAPK/ERK kinase kinase 1 (MAP3K1)	1.0	0.6	1.2	1.9	Upstream member of the MAPK family that activates the ERK and JNK kinase pathways by phosphorylation of MAP2K1 and MAP2K4. Activates CHUK and IKBKB, the central protein kinases of the NF-kappa-B pathway.	NA
MEKK1	Pan-specific	MAPK/ERK kinase kinase 1 (MAP3K1)	1.0	0.9	0.7	0.0	see above	NA
MEKK2	Pan-specific	MAPK/ERK kinase kinase 2 (MAP3K2)	0.5	1.0	1.8	2.7	Upstream member of the MAPK family which regulates the JNK and ERK5 pathways by phosphorylating and activating MAP2K5 and MAP2K7. Plays a role in caveolae kiss-and-run dynamics.	NA
MEKK2	S239	MAPK/ERK kinase kinase 2 (MAP3K2)	0.1	0.8	1.7	0.9	see above	No data available.
MERTK	Y749+Y753	Tyrosine-protein kinase Mer (MER)	-0.4	1.9	1.6	1.1	Receptor tyrosine kinase that transduces signals from the ECM into the cytoplasm by binding to several ligands including LGALS3, TUB, TULP1 or GAS6. Regulates many physiological processes including cell survival, migration, differentiation, and phagocytosis of apoptotic cells (efferocytosis). Ligand binding at the cell surface induces autophosphorylation of MERTK, providing docking sites for downstream signaling molecules. Following activation by ligand, interacts with GRB2 or PLCG2 and induces phosphorylation of MAPK1, MAPK2, FAK/PTK2 or RAC1.	Stimulates phosphotransferase activity. Y749 and Y753 are phosphorylated by MER (MERTK).
MERTK	Y749	Tyrosine-protein kinase Mer (MER)	-0.2	0.5	1.1	-0.1	see above	Stimulates phosphotransferase activity. Y749 and Y753 are phosphorylated by MER (MERTK).
MET	Pan-specific	Hepatocyte growth factor (HGF) receptor-tyrosine kinase	1.8	0.6	0.6	0.7	Receptor tyrosine kinase that transduces signals from the ECM into the cytoplasm by binding to hepatocyte growth factor/HGF ligand. Regulates many physiological processes including proliferation, scattering, morphogenesis and survival. Ligand binding induces autophosphorylation of MET, providing docking sites for downstream signaling molecules. Following activation, interacts with the PI3K subunit PIK3R1, PLCG1, SRC, GRB2, STAT3 or the adapter GAB1. Recruitment of these effectors leads to activation of RAS-ERK, PI3K-AKT, and PLCgamma-PKC signaling.	NA
MET	Pan-specific	Hepatocyte growth factor (HGF) receptor-tyrosine kinase	1.5	0.9	0.8	0.7	see above	NA
MET	Y1234+Y1235+S1236	Hepatocyte growth factor (HGF) receptor-tyrosine kinase	0.0	0.4	1.8	0.7	see above	Stimulates phosphotransferase activity. Phosphorylation also regulates protein interaction. Y1234 and Y1235 are phosphorylated by Met, Ron (MST1R).



MET	Y1003	Hepatocyte growth factor (HGF) receptor-tyrosine kinase	0.8	0.7	1.7	1.4	see above	Stimulates phosphotransferase activity. Phosphorylation regulates cell growth, receptor desensitization, protein stabilization, ubiquitination, protein and molecular association. Y1003 is phosphorylated by Met.
MET	S1236	Hepatocyte growth factor (HGF) receptor-tyrosine kinase	-0.2	0.7	1.5	0.8	see above	Stimulates phosphotransferase activity.
MET	Y1234+Y1235	Hepatocyte growth factor (HGF) receptor-tyrosine kinase	0.1	0.1	1.4	0.9	see above	Stimulates phosphotransferase activity. Phosphorylation also regulates protein interaction. Y1234 and Y1235 are phosphorylated by Met, Ron (MST1R).
MET	T1241	Hepatocyte growth factor (HGF) receptor-tyrosine kinase	0.1	0.5	1.4	0.7	see above	Stimulates phosphotransferase activity.
MKK3	S218	MAPK/ERK protein-serine kinase 3 beta isoform (MEK3 beta, MAP2K3)	0.3	1.6	0.6	1.0	Dual specificity MAPK family kinase that is activated by cytokines and environmental stress in vivo. Phosphorylates and activates MAPK p38. Part of a signaling cascade that begins with the activation of the adrenergic receptor ADRA1B and leads to the activation of MAPK14.	Stimulates phosphotransferase activity and regulates transcription. S218 is phosphorylated by ASK1 (MAP3K5), COT (MAP3K8), MEKK3 (MAP3K3), MKK3 (MAP2K3, MEK3), MLK3 (MAP3K11).
MKK3	Pan-specific	MAPK/ERK protein-serine kinase 3 beta isoform (MEK3 beta, MAP2K3)	0.1	1.1	1.5	1.4	see above	NA
MKK4	S80	MAPK/ERK protein-serine kinase 4 (MEK4, MAP2K4)	0.0	0.5	1.1	-0.1	Dual specificity MAPK family kinase. With MAP2K7/MKK7, it is the one of the only known kinases to directly activate MAPK8/JNK1, MAPK9/JNK2 and MAPK10/JNK3.	Inhibits phosphotransferase activity. Phosphorylation regulates apoptosis. S80 is phosphorylated by Akt1 (PKBa), Akt3 (PKBg), SGK1.
MLC	S19	Myosin regulatory light chain 2, smooth muscle isoform (MYL12B, MRLC2)	-0.4	1.1	-0.8	-1.1	Myosin regulatory subunit that plays an important role in regulation of both smooth muscle and nonmuscle cell contractile activity via its phosphorylation. Implicated in cytokinesis, receptor capping, and cell locomotion.	Phosphorylation increases an actomyosin contractile response by triggering cross-bridge cycling and force development. S19 is phosphorylated by MLCK, ROCK1, ZIPK, ILK1, PAK3.
MLK3	Pan-specific	Mixed-lineage protein-serine kinase 3 (MAP3K11)	1.4	1.3	2.2	2.7	Activates the JUN N-terminal pathway. Required for serum-stimulated cell proliferation and for mitogen and cytokine activation of MAPK14 (p38), MAPK3 (ERK) and MAPK8 (JNK1) through phosphorylation and activation of MAP2K4/MKK4 and MAP2K7/MKK7.	NA

MLK3	T277+S281	Mixed-lineage protein-serine kinase 3 (MAP3K11)	-0.8	0.4	-0.9	-1.3	see above	Stimulates phosphotransferase activity. Phosphorylation regulates molecular association, including inducing interaction with GEFT. T277 is phosphorylated by MLK3 (MAP3K11). S281 is phosphorylated by HPK1 (MAP4K1), MLK3 (MAP3K11).
MOK	T159+Y161	MOK protein kinase (RAGE)	0.0	1.1	0.4	0.3	Able to phosphorylate several exogenous substrates and to undergo autophosphorylation. Negatively regulates cilium length in a cAMP and mTORC1 signaling-dependent manner.	Stimulates phosphotransferase activity.
MSK1	S212	Mitogen & stress-activated protein-serine kinase 1 (RPS6KA5)	0.9	0.1	1.5	1.1	Serine/threonine kinase that is required for mitogen, cytokine, or other stress-induced phosphorylation of CREB1 and ATF1 and for the regulation of RELA, STAT3 and ETV1/ER81 in response to these stressors. This contributes to gene activation by histone phosphorylation and functions in the regulation of inflammatory genes.	Stimulates phosphotransferase activity. S212 is phosphorylated by MSK1 (RPS6KA5).
MSK1	S376	Mitogen & stress-activated protein-serine kinase 1 (RPS6KA5)	-0.4	0.2	3.4	4.6	see above	Stimulates phosphotransferase activity. S376 is phosphorylated by MSK1 (RPS6KA5).
MST1	Pan-specific	Mammalian STE20-like protein-serine kinase 1 (MST1, STK4)	0.9	0.7	1.3	1.3	Stress-activated, pro-apoptotic kinase which, following caspase-cleavage, enters the nucleus and induces chromatin condensation followed by internucleosomal DNA fragmentation. Key component of the Hippo signaling pathway which plays a pivotal role in organ size control and tumor suppression by restricting proliferation and promoting apoptosis. STK3/MST2 and STK4/MST1, in complex with SAV1, phosphorylate and activate LATS1/2 in complex with its regulatory protein MOB1. This leads to phosphorylation and inactivation of YAP1 and WWTR1/TAZ.	NA
MST1	Pan-specific	Mammalian STE20-like protein-serine kinase 1 (KRS2, STK4)	0.6	1.0	2.2	3.4	see above	NA
MST1	Pan-specific	Mammalian STE20-like protein-serine kinase 1 (KRS2, STK4)	0.8	0.5	1.2	0.8	see above	NA
MST2	Pan-specific	Mammalian STE20-like protein-serine kinase 2 (KRS1)	0.5	0.7	2.0	1.6	Scaffolding protein that is part of a multiprotein signaling complex. Promotes phosphorylation of Raf family members and activation of downstream MAPKs. Promotes activation of MAPK1 and MAPK3, both in response to EGF and to cAMP.	NA
MST2	Pan-specific	Mammalian STE20-like protein-serine kinase 2 (KRS1)	1.6	1.1	0.2	0.5	see above	NA
MST3	T184	Mammalian STE20-like protein-serine kinase 3 (STK24)	1.0	0.7	1.1	0.6	Serine/threonine-protein kinase that acts on both serine and threonine residues and promotes apoptosis in response to stress stimuli and caspase activation. Mediates oxidative-stress-induced cell death by modulating phosphorylation of JNK1, JNK2, and p38.	Predicted to be stimulatory for phosphotransferase activity.

NBS1	S343	Nijmegen breakage syndrome protein 1 (NBN, Nibrin)	0.2	0.8	1.3	1.3	Component of the MRE11-RAD50-NBN (MRN complex) which plays a critical role in the cellular response to DNA damage and the maintenance of chromosome integrity. The complex is involved in double-strand break repair, DNA recombination, maintenance of telomere integrity, cell cycle checkpoint control and meiosis.	S343 is phosphorylated by ATM.
NDR1	S281+T282	Serine/threonine-protein kinase 38 (NDR, STK38)	0.8	0.6	1.1	0.5	Negative regulator of MAP3K1/2 signaling. Converts MAP3K2 from its phosphorylated form to its non-phosphorylated form and inhibits autophosphorylation of MAP3K2.	Stimulates phosphotransferase activity and protein interaction. Phosphorylation regulates intracellular location. S281 is phosphorylated by NDR1 (NDR; STK38).
NEK2	Pan-specific	NIMA (never-in-mitosis)-related protein-serine kinase 2	3.2	1.4	2.4	4.1	Protein kinase which is involved in the control of centrosome separation and bipolar spindle formation in mitotic cells and chromatin condensation in meiotic cells. Regulates centrosome separation by phosphorylating CROCC, CEP250 and NINL. Regulates kinetochore microtubule attachment stability via phosphorylation of NDC80. Involved in regulation of mitotic checkpoint protein complex via phosphorylation of CDC20 and MAD2L1. Regulates chromatin condensation through phosphorylation of HMGA2.	NA
NEK2	Pan-specific	NIMA (never-in-mitosis)-related protein-serine kinase 2	1.9	1.4	3.2	4.0	see above	NA
NFkappaB p50	Pan-specific	NF-kappa-B p50 nuclear transcription factor	0.9	1.4	3.6	5.8	NF-kappa-B is a pleiotropic transcription factor present in almost all cell types and is the endpoint of a series of signal transduction events that are initiated by a vast array of stimuli related to many biological processes such as inflammation, immunity, differentiation, cell growth, tumorigenesis and apoptosis. NF-kappa-B is a homo- or heterodimeric complex formed by the Rel-like domain-containing proteins RELA/p65, RELB, NFKB1/p105, NFKB1/p50, REL and NFKB2/p52 and the heterodimeric p65-p50 complex appears to be most abundant one.	NA
NFkappaB p65	Pan-specific	NF-kappa-B p65 nuclear transcription factor (Rel A)	0.5	0.7	1.8	3.1	see above	NA
NFkappaB p65	S529	NF-kappa-B p65 nuclear transcription factor (Rel A)	-0.2	-0.1	1.3	0.9	see above	S529 is phosphorylated by CK2a1 (CSNK2A1).
NFkappaB p65	S276	NF-kappa-B p65 nuclear transcription factor (Rel A)	0.0	0.6	1.0	1.3	see above	S276 is phosphorylated by MSK1 (RPS6KA5), MSK2 (RPS6KA4), PKACa (PRKACA), PKCa (PRKCA).
NR1 (NMDAR1)	S896	N-methyl-D-aspartate (NMDA) glutamate receptor 1 subunit zeta	0.8	-0.2	2.1	2.9	NMDA receptor subtype of glutamate-gated ion channels with high calcium permeability and voltage-dependent sensitivity to magnesium. Mediated by glycine. This protein plays a key role in synaptic plasticity, synaptogenesis, excitotoxicity, memory acquisition and learning. It mediates neuronal functions in glutamate neurotransmission.	S896 is phosphorylated by the following protein kinases in vitro: PKCa (PRKCA).

p38a MAPK	Pan-specific	Mitogen-activated protein-serine kinase p38 alpha (MAPK14)	1.7	2.9	0.5	0.1	Serine/threonine kinase of the MAPK signal transduction pathway. One of the four p38 MAPKs which play an important role in the cascades of cellular responses evoked by extracellular stimuli such as proinflammatory cytokines or physical stress leading to direct activation of transcription factors. The p38 MAPKs phosphorylate a broad range of proteins and may have 200 to 300 substrates each. Many targets are kinases which phosphorylate additional downstream targets. RPS6KA5/MSK1 and RPS6KA4/MSK2 can directly phosphorylate/activate transcription factors CREB1, ATF1, the NF-kappa-B isoform RELA/NFKB3, STAT1 and STAT3, but can also phosphorylate histone H3 and nucleosomal protein HMG1.	NA
p38a MAPK	T180+Y182	Mitogen-activated protein-serine kinase p38 alpha (MAPK14)	1.3	1.0	0.0	-0.1	see above	Stimulates phosphotransferase activity. Phosphorylation regulates apoptosis, cell adhesion, cell cycle progression, cell motility, cytoskeletal reorganization, and molecular association, including inducing interaction with Fyn, Nck1, p38-alpha. T180 is phosphorylated by MKK3 (MAP2K3, MEK3), MKK4 (MAP2K4, MEK4), MKK6 (MAP2K6, MEK6), p38a MAPK (MAPK14), PBK (TOPK).
p38d MAPK	Y182	Mitogen-activated protein-serine kinase p38 delta (MAPK13)	0.5	1.1	0.5	-0.5	Serine/threonine kinase and essential component of the MAPK signal transduction pathway. One of the four p38 MAPKs which play an important role in the cascades of cellular responses evoked by extracellular stimuli such as proinflammatory cytokines or physical stress leading to direct activation of transcription factors such as ELK1 and ATF2.	Stimulates phosphotransferase activity. Y182 is phosphorylated by MKK3 (MAP2K3, MEK3), MKK4 (MAP2K4, MEK4), MKK6 (MAP2K6, MEK6), p38a MAPK (MAPK14), PBK (TOPK).
p38g MAPK	Pan-specific	Mitogen-activated protein-serine kinase p38 gamma, ((MAPK12, ERK6)	0.7	2.3	0.5	0.1	Serine/threonine kinase and essential component of the MAPK signal transduction pathway. One of the four p38 MAPKs which play an important role in the cascades of cellular responses evoked by extracellular stimuli such as proinflammatory cytokines or physical stress leading to direct activation of transcription factors such as ELK1 and ATF2.	NA
p38g MAPK	Pan-specific	Mitogen-activated protein-serine kinase p38 gamma, ((MAPK12, ERK6)	0.4	1.5	0.5	0.1	see above	NA
p38g MAPK	Pan-specific	Mitogen-activated protein-serine kinase p38 gamma, ((MAPK12, ERK6)	0.7	1.2	0.2	0.2	see above	NA
p53	Pan-specific	Tumor suppressor protein p53 (antigenNY-CO-13) (TP53)	1.7	1.6	2.0	3.0	Induces growth arrest or apoptosis depending on the physiological circumstances and cell type. Involved in cell cycle regulation as a trans-activator that acts to negatively regulate cell division by controlling genes required for this process. One of the activated genes is an inhibitor of cyclin-dependent kinases. Apoptosis induction is mediated either by stimulation of BAX and FAS antigen expression, or by repression of Bcl-2 expression. In cooperation with mitochondrial PPIF, is involved in activating oxidative stress-induced necrosis (largely independent of transcription).	NA

p70 S6K	Pan-specific	Ribosomal protein S6 kinase beta-1 (RPS6KB1 p70S6Ka)	2.1	0.3	1.2	2.3	Serine/threonine kinase that acts downstream of mTOR signaling in response to growth factors and nutrients to promote cell proliferation, cell growth and cell cycle progression. Regulates protein synthesis through phosphorylation of EIF4B, RPS6 and EEF2K, and contributes to cell survival by repressing the pro-apoptotic function of BAD. Under conditions of nutrient depletion, the inactive form associates with the EIF3 translation initiation complex to inhibit activity.	NA
p70 S6K	T252	Ribosomal protein S6 kinase beta-1 (RPS6KB1, p70S6Ka)	0.9	9.6	-0.8	14.5	see above	Stimulates phosphotransferase activity. Phosphorylation regulates protein translation and protein conformation. T252 is phosphorylated by PDK1 (PDPK1), PIK3CD.
PAK1	Pan-specific	p21-activated kinase 1 (alpha) (serine/threonine-protein kinase PAK 1) (PAKa)	2.1	0.0	3.0	4.4	Protein kinase involved in intracellular signaling downstream of integrins and receptor-type kinases that plays an important role in actin and microtubule cytoskeleton dynamics (including actin stress fibers, focal adhesion complexes, and microtubule biogenesis and organization), in cell adhesion, migration, proliferation, apoptosis, mitosis, and in vesicle-mediated transport processes. Phosphorylates BAD to protect cells against apoptosis. Activated by interaction with CDC42 and RAC1. Functions as GTPase effector that links the Rho-related GTPases CDC42 and RAC1 to the JNK MAP kinase pathway. Phosphorylates and activates MAP2K1, and thereby mediates activation of downstream MAP kinases. Plays a role in the regulation of insulin secretion in response to elevated glucose levels.	NA
PAK1	S144/S141/S154	p21-activated kinase 1 (alpha) (serine/threonine-protein kinase PAK 1) (PAKa)	0.7	0.5	1.2	0.7	see above	Stimulates phosphotransferase activity and regulates cytoskeletal reorganization, and intracellular location. S144 is phosphorylated by PAK1.
PAK3	Pan-specific	p21-activated kinase 3 (beta) (serine/threonine-protein kinase PAK 3) (PAKb)	0.6	0.0	1.4	1.1	Serine/threonine protein kinase that plays a role in a variety of different signaling pathways including cytoskeleton regulation, cell migration, or cell cycle regulation. Plays a role in dendrite spine morphogenesis as well as synapse formation and plasticity. Acts as downstream effector of the small GTPases CDC42 and RAC1. Activation by the binding of active CDC42 and RAC1 results in a conformational change and a subsequent autophosphorylation on several serine and/or threonine residues. Phosphorylates MAPK4 and MAPK6 and activates the downstream target MAPKAPK5, a regulator of F-actin polymerization and cell migration. Additionally, phosphorylates TNNI3/troponin I to modulate calcium sensitivity and relaxation kinetics of thin myofilaments. May also be involved in early neuronal development.	NA
Paxillin 1	Y118	Paxillin 1 (PXN)	0.5	-0.6	1.0	1.2	Cytoskeletal protein involved in actin-membrane attachment at sites of cell adhesion to the extracellular matrix (focal adhesion).	Activation and binding to CrkL, Src. Y118 is phosphorylated by Abl1, Brk (PTK6), FAK (PTK2), Fyn, PYK2 (PTK2B), Src.

PDGFRa	Y754	Platelet-derived growth factor receptor kinase alpha	0.1	2.5	-0.5	-0.9	Tyrosine kinase that acts as a cell-surface receptor for PDGFA, PDGFB and PDGFC and plays an essential role in the regulation of embryonic development, cell proliferation, survival and chemotaxis. Depending on the context, promotes or inhibits cell proliferation and cell migration. Plays an important role in the differentiation of bone marrow-derived mesenchymal stem cells. Required for normal skeleton development and cephalic closure during embryonic development. Required for normal development of the mucosa lining the gastrointestinal tract, and for recruitment of mesenchymal cells and normal development of intestinal villi. Plays a role in cell migration and chemotaxis in wound healing. Plays a role in platelet activation, secretion of agonists from platelet granules, and in thrombin-induced platelet aggregation.	Y754 is phosphorylated by PDGFRA, PDGFRB.
PDK1	S241	3-phosphoinositide-dependent protein-serine kinase 1 (PDPK1)	0.6	0.4	0.5	1.0	Serine/threonine kinase which acts as a master kinase, phosphorylating and activating a subgroup of the AGC family of protein kinases. Its targets include: PKB/AKT1, PKB/AKT2, PKB/AKT3, RPS6KB1, RPS6KA1, RPS6KA2 and RPS6KA3, PRKACA, PRKCD, PRKCZ, SGK1, SGK2 and SGK3, PAK1, PKN1 and PKN2. Plays a central role in the transduction of signals from insulin by activating PKB/AKT1. Negatively regulates the TGF-beta-induced signaling through modulation of SMAD phosphorylation, localization, and association with TGF-beta receptor. Activates PPARG transcriptional activity and promotes adipocyte differentiation. Activates the NF-kappa-B pathway via phosphorylation of IKKB. The tyrosine phosphorylated form regulates focal adhesions via angiotensin II.	Stimulatory for phosphotransferase activity. Phosphorylation induces interaction with 14-3-3 eta and 14-3-3 theta. S241 is phosphorylated by PDK1 (PDPK1).
PECAM-1	Y713	Platelet endothelial cell adhesion molecule	1.8	-0.4	0.5	0.9	Cell adhesion molecule which is required for leukocyte transendothelial migration (TEM) under most inflammatory conditions. Prevents phagocyte ingestion of closely apposed viable cells by transmitting 'detachment' signals, and changes function on apoptosis; the encounter of a viable cell with a phagocyte via the homophilic interaction of PECAM1 on both cell surfaces leads to the viable cell's repulsion from the phagocyte. During apoptosis, the inside-out signaling of PECAM1 is disabled so that the apoptotic cell no longer rejects the phagocyte.	Induces activity and binding to SHP-2 and STAT5A. Y713 is phosphorylated by CSK, Fer, Fes, Fyn, Lck.
PI3K	Pan-specific	Phosphatidylinositol 3-kinase regulatory subunit alpha	0.5	1.3	0.5	4.8	Binds to activated (phosphorylated) protein-Tyr kinases, through its SH2 domain, and acts as an adapter, mediating the association of the p110 catalytic unit to the PM. Necessary for insulin-stimulated increase in glucose uptake and glycogen synthesis in insulin-sensitive tissues. Involved in signaling from FGFR1, FGFR2, FGFR3, FGFR4, KITLG/SCF, KIT, PDGFRA, PDGFRB, and ITGB2. Modulates the cellular response to ER stress and metabolic overloading to improve glucose tolerance.	NA
PKCa	Pan-specific	Protein-serine kinase C alpha (PRKCA)	0.5	1.2	0.6	0.9	Calcium-activated, phospholipid- and diacylglycerol (DAG)-dependent serine/threonine kinase that is involved in positive and negative regulation of cell proliferation, apoptosis, differentiation, migration and adhesion, tumorigenesis, cardiac hypertrophy, angiogenesis, platelet function and inflammation, by directly phosphorylating targets such as RAF1, BCL2, CSPG4, TNNT2/CTNT, or activating signaling cascade involving ERK1/2 and RAP1GAP. Involved in cell proliferation and cell growth arrest by positive and negative regulation of the cell cycle.	NA
PKCa	Y195	Protein-serine kinase C alpha (PRKCA)	0.1	0.1	0.6	1.1	see above	No data available.

PKCb	Pan-specific	Protein-serine kinase C beta 1 (PRKCB1)	1.1	0.2	2.0	2.3	Calcium-activated, phospholipid- and diacylglycerol (DAG)-dependent serine/threonine kinase involved in various cellular processes such as regulation of the B-cell receptor (BCR) signalosome, oxidative stress-induced apoptosis, androgen receptor-dependent transcription regulation, insulin signaling and endothelial cell proliferation. Plays a key role in B-cell activation by regulating BCR-induced NF-kappa-B activation. Mediates the activation of the canonical NF-kappa-B pathway.	NA
PKCb	S661	Protein-serine kinase C beta 1 (PRKCB1)	-0.6	-1.1	-0.9	-0.7	see above	Inhibits phosphotransferase activity. Phosphorylation inhibits membrane binding and causes release into cytoplasm. S661 is phosphorylated by PKCb1 (PRKCB1).
PKCd	Pan-specific	Protein-serine kinase C delta (PRKCD)	0.7	0.1	1.6	1.6	Calcium-independent, phospholipid- and DAG-dependent serine/threonine kinase that plays contrasting roles in cell death and cell survival by functioning as a pro-apoptotic protein during DNA damage-induced apoptosis (via BCLAF1/Btf and p53), but acting as an anti-apoptotic protein during cytokine receptor-initiated cell death. Required for oxygen radical production by NADPH oxidase and acts as positive or negative regulator in platelet functional responses. Negatively regulates B cell proliferation and also has an important function in self-antigen induced B cell tolerance induction. In response to oxidative stress, activates CHUK/IKKA, causing the phosphorylation of p53/TP53. During ER stress or DNA damage-induced apoptosis, complexes with ABL1 to trigger apoptosis independently of p53/TP53. In the cytosol it triggers apoptosis by activating MAPK11 or MAPK14, inhibiting AKT1 and decreasing the level of XIAP, but in nucleus it induces apoptosis via the activation of MAPK8 or MAPK9. Upon ionizing radiation, it is required for the activation of BAX and BAK, which trigger the mitochondrial cell death pathway.	NA
PKCd	Y313	Protein-serine kinase C delta (PRKCD)	0.3	-0.1	0.6	1.3	see above	Stimulates phosphotransferase activity. Phosphorylation regulates transcription and apoptosis. Y313 is phosphorylated by EGFR, Fyn, Lck, Lyn, PDGFRA, PKCd (PRKCD), Src, Yes.
PKCd	Y313	Protein-serine kinase C delta (PRKCD)	0.1	0.6	-1.0	-1.1	see above	Stimulates phosphotransferase activity. Phosphorylation regulates transcription and apoptosis. Y313 is phosphorylated by EGFR, Fyn, Lck, Lyn, PDGFRA, PKCd (PRKCD), Src, Yes.



PKCe	Pan-specific	Protein-serine kinase C epsilon (PRKCE)	1.1	0.3	1.8	2.1	Calcium-independent, phospholipid- and diacylglycerol (DAG)-dependent serine/threonine kinase that plays essential roles in the regulation of multiple cellular processes linked to cytoskeletal proteins, such as cell adhesion, motility, migration and cell cycle, functions in neuron growth and ion channel regulation, and is involved in immune response, cancer cell invasion and regulation of apoptosis. Mediates cell adhesion to the ECM via integrin-dependent signaling, by mediating angiotensin-2-induced activation of integrin beta-1 (ITGB1) in cardiac fibroblasts. Phosphorylates MARCKS, which phosphorylates and activates PTK2/FAK. Involved in the control of the directional transport of ITGB1 in mesenchymal cells by phosphorylating vimentin (VIM), an intermediate filament (IF) protein. In epithelial cells, associates with and phosphorylates keratin-8 (KRT8), which induces targeting of desmoplakin at desmosomes and regulates cell-cell contact.	NA
PKCe	Pan-specific	Protein-serine kinase C epsilon (PRKCE)	1.0	0.4	1.5	1.9	see above	NA
PKCg	T674	Protein-serine kinase C gamma (PRKCG)	0.6	1.1	-0.4	-0.4	Calcium-activated, phospholipid- and diacylglycerol (DAG)-dependent serine/threonine kinase that plays diverse roles in neuronal cells and eye tissues, such as regulation of the neuronal receptors GRIA4/GLUR4 and GRIN1/NMDAR1, modulation of receptors and neuronal functions related to sensitivity to opiates, pain and alcohol, mediation of synaptic function and cell survival after ischemia, and inhibition of gap junction activity after oxidative stress.	Stimulates phosphotransferase activity. T674 is phosphorylated by PKCg (PRKCG).
PKCg	T514	Protein-serine kinase C gamma (PRKCG)	-0.4	0.0	-1.0	-1.2	see above	Stimulates phosphotransferase activity. Phosphorylation induces preactivation of PKC. T514 is phosphorylated by PDK1 (PDPK1).
PKCh	Pan-specific	Protein-serine kinase C eta (PRKCH)	1.0	0.9	1.6	1.5	Calcium-independent, phospholipid- and DAG-dependent serine/threonine kinase involved in regulating cell differentiation in keratinocytes, pre-B cell receptor signaling, epithelial tight junction integrity and foam cell formation, actin depolymerization, and proliferation and apoptosis in some cell types. Activates FYN, which blocks EGFR signaling and leads to growth arrest and differentiation in some cell types. Associates with the cyclin CCNE1-CDK2-CDKN1B complex and inhibits CDK2 kinase activity, leading to RB1 dephosphorylation and G1 arrest. Regulates tight junctions (TJs) by phosphorylating occludin (OCLN), which is necessary for assembly and maintenance of TJs. In association with PLD2 and via TLR4 signaling, is involved in LPS-induced RGS2 down-regulation and foam cell formation. Can activate the mTOR pathway, the PI3K/AKT pathway and ERK1. Can regulate NF-kappa-B by activating IKBKB, and confer protection against DNA damage-induced apoptosis. Promotes oncogenic functions of ATF2 in the nucleus while blocking its apoptotic function at mitochondria.	NA
PKCh	T656	Protein-serine kinase C eta (PRKCH)	0.8	1.6	-0.6	-0.7	see above	Stimulates phosphotransferase activity. T656 is phosphorylated by PKCh (PRKCH).

PKCI/I	Pan-specific	Protein-serine kinase C lambda/iota (PRKCI)	0.4	0.6	2.2	2.7	Calcium- and diacylglycerol-independent serine/ threonine kinase that plays a general protective role against apoptotic stimuli, is involved in NF-kappa-B activation, cell survival, differentiation and polarity, and contributes to the regulation of microtubule dynamics in the early secretory pathway. Is necessary for BCR-ABL oncogene-mediated resistance to apoptotic drugs in leukemia cells. In cultured neurons, prevents amyloid beta protein-induced apoptosis by interrupting cell death process at a very early step.	NA
PKCI/I	T564	Protein-serine kinase C lambda/iota (PRKCI)	0.2	-0.5	1.0	0.7	see above	No data available for this site, but all other documented sites stimulate phosphotransferase activity.
PKCm	Pan-specific	Protein-serine kinase C mu (Protein kinase D) (PRKD1, PKD1, PRKCM)	2.2	1.0	3.0	3.2	Serine/threonine kinase that converts transient DAG signals into prolonged physiological effects downstream of PKC, and is involved in the regulation of MAPK8/JNK1 and Ras signaling, Golgi membrane integrity and trafficking, cell survival through NF-kappa-B activation, cell migration, cell differentiation by mediating HDAC7 nuclear export, cell proliferation via ERK1/2 signaling, and plays a role in cardiac hypertrophy, VEGFA-induced angiogenesis, genotoxic-induced apoptosis and flagellin-stimulated inflammatory response. Phosphorylates EGFR, which leads to the suppression of EGF-induced MAPK8/JNK1 activation and subsequent JUN phosphorylation.	NA
PKCm	S910	Protein-serine kinase C mu (Protein kinase D) (PRKD1, PKD1, PRKCM)	0.3	1.1	0.4	0.9	see above	Stimulates phosphotransferase activity. S910 is phosphorylated by PKD1 (PRKCM).
PKCq	S676	Protein-serine kinase C theta (PRKCQ)	0.8	0.2	2.5	2.3	Calcium-independent, phospholipid- and DAG-dependent serine/threonine-protein kinase that mediates non-redundant functions in T-cell receptor (TCR) signaling, including T-cell activation, proliferation, differentiation and survival, by mediating activation of multiple transcription factors such as NF-kappa-B, JUN, NFATC1 and NFATC2. In TCR-CD3/CD28-co-stimulated T-cells, it is required for the activation of NF-kappa-B and JUN, which in turn are essential for IL2 production, and participates in the calcium-dependent NFATC1 and NFATC2 transactivation.	Stimulates phosphotransferase activity. Phosphorylation regulates transcription. S676 is phosphorylated by PKCt (PRKCQ).
PKCq	S695	Protein-serine kinase C theta (PRKCQ)	0.3	0.1	1.6	1.9	see above	Stimulates phosphotransferase activity. Phosphorylation induces interaction with PDK1 and protein stabilization. S695 is phosphorylated by PKCt (PRKCQ).
PKCq	S695	Protein-serine kinase C theta (PRKCQ)	0.8	0.2	1.4	1.1	see above	Stimulates phosphotransferase activity. Phosphorylation induces interaction with PDK1 and protein stabilization. S695 is phosphorylated by PKCt (PRKCQ).

PKCz	T410	Protein-serine kinase C zeta (PRKCZ)	0.0	0.7	1.4	1.0	Calcium- and DAG-independent serine/threonine kinase that functions in PI3K pathway and MAPK cascade, and is involved in NF-kappa-B activation, mitogenic signaling, cell proliferation, cell polarity, inflammatory response and maintenance of long-term potentiation (LTP). Upon lipopolysaccharide (LPS) treatment in macrophages, or following mitogenic stimuli, functions downstream of PI3K to activate MAP2K1/MEK1-MAPK1/ERK2 signaling cascade independently of RAF1 activation. Required for insulin-dependent activation of AKT3, but may function as an adapter rather than a direct activator.	Stimulates phosphotransferase activity. Phosphorylation regulates cytoskeletal reorganization, protein conformation, and molecular association, including increased binding to MYO1C, TNNI1, TPM1 and desmin. T410 is phosphorylated by PDK1 (PDPK1).
PKCz	Pan-specific	Protein-serine kinase C zeta (PRKCZ)	0.6	0.8	1.3	1.1	see above	NA
PKM2	Y390	Pyruvate kinase isozymes M1/M2	0.5	0.5	1.5	1.5	Glycolytic enzyme that catalyzes the transfer of a phosphoryl group from phosphoenolpyruvate (PEP) to ADP, generating ATP. Stimulates POU5F1-mediated transcriptional activation. Plays a general role in caspase independent cell death.	No data available.
PKR1	Pan-specific	Double stranded RNA dependent protein-serine kinase (PRKR; EIF2AK2)	1.6	0.8	1.2	1.3	IFN-induced dsRNA-dependent serine/threonine kinase which regulates the innate immune response to viral infection and is also involved in the regulation of signal transduction, apoptosis, cell proliferation and differentiation. Regulates replication via EIF2S1. Phosphorylates p53/TP53, PPP2R5A, DHX9, ILF3, IRS1 and the HHV-1 viral protein US11. Also has tyrosine-protein kinase activity and phosphorylates CDK1 upon DNA damage, facilitating its ubiquitination and proteosomal degradation. Either as an adapter protein and/or via its kinase activity, can regulate signaling through p38 MAP kinase, NF-kappa-B and insulin signaling pathways and transcription factors (JUN, STAT1, STAT3, IRF1, ATF3) regulating proinflammatory cytokines and IFNs.	NA
PLCg1	Y783	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase gamma-2	0.6	2.3	3.3	2.0	Mediates the production of the second messenger molecules diacylglycerol (DAG) and inositol 1,4,5-trisphosphate (IP3). Plays an important role in the regulation of intracellular signaling cascades. Becomes activated in response to ligand-mediated activation of receptor-type tyrosine kinases, such as PDGFRA, PDGFRB, FGFR1, FGFR2, FGFR3 and FGFR4. Plays a role in actin reorganization and cell migration.	Stimulates phospholipase activity and regulates cell motility and molecular association, including inducing interaction with Grb2 and VEGFR-2. Y783 is phosphorylated by EGFR, Itk, Src, Syk, TrkB (NTRK2), ZAP70.
PLCg1	Y771	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase gamma-1	-0.9	1.7	-0.1	-0.6	see above	Y771 is phosphorylated by EGFR, Syk.
PLCg1	Y783	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase gamma-1	-0.1	1.0	1.4	0.2	see above	Stimulates phospholipase activity and regulates cell motility and molecular association, including inducing interaction with Grb2 and VEGFR-2. Y783 is phosphorylated by EGFR, Itk, Src, Syk, TrkB (NTRK2), ZAP70.

PLCg2	Y753	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase gamma-2 (PLC R)	0.9	1.8	2.1	1.2	The production of the second messenger molecules diacylglycerol (DAG) and inositol 1,4,5-trisphosphate (IP3) is mediated by activated phosphatidylinositol-specific phospholipase C enzymes. It is a crucial enzyme in transmembrane signaling.	Stimulates phospholipase activity, and regulates molecular association, including inducing interaction with Lyn. Y753 is phosphorylated by the following protein kinases in vitro: Btk, Fyn, Lck, Src
PLCg2	Pan-specific	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase gamma-2 (PLC R)	0.7	1.4	0.0	-0.5	see above	NA
PLCg2	Y759	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase gamma-2 (PLC R)	0.8	0.4	1.6	2.3	see above	Stimulates phospholipase activity, and regulates molecular association, including inducing interaction with Lyn. Y759 is phosphorylated by Btk, Fyn, Lck, Src, Syk.
PLK4	T170	Polo-like protein kinase 3 (cytokine- inducible kinase (CNK) (SAK, STK18)	0.5	0.4	1.2	0.7	Serine/threonine-protein kinase that plays a central role in centriole duplication. Able to trigger procentriole formation on the surface of the parental centriole cylinder, leading to the recruitment of centriole biogenesis proteins such as SASS6, CENPJ/CPAP, CCP110, CEP135 and gamma-tubulin.	Predicted to be stimulatory for phosphotransferase activity.
PRK1	T774	Protein kinase C-related protein-serine kinase 1 (PKN1, PRKCL1)	0.2	3.2	0.5	0.0	PKC-related serine/threonine-protein kinase involved in various processes such as regulation of the intermediate filaments of the actin cytoskeleton, cell migration, tumor cell invasion and transcription regulation.	Stimulates phosphotransferase activity. Phosphorylation regulates cytoskeletal reorganization and molecular association. T774 is phosphorylated by PDK1 (PDPK1), PKN1 (PRKCL1).
PRKACA	T198	cAMP-dependent protein kinase catalytic subunit alpha	-0.7	0.6	-0.8	-1.3	Phosphorylates a large number of substrates in the cytoplasm and the nucleus. Regulates the abundance of compartmentalized pools of its regulatory subunits through phosphorylation of PJA2 which binds and ubiquitinates these subunits, leading to proteolysis. Phosphorylates CDC25B, ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA and VASP. Involved in the regulation of platelets in response to thrombin and collagen; maintains circulating platelets in a resting state by phosphorylating proteins in numerous platelet inhibitory pathways when in complex with NF-kappa-B and I-kappa-B-alpha. Thrombin and collagen disrupt these complexes and free active PRKACA stimulates platelets and leads to platelet aggregation by phosphorylating VASP.	Stimulates phosphotransferase activity and regulates stability. T198 is phosphorylated by PDK1 (PDPK1), PKACa (PRKACA).
PRKX	T201+T203	Serine/threonine-protein kinase PRKX	1.4	1.2	1.8	1.6	Serine/threonine protein kinase regulated by and mediating cAMP signaling in cells. Acts through phosphorylation of downstream targets that may include CREB, SMAD6 and PKD1 and has multiple functions in cellular differentiation and epithelial morphogenesis. Regulates myeloid cell differentiation through SMAD6 phosphorylation. Involved in nephrogenesis by stimulating renal epithelial cell migration and tubulogenesis. Also involved in angiogenesis through stimulation of endothelial cell proliferation, migration and vascular-like structure formation.	Predicted to be stimulatory for phosphotransferase activity.

PTEN	Pan-specific	Phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase and protein phosphatase and tensin homolog deleted on chromosome 10	2.4	1.2	1.7	2.4	Acts as a dual-specificity protein phosphatase, dephosphorylating tyrosine-, serine- and threonine-phosphorylated proteins. Also acts as a lipid phosphatase, removing the phosphate in the D3 position of the inositol ring from phosphatidylinositols. Antagonizes the PI3K-AKT/PKB signaling pathway by dephosphorylating phosphoinositides and thereby modulating cell cycle progression and cell survival. The unphosphorylated form cooperates with AIP1 to suppress AKT1 activation.	NA
PTEN	S380+T382+T383	Phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase and protein phosphatase and tensin homolog deleted on chromosome 10	0.2	0.6	1.7	1.1	see above	Inhibits phosphatase activity, regulates cell differentiation, cell motility, transcription, and induces/inhibits interaction with PTEN. S380 is phosphorylated by CK2a1 (CSNK2A1), LKB1 (STK11), PKCz (PRKCZ). T382/T383 are phosphorylated by CK2a1 (CSNK2A1), LKB1 (STK11), MAGI2 (AIP1), PKCz (PRKCZ).
PTEN	Pan-specific	Phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase and protein phosphatase and tensin homolog deleted on chromosome 10	0.7	0.8	1.6	1.9	see above	NA
PTEN	S380+T382+T383	Phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase and protein phosphatase and tensin homolog deleted on chromosome 10	0.1	0.8	1.4	0.4	see above	Inhibits phosphatase activity, regulates cell differentiation, cell motility, transcription, and induces/inhibits interaction with PTEN. S380 is phosphorylated by CK2a1 (CSNK2A1), LKB1 (STK11), PKCz (PRKCZ). T382/T383 are phosphorylated by CK2a1 (CSNK2A1), LKB1 (STK11), MAGI2 (AIP1), PKCz (PRKCZ).
PTP1D	S580	Protein-tyrosine phosphatase 1D (SHP2, SHPTP2, Syp, PTP2C, PTPN11)	2.9	2.5	11.0	4.4	Acts downstream of various receptor and cytoplasmic protein tyrosine kinases to participate in the signal transduction from the cell surface to the nucleus. Positively regulates MAPK signal transduction pathway .	S580 is phosphorylated by PKCa (PRKCA), PKCb1 (PRKCB1), PKCb2 (PRKCB2), PKCh (PRKCH).

PYK2	Pan-specific	Protein-tyrosine kinase 2 (PTK2B)	2.0	1.5	1.8	1.2	Non-receptor tyrosine kinase that regulates reorganization of the actin cytoskeleton, cell polarization, cell migration, adhesion, spreading and bone remodeling. Plays a role in the regulation of the humoral immune response, and B-cell regulation in lymphoid tissues. Required for normal macrophage polarization and migration towards sites of inflammation. Regulates cytoskeleton rearrangement and the regulation of T-cell responses. Promotes osteoclastic bone resorption. Functions in signaling downstream of integrin and collagen receptors, immune receptors, GPCRs, cytokine, chemokine and growth factor receptors, and mediates responses to cellular stress. Forms multisubunit signaling complexes with PDPK1, SRC and SRC family members upon activation to create binding sites for scaffold proteins, effectors and substrates. Promotes activation of NOS3, cGMP, RHOA, RAC1, and the PI3K-AKT1 and MAPK ERK1/2 and JNK signaling cascades. Recruits MDM2 to P53/TP53 in the nucleus to regulate P53/TP53 activity.	NA
PYK2	Y579+Y580	Protein-tyrosine kinase 2 (PTK2B)	0.6	1.0	0.8	0.2	see above	Stimulates phosphotransferase activity. Y579 and Y580 are phosphorylated by Src.
PYK2	Y402	Protein-tyrosine kinase 2 (PTK2B)	-0.3	0.6	1.5	0.0	see above	Stimulates phosphotransferase activity. Phosphorylation regulates cell cycle progression, cell motility, alters intracellular location, and induces binding to ErbB2, RASA1 and Src. Y402 is phosphorylated by PYK2 (PTK2B), Src.
Rb	S807	Retinoblastoma-associated protein 1	-0.2	1.1	-0.2	-0.7	Key regulator of entry into cell division that acts as a tumor suppressor. Promotes G0-G1 transition when phosphorylated by CDK3/cyclin-C. Acts as a transcription repressor of E2F1 target genes. The underphosphorylated, active form of RB1 interacts with E2F1 and represses its transcription activity, leading to cell cycle arrest. Directly involved in heterochromatin formation by maintaining overall chromatin structure and stabilizing histone methylation. Recruits and targets histone methyltransferases SUV39H1, KMT5B and KMT5C, leading to epigenetic transcriptional repression.	Inhibits interaction with Abl and EF21. S807 is phosphorylated by CDK1 (CDC2), CDK2, CDK3, CDK4, CDK6, CDK9.
Rb	T821	Retinoblastoma-associated protein 1	0.4	1.0	0.0	-0.3	see above	Inhibits interaction with E2F1, Elf-1 and TFDP1, and induces binding with Rb. T821 is phosphorylated by the following protein kinases in vitro: CDK2, CDK6.
Rb	S612	Retinoblastoma-associated protein 1	-0.5	0.6	-0.6	-1.1	see above	Reported to either induce and inhibit binding to E2F1. S612 is phosphorylated by CDK2, CDK6, Chk1 (CHEK1), Chk2 (CHEK2).

RET	Y905	Proto-oncogene tyrosine-protein kinase receptor Ret	-0.4	-0.6	0.8	1.2	Receptor tyrosine kinase involved in numerous cellular mechanisms including cell proliferation, neuronal navigation, cell migration, and cell differentiation upon binding with glial cell derived neurotrophic factor family ligands. Phosphorylates PTK2/FAK1. Regulates both cell death/survival balance and positional information. Regulates intestine organogenesis, development of enteric nervous system, the neural crest, and renal organogenesis during embryonic life, and promotes the formation of Peyer's patch-like structures (gut-associated lymphoid tissue). Modulates cell adhesion via its cleavage by caspase and mediates cell migration in an integrin (e.g. ITGB1 and ITGB3)-dependent manner. Active in the absence of ligand, triggering apoptosis in a caspase-dependent manner.	Stimulates phosphotransferase activity, and regulates cell growth. Y905 is phosphorylated by FAK (PTK2), Ret, Src.
RIPK1	Pan-specific	Receptor-interacting protein-serine kinase 1	0.2	1.2	0.9	1.2	Serine-threonine kinase which transduces inflammatory and cell-death signals (programmed necrosis) following death receptors ligation, activation of pathogen recognition receptors (PRRs), and DNA damage. Upon activation of TNFR1 by the TNF-alpha family cytokines, TRADD and TRAF2 are recruited to the receptor. Activates the MAPK-JNK apoptotic cascade and pro-inflammatory NF-kappa-B signaling. Interaction with other cellular RHIM-containing adapters initiates gene activation and cell death. RIPK1 and RIPK3 association, in particular, forms a necrosis-inducing complex.	NA
RIPK2	Y381	Receptor-interacting serine/threonine-protein kinase 2 (RIPK2, RIP2, RICK)	-0.1	0.1	1.2	1.3	Serine/threonine/tyrosine kinase that plays an essential role in modulation of innate and adaptive immune responses. Upon stimulation by bacterial peptidoglycans, NOD1 and NOD2 are activated, oligomerize and recruit RIPK2 through CARD-CARD domains. Contributes to the tyrosine phosphorylation of the guanine exchange factor ARHGEF2 through Src tyrosine kinase leading to NF-kappaB activation by NOD2. Once recruited, RIPK2 autophosphorylates and undergoes 'Lys-63'-linked polyubiquitination and mediates the recruitment of MAP3K7/TAK1 to IKBKG/NEMO. This ultimately leads to activation of IKBKB/IKKB and subsequent NF-kappa-B activation, which drives the transcription of genes involved in immune response, growth control, or protection against apoptosis. Also plays a role during engagement of the T-cell receptor (TCR).	No data available.
ROCK1	Pan-specific	RhoA protein-serine kinase beta (ROKb)	1.5	1.1	1.6	0.8	Protein kinase which is a key regulator of actin cytoskeleton and cell polarity. Involved in regulation of smooth muscle contraction, actin cytoskeleton organization, stress fiber and focal adhesion formation, neurite retraction, cell adhesion and motility via phosphorylation of DAPK3, GFAP, LIMK1, LIMK2, MYL9/MLC2, PFN1 and PPP1R12A. Phosphorylates FHOD1 and acts synergistically with it to promote SRC-dependent non-apoptotic plasma membrane blebbing. Phosphorylates JIP3 and regulates the recruitment of JNK to JIP3 upon UVB-induced stress. Acts as a suppressor of inflammatory cell migration by regulating PTEN phosphorylation and stability. Acts as a negative regulator of VEGF-induced angiogenic endothelial cell activation.	NA



ROCK2	Y722	Rho-associated protein kinase 2 (ROKa)	-0.3	-0.1	0.9	1.2	Protein kinase which is a key regulator of actin cytoskeleton and cell polarity. Involved in regulation of smooth muscle contraction, actin cytoskeleton organization, stress fiber and focal adhesion formation, neurite retraction, cell adhesion and motility via phosphorylation of ADD1, BRCA2, CNN1, EZR, DPYSL2, EP300, MSN, MYL9/MLC2, NPM1, RDX, PPP1R12A and VIM. Phosphorylates SORL1 and IRF4. Acts as a negative regulator of VEGF-induced angiogenic endothelial cell activation. Positively regulates the activation of p42/MAPK1-p44/MAPK3 and of p90RSK/RPS6KA1 during myogenic differentiation. Plays an important role in the timely initiation of centrosome duplication.	Phosphorylation inhibits phosphotransferase activity and inhibits interaction with RhoA.
ROCK2	Pan-specific	Rho-associated protein kinase 2 (ROKa)	1.6	0.9	2.7	3.4	see above	NA
Ron	Pan-specific	Macrophage-stimulating protein receptor alpha chain (RONa)	0.6	0.3	1.7	3.3	Receptor tyrosine kinase that transduces signals from the ECM into the cytoplasm by binding to MST1 ligand or GFs. Regulates many physiological processes including cell survival, migration and differentiation. Ligand binding at the cell surface induces autophosphorylation of RON on its intracellular domain that provides docking sites for downstream signaling molecules. This leads to interaction with PI3K subunit PIK3R1, PLCG1 or the adapter GAB1 and subsequent activation of several signaling cascades including the RAS-ERK, PI3K-AKT, or PLCgamma-PKC. RON signaling activates the wound healing response, proliferation as well as survival at the wound site. Also plays a role in the innate immune response by regulating the migration and phagocytic activity of macrophages.	NA
RPS6	S235	40S ribosomal protein S6	0.3	0.2	1.1	1.7	May play an important role in controlling cell growth and proliferation through the selective translation of particular classes of mRNA.	Phosphorylation at S235 and S236 facilitates the assembly of the preinitiation complex. S235 is phosphorylated by Akt1 (PKBa), Akt2 (PKBb), AurB (STK12), p70S6K (RPS6KB1), PKACa (PRKACA), PKCd (PRKCD), RSK1 (RPS6KA2), RSK2 (RPS6KA3).
RSK1	Pan-specific	Ribosomal S6 protein-serine kinase 1 (RPS6KA1, p90RSK)	1.7	1.2	3.0	4.6	Serine/threonine kinase that acts downstream of ERK signaling and positively regulates mitogenic and stress-induced activation of CREB1, CREBBP, ETV1/ER81 and NR4A1/NUR77, positively regulates translation through RPS6 and EIF4B phosphorylation, and mediates cellular proliferation, survival, and differentiation by modulating mTOR signaling and repressing pro-apoptotic function of BAD and DAPK1. Upon insulin-derived signal, phosphorylates GSK3B to inhibit its activity and EIF4B to enhance EIF4B affinity for the EIF3 complex to stimulating cap-dependent translation. Involved in the mTOR nutrient-sensing pathway by phosphorylating TSC2 to prevent its suppression of mTOR signaling, and via phosphorylation of RPTOR (regulates mTORC1 activity). Involved in cell cycle regulation by phosphorylating the CDK inhibitor CDKN1B. Phosphorylates EPHA2 to regulate cell migration.	NA
RSK1	S363	Ribosomal S6 protein-serine kinase 1 (RPS6KA1, p90RSK)	0.2	-0.5	1.0	2.0	see above	Stimulates phosphotransferase activity. S363 is phosphorylated by the following protein kinases in vitro: ERK1 (MAPK3), ERK2 (MAPK1), PDK1 (PDPK1), PKCa (PRKCA).

RSK1	S380	Ribosomal S6 protein-serine kinase 1 (RPS6KA1, p90RSK)	0.0	0.0	0.7	1.4	see above	Stimulates phosphotransferase activity. S380 is phosphorylated by JNK1 (MAPK8), JNK2 (MAPK9), p70S6K (RPS6KB1), RSK1 (RPS6KA2).
RSK1	T359	Ribosomal S6 protein-serine kinase 1 (RPS6KA1, p90RSK)	-0.1	-0.9	0.9	1.0	see above	Stimulates phosphotransferase activity. T359 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1).
RSK3	Y217+S218	Ribosomal protein S6 kinase alpha-3 (RPS6KA2, p90RSK)	0.2	0.1	1.1	0.9	Serine/threonine-protein kinase that acts downstream of ERK (MAPK1/ERK2 and MAPK3/ERK1) signaling and mediates mitogenic and stress-induced activation of transcription factors, regulates translation, and mediates cellular proliferation, survival, and differentiation. May function as tumor suppressor in epithelial ovarian cancer cells.	Predicted to be stimulatory for phosphotransferase activity. S218 is phosphorylated by RSK3 (RPS6KA2).
SCYL1	S754	N-terminal kinase-like protein	-0.1	0.0	1.3	1.2	Regulates COPI-mediated retrograde protein traffic at the interface between the Golgi apparatus and the endoplasmic reticulum.	No data available.
Sgk223	Y413	Tyrosine-protein kinase Sgk223	-0.2	-0.4	0.9	1.3	Tyrosine protein kinase family; a similar protein in rat binds to Rho family GTPases and regulates neurite outgrowth via activation of RhoA.	No data available.
Shc1	Y349	SH2 domain-containing transforming protein 1	0.3	0.4	1.0	1.3	Signaling adapter that couples activated growth factor receptors to signaling pathways. Participates in a signaling cascade initiated by activated KIT and KITLG/SCF. Once phosphorylated, some isoforms couple activated receptor tyrosine kinases to Ras via the recruitment of the GRB2/SOS complex and are implicated in the cytoplasmic propagation of mitogenic signals while other isoforms are involved in signal transduction pathways that regulate apoptosis in response to oxidative stress downstream of p53.	Regulates apoptosis and molecular association, including inducing interaction with Grb2. Y349 is phosphorylated by EGFR, Lck, Src, ZAP70.
Shc1	Y349+Y350	SH2 domain-containing transforming protein 1	-0.6	0.6	-0.7	-1.2	see above	Regulates apoptosis and molecular association, including inducing interaction with Grb2. Y349 is phosphorylated by EGFR, Lck, Src, ZAP70. Y350 is phosphorylated by the following protein kinases in vitro: EGFR, Lck, Src, ZAP70.

SIK (SIK1)	T182	Salt-inducible kinase	-0.2	0.3	1.5	1.2	Serine/threonine-protein kinase involved in various processes such as cell cycle regulation, gluconeogenesis and lipogenesis regulation, muscle growth and differentiation and tumor suppression. Phosphorylates HDAC4, HDAC5, PPME1 (subunit of PP2A), SREBF1, CRTC1/TORC1 and CRTC2/TORC2. Regulates p53/TP53-dependent anoikis (apoptosis triggered by cell detachment) via phosphorylation of p53. Following increases in intracellular sodium, SIK1 is activated by CaMK1 and phosphorylates PP2A, leading to dephosphorylation of sodium/potassium-transporting ATPase ATP1A1 and subsequent increase activity of ATP1A1. Acts as a regulator of muscle cells via phosphorylation of HDAC4 and HDAC5, leading to promote expression of MEF2 target genes.	Predicted to be stimulatory for phosphotransferase activity. This phosphosite is located in the kinase activation loop between catalytic subdomains VII and VIII. T182 is phosphorylated by the following protein kinases in vitro: GSK3b, LKB1 (STK11)
SIK2 (QIK)	S358	Salt-inducible kinase 2	-0.3	-0.2	0.9	1.3	Phosphorylates 'Ser-794' of IRS1 in insulin-stimulated adipocytes, potentially modulating the efficiency of insulin signal transduction. Inhibits CREB activity by phosphorylating and repressing TORCs, the CREB-specific coactivators.	Stimulates phosphotransferase activity. S358 is phosphorylated by Akt1 (PKBa), Akt2 (PKBb).
SIK3 (QSK)	Pan-specific	Serine/threonine-protein kinase SIK3	2.8	0.9	1.3	2.4	Phosphorylates 'Ser-794' of IRS1 in insulin-stimulated adipocytes, potentially modulating the efficiency of insulin signal transduction. Inhibits CREB activity by phosphorylating and repressing TORCs, the CREB-specific coactivators.	NA
SIK3 (QSK)	T163	Salt-inducible kinase 3	1.1	0.7	2.1	4.4	see above	Predicted to stimulate phosphotransferase activity. T163 is phosphorylated by LKB1 (STK11).
SIK3 (QSK)	Pan-specific	Serine/threonine-protein kinase SIK3	1.1	1.8	0.5	2.2	see above	NA
SLK	S189	STE20-like serine/threonine-protein kinase (STK2)	0.4	0.1	1.1	0.8	Mediates apoptosis and actin stress fiber dissolution.	Predicted to be stimulatory for phosphotransferase activity.
Smad2	S467	Mothers against decapentaplegic homolog 2	0.1	-0.2	1.3	1.0	Receptor-regulated SMAD that is an intracellular signal transducer and transcriptional modulator activated by TGF-beta and activin type 1 receptor kinases. On formation of the SMAD2/SMAD4 complex, activates transcription. Positively regulates PDPK1 kinase activity by stimulating its dissociation from the 14-3-3 protein YWHAQ which acts as a negative regulator.	S467 is phosphorylated by BMPR1B (ACVR1), TGFbR1.
SMC1	S957	Structural maintenance of chromosomes protein 1A	0.3	-0.2	1.2	1.0	Involved in chromosome cohesion during cell cycle and in DNA repair. Central component of cohesin complex. The cohesin complex is required for the cohesion of sister chromatids after DNA replication. The cohesin complex may also play a role in spindle pole assembly during mitosis. Involved in DNA repair via its interaction with BRCA1 and its related phosphorylation by ATM, or via its phosphorylation by ATR. Works as a downstream effector both in the ATM/NBS1 branch and in the ATR/MSH2 branch of S-phase checkpoint.	S957 is phosphorylated by ATM, ATR.

SMG1	T3550	Lambda/iota protein kinase C-interacting protein	0.8	1.7	1.3	1.0	Serine/threonine protein kinase involved in both mRNA surveillance and genotoxic stress response pathways. Plays a central role in nonsense-mediated decay of mRNAs containing premature stop codons by phosphorylating UPF1/RENT1. Recruited by release factors to stalled ribosomes together with SMG8 and SMG9 and UPF1 to form the transient SURF complex. In Also acts as a genotoxic stress-activated protein kinase that displays some functional overlap with ATM. Can phosphorylate p53/TP53 and is required for optimal p53/TP53 activation after cellular exposure to genotoxic stress. May activate PRKCI.	No data available.
SNCA	S129	Alpha-synuclein	1.3	0.1	2.9	2.9	May be involved in the regulation of dopamine release and transport. Induces fibrillization of microtubule-associated protein tau. Reduces neuronal responsiveness to various apoptotic stimuli, leading to a decreased caspase-3 activation.	S129 is phosphorylated by BARK1 (GRK2; ADRBK1), CaMK2a, CK1a1 (CSNK1A1), CK2a1 (CSNK2A1), GPRK5 (GRK5), Plk2 (SNK), Plk3 (CNK).
SOX9	S181	SRY (sex determining region Y)-box 9 (campomelic dysplasia, autosomal sex-reversal)	0.0	1.2	-0.7	-1.0	Transcription factor that plays an important role in the normal skeletal development.	Stimulates transcriptional activity by increasing SOX9's DNA binding and transcriptional activation, and regulates cytoskeletal reorganization, intracellular location and molecular association, including inducing interaction with KPNB1. S181 is phosphorylated by PKACa (PRKACA).
SRC	Pan-specific	Src proto-oncogene-encoded protein-tyrosine kinase	1.3	2.9	2.7	2.7	Non-receptor protein tyrosine kinase which is activated following engagement of many different classes of cellular receptors including immune response receptors, integrins and other adhesion receptors, receptor protein tyrosine kinases, G protein-coupled receptors as well as cytokine receptors. Participates in signaling pathways that control a diverse spectrum of biological activities including gene transcription, immune response, cell adhesion, cell cycle progression, apoptosis, migration, and transformation. Receptor clustering or dimerization leads to recruitment of SRC to the receptor complexes where it phosphorylates the tyrosine residues within the receptor cytoplasmic domains.	NA
SRPK1	S222	Serine/arginine-rich protein-specific kinase 1	0.2	0.2	1.0	0.5	Serine/arginine-rich protein-specific kinase which specifically phosphorylates its substrates at serine residues located in regions rich in arginine/serine dipeptides, known as RS domains and is involved in the phosphorylation of SR splicing factors and the regulation of splicing. Can influence additional steps of mRNA maturation, as well as other cellular activities, such as chromatin reorganization and cell cycle progression.	Stimulates phosphotransferase activity.

STAT1	Y701	Signal transducer and activator of transcription 1 beta	0.5	0.4	2.5	1.2	Signal transducer and transcription activator that mediates cellular responses to interferons (IFNs), cytokine KITLG/SCF and other cytokines and other growth factors. Following type I IFN (IFN-alpha and IFN-beta) binding to cell surface receptors, signaling via protein kinases leads to activation of Jak kinases (TYK2 and JAK1) and to tyrosine phosphorylation of STAT1 and STAT2. In response to type II IFN (IFN-gamma), STAT1 is tyrosine- and serine-phosphorylated. It then forms a homodimer termed IFN-gamma-activated factor (GAF), migrates into the nucleus and binds to the IFN gamma activated sequence (GAS) to drive the expression of the target genes. Activation of the JAK-STAT pathway drives the cell into an antiviral state. May mediate cellular responses to activated FGFR1, FGFR2, FGFR3 and FGFR4.	S222 is phosphorylated by CK2a1 (CSNK2A1), CK2a2 (CSNK2A2).
STAT3	Pan-specific	Signal transducer and activator of transcription 3 (acute phase response factor)	0.1	-1.4	3.6	4.5	Signal transducer and transcription activator that mediates cellular responses to interleukins, KITLG/SCF, LEP and other growth factors.	NA
STAT5A	S780	Signal transducer and activator of transcription 5A	0.8	-0.1	3.2	3.6	Carries out a dual function: signal transduction and activation of transcription. Mediates cellular responses to the cytokine KITLG/SCF and other growth factors. Mediates cellular responses to ERBB4. May mediate cellular responses to activated FGFR1, FGFR2, FGFR3 and FGFR4. Binds to the GAS element and activates PRL-induced transcription. Regulates the expression of milk proteins during lactation.	Regulates molecular association, including inhibiting interaction with ERK1. S780 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1), PAK1.
STAT5A	Pan-specific	Signal transducer and activator of transcription 5A	0.8	-0.4	2.3	2.9	see above	NA
STAT5A	Y694	Signal transducer and activator of transcription 5A	0.7	0.1	1.8	2.2	see above	Stimulates transcriptional activity. Y694 is phosphorylated by Btk, JAK1, JAK2, JAK3, Lck, Lyn, Src.
STAT5B	Pan-specific	Signal transducer and activator of transcription 5B	0.5	-0.4	2.5	3.0	see above	NA
TEK	Pan-specific	Spleen protein-tyrosine kinase	1.8	0.2	3.1	3.5	Non-receptor tyrosine kinase which mediates signal transduction downstream of a variety of transmembrane receptors including classical immunoreceptors like the B-cell receptor (BCR). Regulates several biological processes including innate and adaptive immunity, cell adhesion, osteoclast maturation, platelet activation and vascular development. Assembles into signaling complexes with activated receptors at the plasma membrane via interaction between its SH2 domains and the receptor tyrosine-phosphorylated ITAM domains.	NA

TAK1	S439	TGF-beta-activated protein-serine kinase 1 (MAP3K7)	0.9	0.7	1.8	1.2	Plays a crucial role in innate immune response to fungal, bacterial and viral pathogens including ROS production. Activates the inflammasome and NF-kappa-B-mediated transcription of chemokines and cytokines in the presence of pathogens. Regulates neutrophil degranulation and phagocytosis through activation of the MAPK signaling cascade and mediates the activation of dendritic cells by cell necrosis stimuli. Also involved in mast cells activation. It can function downstream of receptors mediating cell adhesion such as integrins and aids in recruitment of leukocytes to inflammatory loci. Involved in vascular development where it may regulate blood and lymphatic vascular separation.	No data available.
TAK1	T184+T187	TGF-beta-activated protein-serine kinase 1 (MAP3K7)	0.7	0.9	0.7	1.7	see above	Stimulates phosphotransferase activity. T184 is phosphorylated by TAK1 (MAP3K7).
Tau	T522	Microtubule-associated protein tau (MAPT)	0.5	-0.5	1.3	1.8	Promotes microtubule assembly and stability, and might be involved in the establishment and maintenance of neuronal polarity. The C-terminus binds axonal microtubules while the N-terminus binds neural plasma membrane components, suggesting that tau functions as a linker protein between both. The short isoforms allow plasticity of the cytoskeleton whereas the longer isoforms may preferentially play a role in its stabilization.	Phosphorylation disrupts tau binding to microtubules. T522 is phosphorylated by GSK3-beta, CDK5, CK1-delta.
TBK1	Pan-specific	Serine/threonine-protein kinase TBK1	1.4	0.8	2.9	1.4	Serine/threonine kinase that plays an essential role in regulating inflammatory responses to foreign agents. Following activation of toll-like receptors by viral or bacterial components, associates with TRAF3 and TANK and phosphorylates interferon regulatory factors (IRFs) IRF3 and IRF7 as well as DDX3X to promote inflammatory responses. Several scaffolding molecules including FADD, TRADD, MAVS, AZI2, TANK or TBKBP1/SINTBAD can be recruited to the TBK1-containing-complexes. Can induce NF-kappa-B and AKT1 activation. Restricts bacterial proliferation by phosphorylating the autophagy receptor OPTN/Optineurin on 'Ser-177', thus enhancing LC3 binding affinity and antibacterial autophagy. Phosphorylates SMCR8 component of the C9orf72-SMCR8 complex, promoting autophagosome maturation.	NA
TGM2	Y369	Protein-glutamine gamma-glutamyltransferase 2	-0.2	0.0	1.0	1.1	Catalyzes the cross-linking of proteins and the conjugation of polyamines to proteins.	No data available.

TIE2	Y992	Angiopoietin-1 receptor (TEK)	0.3	0.6	0.8	2.0	Tyrosine-protein kinase that acts as cell-surface receptor for ANGPT1, ANGPT2 and ANGPT4 and regulates angiogenesis, endothelial cell survival, proliferation, migration, adhesion and cell spreading, reorganization of the actin cytoskeleton, and maintenance of vascular quiescence. Has anti-inflammatory effects by preventing the leakage of proinflammatory plasma proteins and leukocytes from blood vessels. Required for normal angiogenesis and heart development during embryogenesis and for post-natal hematopoiesis. Inhibits angiogenesis and promotes vascular stability in quiescent vessels via ANGPT1, TEK and PI3K-AKT1 signaling. In migrating endothelial cells that lack cell-cell adhesions, ANG1 recruits TEK to contacts with the ECM, leading to formation of focal adhesion complexes, activation of PTK2/FAK and ERK1/2, and stimulation of sprouting angiogenesis.	Stimulates phosphotransferase activity. Y992 is phosphorylated by Tie2.
TLN1	Y70	Talin 1	0.5	0.5	1.0	1.1	Probably involved in connections of major cytoskeletal structures to the plasma membrane. High molecular weight cytoskeletal protein concentrated at regions of cell-substratum contact and, in lymphocytes, at cell-cell contacts.	No data available.
TNK1	Y277	Non-receptor tyrosine-protein kinase TNK1	1.7	0.8	0.4	1.0	Involved in negative regulation of cell growth. Has tumor suppressor properties. Plays a negative regulatory role in the Ras-MAPK pathway. May function in signaling pathways utilized broadly during fetal development and more selectively in adult tissues and in cells of the lymphohematopoietic system. Could specifically be involved in phospholipid signal transduction.	Predicted to be stimulatory for phosphotransferase activity.
TRKA	Y680+Y681	Nerve growth factor (NGF) receptor-tyrosine kinase (NGFR, NTRK1)	0.5	0.1	1.0	1.1	Receptor tyrosine kinase involved in the development and the maturation of the central and peripheral nervous systems through regulation of proliferation, differentiation and survival of sympathetic and nervous neurons.	Stimulates phosphotransferase activity. Y680 is phosphorylated by TrkA (NTRK1).
TRKB	Y706	BDNF/NT3/4/5 receptor-tyrosine kinase (NTRK2)	0.0	0.4	0.7	1.5	Receptor tyrosine kinase involved in the development and the maturation of the central and the peripheral nervous systems through regulation of neuron survival, proliferation, migration, differentiation, and synapse formation and plasticity.	Stimulates phosphotransferase activity. Y706 is phosphorylated by TrkB (NTRK2).
TYK2	Y292	Protein-tyrosine kinase 2 (Jak-related)	0.0	1.3	0.3	0.3	Involved in intracellular signal transduction by being involved in the initiation of type I IFN signaling. Phosphorylates the interferon-alpha/beta receptor alpha chain.	No data available.
TYK2	Pan-specific	Protein-tyrosine kinase 2 (Jak-related)	0.8	0.3	2.4	2.0	see above	NA
VEGFR1 (FLT1)	Y1048	Vascular endothelial growth factor receptor 1	0.2	0.8	0.9	1.4	Tyrosine-protein kinase that acts as a cell-surface receptor for VEGFA, VEGFB and PGF, and plays an essential role in the development of embryonic vasculature, the regulation of angiogenesis, cell survival, cell migration, macrophage function, chemotaxis, and cancer cell invasion. May play an essential role as a negative regulator of embryonic angiogenesis by inhibiting excessive proliferation of endothelial cells.	Predicted to be stimulatory for phosphotransferase activity.



VEGFR2 (KDR)	Pan-specific	Vascular endothelial growth factor receptor-tyrosine kinase 2 (Flk1)	1.0	0.5	0.2	0.7	Tyrosine-protein kinase that acts as a cell-surface receptor for VEGFA, VEGFC and VEGFD. Plays an essential role in the regulation of angiogenesis, vascular development, vascular permeability, and embryonic hematopoiesis. Promotes proliferation, survival, migration and differentiation of endothelial cells. Promotes reorganization of the actin cytoskeleton.	NA
VEGFR2 (KDR)	Y1059	Vascular endothelial growth factor receptor-tyrosine kinase 2 (Flk1)	0.5	0.5	1.0	2.0	see above	Stimulates phosphotransferase activity and induces interaction with Cbl, PLCG1 and Src. Y1059 is phosphorylated by KDR (VEGFR2).
VEGFR3 (FLT4)	Pan-specific	Vascular endothelial growth factor receptor-protein-tyrosine kinase 3 (VEGFR3)	1.1	0.3	0.9	0.8	Tyrosine-protein kinase that acts as a cell-surface receptor for VEGFC and VEGFD, and plays an essential role in adult lymphangiogenesis and in the development of the vascular network and the cardiovascular system during embryonic development. Promotes proliferation, survival and migration of endothelial cells, and regulates angiogenic sprouting. Signaling by activated FLT4 leads to enhanced production of VEGFC, and to a lesser degree VEGFA, thereby creating a positive feedback loop that enhances FLT4 signaling. Modulates KDR signaling by forming heterodimers.	NA
Vimentin	S34	VIM (Vimentin)	-0.2	0.9	0.3	1.2	Vimentins are class-III intermediate filaments found in various non-epithelial cells, especially mesenchymal cells. Vimentin is attached to the nucleus, endoplasmic reticulum, and mitochondria, either laterally or terminally.	S34 is phosphorylated by PKCa (PRKCA).
WNK1	Pan-specific	Serine/threonine-protein kinase WNK1 (PRKWINK1)	1.1	0.8	0.4	0.6	Serine/threonine kinase which plays an important role in the regulation of electrolyte homeostasis, cell signaling, survival, and proliferation. Acts as an activator and inhibitor of sodium-coupled chloride cotransporters and potassium-coupled chloride cotransporters respectively. Activates SCNN1A, SCNN1B, SCNN1D and SGK1. Controls sodium and chloride ion transport by inhibiting the activity of WNK4. WNK4 regulates the activity of the thiazide-sensitive Na-Cl cotransporter, SLC12A3, by phosphorylation. WNK1 may also play a role in actin cytoskeletal reorganization.	NA
WNK1	T60	Serine/threonine-protein kinase WNK1 (PRKWINK1)	0.4	0.5	1.3	1.8	see above	Stimulates phosphotransferase activity. T60 is phosphorylated by Akt1 (PKBa), Akt3 (PKBg), MSK1 (RPS6KA5), SGK1.
YES	Pan-specific	Yamaguchi sarcoma proto-oncogene-encoded tyrosine kinase	1.3	1.1	2.6	2.7	Non-receptor protein tyrosine kinase that is involved in the regulation of cell growth and survival, apoptosis, cell-cell adhesion, cytoskeleton remodeling, and differentiation. Stimulation by receptor tyrosine kinases (RTKs) including EGRF, PDGFR, CSF1R and FGFR leads to recruitment of YES1 to the phosphorylated receptor, and activation and phosphorylation of downstream substrates. Upon EGRF activation, promotes the phosphorylation of PARD3 to favor epithelial tight junction assembly. Participates in the phosphorylation of specific junctional components such as CTNND1 by stimulating the FYN and FER tyrosine kinases at cell-cell contacts.	NA
YES	Y222+Y223	Yamaguchi sarcoma proto-oncogene-encoded tyrosine kinase	0.1	-0.1	0.9	1.4	see above	No data available.

ZAP70	Pan-specific	Zeta-chain (TCR) associated protein-tyrosine kinase, 70 kDa	1.6	0.6	2.4	2.6	<p>Tyrosine kinase that plays an essential role in regulation of the adaptive immune response. Regulates motility, adhesion and cytokine expression of mature T-cells, as well as thymocyte development. Contributes also to the development and activation of primary B-lymphocytes. Release of ZAP70 active conformation is stabilized by phosphorylation mediated by LCK. ZAP70 phosphorylates at least 2 essential adapter proteins: LAT and LCP2. In turn, a large number of signaling molecules are recruited and ultimately lead to lymphokine production, T-cell proliferation and differentiation. Furthermore, ZAP70 controls cytoskeleton modifications, adhesion and mobility of T-lymphocytes, thus ensuring correct delivery of effectors to the APC.</p>	NA
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**Table S2: dT-HESC 3hr Post-Infection Array Analysis with Fold Changes Compared to Mock Infection and Annotated Functions.** Proteins with z-score ratios greater than 1.0 (red) or less than -1.0 (blue) were considered significant.

Target Protein Name	Phospho Site (Human)	Full Target Protein Name	Fold Ch. GB112	Fold Ch. GB411	Fold Ch. GB590	Fold Ch. GB653	Function as summarized from the Uniprot Database ( <a href="http://www.uniprot.com">www.uniprot.com</a> )	Phospho Site Information (Kinexus PhosphoNET Database)
A6r	Y309	Twinfilin-2	8	7	9	7	Actin-binding protein involved in motile and morphological processes. Inhibits actin polymerization, likely by sequestering G-actin. By capping the barbed ends of filaments, it also regulates motility. Seems to play an important role in clathrin-mediated endocytosis and distribution of endocytic organelles.	No data available.
ABL1	Pan-specific	Abelson proto-oncogene-encoded protein-tyrosine kinase	9	6	5	5	Non-receptor tyrosine-protein kinase that plays a role in many key processes linked to cell growth and survival such as cytoskeleton remodeling in response to extracellular stimuli, cell motility and adhesion, receptor endocytosis, autophagy, DNA damage response and apoptosis. Pathogens can hijack ABL1 kinase signaling to reorganize the host actin cytoskeleton for entry, facilitating intracellular movement and host cell exit.	No data available.
ABL1	Y139	Abelson proto-oncogene-encoded protein-tyrosine kinase	11	9	9	11	see above	Stimulates phosphotransferase activity. Y139 is phosphorylated by Fyn, Hck, Lyn.
ABL1	Y257	Abelson proto-oncogene-encoded protein-tyrosine kinase	6	4	5	5	see above	Predicted to be inhibitory for phosphotransferase activity.
ABL1	Pan-specific	Abelson proto-oncogene-encoded protein-tyrosine kinase	4	3	9	4	see above	NA
ACK1	Pan-specific	Activated CDC42 kinase 1 (TNK2)	3	3	7	5	Non-receptor tyrosine-protein and serine/threonine-protein kinase that is implicated in cell spreading and migration, cell survival, cell growth and proliferation. Transduces extracellular signals to cytosolic and nuclear effectors. Implicated in trafficking and clathrin-mediated endocytosis through binding to EGFR and clathrin. Regulates ligand-induced degradation of EGFR, thereby contributing to the accumulation of EGFR at the limiting membrane of early endosomes. Downstream effector of CDC42 which mediates CDC42-dependent cell migration.	NA

ACTB	Y53	Actin, cytoplasmic 1 (Beta-actin)	9	13	10	10	Actins are highly conserved proteins that are involved in various types of cell motility and are ubiquitously expressed in all eukaryotic cells.	Phosphorylated by PKACa.
ACTN1	Y246	Alpha-actinin-1	3	1	2	2	F-actin cross-linking protein which is thought to anchor actin to a variety of intracellular structures. This is a bundling protein.	No data available; other sites are phosphorylated by FAK and PKACA.
Adducin a/g	S726	Adducin alpha, gamma (ADD 1/3)	24	34	23	17	Membrane-cytoskeleton-associated protein that promotes the assembly of the spectrin-actin network. Plays a role in actin filament capping. Binds to calmodulin.	Phosphorylated by PKACA, PKAc, PKCz.
AKT1 (PKBa)	T308	RAC-alpha serine/threonine-protein kinase	4	3	3	3	Serine/threonine-protein kinase which regulates many processes including metabolism, proliferation, cell survival, growth and angiogenesis. This is mediated through serine and/or threonine phosphorylation of a range of downstream substrates. Over 100 substrate candidates have been reported.	Stimulates phosphotransferase activity. Phosphorylation regulates transcription, translation, protein conformation, ubiquitination, and cell growth, differentiation and apoptosis. T308 is phosphorylated by MKK1, ERK1 (MAPK3), p38a MAPK (MAPK14), PDK1 (PDPK1), PIK3CA, PKCa (PRKCA), PKCb1 (PRKCB1), PKCe (PRKCE), PKD1 (PRKCM).
AKT1 (PKBa)	Pan-specific	RAC-alpha serine/threonine-protein kinase	2	3	3	1	see above	NA
AKT2 (PKBb)	Pan-specific	RAC-beta serine/threonine-protein kinase	4	3	3	4	Serine/threonine-protein kinase which regulates many processes including metabolism, proliferation, cell survival, growth and angiogenesis. This is mediated through serine and/or threonine phosphorylation of a range of downstream substrates. Over 100 substrate candidates have been reported.	NA
AKT2 (PKBb)	Pan-specific	RAC-beta serine/threonine-protein kinase	3	3	7	4	see above	NA

ALK	Pan-specific	Anaplastic lymphoma kinase	10	22	9	6	Neuronal receptor tyrosine kinase that is essentially and transiently expressed in specific regions of the central and peripheral nervous systems and plays an important role in the genesis and differentiation of the nervous system.	NA
ANXA1	Y207	Annexin A1	3	4	5	5	Plays important roles in the innate immune response as an effector of glucocorticoid-mediated responses and as a negative regulator of the inflammatory process. Promotes resolution of inflammation and wound healing. Promotes chemotaxis of granulocytes and monocytes via activation of the formyl peptide receptors. Contributes to the adaptive immune response by enhancing signaling cascades that are triggered by T-cell activation, regulates differentiation and proliferation of activated T-cells. Promotes the differentiation of T-cells into Th1 cells and negatively regulates differentiation into Th2 cells.	No data available.
ANXA2	Y238	Annexin A2	2	2	7	3	Calcium-regulated membrane-binding protein whose affinity for calcium is greatly enhanced by anionic phospholipids. May be involved in heat-stress response.	No data available.
Arrestin b	S412	Arrestin beta 1 (ARRB1)	30	38	24	18	Functions in regulating agonist-mediated GPCR signaling by mediating both receptor desensitization and resensitization processes. Targets many receptors for internalization by acting as an endocytic adapter (CLASPs, clathrin-associated sorting proteins) and recruiting the GPCRs to the adapter protein 2 complex 2 (AP-2) in clathrin-coated pits (CCPs). Can also play a role in MAPK, AKT and NFkB signaling.	S412 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1).
ASK1	Pan-specific	Apoptosis signal regulating protein-serine kinase 1 (MAP3K5)	4	3	2	3	Serine/threonine kinase which acts as an essential component of the MAPK pathway in response to changes in the environment to determine cell fates such as differentiation and survival. Regulates apoptosis through mitochondria-dependent caspase activation, and is required for the innate immune response. Mediates signal transduction of various stressors such as oxidative stress as receptor-mediated inflammatory signals (i.e. TNF and LPS). Acts as an upstream activator of the MKK/JNK and p38 MAPK signal transduction cascades through the phosphorylation and activation of MAP2Ks (MAP2K4/SEK1, MAP2K3/MKK3, MAP2K6/MKK6 and MAP2K7/MKK7).	NA
ASK1	Pan-specific	Apoptosis signal regulating protein-serine kinase 1 (MAP3K5)	3	3	7	4	see above	NA
ATM	S1981	Ataxia telangiectasia mutated	4	4	4	6	Serine/threonine protein kinase which activates checkpoint signaling upon double strand breaks (DSBs), apoptosis, and genotoxic stresses (i.e. UV light), thereby acting as a DNA damage sensor. Also involved in signal transduction and cell cycle control. May function as a tumor suppressor. Necessary for activation of ABL1 and SAPK.	Stimulates phosphotransferase activity and protein interaction. S1981 is phosphorylated by ATM, ATR.

ATM	Y2969	Ataxia telangiectasia mutated	2	1	2	3	see above	No data available.
ATR	S435+S436	Ataxia telangiectasia and Rad3 related	2	3	3	4	Serine/threonine protein kinase which activates checkpoint signaling upon genotoxic stresses (ionizing radiation, UV light, DNA replication stalling), thereby acting as a DNA damage sensor. Phosphorylates BRCA1, CHEK1, MCM2, RAD17, RPA2, SMC1 and p53/TP53, which collectively inhibit DNA replication and mitosis and promote DNA repair, recombination and apoptosis.	Stimulates phosphotransferase activity.
AurKA (Aurora A)	Pan-specific	Aurora Kinase A (serine/threonine protein kinase 6), (AIK, STK15)	7	7	6	7	Mitotic serine/threonine kinase that contributes to the regulation of cell cycle progression at several stages of mitosis. Also regulates the p53/TP53 pathway by phosphorylating and stabilizing p53/TP53.	NA
AurKA (Aurora A)	T287+T288	Aurora Kinase A (serine/threonine protein kinase 6), (AIK, STK15)	4	5	3	5	see above	Stimulates phosphotransferase activity. T287 is phosphorylated by AurA (STK15). T288 is phosphorylated by AurA (STK15), PAK1, PKACa (PRKACA).
AurKB (Aurora B)	Pan-specific	Aurora Kinase B (serine/threonine protein kinase 12), (AIM-1)	5	3	3	4	Serine/threonine-protein kinase component of the chromosomal passenger complex (CPC), a complex that acts as a key regulator of mitosis that ensures correct chromosome alignment and segregation as well as chromatin-induced microtubule stabilization and spindle assembly. Involved in the bipolar attachment of spindle microtubules to kinetochores and is a key regulator for the onset of cytokinesis during mitosis.	NA
AurKB (Aurora B)	Pan-specific	Aurora Kinase B (serine/threonine protein kinase 12), (AIM-1)	3	1	2	4	see above	NA
BAK	Pan-specific	Bcl2 homologous antagonist/killer (BCK2L7)	2	1	6	6	In the presence of an appropriate stimulus, accelerates programmed cell death by binding to, and antagonizing the anti-apoptotic action of BCL2.	NA
BARK1	S670	Beta-adrenergic receptor kinase 1 (GRK2, ADRBK1)	6	5	3	2	Specifically phosphorylates the agonist-occupied form of the beta-adrenergic and closely related receptors, probably inducing a desensitization of them. Key regulator of LPAR1 signaling. Competes with RALA for binding to LPAR1 thus affecting the signaling properties of the receptor.	Inhibits phosphotransferase activity. Phosphorylation regulates cell cycle progression, cell growth, protein degradation, and molecular association. S670 is phosphorylated by ERK1 (MAPK3).

BCR	Y177	Breakpoint cluster region protein	3	3	2	2	GTPase-activating protein for RAC1 and CDC42. Promotes the exchange of RAC or CDC42-bound GDP by GTP, thereby activating them. Displays serine/threonine kinase activity.	Induces interaction with Gab2, Grb2 and SOS1, and inhibits interaction with Hck. Y177 is phosphorylated by Abl1, Bcr, Fes, Fyn, Hck, Lyn.
BLK	Y389	B lymphoid tyrosine kinase	4	4	3	4	Non-receptor tyrosine kinase involved in B-lymphocyte development, differentiation and signaling. Binding of antigen to the BCR triggers signaling that ultimately leads to B-cell activation. Signaling through BLK plays an important role in transmitting signals through surface immunoglobulins and supports the pro-B to pre-B transition, as well as the signaling for growth arrest and apoptosis downstream of B-cell receptor.	Stimulates phosphotransferase activity.
BLK	Y188	B lymphoid tyrosine kinase	3	2	2	3	see above	No data available
BLNK	Y84	B-cell linker protein	4	8	5	3	Functions as a central linker protein, downstream of the B-cell receptor (BCR), bridging the SYK kinase to a multitude of signaling pathways and regulating biological outcomes of B-cell function and development. Plays a role in the activation of ERK/EPHB2, MAP kinase p38, JNK, AP1, NF-kappa-B and NFAT. Plays an important role in BCR-mediated PLCG1 and PLCG2 activation and Ca2+ mobilization and is required for trafficking of the BCR to late endosomes. Plays a critical role in orchestrating the pro-B cell to pre-B cell transition and in BCR-induced B-cell apoptosis.	Regulates transcription and molecular association, including inducing interaction with Btk, Nck2, PLCG1, VAV1. Y84 is phosphorylated by Syk.
B-Raf (RafB)	Pan-specific	RafB proto-oncogene-encoded protein-serine kinase	-1	-1	-2	-2	Protein kinase involved in the transduction of mitogenic signals from the cell membrane to the nucleus. Contributes to MAPK signaling via phosphorylation of MAP2K1.	NA
B-Raf (RafB)	S446+S447	RafB proto-oncogene-encoded protein-serine kinase	3	3	3	2	see above	Stimulates phosphotransferase activity and induces interaction with H-Ras-1. S446 is phosphorylated by PAK1, PKACa (PRKACA).
BTK	Y223+Y225	Bruton's agammaglobulinemia tyrosine kinase	6	7	8	7	Non-receptor tyrosine kinase that regulates apoptosis and is required for B lymphocyte development, differentiation and signaling. After BCR engagement and activation, phosphorylates PLCG2, igniting the downstream signaling pathway through calcium mobilization, followed by activation of PKC family members.	Stimulates phosphotransferase activity, may serve as a docking site for an SH2 domain containing protein, and regulates cell growth. Y223 is phosphorylated by Abl1, Btk, Itk, Lyn, PIK3CD, Tec.



BTK	Pan-specific	Bruton's agammaglobulinemia tyrosine kinase	2	1	4	3	see above	NA
BUB1B	S670	Mitotic checkpoint serine/threonine-protein kinase BUB1 beta (Bub1R)	3	3	4	3	Essential component of the mitotic checkpoint. Required for normal mitosis progression. The mitotic checkpoint delays anaphase until all chromosomes are properly attached to the mitotic spindle.	Induces interaction with PPP2R5A and regulates cell cycle progression. S670 is phosphorylated by CDK1 (CDC2), TTK.
Caldesmon	S789	Caldesmon	-2	-1	-1	-1	Actin- and myosin-binding protein implicated in the regulation of actomyosin interactions in smooth muscle and nonmuscle cells (could act as a bridge between myosin and actin filaments). Stimulates actin binding of tropomyosin which increases the stabilization of actin filament structure.	S789 is phosphorylated by CDK1 (CDC2), CDK6, ERK1 (MAPK3), ERK2 (MAPK1), p38a MAPK (MAPK14), PKCa (PRKCA).
CaMK1d	T180	Calcium/calmodulin-dependent protein-serine kinase 1 delta	6	6	10	9	Calcium/calmodulin-dependent protein kinase that operates in the calcium-triggered CaMKK-CaMK1 signaling cascade and, upon calcium influx, activates CREB-dependent gene transcription, regulates calcium-mediated granulocyte function and respiratory burst and promotes basal dendritic growth of hippocampal neurons. In neutrophil cells, required for cytokine-induced proliferative responses and activation of the respiratory burst.	Stimulates phosphotransferase activity. T180 is phosphorylated by CaMKK1.
CaMK4	Pan-specific	Calcium/calmodulin-dependent protein-serine kinase 4 (CaMPK4)	15	17	14	11	Calcium/calmodulin-dependent protein kinase that operates in the calcium-triggered CaMKK-CaMK4 signaling cascade and regulates, mainly by phosphorylation, the activity of several transcription activators, such as CREB1, MEF2D, JUN and RORA, which play pivotal roles in immune response, inflammation, and memory consolidation. Can activate the MAP kinases MAPK1/ERK2, MAPK8/JNK1 and MAPK14/p38 and stimulate transcription through the phosphorylation of ELK1 and ATF2.	NA
CaMK4	Pan-specific	Calcium/calmodulin-dependent protein-serine kinase 4 (CaMPK4)	9	5	10	9	see above	NA
Caveolin 1	Y14	Caveolin 1 (CAV1)	-1	-1	-1	-1	May act as a scaffolding protein within caveolar membranes. Interacts directly with G-protein alpha subunits and can functionally regulate their activity (By similarity). Involved in the costimulatory signal essential for T-cell receptor (TCR)-mediated T-cell activation. Its binding to DPP4 induces T-cell proliferation and NF-kappa-B activation in a T-cell receptor/CD3-dependent manner. Recruits CTNNB1 to caveolar membranes and may regulate CTNNB1-mediated signaling through the Wnt pathway. Negatively regulates TGFB1-mediated activation of SMAD2/3 by mediating the internalization of TGFBR1 from membrane rafts leading to its subsequent degradation.	Y14 is phosphorylated by Fyn, InsR, Src.

Caveolin 2	S36	Caveolin 2 (CAV2)	6	8	8	9	May act as a scaffolding protein within caveolar membranes. Interacts directly with G-protein alpha subunits and can functionally regulate their activity. Acts as an accessory protein in conjunction with CAV1 in targeting to lipid rafts and driving caveolae formation. The Ser-36 phosphorylated form has a role in modulating mitosis in endothelial cells. Positive regulator of cellular mitogenesis of the MAPK signaling pathway. Required for the insulin-stimulated nuclear translocation and activation of MAPK1 and STAT3, and the subsequent regulation of cell cycle progression.	S36 is phosphorylated by CK2a1 (CSNK2A1).
CDC7	T376	Cell division cycle 7-related protein kinase	6	5	2	5	Seems to phosphorylate critical substrates that regulate the G1/S phase transition and/or DNA replication. Can phosphorylates MCM2 and MCM3.	Originally suggested to be stimulatory based on loss of phosphotransferase activity with an alanine substitution. However, it is predicted to be inhibitory for phosphotransferase activity. T376 is phosphorylated by CDK1 (CDC2), CDK2.
CDK1	Pan-specific	Cyclin-dependent protein-serine kinase 1 (CDC2)	19	40	19	18	Plays a key role in the control of the eukaryotic cell cycle by modulating the centrosome cycle and mitotic onset; promotes G2-M transition, and regulates G1 progress and G1-S transition via association with multiple interphase cyclins. Required for entry into S-phase and mitosis.	NA
CDK1	Y19	Cyclin-dependent protein-serine kinase 1 (CDC2)	7	4	3	5	see above	Predicted to be inhibitory for phosphotransferase activity.
CDK1	Pan-specific	Cyclin-dependent protein-serine kinase 1 (CDC2)	3	2	6	8	see above	NA
CDK1/2	Pan-specific	Cyclin-dependent protein-serine kinase 1/2 (CDC2)	11	9	8	11	see above	NA
CDK1/2	T14+Y15	Cyclin-dependent protein-serine kinase 1/2 (CDC2)	5	4	2	8	see above	Inhibits phosphotransferase activity, and regulates cell cycle progression and apoptosis. Y15 is phosphorylated by CDK1 (CDC2), Chk1 (CHEK1), MYT1 (PKMYT1), Src, Wee1.

CDK2	Pan-specific	Cyclin-dependent protein-serine kinase 2	4	1	7	6	Serine/threonine-protein kinase involved in the control of the cell cycle; essential for meiosis, but dispensable for mitosis. Phosphorylates CTNNB1, USP37, p53/TP53, NPM1, CDK7, RB1, BRCA2, MYC, NPAT, EZH2. Triggers duplication of centrosomes and DNA. Acts at the G1-S transition to promote the E2F transcriptional program and the initiation of DNA synthesis, and modulates G2 progression; controls the timing of entry into mitosis/meiosis by controlling the activation of cyclin B/CDK1 by phosphorylation. Orchestrates the balance between cellular proliferation, cell death, and DNA repair.	NA
CDK2	Pan-specific	Cyclin-dependent protein-serine kinase 2	3	2	6	8	see above	NA
CDK4	Pan-specific	Cyclin-dependent protein-serine kinase 4	2	0	5	3	Ser/Thr-kinase component of cyclin D-CDK4 (DC) complexes that phosphorylate and inhibit members of the retinoblastoma (RB) protein family including RB1 and regulate the cell-cycle during G1/S transition. Phosphorylation of RB1 allows dissociation of the transcription factor E2F from the RB/E2F complexes and the subsequent transcription of E2F target genes which are responsible for the progression through the G1 phase.	NA
CDK5	Pan-specific	Cyclin-dependent protein-serine kinase 5	5	2	5	7	Proline-directed serine/threonine-protein kinase essential for neuronal cell cycle arrest and differentiation and may be involved in apoptotic cell death in neuronal diseases. Interacts with D1 and D3-type G1 cyclins. Phosphorylates SRC, NOS3, VIM/vimentin, p35/CDK5R1, MEF2A, SIPA1L1, SH3GLB1, PXN, PAK1, MCAM/MUC18, SEPT5, SYN1, DNM1, AMPH, SYNJ1, CDK16, RAC1, RHOA, CDC42, TONEBP/NFAT5, MAPT/TAU, MAP1B, histone H1, p53/TP53, HDAC1, APEX1, PTK2/FAK1, huntingtin/HTT, ATM, MAP2, NEFH and NEFM. Regulates several neuronal development and physiological processes.	NA
CDK6	Pan-specific	Cyclin-dependent protein-serine kinase 6	25	18	14	19	Serine/threonine-protein kinase involved in the control of the cell cycle and differentiation; promotes G1/S transition. Phosphorylates pRB/RB1 and NPM1. Interacts with D-type G1 cyclins during interphase at G1 to form a pRB/RB1 kinase and controls the entrance into the cell cycle. Involved in initiation and maintenance of cell cycle exit during cell differentiation; prevents cell proliferation in most cell types and negatively regulates differentiation. Required for thymocyte development. Promotes the production of newborn neurons and changes in the actin cytoskeleton including loss of stress fibers, and enhanced motility during cell differentiation.	NA
CDK6	Y13	Cyclin-dependent protein-serine kinase 6	4	2	2	4	see above	No data available.

CDK6	Y13	Cyclin-dependent protein-serine kinase 6	-1	-1	-1	-1	see above	No data available.
CDK7	Pan-specific	Cyclin-dependent protein-serine kinase 7	2	2	4	4	Serine/threonine kinase involved in cell cycle control and in RNA polymerase II-mediated RNA transcription. Required for both activation and complex formation of CDK1/cyclin-B during G2-M transition, and for activation of CDK2/cyclins during G1-S transition. CDK7 is the catalytic subunit of the CDK-activating kinase (CAK) complex. Upon DNA damage, triggers p53/TP53 activation (phosphorylation), allowing cell cycle arrest and recovery or apoptosis.	NA
CDK9	T186	Cyclin-dependent protein-serine kinase 9	3	3	2	4	Protein kinase involved in the regulation of transcription, cotranscriptional histone modification, and mRNA processing and export. . Member of the CDK9/cyclin-T complex (aka P-TEFb), which facilitates the transition from abortive to productive elongation by phosphorylating RNA polymerase II (RNAP II). Regulates cytokine inducible transcription networks by facilitating promoter recognition of target transcription factors (e.g. TNF-inducible RELA/p65 activation and IL-6-inducible STAT3 signaling). Promotes RNA synthesis for cell growth and differentiation. The CDK9/cyclin-K complex is required for genome integrity maintenance, by promoting cell cycle recovery from replication arrest and limiting ss-DNA in response to replication stress.	Stimulates phosphotransferase activity and regulates transcription and binding to EDG-1, RNA an TEAD1. T186 is phosphorylated by CDK9.
CHK1	Pan-specific	Checkpoint protein-serine kinase 1 (CHEK1)	4	1	4	7	Serine/threonine-protein kinase which is required for checkpoint-mediated cell cycle arrest and activation of DNA repair in response to the presence of DNA damage or unreplicated DNA. May also negatively regulate cell cycle progression during unperturbed cell cycles.	NA
CHK1	S345	Checkpoint protein-serine kinase 1 (CHEK1)	2	1	0	3	see above	Stimulates phosphotransferase activity. Phosphorylation regulates apoptosis, cell cycle progression, intracellular location, and protein degradation. It induces binding to 14-3-3-sigma, claspin, p21Cip1 and p53. S345 is phosphorylated by ATM, ATR, COT (MAP3K8).
CHK1	Pan-specific	Checkpoint protein-serine kinase 1 (CHEK1)	2	1	2	3	see above	NA

CHK2	Pan-specific	Checkpoint protein-serine kinase 2 (CHEK2)	4	1	5	7	Serine/threonine-protein kinase which is required for checkpoint-mediated cell cycle arrest, activation of DNA repair and apoptosis in response to the presence of DNA double-strand breaks. May also negatively regulate cell cycle progression during unperturbed cell cycles.	NA
CHK2	T68	Checkpoint protein-serine kinase 2 (CHEK2)	-1	-1	-1	-1	see above	Stimulates phosphotransferase activity, and induces interactions with Chk2 (homodimerization), MDC1, NBS1 and Plk1. T68 is phosphorylated by ATM, ATR, Chk2 (CHEK2), DNAPK (PRKDC), Plk1 (PLK), TTK, ZAK (MLTK).
CLK1	S337+T338	Dual specificity protein kinase CLK1	4	4	2	2	Dual specificity kinase acting on both serine/threonine and tyrosine-containing substrates. Phosphorylates serine- and arginine-rich (SR) proteins of the spliceosomal complex and may be a constituent of a network of regulatory mechanisms that enable SR proteins to control RNA splicing. Phosphorylates: SRSF1, SRSF3 and PTPN1.	Predicted to be stimulatory for phosphotransferase activity.
CLK1	S337	Dual specificity protein kinase CLK1	1	1	3	2	see above	Predicted to be stimulatory for phosphotransferase activity.
Cofilin 1	Pan-specific	Cofilin 1 (CFL1)	2	4	5	3	Binds to F-actin and exhibits pH-sensitive F-actin depolymerizing activity. Important for normal progress through mitosis and normal cytokinesis. Plays a role in the regulation of cell morphology and cytoskeletal organization. Required for the up-regulation of atypical chemokine receptor ACKR2 from endosomal compartment to cell membrane, increasing its efficiency in chemokine uptake and degradation.	NA
Connexin 43	S368	Gap junction alpha-1 protein (Cx43, GJA1)	4	4	5	4	Gap junction protein that acts as a regulator of bladder capacity and communication in the ventricles. A gap junction consists of a cluster of closely packed pairs of transmembrane channels, the connexons, through which materials of low MW diffuse from one cell to a neighboring cell. May play a critical role in the physiology of hearing by participating in the recycling of potassium to the cochlear endolymph. May play a role in cell growth inhibition.	S368 is phosphorylated by PKACa (PRKACA), PKCa (PRKCA), PKCe (PRKCE).
COT	Pan-specific	Osaka thyroid oncogene protein-serine kinase (TPL2) (MAP3K8)	7	9	6	7	Required for LPS-induced, TLR4-mediated activation of the MAPK/ERK pathway in macrophages, thus being critical for production of the proinflammatory cytokine production (i.e. TNF). Involved in the regulation of T-helper cell differentiation and IFNG expression. Involved in mediating host resistance to bacterial infection through negative regulation of type I interferon (IFN) production. Activates MAPK/ERK pathway in response to IL1 in an IRAK1-independent manner, leading to up-regulation of IL8 and CCL4. Transduces CD40 and TNFRSF1A signals that activate ERK in B-cells and macrophages. May also play a role in the transduction of TNF signals that activate JNK and NF-kappa-B in some cell types. Plays a role in the cell cycle.	NA

COT	Pan-specific	Osaka thyroid oncogene protein-serine kinase (TPL2) (MAP3K8)	8	13	13	11	see above	NA
Crystallin aB	S19	Crystallin alpha B (heat-shock 20 kDa like-protein) (HspB5; CRYA2; CRYAB)	21	25	16	12	Has chaperone-like activity, preventing aggregation of various proteins under a wide range of stress conditions.	Regulates conformation, intracellular location, protein degradation, and molecular association.
Crystallin aB	S45	Crystallin alpha B (heat-shock 20 kDa like-protein) (HspB5; CRYA2; CRYAB)	19	20	12	10	see above	S45 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1).
CSF1R	Y699	Macrophage colony-stimulating factor 1 receptor (Fms)	12	18	9	9	Tyrosine-protein kinase that acts as cell-surface receptor for CSF1 and IL34 and aids in the regulation of survival, proliferation and differentiation of hematopoietic precursor cells (i.e. macrophages and monocytes). Promotes the release of proinflammatory chemokines in response to IL34 and CSF1. Regulates osteoclast proliferation and differentiation, bone resorption, and bone and tooth development. Required for normal male and female fertility, and for normal development of milk ducts and acinar structures in the mammary gland during pregnancy.	Induces binding to PIK3CB and Grb2. Y699 is phosphorylated by CSF1R.
CSF1R	S807+Y809	Macrophage colony-stimulating factor 1 receptor (Fms)	5	5	8	5	see above	(807) Predicted to be stimulatory for phosphotransferase activity. (809) Induces interaction with and activation of Src family members, including Fyn, Yes1 and Src as well as binding to PLCG2. Y809 is phosphorylated by CSF1R.
CSK	Pan-specific	C-terminus of Src tyrosine kinase	16	11	39	30	Non-receptor tyrosine-protein kinase that plays an important role in the regulation of cell growth, differentiation, migration and immune response. Phosphorylates Src-family kinases (SFKs) including LCK, SRC, HCK, FYN, LYN or YES1.	NA
CSK	Pan-specific	C-terminus of Src tyrosine kinase	4	11	11	6	see above	NA

Cyclin B1	Pan-specific	Cyclin B1 (CCNB1)	3	2	6	7	Essential for the control of the cell cycle at the G2/M (mitosis) transition.	NA
Cyclin E1	Pan-specific	Cyclin E1 (CCNE1)	5	3	6	6	Essential for the control of the cell cycle at the G1/S (start) transition.	NA
DDR2	Y736	Discoidin domain-containing receptor 2 (Tyro10)	4	7	5	5	Tyrosine kinase that functions as cell surface receptor for fibrillar collagen and regulates cell differentiation, remodeling of the extracellular matrix, cell migration and cell proliferation. Required for normal bone development. Regulates osteoblast differentiation and chondrocyte maturation via a signaling pathway that involves MAPKs and leads to the activation of the transcription factor RUNX2. Regulates remodeling of the extracellular matrix by up-regulation of the collagenases MMP1, MMP2 and MMP13, and thereby facilitates cell migration and tumor cell invasion. Promotes fibroblast migration and proliferation, and thereby contributes to cutaneous wound healing.	Stimulates phosphotransferase activity. Y736 is phosphorylated by Src.
DYRK1A	Y321	Dual specificity tyrosine-phosphorylation-regulated kinase 1A	5	4	6	9	Dual-specificity kinase which possesses both serine/threonine and tyrosine kinase activities. May play a role in a signaling pathway regulating nuclear functions of cell proliferation. Modulates alternative splicing by phosphorylating the splice factor SRSF6. Has pro-survival function and negatively regulates the apoptotic process. Promotes cell survival upon genotoxic stress through phosphorylation of SIRT1. This in turn inhibits TP53 activity and apoptosis.	Stimulates phosphotransferase activity. Y321 is phosphorylated by DYRK1A.
DYRK2	Y382	Dual specificity tyrosine-phosphorylation-regulated kinase 2	5	6	5	5	Serine/threonine-protein kinase involved in the regulation of the mitotic cell cycle, cell proliferation, apoptosis, organization of the cytoskeleton and neurite outgrowth. Functions in part via its role in ubiquitin-dependent proteasomal protein degradation. Functions downstream of ATM and phosphorylates p53/TP53 at 'Ser-46', and thereby contributes to the induction of apoptosis in response to DNA damage.	Predicted to be stimulatory for phosphotransferase activity.
EGFR	Y1110	Epidermal growth factor receptor-tyrosine kinase (ErbB1)	-1	-1	-1	-1	Receptor tyrosine kinase binding ligands of the EGF family and activating several signaling cascades to convert extracellular cues into appropriate cellular responses. Known ligands: EGF, TGFA/TGF-alpha, amphiregulin, epigen/EPGN, BTC/betacellulin, epiregulin/EREG and HBEGF/heparin-binding EGF. Ligand binding triggers receptor homo- and/or heterodimerization and autophosphorylation on key cytoplasmic residues. The phosphorylated receptor recruits adapter proteins like GRB2 which activate downstream signaling cascades. Activates at least 4 major pathways including the RAS-RAF-MEK-ERK, PI3 kinase-AKT, PLCgamma-PKC and STATs modules. May also activate the NF-kappa-B signaling.	Stimulates phosphotransferase activity, induces binding of STAT3, and regulates transcription, protein conformation, intracellular location, receptor internalization, molecular association, and ubiquitination. Y1110 is phosphorylated by EGFR.



EGFR	T693	Epidermal growth factor receptor-tyrosine kinase (ErbB1)	3	5	14	3	see above	Inhibits phosphotransferase activity. T693 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1), p38a MAPK (MAPK14), PRKD1.
EGFR	Y869	Epidermal growth factor receptor-tyrosine kinase (ErbB1)	1	3	3	17	see above	Stimulates phosphotransferase activity and protein interaction. Y869 is phosphorylated by Src.
eIF4B	S422	Eukaryotic translation initiation factor 4B	6	10	12	11	Required for the binding of mRNA to ribosomes. Functions in close association with EIF4-F and EIF4-A. Binds near the 5'-terminal cap of mRNA in presence of EIF-4F and ATP. Promotes the ATPase activity and the ATP-dependent RNA unwinding activity of both EIF4-A and EIF4-F.	S422 is phosphorylated by p70S6K (RPS6KB1), RSK1 (RPS6KA2).
eIF4E	S209	Eukaryotic translation initiation factor 4 (mRNA cap binding protein)	18	31	25	21	Recognizes and binds the 7-methylguanosine-containing mRNA cap during an early step in the initiation of protein synthesis and facilitates ribosome binding by inducing the unwinding of the mRNAs secondary structures. Component of the CYFIP1-EIF4E-FMR1 complex which binds to the mRNA cap and mediates translational repression.	Increases the affinity of this protein for the 7-methylguanosine-containing mRNA cap, although another report describes inhibition of interaction with RNA. S209 is phosphorylated by MNK1 (MKNK1), PKCa (PRKCA).
ENO2	Y25	Gamma-enolase	4	9	6	5	Has neurotrophic and neuroprotective properties on a broad spectrum of central nervous system (CNS) neurons. Binds, in a calcium-dependent manner, to cultured neocortical neurons and promotes cell survival.	No data available.
EphA1	Pan-specific	Ephrin type-A receptor 1 protein-tyrosine kinase	7	8	12	10	Receptor tyrosine kinase which binds promiscuously membrane-bound ephrin-A family ligands residing on adjacent cells, leading to contact-dependent bidirectional signaling into neighboring cells.	NA
EphB2	Y780	Ephrin type-B receptor 2 protein-tyrosine kinase	3	2	3	3	Receptor tyrosine kinase which binds promiscuously transmembrane ephrin-B family ligands residing on adjacent cells, leading to contact-dependent bidirectional signaling into neighboring cells.	No data available.
EphB3	Y600	Ephrin type-B receptor 3 protein-tyrosine kinase	3	3	2	2	Receptor tyrosine kinase which binds promiscuously transmembrane ephrin-B family ligands residing on adjacent cells, leading to contact-dependent bidirectional signaling into neighboring cells.	No data available.

ErbB2 (HER2)	Y877	ErbB2 (Neu) receptor-tyrosine kinase	3	4	5	5	Protein tyrosine kinase that is part of several cell surface receptor complexes but needs a coreceptor for ligand binding. Essential component of a neuregulin-receptor complex. GP30 is a potential ligand. Regulates outgrowth and stabilization of peripheral microtubules (MTs). Upon ERBB2 activation, the MEMO1-RHOA-DIAPH1 signaling pathway elicits the phosphorylation and inhibition of GSK3B at cell membrane. This prevents the phosphorylation of APC and CLASP2, allowing its association with the cell membrane. Membrane-bound APC allows the localization of MACF1 to the cell membrane, which is required for microtubule capture and stabilization.	Stimulates phosphotransferase activity. Phosphorylation regulates cell growth.
ErbB3 (HER3)	Pan-specific	Tyrosine kinase-type cell surface receptor HER3	-1	-1	-1	-1	Tyrosine-protein kinase that plays an essential role as cell surface receptor for neuregulins. Binds to neuregulin-1 (NRG1) and is activated by it; ligand-binding increases phosphorylation on tyrosine residues and promotes its association with the p85 subunit of phosphatidylinositol 3-kinase.	NA
ErbB4 (HER4)	Y733	Receptor tyrosine-protein kinase erbB-4	1	5	3	3	Tyrosine-protein kinase that plays an essential role as cell surface receptor for neuregulins and EGF family members and regulates development of the heart, the central nervous system and the mammary gland, gene transcription, cell proliferation, differentiation, migration and apoptosis. Required for normal cardiac muscle differentiation during embryonic development, and for postnatal cardiomyocyte proliferation. Required for normal development of the embryonic central nervous system, especially for normal neural crest cell migration and normal axon guidance. Required for mammary gland differentiation, induction of milk proteins and lactation.	No data available.
ERK1 (MAPK3)	Pan-specific	Extracellular regulated protein-serine kinase 1 (p44 MAP kinase)	-1	-1	-1	-1	Serine/threonine kinase; major effector of the MAPK/ERK cascade. Depending on the cellular context, this cascade mediates diverse biological functions such as cell growth, adhesion, survival and differentiation through the regulation of transcription, translation, cytoskeletal rearrangements. Also plays a role in initiation and regulation of meiosis, mitosis, and postmitotic functions in differentiated cells by phosphorylating a number of transcription factors. Participates in a signaling cascade initiated by activated KIT and KITLG/SCF.	NA
ERK2 (MAPK1)	Pan-specific	Extracellular regulated protein-serine kinase 2 (p42 MAP kinase)	1	4	2	3	Serine/threonine kinase; major effector of the MAPK/ERK cascade. Depending on the cellular context, this cascade mediates diverse biological functions such as cell growth, adhesion, survival and differentiation through the regulation of transcription, translation, cytoskeletal rearrangements. Also plays a role in initiation and regulation of meiosis, mitosis, and postmitotic functions in differentiated cells by phosphorylating a number of transcription factors. Participates in a signaling cascade initiated by activated KIT and KITLG/SCF.	NA
ERK4 (MAPK4)	Pan-specific	Extracellular regulated protein-serine kinase 4	5	4	5	6	Atypical MAPK protein. Phosphorylates microtubule-associated protein 2 (MAP2) and MAPKAPK5. The precise role of the complex formed with MAPKAPK5 is still unclear, but the complex follows a complex set of phosphorylation events: upon interaction with atypical MAPKAPK5, ERK4/MAPK4 is phosphorylated and mediates phosphorylation and activation of MAPKAPK5, which phosphorylates ERK4/MAPK4. May promote entry in the cell cycle.	NA

ERK4 (MAPK4)	S186	Extracellular regulated protein-serine kinase 4	-1	-1	-1	-1	see above	Stimulates phosphotransferase activity. Phosphorylation induces interaction with MAPKAPK5. S186 is phosphorylated by PAK1, PAK2, PAK3.
FAK (PTK2)	Pan-specific	Focal adhesion protein-tyrosine kinase	4	4	7	9	Non-receptor tyrosine kinase that regulates cell migration, adhesion, spreading, reorganization of the actin cytoskeleton, formation and disassembly of focal adhesions and cell protrusions, cell cycle progression, cell proliferation and apoptosis. Required for early embryonic development, placenta development, embryonic angiogenesis, normal cardiomyocyte migration and proliferation, and normal heart development. Regulates axon growth and neuronal cell migration, axon branching and synapse formation; required for normal development of the nervous system. Plays a role in osteogenesis and differentiation of osteoblasts. Functions in signaling downstream of integrins, growth factor receptors, GPCRs, EPHA2, netrin receptors and LDL receptors. Forms multisubunit signaling complexes with SRC and SRC family members, leading to SRC activation and the creation of binding sites for scaffold proteins, effectors and substrates. Promotes activation of PI3K-AKT1 signaling, the MAPK pathway and RAC1. Promotes activation of GEFs and GAPs to regulate activity of Rho family GTPases. Recruits MDM2 to P53/TP53 in the nucleus, and phosphorylates ACTN1, ARHGEF7, GRB7, RET and WASL. Promotes phosphorylation of PXN, STAT1, BCAR1, GIT2, SHC1, BMX and PIK3R1.	NA
FES	Pan-specific	Fes/Fps protein-tyrosine kinase	8	7	5	7	Tyrosine-protein kinase that acts downstream of cell surface receptors such as FCER1 and KIT and plays a role in the regulation of the actin cytoskeleton, microtubule assembly, cell attachment and cell spreading. Aids in regulation of degranulation in mast cells, cell differentiation and neurite outgrowth in response to NGF signaling, as well as cell scattering and cell migration in response to HGF-induced activation of EZR. Phosphorylates BCR and down-regulates BCR kinase activity. Phosphorylates HCLS1/HS1, PECAM1, STAT3 and TRIM28.	NA
FES	Y713	Fes/Fps protein-tyrosine kinase	10	8	12	12	see above	Stimulates phosphotransferase activity, and regulates cell differentiation, cell growth and molecular association, including inducing interaction with Fes. Y713 is phosphorylated by Fes.

FGFR2	Pan-specific	Fibroblast growth factor receptor-tyrosine kinase 2 (BEK)	-1	-1	-1	-1	Tyrosine-protein kinase that acts as cell-surface receptor for fibroblast growth factors and plays an essential role in the regulation of cell proliferation, differentiation, migration and apoptosis, and in the regulation of embryonic development. Required for normal embryonic patterning, trophoblast function, limb bud development, lung morphogenesis, osteogenesis and skin development. Plays an essential role in the regulation of osteoblast differentiation, proliferation and apoptosis, and is required for normal skeleton development. Promotes cell proliferation in keratinocytes and immature osteoblasts, but promotes apoptosis in differentiated osteoblasts. Phosphorylates PLCG1, FRS2 and PAK4, leading to PI and DAG signaling, recruitment of GRB2, GAB1, PIK3R1 and SOS1, and activation of RAS, ERK1/2 and AKT1 signaling.	NA
FGFR2	Y656+Y657	Fibroblast growth factor receptor-tyrosine kinase 2 (BEK)	3	3	3	3	see above	Predicted to be stimulatory for phosphotransferase activity.
FGR	Y412	Gardner-Rasheed feline sarcoma viral (v-fgr) oncogene	4	4	5	5	Non-receptor tyrosine-protein kinase that transmits signals from cell surface receptors devoid of kinase activity and contributes to the regulation of immune responses, including neutrophil, monocyte, macrophage and mast cell functions, cytoskeleton remodeling in response to extracellular stimuli, phagocytosis, cell adhesion and migration. Promotes mast cell degranulation, release of inflammatory cytokines and IgE-mediated anaphylaxis. Acts downstream of Fc-receptors, such as MS4A2/FCER1B, FCGR2A and/or FCGR2B as well as ITGB1 and ITGB2 to regulate actin cytoskeleton reorganization, cell spreading and adhesion. Negative regulator of ITGB2 signaling, phagocytosis and SYK activity in monocytes. Required for normal ITGB1 and ITGB2 signaling, normal cell spreading and adhesion in neutrophils and macrophages. Positive regulator of cell migration and regulates cytoskeleton reorganization via RAC1 activation. Phosphorylates SYK to promote AKT1 and MAPK signaling. Phosphorylates PLD2 in antigen-stimulated mast cells, leading to PLD2 activation. Promotes activation of PIK3R1. Phosphorylates FASLG, ABL1 and HCLS1. Promotes phosphorylation of CBL, CTTN, PIK3R1, PTK2/FAK1, PTK2B/PYK2 and VAV2.	Predicted to be stimulatory for phosphotransferase activity. Y412 is phosphorylated by Fgr.
FKHR	S256	Forkhead box protein O1 (FOXO1A)	-1	-1	-1	-1	Transcription factor that is the main target of insulin signaling and regulates metabolic homeostasis in response to oxidative stress. Binds to the insulin response element (IRE). Important regulator of cell death acting downstream of CDK1, PKB/AKT1 and SKT4/MST1.	Inhibits transcription by preventing nuclear import, regulates protein degradation and molecular association; phosphorylation induces interaction with 14-3-3 beta, SKP2, and inhibits interaction with DNA. S256 is phosphorylated by Akt1 (PKBa), Akt3 (PKBg).

FOS	Pan-specific	Fos-c FBJ murine osteosarcoma oncoprotein-related transcription factor	0	1	1	3	Nuclear phosphoprotein which forms a complex with the JUN/AP-1 transcription factor. On TGF-beta activation, forms a multimeric SMAD3/SMAD4/JUN/FOS complex at the AP1/SMAD-binding site to regulate TGF-beta signaling. Has an important role in signal transduction, cell proliferation and differentiation. Aids in regulation of cells involved in skeletal development, and, in growing cells, activates phospholipid synthesis, possibly via CDS1 and PI4K2A.	NA
FRS2	Y348	Fibroblast growth factor receptor substrate 2	4	5	5	4	Adapter protein that links activated FGR and NGF receptors to downstream pathways. Aids in activation of MAPKs and phosphorylation of PIK3R1, the regulatory subunit of PI3K, in response to ligand-mediated activation of FGFR1. Modulates signaling via SHC1 by competing for a common binding site on NTRK1.	No data available.
FYN	Y531	Fyn proto-oncogene-encoded protein-tyrosine kinase	7	9	7	8	Non-receptor tyrosine kinase that plays a role in many biological processes including regulation of cell growth and survival, cell adhesion, integrin-mediated signaling, cytoskeletal remodeling, cell motility, immune response and axon guidance. Following activation by PKA, FYN associates with PTK2/FAK1, allowing PTK2/FAK1 phosphorylation, activation and targeting to focal adhesions. Involved in the regulation of cell adhesion and motility through phosphorylation of beta and delta-catenin (CTNNB1, CTNND1). Regulates cytoskeletal remodeling by phosphorylating WAS, MAP2, and MAPT. Promotes cell survival by phosphorylating AGAP2/PIKE-A and preventing its apoptotic cleavage.	Inhibits phosphotransferase activity, regulates cell growth, and alters intracellular location. Y531 is phosphorylated by CSK.
FYN	Pan-specific	Fyn proto-oncogene-encoded protein-tyrosine kinase	3	2	6	8	see above	NA
GATA1	S142	Erythroid transcription factor	-1	-1	-1	-1	Transcriptional activator or repressor which probably serves as a general switch factor for erythroid development.	No data available.
GCK	Pan-specific	Germinal centre protein-serine kinase	2	2	3	5	Serine/threonine kinase; acts as a MAP4K and is an upstream activator of the SAP/JNK signaling pathway and, to a lesser extent, the p38 MAPKs pathway. Required for the efficient activation of JNKs by TRAF6-dependent stimuli, including PAMPs such as polyinosine-polycytidine (poly(IC)), lipopolysaccharides (LPS), lipid A, peptidoglycan (PGN), or bacterial flagellin. IL-1 and engagement of CD40 also stimulate MAP4K2-mediated JNKs activation. Enhances activation of MAP3K1, MAP3K10/MLK2 and MAP3K11/MLK3. May play a role in the regulation of vesicle targeting/fusion.	NA
GRK2 (BARK1)	S670	G protein-coupled receptor-serine kinase 2 (ADRBK1)	20	30	19	19	Specifically phosphorylates the agonist-occupied form of the beta-adrenergic and closely related receptors, probably inducing a desensitization of them. Key regulator of LPAR1 signaling. Competes with RALA for binding to LPAR1 thus affecting the signaling properties of the receptor. Desensitizes LPAR1 and LPAR2 in a phosphorylation-independent manner.	Inhibits phosphotransferase activity. Phosphorylation regulates cell cycle progression, cell growth, protein degradation, and molecular association.

								S670 is phosphorylated by ERK1 (MAPK3).
GRK2 (BARK1)	Pan-specific	G protein-coupled receptor-serine kinase 2 (ADRBK1)	1	2	1	3	see above	NA
GSK3a	S278+Y279	Glycogen synthase-serine kinase 3 alpha	-1	-1	-1	-1	Constitutively active protein kinase that acts as a negative regulator in the hormonal control of glucose homeostasis, Wnt signaling and regulation of transcription factors and microtubules, by phosphorylating and inactivating glycogen synthase, CTNNB1/beta-catenin, APC and AXIN1. May mediate the development of insulin resistance by regulating activation of transcription factors. In Wnt signaling, regulates the level and transcriptional activity of nuclear CTNNB1/beta-catenin. Facilitates amyloid precursor protein (APP) processing and the generation of APP-derived amyloid plaques found in Alzheimer disease. May be involved in the regulation of replication in pancreatic beta-cells. Necessary for the establishment of neuronal polarity and axon outgrowth. Through phosphorylation of the anti-apoptotic protein MCL1, may control cell apoptosis in response to growth factors deprivation.	Stimulates phosphotransferase activity. Stimulates phosphotransferase activity, promotes nuclear localization and regulates apoptosis. Y279 is phosphorylated by GSK3a, MEK1 (MAP2K1), MEK2 (MAP2K2).
GSK3b	Pan-specific	Glycogen synthase-serine kinase 3 beta	6	4	6	5	Constitutively active protein kinase that acts as a negative regulator in the hormonal control of glucose homeostasis, Wnt signaling and regulation of transcription factors and microtubules, by phosphorylating and inactivating glycogen synthase (GYS1 or GYS2), EIF2B, CTNNB1/beta-catenin, APC, AXIN1, DPYSL2/CRMP2, JUN, NFATC1/NFATC, MAPT/TAU and MACF1.	NA
GSK3b	Pan-specific	Glycogen synthase-serine kinase 3 beta	6	6	11	8	see above	NA
GTF2F1	S385+T389	General transcription factor IIF subunit 1	6	3	8	6	TFIIF is a general transcription initiation factor that binds to RNA polymerase II and helps to recruit it to the initiation complex in collaboration with TFIIB. It promotes transcription elongation.	No data available.
HGK	T187	Mitogen-activated protein kinase kinase kinase 4 (ZC1, MAP4K4)	4	3	6	5	Serine/threonine kinase that may play a role in the response to environmental stress and cytokines such as TNF-alpha. Appears to act upstream of the JUN N-terminal pathway. Phosphorylates SMAD1.	Predicted to be stimulatory for phosphotransferase activity.

Histone H3	S10	Histone H3.3 (H3F3A)	5	5	6	6	Variant histone H3 which replaces conventional H3 in a wide range of nucleosomes in active genes. Constitutes the predominant form of histone H3 in non-dividing cells and is incorporated into chromatin independently of DNA synthesis. Deposited at sites of nucleosomal displacement throughout transcribed genes, suggesting that it represents an epigenetic imprint of transcriptionally active chromatin. Nucleosomes wrap and compact DNA into chromatin, limiting DNA accessibility to the cellular machineries which require DNA as a template, causing histones to play a central role in transcription regulation, DNA repair, DNA replication and chromosomal stability.	No data available - <b>not a site?</b>
Histone H3	S28	Histone H3.3 (H3F3A)	3	3	3	1	see above	Phosphorylation may contribute to increased mitotic chromosome condensation.
HSP27	S78	Heat shock 27 kDa protein beta 1 (HspB1)	3	6	4	3	Small heat shock protein which functions as a molecular chaperone probably maintaining denatured proteins in a folding-competent state. Plays a role in stress resistance and actin organization. Through its molecular chaperone activity may regulate numerous biological processes including the phosphorylation and the axonal transport of neurofilament proteins.	Regulates apoptosis, cell cycle progression, cell growth, cytoskeletal reorganization, transcription, alters conformation, alters intracellular location, enzymatic activation, phosphorylation, molecular association, sumoylation, ubiquitination, inhibit interaction with HSF1, TRAF6, induces interaction with TPM1. S78 is phosphorylated by MAPKAPK2, MAPKAPK5, p70S6K (RPS6KB1), PKACa (PRKACA), PKG1 (PRKG1), RSK2 (RPS6KA3).
HSP90a/b	Pan-specific	Heat shock 90 kDa protein alpha/beta	4	3	7	9	Molecular chaperone that promotes the maturation, structural maintenance and proper regulation of specific target proteins involved in cell cycle control and signal transduction. Binds bacterial LPS and mediates LPS-induced inflammatory response, including TNF secretion by monocytes.	NA
Huntingtin	S421	Huntington's disease protein	6	4	10	11	May play a role in microtubule-mediated transport or vesicle function.	No data available - <b>not a site?</b>



IGF1R	Y1165/Y1166	Insulin-like growth factor 1 receptor protein-tyrosine kinase	-2	-1	-1	-1	Receptor tyrosine kinase which mediates the pleiotropic actions of insulin. Binding of insulin leads to phosphorylation of several intracellular substrates, including, insulin receptor substrates (IRS1, 2, 3, 4), SHC, GAB1, CBL and other signaling intermediates. Each of these phosphorylated proteins serve as docking proteins for other signaling proteins that contain Src-homology-2 domains (SH2 domain) that specifically recognize different phosphotyrosine residues, including the p85 regulatory subunit of PI3K and SHP2. Phosphorylation of IRSs proteins lead to the activation of the PI3K-AKT/PKB pathway, which is responsible for most of the metabolic actions of insulin, and the Ras-MAPK pathway, which regulates expression of some genes and cooperates with the PI3K pathway to control cell growth and differentiation.	(1165) Stimulates phosphotransferase activity. Phosphorylation regulates conformation. Phosphorylated by Src. (1166) Stimulates phosphotransferase activity. Phosphorylation regulates cell growth and protein conformation. Y1166 is phosphorylated by IGF1R, Src
IR/IGF1R	Y1189/Y1190	Insulin receptor / Insulin-like growth factor 1 receptor (INSR)	12	23	31	18	see above	Stimulates phosphotransferase activity, receptor internalization and induces interaction with SOCS1, IRS2 and PTP1B. Y1189 and Y1190 are phosphorylated by InsR.
InsR (IR)	Y999	Insulin receptor beta chain	-1	-1	-1	-1	see above	Stimulates phosphotransferase activity and induces interaction with IRS1 and Shc1 (via their PTB/PID domains), STAT5B and SOCS3. Phosphorylation regulates cell cycle progression, receptor internalization, and molecular association. Y999 is phosphorylated by InsR.
IkBα	Pan-specific	Inhibitor of NF-kappa-B alpha (MAD3)	1	2	2	3	Inhibits the activity of dimeric NF-kappa-B/REL complexes by trapping REL dimers in the cytoplasm through masking of their nuclear localization signals. On cellular stimulation by immune and proinflammatory responses, becomes phosphorylated promoting ubiquitination and degradation, enabling the dimeric RELα to translocate to the nucleus and activate transcription.	NA
IkBβ	Pan-specific	Inhibitor of NF-kappa-B beta (thyroid receptor interacting protein 9)	1	1	3	4	see above	NA
IKKα	Pan-specific	Inhibitor of NF-kappa-B protein-serine kinase alpha (CHUK, IKBKA)	3	4	10	9	Serine kinase that plays an essential role in the NF-kappa-B signaling pathway which is activated by multiple stimuli such as inflammatory cytokines, bacterial or viral products, DNA damages or other cellular stresses. Acts as part of the canonical IKK complex in the conventional pathway of NF-kappa-B activation and phosphorylates inhibitors of NF-kappa-B on serine residues.	NA

IKKa	Pan-specific	Inhibitor of NF-kappa-B protein-serine kinase alpha (CHUK, IKBKA)	2	4	4	6	see above	NA
IKKa	Pan-specific	Inhibitor of NF-kappa-B protein-serine kinase alpha (CHUK, IKBKA)	2	0	4	5	see above	NA
ILK1	Pan-specific	Integrin-linked protein-serine kinase 1	4	3	3	5	Receptor-proximal protein kinase regulating integrin-mediated signal transduction. May act as a mediator of inside-out integrin signaling. Focal adhesion protein part of the complex ILK-PINCH. This complex is considered to be one of the convergence points of integrin-and growth factor-signaling pathway. Could be implicated in mediating cell architecture, adhesion to integrin substrates and anchorage-dependent growth in epithelial cells. Phosphorylates beta-1 and beta-3 integrin subunit on serine and threonine residues, but also AKT1 and GSK3B.	NA
Integrin a4	S1021	Integrin alpha 4 (VLA4, ITGA4)	4	8	8	4	Integrins alpha-4/beta-1 (VLA-4) and alpha-4/beta-7 are receptors for fibronectin. They recognize one or more domains within the alternatively spliced CS-1 and CS-5 regions of fibronectin. They are also receptors for VCAM1. Integrin alpha-4/beta-1 recognizes the sequence Q-I-D-S in VCAM1. Integrin alpha-4/beta-7 is also a receptor for MADCAM1.	No data available.
IRAK1	Pan-specific	Interleukin 1 receptor-associated kinase 1 (Pelle-like protein kinase)	6	3	10	14	Serine/threonine-protein kinase that plays a critical role in initiating innate immune response against foreign pathogens. Involved in Toll-like receptor (TLR) and IL-1R signaling pathways.	NA
JAK1	Y1034	Janus protein-tyrosine kinase 1	-2	-1	-1	-1	Tyrosine kinase of the non-receptor type, involved in the IFN-alpha/beta/gamma signal pathway. Involved in IL-2 receptor signaling.	Stimulates phosphotransferase activity.
JAK2	Y1007+Y1008	Janus protein-tyrosine kinase 2	9	13	10	7	Non-receptor tyrosine kinase involved in various processes such as cell growth, development, differentiation or histone modifications. Mediates essential signaling events in both innate and adaptive immunity. In the cytoplasm, plays a pivotal role in signal transduction via its association with type I receptors such as growth hormone (GHR), prolactin (PRLR), leptin (LEPR), erythropoietin (EPOR), thrombopoietin (THPO); or type II receptors including IFN-alpha, IFN-beta, IFN-gamma and multiple interleukins.	Stimulates phosphotransferase activity. Y1007 is phosphorylated by JAK2, PYK2 (PTK2B). Y1008 is phosphorylated by Abi1, JAK2, PYK2 (PTK2B).
JAK2	Pan-specific	Janus protein-tyrosine kinase 2	3	6	4	6	see above	NA

JAK3	Pan-specific	Janus protein-tyrosine kinase 3	8	8	13	13	Non-receptor tyrosine kinase involved in various processes such as cell growth, development, or differentiation. Mediates essential signaling events in both innate and adaptive immunity and plays a crucial role in hematopoiesis during T-cells development. In the cytoplasm, plays a pivotal role in signal transduction via its association with type I receptors sharing the common subunit gamma such as IL2R, IL4R, IL7R, IL9R, IL15R and IL21R.	NA
JAK3	Pan-specific	Janus protein-tyrosine kinase 3	7	9	13	11	see above	NA
JNK 1/2/3	T183+Y185	Jun N-terminus protein-serine kinase (stress-activated protein kinase (SAPK)) 1 (SAPKg, MAPK8)	2	5	3	3	Serine/threonine-protein kinase involved in various processes such as cell proliferation, differentiation, migration, transformation and programmed cell death. Extracellular stimuli such as proinflammatory cytokines or physical stress stimulate the stress-activated protein kinase/c-Jun N-terminal kinase (SAP/JNK) signaling pathway. Activated by MAP2K4/MKK4 and MAP2K7/MKK7. Phosphorylates a number of transcription factors, primarily components of AP-1 such as JUN, JDP2 and ATF2.	Stimulates phosphotransferase activity. Phosphorylation regulates apoptosis, cell adhesion and transcription. T183 and Y185 are phosphorylated by MEKK1 (MAP3K1), MKK4 (MAP2K4, MEK4), MKK7 (MAP2K7, MEK7).
JNK1	Y185	Jun N-terminus protein-serine kinase (stress-activated protein kinase (SAPK)) 1 (SAPKg, MAPK8)	3	5	6	6	see above	Stimulates phosphotransferase activity. Phosphorylation regulates apoptosis, cell adhesion and transcription. T183 and Y185 are phosphorylated by MEKK1 (MAP3K1), MKK4 (MAP2K4, MEK4), MKK7 (MAP2K7, MEK7).
JNK3	Pan-specific	Jun N-terminus protein-serine kinase (stress-activated protein kinase (SAPKb)) 3 (SAPKb, MAPK10)	16	15	15	21	Serine/threonine-protein kinase involved in various processes such as neuronal proliferation, differentiation, migration and programmed cell death. Extracellular stimuli such as proinflammatory cytokines or physical stress stimulate the stress-activated protein kinase/c-Jun N-terminal kinase (SAP/JNK) signaling pathway. In this cascade, MKK4 and MKK7 activate JNK3. In turn, JNK3 phosphorylates a number of transcription factors, primarily components of AP-1 such as JUN and ATF2 and thus regulates AP-1 transcriptional activity.	NA
JUN	S73	Jun proto-oncogene-encoded AP1 transcription factor (c-Jun)	17	20	16	12	Transcription factor that recognizes and binds to the enhancer heptamer motif 5'-TGA[CG]TCA-3'. Promotes activity of NR5A1 when phosphorylated by HIPK3 leading to increased steroidogenic gene expression upon cAMP signaling pathway stimulation.	Stimulates transcriptional activity. S73 is phosphorylated by CDK1 (CDC2), CDK3, CK2a1 (CSNK2A1), ERK1 (MAPK3), ERK2 (MAPK1), JNK1 (MAPK8), JNK2 (MAPK9), JNK3

									(MAPK10), PIK3 (CNK), VRK1.
JUN	S243	Jun proto-oncogene-encoded AP1 transcription factor (c-Jun)	-2	-1	-1	-1	see above		Inhibits transcriptional activity - reducing binding of DNA. S243 is phosphorylated by CDK1 (CDC2), CK2a1 (CSNK2A1), DYRK2, ERK1 (MAPK3), ERK2 (MAPK1), GSK3b.
JUN	Y170	Jun proto-oncogene-encoded AP1 transcription factor (c-Jun)	-1	-1	-1	-1	see above		Y170 is phosphorylated by Abl1.
KHS1	Y31	Kinase homologous to SPS1/STE20 (MAP kinase kinase kinase protein-serine kinase 5 (MEKKK5))	4	7	8	8	May play a role in the response to environmental stress. Appears to act upstream of the JUN N-terminal pathway.		Predicted to be inhibitory for phosphotransferase activity.
KIT	Y730	'Mast/stem cell growth factor receptor Kit	22	32	26	20	Tyrosine-protein kinase that acts as cell-surface receptor for the cytokine KITLG/SCF, leading to regulation of cell survival and proliferation, hematopoiesis, stem cell maintenance, gametogenesis, mast cell development, migration and function, and in melanogenesis. Phosphorylates PIK3R1, PLCG1, SH2B2/APS and CBL. Activates the AKT1 signaling pathway by phosphorylation of PIK3R1, the regulatory subunit of PI3K. Activated KIT also signals via GRB2 and activation of RAS, RAF1 and ERK1/2 MAPKs. Promotes activation of STAT family members STAT1, STAT3, STAT5A and STAT5B.		No data available.
KIT	Y703	'Mast/stem cell growth factor receptor Kit	7	13	8	6	see above		Induces interaction with Grb2. Y703 is phosphorylated by Kit.
KIT	Y936	'Mast/stem cell growth factor receptor Kit	7	43	110	176	see above		Stimulates phosphotransferase activity and induces interaction with Grb2 and Grb7. Phosphorylation also induces receptor internalization and protein degradation. Y936 is phosphorylated by Kit.

KSR	Pan-specific	Protein-serine kinase suppressor of Ras 1	7	11	13	14	Scaffolding protein that is part of a multiprotein signaling complex. Promotes phosphorylation of Raf family members and activation of downstream MAP kinases. Promotes activation of MAPK1 and/or MAPK3, both in response to EGF and to cAMP.	NA
LCK	S158	Lymphocyte-specific protein-tyrosine kinase	28	42	32	25	Non-receptor tyrosine kinase that plays an essential role in the selection and maturation of developing T-cells in the thymus and in the function of mature T-cells. Plays a key role in T-cell antigen receptor (TCR)-linked signal transduction pathways.	No data available.
LCK	Y192	Lymphocyte-specific protein-tyrosine kinase	15	25	17	12	see above	Inhibits phosphotransferase activity. Phosphorylation regulates molecular association.
LCK	Y394	Lymphocyte-specific protein-tyrosine kinase	9	17	19	12	see above	Stimulates phosphotransferase activity. Phosphorylation regulates cell growth and molecular association. Y394 is phosphorylated by Lck.
LCK	Pan-specific	Lymphocyte-specific protein-tyrosine kinase	4	3	10	10	see above	NA
LCK	Y505	Lymphocyte-specific protein-tyrosine kinase	3	4	6	5	see above	Inhibits phosphotransferase activity, and regulates cell growth and molecular association, including inducing interaction with Lck. Y505 is phosphorylated by CSK, Lck.
LTK	Y672	Leukocyte tyrosine kinase receptor	2	4	4	4	Receptor with a tyrosine kinase activity. The exact function is not known but may promote cell growth and survival. Signaling appears to involve the PI3 kinase pathway.	No data available.
LYN	Pan-specific	Yes-related protein-tyrosine kinase	4	4	10	10	Non-receptor tyrosine kinase that transmits signals from cell surface receptors and plays an important role in the regulation of innate and adaptive immune responses, hematopoiesis, responses to growth factors and cytokines, integrin signaling, but also responses to DNA damage and genotoxic agents. Functions primarily as negative regulator, but also as an activator in certain circumstances. Required for both the initiation and termination of the B-cell response, and aids in regulation of B-cell differentiation, proliferation, survival and apoptosis. It is also important for immune self-tolerance.	NA

LYN	Y508	Yes-related protein-tyrosine kinase	3	4	3	5	see above	Inhibits phosphotransferase activity. Y508 is phosphorylated by CSK, CTK (MATK).
MAK	T157	Male germ cell-associated protein-serine kinase	2	4	3	2	Essential for the regulation of ciliary length and required for the long-term survival of photoreceptors. Phosphorylates FZR1 in a cell cycle-dependent manner. Plays a role in the transcriptional coactivation of AR.	Stimulates phosphotransferase activity.
MAPKAPK2	Pan-specific	Mitogen-activated protein kinase-activated protein kinase 2	3	3	8	9	Stress-activated serine/threonine-protein kinase involved in cytokine production, endocytosis, reorganization of the cytoskeleton, cell migration, cell cycle control, chromatin remodeling, DNA damage response and transcriptional regulation. Following stress, it is phosphorylated and activated by MAPK p38-alpha/MAPK14, leading to phosphorylation of substrates.	NA
MARK3	T507	MAP/microtubule affinity-regulating protein-serine kinase 3	4	4	4	3	Involved in the specific phosphorylation of microtubule-associated proteins for tau, MAP2 and MAP4. Phosphorylates CDC25C on 'Ser-216'. Regulates localization and activity of some histone deacetylases by mediating phosphorylation of HDAC7, promoting subsequent interaction between HDAC7 and 14-3-3 and export from the nucleus. Negatively regulates the Hippo signaling pathway and antagonizes the phosphorylation of LATS1. Cooperates with DLG5 to inhibit the kinase activity of STK3/MST2 toward LATS1.	No data available - <a href="#">not a site?</a>
MEK1	S298	MAPK/ERK protein-serine kinase 1 (MKK1, MAP2K1)	16	17	11	6	Dual specificity kinase which acts as an essential component of the MAPK signal transduction pathway. Binding of extracellular ligands such as growth factors, cytokines and hormones to their cell-surface receptors activates RAS and initiates RAF1 activation. RAF1 activates the MAP2K1/MEK1 and MAP2K2/MEK2. Both MAP2K1/MEK1 and MAP2K2/MEK2 phosphorylate and activate MAPK3/ERK1 and MAPK1/ERK2. Depending on the cellular context, this pathway mediates diverse biological functions such as cell growth, adhesion, survival and differentiation, predominantly through the regulation of transcription, metabolism and cytoskeletal rearrangements.	Stimulates phosphotransferase activity. Phosphorylation regulates cell growth and molecular association. MAPK1/ERK2 phosphorylation of Thr-292 in response to cellular adhesion leads to inhibition of S298 phosphorylation by PAK. S298 is phosphorylated by MEK1 (MAP2K1), PAK1, PAK2, PAK3.
MEK1	T386	MAPK/ERK protein-serine kinase 1 (MKK1, MAP2K1)	14	12	9	5	see above	Phosphorylation induces interaction with ERK2 and regulates intracellular location. T386 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1).

MEK1	T292	MAPK/ERK protein-serine kinase 1 (MKK1, MAP2K1)	10	11	7	4	see above	Stimulates phosphotransferase activity. Phosphorylation regulates cell growth and molecular association. MAPK1/ERK2 phosphorylation of Thr-292 in response to cellular adhesion leads to inhibition of S298 phosphorylation by PAK. T292 is phosphorylated by CDK1 (CDC2), ERK1 (MAPK3), ERK2 (MAPK1), MEKK1 (MAP3K1).
MEK1	T386	MAPK/ERK protein-serine kinase 1 (MKK1, MAP2K1)	6	5	5	3	see above	Phosphorylation induces interaction with ERK2 and regulates intracellular location. T386 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1).
MEK1	Pan-specific	MAPK/ERK protein-serine kinase 1 (MKK1, MAP2K1)	2	2	3	4	see above	NA
MEK1/2	S218+S222	MAPK/ERK protein-serine kinase 1/2 (MKK1/2, MAP2K1/2)	-1	-1	-1	-1	see above	Stimulates phosphotransferase activity and regulates cell cycle progression and cell growth. S218 is phosphorylated by B-Raf, COT (MAP3K8), MEKK1 (MAP3K1), Mos, Raf1, RafA. S222 is phosphorylated by B-Raf, COT (MAP3K8), MEKK1 (MAP3K1), Mos, PDK1 (PDPK1), Raf1, RafA.
MEK2	T394	MAPK/ERK protein-serine kinase 2 (MKK2, MAP2K2) (mouse)	23	31	19	15	Upstream component of the MAPK pathway. Activates the ERK1 and ERK2 MAPKs.	No data available.
MEK2	T394	MAPK/ERK protein-serine kinase 2 (MKK2, MAP2K2)	4	6	5	4	see above	No data available.



MEK2	Pan-specific	MAPK/ERK protein-serine kinase 2 (MKK2, MAP2K2)	3	3	3	5	see above	NA
MEK3	Pan-specific	MAPK/ERK protein-serine kinase 3 beta isoform (MKK3 beta, MAP2K3)	4	2	6	7	Dual specificity kinase. Is activated by cytokines and environmental stress in vivo. Phosphorylates and activates the MAPK p38. Part of a signaling cascade that begins with the activation of the adrenergic receptor ADRA1B and leads to the activation of MAPK14.	NA
MEK3/6	S218/S207	MAPK/ERK protein-serine kinase 3 beta isoform (MKK3 beta, MAP2K3)	-1	-1	-2	-1	see above	Stimulates phosphotransferase activity and regulates transcription. S218 is phosphorylated by ASK1 (MAP3K5), COT (MAP3K8), MEKK3 (MAP3K3), MKK3 (MAP2K3, MEK3), MLK3 (MAP3K11).
MEK4	Pan-specific	MAPK/ERK protein-serine kinase 4 (MKK4, MAP2K4)	5	2	6	6	Dual specificity protein kinase which acts as an essential component of the MAPK signal transduction pathway. With MAP2K7/MKK7, is one of the only known kinases to directly activate the MAPK8/JNK1, MAPK9/JNK2 and MAPK10/JNK3.	NA
MEK5	Pan-specific	MAPK/ERK protein-serine kinase 5 (MKK5, MAP2K5)	3	3	9	8	see above	NA
MEKK1	Pan-specific	MAPK/ERK kinase kinase 1 (MAP3K1)	3	1	4	3	Upstream member of the MAPK family that activates the ERK and JNK kinase pathways by phosphorylation of MAP2K1 and MAP2K4. Activates CHUK and IKBKB, the central protein kinases of the NF-kappa-B pathway.	NA
MEKK2	Pan-specific	MAPK/ERK kinase kinase 2 (MAP3K2)	3	3	7	6	Upstream member of the MAPK family which regulates the JNK and ERK5 pathways by phosphorylating and activating MAP2K5 and MAP2K7. Plays a role in caveolae kiss-and-run dynamics.	NA
MERTK	Y749	Tyrosine-protein kinase Mer (MER)	3	4	5	4	Receptor tyrosine kinase that transduces signals from the ECM into the cytoplasm by binding to several ligands including LGALS3, TUB, TULP1 or GAS6. Regulates many physiological processes including cell survival, migration, differentiation, and phagocytosis of apoptotic cells (efferocytosis). Ligand binding at the cell surface induces autophosphorylation of MERTK, providing docking sites for downstream signaling molecules. Following activation by ligand, interacts with GRB2 or PLCG2 and induces phosphorylation of MAPK1, MAPK2, FAK/PTK2 or RAC1.	Stimulates phosphotransferase activity. Y749 is phosphorylated by MER (MERTK).

MKK4	Pan-specific	MAPK/ERK protein-serine kinase 4 (MEK4, MAP2K4)	11	6	5	5	Dual specificity MAPK family kinase. With MAP2K7/MKK7, it is the one of the only known kinases to directly activate MAPK8/JNK1, MAPK9/JNK2 and MAPK10/JNK3.	NA
MKK4	S257	MAPK/ERK protein-serine kinase 4 (MEK4, MAP2K4)	6	5	5	6	see above	Stimulates phosphotransferase activity. S257 is phosphorylated by ASK1 (MAP3K5), MEKK1 (MAP3K1), MEKK4 (MAP3K4), MLK2 (MAP3K10), MLK3 (MAP3K11).
MKK4	S80	MAPK/ERK protein-serine kinase 4 (MEK4, MAP2K4)	8	6	9	10	see above	Inhibits phosphotransferase activity. Phosphorylation regulates apoptosis. S80 is phosphorylated by Akt1 (PKBa), Akt3 (PKBg), SGK1.
MKK6	Pan-specific	MAPK/ERK protein-serine kinase 6 (MEK6, MAP2K6)	13	10	13	8	Dual specificity protein MAPK protein which, with MAP3K3/MKK3, catalyzes the concomitant phosphorylation of p38 MAPK11, MAPK12, MAPK13 and MAPK14 and plays an important role in the regulation of cellular responses to cytokines and all kinds of stresses. MAP2K3/MKK3 and MAP2K6/MKK6 are both essential for the activation of MAPK11 and MAPK13 induced by environmental stress, whereas MAP2K6/MKK6 is the major MAPK11 activator in response to TNF. MAP2K6/MKK6 also phosphorylates and activates PAK6. Nuclear targets of p38 MAPK include ATF2 and ELK1. Within the p38 MAPK pathway, MAP3K6/MKK6 mediates phosphorylation of STAT4 through MAPK14 activation, and is therefore required for STAT4 activation and STAT4-regulated gene expression in response to IL-12 stimulation.	NA
MLC	S19	Myosin regulatory light chain 2, smooth muscle isoform (MYL12B, MRLC2)	18	30	22	19	Myosin regulatory subunit that plays an important role in regulation of both smooth muscle and nonmuscle cell contractile activity via its phosphorylation. Implicated in cytokinesis, receptor capping, and cell locomotion.	Phosphorylation increases an actomyosin contractile response by triggering cross-bridge cycling and force development. S19 is phosphorylated by MLCK, ROCK1, ZIPK, ILK1, PAK3.

MLK3	T277+S281	Mixed-lineage protein-serine kinase 3 (MAP3K11)	40	34	27	21	Activates the JUN N-terminal pathway. Required for serum-stimulated cell proliferation and for mitogen and cytokine activation of MAPK14 (p38), MAPK3 (ERK) and MAPK8 (JNK1) through phosphorylation and activation of MAP2K4/MKK4 and MAP2K7/MKK7.	(277) Phosphorylation regulates molecular association, including inducing interaction with GEFT. Predicted to be stimulatory for phosphotransferase activity. T277 is phosphorylated by MLK3 (MAP3K11). (281) Stimulates phosphotransferase activity. Phosphorylation regulates molecular association, including inducing interaction with GEFT. S281 is phosphorylated by HPK1 (MAP4K1), MLK3 (MAP3K11).
MLK3	Pan-specific	Mixed-lineage protein-serine kinase 3 (MAP3K11)	4	2	6	6	see above	NA
MLTK	T161+T162	Mitogen-activated protein kinase kinase kinase MLT (ZAK)	10	6	6	7	Stress-activated component of a protein kinase signal transduction cascade. Regulates the JNK and p38 pathways. Part of a signaling cascade that begins with the activation of the adrenergic receptor ADRA1B and leads to the activation of MAPK14. Pro-apoptotic. Regulates S and G2 cell cycle checkpoints by phosphorylation of CHEK2.	Stimulates phosphotransferase activity. T161 and T162 are phosphorylated by ZAK (MLTK).
MOK	Y167	MOK protein kinase (RAGE)	4	1	1	1	Able to phosphorylate several exogenous substrates and to undergo autophosphorylation. Negatively regulates cilium length in a cAMP and mTORC1 signaling-dependent manner.	No data available.
MOS	Y263	Moloney sarcoma oncogene-encoded protein-serine kinase	6	3	8	5	Involved in MAPK signaling and cytoskeletal rearrangement.	No data available.
MSK2	T687	Ribosomal protein S6 kinase alpha-4 (RPS6KA4)	3	2	3	5	Serine/threonine-protein kinase that is required for the mitogen or stress-induced phosphorylation of the transcription factors CREB1 and ATF1 and for the regulation of the transcription factor RELA, and that contributes to gene activation by histone phosphorylation and functions in the regulation of inflammatory genes. Phosphorylates CREB1 and ATF1 in response to mitogenic or stress stimuli (i.e. UV, EGF, and anisomycin).	Stimulates phosphotransferase activity. T687 is phosphorylated by ERK1 (MAPK3), ERK2 (MAPK1), p38a MAPK (MAPK14).

MST1	Pan-specific	Mammalian STE20-like protein-serine kinase 1 (MST1, STK4)	3	4	12	9	Stress-activated, pro-apoptotic kinase which, following caspase-cleavage, enters the nucleus and induces chromatin condensation followed by internucleosomal DNA fragmentation. Key component of the Hippo signaling pathway which plays a pivotal role in organ size control and tumor suppression by restricting proliferation and promoting apoptosis. STK3/MST2 and STK4/MST1, in complex with SAV1, phosphorylate and activate LATS1/2 in complex with its regulatory protein MOB1. This leads to phosphorylation and inactivation of YAP1 and WWTR1/TAZ.	NA
MST1	Pan-specific	Mammalian STE20-like protein-serine kinase 1 (KRS2, STK4)	3	2	6	6	see above	NA
MST1	Pan-specific	Mammalian STE20-like protein-serine kinase 1 (KRS2, STK4)	0	0	4	2	see above	NA
MST2	Pan-specific	Mammalian STE20-like protein-serine kinase 2 (KRS1)	3	3	12	14	Scaffolding protein that is part of a multiprotein signaling complex. Promotes phosphorylation of Raf family members and activation of downstream MAPKs. Promotes activation of MAPK1 and MAPK3, both in response to EGF and to cAMP.	NA
MST3	T184	Mammalian STE20-like protein-serine kinase 3 (STK24)	5	2	4	4	Serine/threonine-protein kinase that acts on both serine and threonine residues and promotes apoptosis in response to stress stimuli and caspase activation. Mediates oxidative-stress-induced cell death by modulating phosphorylation of JNK1, JNK2, and p38.	Predicted to be stimulatory for phosphotransferase activity.
NEK2	Pan-specific	NIMA (never-in-mitosis)-related protein-serine kinase 2	11	5	12	10	Protein kinase which is involved in the control of centrosome separation and bipolar spindle formation in mitotic cells and chromatin condensation in meiotic cells. Regulates centrosome separation by phosphorylating CROCC, CEP250 and NINL. Regulates kinetochore microtubule attachment stability via phosphorylation of NDC80. Involved in regulation of mitotic checkpoint protein complex via phosphorylation of CDC20 and MAD2L1. Regulates chromatin condensation through phosphorylation of HMGA2.	NA
NEK2	T170+S171	NIMA (never-in-mitosis)-related protein-serine kinase 2	8	8	6	7	see above	Stimulates phosphotransferase activity.
NEK2	Pan-specific	NIMA (never-in-mitosis)-related protein-serine kinase 2	8	3	17	11	see above	NA

NEK6	S206	NIMA (never-in-mitosis)-related protein-serine kinase 6	5	3	5	6	Protein kinase which plays an important role in mitotic cell cycle progression. Required for chromosome segregation at metaphase-anaphase transition, robust mitotic spindle formation and cytokinesis. Phosphorylates KIF11, ATF4, CIR1, PTN, RAD26L, RBBP6, RPS7, RPS6KB1, TRIP4, STAT3 and histones H1 and H3. Involved in G2/M phase cell cycle arrest induced by DNA damage. Inhibition of activity results in apoptosis. Suppresses p53/TP53-induced cancer cell senescence.	Stimulates phosphotransferase activity. S206 is phosphorylated by NEK9.
NEK7	Pan-specific	NIMA (never-in-mitosis)-related protein-serine kinase 7	12	8	9	10	Protein kinase which plays an important role in mitotic cell cycle progression. Required for microtubule nucleation activity of the centrosome, robust mitotic spindle formation and cytokinesis. Phosphorylates RPS6KB1.	NA
NFkappaB p65	S529	NF-kappa-B p65 nuclear transcription factor (Rel A)	-1	-1	-1	-1	NF-kappa-B is a pleiotropic transcription factor present in almost all cell types and is the endpoint of a series of signal transduction events that are initiated by a vast array of stimuli related to many biological processes such as inflammation, immunity, differentiation, cell growth, tumorigenesis and apoptosis. NF-kappa-B is a homo- or heterodimeric complex formed by the Rel-like domain-containing proteins RELA/p65, RELB, NFKB1/p105, NFKB1/p50, REL and NFKB2/p52 and the heterodimeric p65-p50 complex appears to be most abundant one.	S529 is phosphorylated by CK2a1 (CSNK2A1).
p38a MAPK	Pan-specific	Mitogen-activated protein-serine kinase p38 alpha (MAPK14)	15	10	10	9	Serine/threonine kinase of the MAPK signal transduction pathway. One of the four p38 MAPKs which play an important role in the cascades of cellular responses evoked by extracellular stimuli such as proinflammatory cytokines or physical stress leading to direct activation of transcription factors. The p38 MAPKs phosphorylate a broad range of proteins and may have 200 to 300 substrates each. Many targets are kinases which phosphorylate additional downstream targets. RPS6KA5/MSK1 and RPS6KA4/MSK2 can directly phosphorylate/activate transcription factors CREB1, ATF1, the NF-kappa-B isoform RELA/NFKB3, STAT1 and STAT3, but can also phosphorylate histone H3 and nucleosomal protein HMGN1.	NA
p38a MAPK	Pan-specific	Mitogen-activated protein-serine kinase p38 alpha (MAPK14)	13	8	7	9	see above	NA
p38a MAPK	T180+Y182	Mitogen-activated protein-serine kinase p38 alpha (MAPK14)	4	3	4	4	see above	Stimulates phosphotransferase activity. Phosphorylation regulates apoptosis, cell adhesion, cell cycle progression, cell motility, cytoskeletal reorganization, and molecular association, including inducing interaction with Fyn, Nck1, p38-alpha. T180 is phosphorylated by MKK3 (MAP2K3, MEK3), MKK4

								(MAP2K4, MEK4), MKK6 (MAP2K6, MEK6), p38a MAPK (MAPK14), PBK (TOPK).
p38a MAPK	T180+Y182	Mitogen-activated protein-serine kinase p38 alpha (MAPK14)	4	2	3	3	see above	Stimulates phosphotransferase activity. Phosphorylation regulates apoptosis, cell adhesion, cell cycle progression, cell motility, cytoskeletal reorganization, and molecular association, including inducing interaction with Fyn, Nck1, p38-alpha. T180 is phosphorylated by MKK3 (MAP2K3, MEK3), MKK4 (MAP2K4, MEK4), MKK6 (MAP2K6, MEK6), p38a MAPK (MAPK14), PBK (TOPK).
p38g MAPK	Pan-specific	Mitogen-activated protein-serine kinase p38 gamma, ((MAPK12, ERK6)	6	9	5	4	Serine/threonine kinase and essential component of the MAPK signal transduction pathway. One of the four p38 MAPKs which play an important role in the cascades of cellular responses evoked by extracellular stimuli such as proinflammatory cytokines or physical stress leading to direct activation of transcription factors such as ELK1 and ATF2.	NA
p53	Pan-specific	Tumor suppressor protein p53 (antigenNY-CO-13) (TP53)	3	2	5	5	Induces growth arrest or apoptosis depending on the physiological circumstances and cell type. Involved in cell cycle regulation as a trans-activator that acts to negatively regulate cell division by controlling genes required for this process. One of the activated genes is an inhibitor of cyclin-dependent kinases. Apoptosis induction is mediated either by stimulation of BAX and FAS antigen expression, or by repression of Bcl-2 expression. In cooperation with mitochondrial PPIF, is involved in activating oxidative stress-induced necrosis (largely independent of transcription).	NA
p53	S6	Tumor suppressor protein p53 (antigenNY-CO-13) (TP53)	-1	-2	-1	-1	see above	Activation of transcriptional activity. S6 is phosphorylated by ATM, CK1d1 (CSNK1D), CK1e1 (CSNK1E).

p70 S6K	Pan-specific	Ribosomal protein S6 kinase beta-1 (RPS6KB1 p70S6Ka)	4	7	5	6	Serine/threonine-protein kinase that acts downstream of mTOR signaling in response to growth factors and nutrients to promote cell proliferation, cell growth and cell cycle progression. Regulates protein synthesis through phosphorylation of EIF4B, RPS6 and EEF2K, and contributes to cell survival by repressing the pro-apoptotic function of BAD. During nutrient depletion, the inactive form associates with the EIF3 translation initiation complex. Upon mitogenic stimulation, phosphorylation by mTORC1 leads to dissociation and activation.	NA
p70 S6K	S434	Ribosomal protein S6 kinase beta-1 (RPS6KB1, p70S6Ka)	-1	-2	-1	-1	Serine/threonine kinase that acts downstream of mTOR signaling in response to growth factors and nutrients to promote cell proliferation, cell growth and cell cycle progression. Regulates protein synthesis through phosphorylation of EIF4B, RPS6 and EEF2K, and contributes to cell survival by repressing the pro-apoptotic function of BAD. Under conditions of nutrient depletion, the inactive form associates with the EIF3 translation initiation complex to inhibit activity.	Stimulates phosphotransferase activity. S434 is phosphorylated by CDK1 (CDC2), CDK5, ERK1 (MAPK3), ERK2 (MAPK1), FRAP1 (mTOR), JNK1 (MAPK8), JNK2 (MAPK9).
p70 S6K	T252	Ribosomal protein S6 kinase beta-1 (RPS6KB1, p70S6Ka)	17	47	19	47	see above	Stimulates phosphotransferase activity. Phosphorylation regulates protein translation and protein conformation. T252 is phosphorylated by PDK1 (PDPK1), PIK3CD.
p70 S6K	T412	Ribosomal protein S6 kinase beta-1 (RPS6KB1 p70S6Ka)	-1	-1	-1	-1	see above	Stimulates phosphotransferase activity. Phosphorylation regulates cell adhesion, cell cycle progression, translation, and alters intracellular location. T412 is phosphorylated by FRAP1 (mTOR), NEK6, p70S6K (RPS6KB1), PDK1 (PDPK1), PIK3CD.
PAK1	S144	p21-activated kinase 1 (alpha) (serine/threonine-protein kinase PAK 1) (PAKa)	4	3	5	7	Protein kinase involved in intracellular signaling downstream of integrins and receptor-type kinases that plays an important role in actin and microtubule cytoskeleton dynamics (including actin stress fibers, focal adhesion complexes, and microtubule biogenesis and organization), in cell adhesion, migration, proliferation, apoptosis, mitosis, and in vesicle-mediated transport processes. Phosphorylates BAD to protect cells against apoptosis. Activated by interaction with CDC42 and RAC1. Functions as GTPase effector that links the Rho-related GTPases CDC42 and RAC1 to the JNK MAP kinase pathway. Phosphorylates and activates MAP2K1, and thereby mediates activation of downstream MAP kinases. Plays a role in the regulation of insulin secretion in response to elevated glucose levels.	Stimulates phosphotransferase activity and regulates cytoskeletal reorganization, and intracellular location. S144 is phosphorylated by PAK1.



PAK1	Pan-specific	p21-activated kinase 1 (alpha) (serine/threonine-protein kinase PAK 1) (PAKa)	1	0	2	4	see above	NA
PAK2	Y130	p21-activated kinase 2 (gamma) (serine/threonine-protein kinase PAK 2) (PAKg)	4	3	4	6	Serine/threonine protein kinase that plays a role in cytoskeleton regulation, cell motility, cell cycle progression, apoptosis or proliferation. Acts as downstream effector of the small GTPases CDC42 and RAC1. Full-length PAK2 stimulates cell survival and cell growth. Phosphorylates MAPK4 and MAPK6 and activates the downstream target MAPKAPK5, a regulator of F-actin polymerization and cell migration. Phosphorylates JUN and plays a role in EGF-induced cell proliferation. Phosphorylates many other substrates including histone H4 to promote assembly of H3.3 and H4 into nucleosomes, BAD, ribosomal protein S6, or MBP. Apoptotic stimuli such as DNA damage lead to caspase-mediated cleavage of PAK2, generating an active p34 fragment that translocates to the nucleus and promotes apoptosis via the JNK pathway. Caspase-activated PAK2 phosphorylates MKNK1 and reduces cellular translation.	Stimulates phosphotransferase activity. Y130 is phosphorylated by Src.
PAK2	Pan-specific	p21-activated kinase 2 (gamma) (serine/threonine-protein kinase PAK 2) (PAKg)	4	3	6	6	see above	NA
PAK2	Pan-specific	p21-activated kinase 2 (gamma) (serine/threonine-protein kinase PAK 2) (PAKg)	3	3	3	5	see above	NA
PAK3	Pan-specific	p21-activated kinase 3 (beta) (serine/threonine-protein kinase PAK 3) (PAKb)	3	2	7	8	Serine/threonine protein kinase that plays a role in a variety of different signaling pathways including cytoskeleton regulation, cell migration, or cell cycle regulation. Plays a role in dendrite spine morphogenesis as well as synapse formation and plasticity. Acts as downstream effector of the small GTPases CDC42 and RAC1. Activation by the binding of active CDC42 and RAC1 results in a conformational change and a subsequent autophosphorylation on several serine and/or threonine residues. Phosphorylates MAPK4 and MAPK6 and activates the downstream target MAPKAPK5, a regulator of F-actin polymerization and cell migration. Additionally, phosphorylates TNNI3/troponin I to modulate calcium sensitivity and relaxation kinetics of thin myofilaments. May also be involved in early neuronal development.	NA

PAK4	S474	p21-activated kinase 4	2	2	2	5	Serine/threonine protein kinase that plays a role in cytoskeleton regulation, cell migration, growth, proliferation or cell survival. Activated by various effectors including growth factor receptors or active CDC42 and RAC1. Phosphorylates and inactivates the phosphatase SSH1, leading to increased inhibitory phosphorylation of the actin binding/depolymerizing factor cofilin. Decreased cofilin activity may lead to stabilization of actin filaments. Phosphorylates LIMK1, a kinase that also inhibits the activity of cofilin. Phosphorylates integrin beta5/ITGB5 and thus regulates cell motility.	Stimulates phosphotransferase activity. S474 is phosphorylated by PAK4.
PCTAIRE1	Pan-specific	PCTAIRE-1 protein-serine kinase (CDK16, PCK1)	8	6	10	13	Protein kinase that plays a role in vesicle-mediated transport processes and exocytosis. Regulates GH1 release by brain neurons. Phosphorylates NSF, and thereby regulates NSF oligomerization. Regulates neuron differentiation and dendrite development. Plays a role in the regulation of insulin secretion in response to changes in blood glucose levels.	NA
PCTAIRE1	Y176	PCTAIRE-1 protein-serine kinase (CDK16, PCK1)	1	0	2	4	see above	No data available; some of other sites phosphorylated by PKACA.
PCTAIRE2	S180	Cell division protein kinase 17 (CDK17, PCK2)	3	2	4	5	May play a role in terminally differentiated neurons. Has a Ser/Thr-phosphorylating activity for histone H1.	No data available; some of other sites phosphorylated by PKACA.
PDGFRa	Y754	Platelet-derived growth factor receptor kinase alpha	16	27	28	23	Tyrosine kinase that acts as a cell-surface receptor for PDGFA, PDGFB and PDGFC and plays an essential role in the regulation of embryonic development, cell proliferation, survival and chemotaxis. Depending on the context, promotes or inhibits cell proliferation and cell migration. Plays an important role in the differentiation of bone marrow-derived mesenchymal stem cells. Required for normal skeleton development and cephalic closure during embryonic development. Required for normal development of the mucosa lining the gastrointestinal tract, and for recruitment of mesenchymal cells and normal development of intestinal villi. Plays a role in cell migration and chemotaxis in wound healing. Plays a role in platelet activation, secretion of agonists from platelet granules, and in thrombin-induced platelet aggregation.	Y754 is phosphorylated by PDGFRA, PDGFRB.

PDGFRb	Pan-specific	Platelet-derived growth factor receptor kinase beta	-1	-1	-1	-1	Tyrosine-protein kinase that acts as cell-surface receptor for homodimeric PDGFB and PDGFD and for heterodimers formed by PDGFA and PDGFB, and plays an essential role in the regulation of embryonic development, cell proliferation, survival, differentiation, chemotaxis, migration, blood vessel development and vascular injury. Promotes proliferation, migration and recruitment of pericytes and smooth muscle cells to endothelial cells. Required for normal development of the cardiovascular system, recruitment of pericytes in the kidney glomerulus, and formation of a branched network of capillaries in kidney glomeruli. Promotes rearrangement of the actin cytoskeleton and the formation of membrane ruffles. Phosphorylates PLCG1, PIK3R1, PTPN11, RASA1/GAP, CBL, SHC1 and NCK1. Activation of PLCG1 leads to the production of DAG and inositol 1,4,5-trisphosphate, mobilization of cytosolic Ca <sup>2+</sup> and the activation of PKC. Phosphorylation of PIK3R1, the regulatory subunit of PI3K, leads to activation of the AKT1. Phosphorylation of SHC1 or PTPN11 recruits GRB2, resulting in the activation of HRAS, RAF1 and down-stream MAPKs (ERK1/2). Promotes phosphorylation and activation of SRC family kinases, PDCD6IP/ALIX and STAM.	NA
PGK1	Y196	Phosphoglycerate kinase 1	-1	-1	-1	-2	In addition to its role as a glycolytic enzyme, it seems that PGK-1 acts as a polymerase alpha cofactor protein.	No data available.
PI3K	Pan-specific	Phosphatidylinositol 3-kinase regulatory subunit alpha	14	8	14	14	Binds to activated (phosphorylated) protein-Tyr kinases, through its SH2 domain, and acts as an adapter, mediating the association of the p110 catalytic unit to the plasma membrane. Necessary for the insulin-stimulated increase in glucose uptake and glycogen synthesis in insulin-sensitive tissues. Plays an important role in signaling in response to FGFR1, FGFR2, FGFR3, FGFR4, KITLG/SCF, KIT, PDGFRA and PDGFRB. Likewise, plays a role in ITGB2 signaling. Modulates the cellular response to ER stress by promoting nuclear translocation of XBP1 isoform 2 in a ER stress- and/or insulin-dependent manner during metabolic overloading in the liver and hence plays a role in glucose tolerance improvement.	NA
PIK3R1	Y467	Phosphatidylinositol 3-kinase regulatory subunit alpha	-1	-1	-2	-1	see above	No data available.
PIK3R1	Y580	Phosphatidylinositol 3-kinase regulatory subunit alpha	-1	-1	-1	-1	see above	Y580 is phosphorylated by InsR.

PKCb	Pan-specific	Protein-serine kinase C beta 1 (PRKCB1)	25	23	18	18	Calcium-activated, phospholipid- and diacylglycerol (DAG)-dependent serine/threonine kinase involved in various cellular processes such as regulation of the B-cell receptor (BCR) signalosome, oxidative stress-induced apoptosis, androgen receptor-dependent transcription regulation, insulin signaling and endothelial cell proliferation. Plays a key role in B-cell activation by regulating BCR-induced NF-kappa-B activation. Mediates the activation of the canonical NF-kappa-B pathway.	NA
PKCb	Pan-specific	Protein-serine kinase C beta 1 (PRKCB1)	2	1	5	6	see above	NA
PKCd	Y313	Protein-serine kinase C delta (PRKCD)	8	7	4	4	Calcium-independent, phospholipid- and DAG-dependent serine/threonine kinase that plays contrasting roles in cell death and cell survival by functioning as a pro-apoptotic protein during DNA damage-induced apoptosis (via BCLAF1/Btf and p53), but acting as an anti-apoptotic protein during cytokine receptor-initiated cell death. Required for oxygen radical production by NADPH oxidase and acts as positive or negative regulator in platelet functional responses. Negatively regulates B cell proliferation and also has an important function in self-antigen induced B cell tolerance induction. In response to oxidative stress, activates CHUK/IKKA, causing the phosphorylation of p53/TP53. During ER stress or DNA damage-induced apoptosis, complexes with ABL1 to trigger apoptosis independently of p53/TP53. In the cytosol it triggers apoptosis by activating MAPK11 or MAPK14, inhibiting AKT1 and decreasing the level of XIAP, but in nucleus it induces apoptosis via the activation of MAPK8 or MAPK9. Upon ionizing radiation, it is required for the activation of BAX and BAK, which trigger the mitochondrial cell death pathway.	Stimulates phosphotransferase activity. Phosphorylation regulates transcription and apoptosis. Y313 is phosphorylated by EGFR, Fyn, Lck, Lyn, PDGFRA, PKCd (PRKCD), Src, Yes.
PKCd	Y313	Protein-serine kinase C delta (PRKCD)	4	5	2	2	see above	Stimulates phosphotransferase activity. Phosphorylation regulates transcription and apoptosis. Y313 is phosphorylated by EGFR, Fyn, Lck, Lyn, PDGFRA, PKCd (PRKCD), Src, Yes.
PKCd	S645	Protein-serine kinase C delta (PRKCD)	-1	-1	-1	-1	see above	Stimulates phosphotransferase activity. S645 is phosphorylated by PKCd (PRKCD).
PKCd	Pan-specific	Protein-serine kinase C delta (PRKCD)	2	1	4	6	see above	NA

PKCe	Pan-specific	Protein-serine kinase C epsilon (PRKCE)	2	1	4	6	Calcium-independent, phospholipid- and diacylglycerol (DAG)-dependent serine/threonine kinase that plays essential roles in the regulation of multiple cellular processes linked to cytoskeletal proteins, such as cell adhesion, motility, migration and cell cycle, functions in neuron growth and ion channel regulation, and is involved in immune response, cancer cell invasion and regulation of apoptosis. Mediates cell adhesion to the ECM via integrin-dependent signaling, by mediating angiotensin-2-induced activation of integrin beta-1 (ITGB1) in cardiac fibroblasts. Phosphorylates MARCKS, which phosphorylates and activates PTK2/FAK. Involved in the control of the directional transport of ITGB1 in mesenchymal cells by phosphorylating vimentin (VIM), an intermediate filament (IF) protein. In epithelial cells, associates with and phosphorylates keratin-8 (KRT8), which induces targeting of desmoplakin at desmosomes and regulates cell-cell contact.	NA
PKCg	T514	Protein-serine kinase C gamma (PRKCG)	12	13	8	10	Calcium-activated, phospholipid- and diacylglycerol (DAG)-dependent serine/threonine kinase that plays diverse roles in neuronal cells and eye tissues, such as regulation of the neuronal receptors GRIA4/GLUR4 and GRIN1/NMDAR1, modulation of receptors and neuronal functions related to sensitivity to opiates, pain and alcohol, mediation of synaptic function and cell survival after ischemia, and inhibition of gap junction activity after oxidative stress.	Stimulates phosphotransferase activity. Phosphorylation induces preactivation of PKC. T514 is phosphorylated by PDK1 (PDPK1).
PKCg	T514	Protein-serine kinase C gamma (PRKCG)	5	5	2	2	see above	Stimulates phosphotransferase activity. Phosphorylation induces preactivation of PKC. T514 is phosphorylated by PDK1 (PDPK1).
PKCg	T674	Protein-serine kinase C gamma (PRKCG)	3	4	2	1	see above	Stimulates phosphotransferase activity. T674 is phosphorylated by PKCg (PRKCG).
PKCg	Pan-specific	Protein-serine kinase C gamma (PRKCG)	1	0	2	4	see above	NA

PKCh	T656	Protein-serine kinase C eta (PRKCH)	14	17	12	13	Calcium-independent, phospholipid- and DAG-dependent serine/threonine kinase involved in regulating cell differentiation in keratinocytes, pre-B cell receptor signaling, epithelial tight junction integrity and foam cell formation, actin depolymerization, and proliferation and apoptosis in some cell types. Activates FYN, which blocks EGFR signaling and leads to growth arrest and differentiation in some cell types. Associates with the cyclin CCNE1-CDK2-CDKN1B complex and inhibits CDK2 kinase activity, leading to RB1 dephosphorylation and G1 arrest. Regulates tight junctions (TJs) by phosphorylating occludin (OCLN), which is necessary for assembly and maintenance of TJs. In association with PLD2 and via TLR4 signaling, is involved in LPS-induced RGS2 down-regulation and foam cell formation. Can activate the mTOR pathway, the PI3K/AKT pathway and ERK1. Can regulate NF-kappa-B by activating IKBKB, and confer protection against DNA damage-induced apoptosis. Promotes oncogenic functions of ATF2 in the nucleus while blocking its apoptotic function at mitochondria.	Stimulates phosphotransferase activity. T656 is phosphorylated by PKCh (PRKCH).
PKCh	Pan-specific	Protein-serine kinase C eta (PRKCH)	2	2	7	10	see above	NA
PKCI/I	Pan-specific	Protein-serine kinase C lambda/iota (PRKCI)	2	2	7	8	Calcium- and diacylglycerol-independent serine/threonine kinase that plays a general protective role against apoptotic stimuli, is involved in NF-kappa-B activation, cell survival, differentiation and polarity, and contributes to the regulation of microtubule dynamics in the early secretory pathway. Is necessary for BCR-ABL oncogene-mediated resistance to apoptotic drugs in leukemia cells. In cultured neurons, prevents amyloid beta protein-induced apoptosis by interrupting cell death process at a very early step.	NA
PKCm	Pan-specific	Protein-serine kinase C mu (Protein kinase D) (PRKD1, PKD1, PRKCM)	3	1	7	8	Serine/threonine kinase that converts transient DAG signals into prolonged physiological effects downstream of PKC, and is involved in the regulation of MAPK8/JNK1 and Ras signaling, Golgi membrane integrity and trafficking, cell survival through NF-kappa-B activation, cell migration, cell differentiation by mediating HDAC7 nuclear export, cell proliferation via ERK1/2 signaling, and plays a role in cardiac hypertrophy, VEGFA-induced angiogenesis, genotoxic-induced apoptosis and flagellin-stimulated inflammatory response. Phosphorylates EGFR, which leads to the suppression of EGF-induced MAPK8/JNK1 activation and subsequent JUN phosphorylation.	NA
PKCq	S695	Protein-serine kinase C theta (PRKCQ)	-2	-1	-1	-1	Calcium-independent, phospholipid- and DAG-dependent serine/threonine-protein kinase that mediates non-redundant functions in T-cell receptor (TCR) signaling, including T-cell activation, proliferation, differentiation and survival, by mediating activation of multiple transcription factors such as NF-kappa-B, JUN, NFATC1 and NFATC2. In TCR-CD3/CD28-co-stimulated T-cells, it is required for the activation of NF-kappa-B and JUN, which in turn are essential for IL2 production, and participates in the calcium-dependent NFATC1 and NFATC2 transactivation.	Stimulates phosphotransferase activity. Phosphorylation induces interaction with PDK1 and protein stabilization. S695 is phosphorylated by PKCt (PRKCQ).

PKCq	S676	Protein-serine kinase C theta (PRKCQ)	-1	-1	-1	-1	see above	Stimulates phosphotransferase activity. Phosphorylation regulates transcription. S676 is phosphorylated by PKCt (PRKCQ).
PKCz	Pan-specific	Protein-serine kinase C zeta (PRKCZ)	1	1	4	4	Calcium- and DAG-independent serine/threonine kinase that functions in PI3K pathway and MAPK cascade, and is involved in NF-kappa-B activation, mitogenic signaling, cell proliferation, cell polarity, inflammatory response and maintenance of long-term potentiation (LTP). Upon lipopolysaccharide (LPS) treatment in macrophages, or following mitogenic stimuli, functions downstream of PI3K to activate MAP2K1/MEK1-MAPK1/ERK2 signaling cascade independently of RAF1 activation. Required for insulin-dependent activation of AKT3, but may function as an adapter rather than a direct activator.	NA
PKN	Pan-specific	Protein kinase C-related protein-serine kinase 1 (PRKCL1, PRK1)	2	3	5	5	PKC-related serine/threonine-protein kinase involved in various processes such as regulation of the intermediate filaments of the actin cytoskeleton, cell migration, tumor cell invasion and transcription regulation. Downstream of the adrenergic receptor ADRA1B; signaling leads to the activation of MAPK14. Regulates the cytoskeletal network by phosphorylating proteins such as VIM and neurofilament proteins NEFH, NEFL and NEFM, leading to inhibit their polymerization. Phosphorylates MAPT/Tau, lowering its ability to bind to microtubules, resulting in disruption of tubulin assembly. Acts as a coactivator of ANDR-dependent transcription, by being recruited to ANDR target genes and phosphorylating histone H3 (H3T11ph). Phosphorylates HDAC5, HDAC7 and HDAC9, leading to impair their import in the nucleus. Phosphorylates PP1R14A, MARCKS, GFAP and RPS6.	NA
PKR1	Pan-specific	Double stranded RNA dependent protein-serine kinase (PRKR; EIF2AK2)	3	3	7	8	IFN-induced dsRNA-dependent serine/threonine kinase which regulates the innate immune response to viral infection and is also involved in the regulation of signal transduction, apoptosis, cell proliferation and differentiation. Regulates replication via EIF2S1. Phosphorylates p53/TP53, PPP2R5A, DHX9, ILF3, IRS1 and the HHV-1 viral protein US11. Also has tyrosine-protein kinase activity and phosphorylates CDK1 upon DNA damage, facilitating its ubiquitination and proteosomal degradation. Either as an adapter protein and/or via its kinase activity, can regulate signaling through p38 MAP kinase, NF-kappa-B and insulin signaling pathways and transcription factors (JUN, STAT1, STAT3, IRF1, ATF3) regulating proinflammatory cytokines and IFNs.	NA
PKR1	T446	Double stranded RNA dependent protein-serine kinase (PRKR; EIF2AK2)	-1	-1	-1	-2	see above	Stimulates phosphotransferase activity. Phosphorylation regulates cell cycle progression and cell growth. T446 is phosphorylated by PKR (PRKR; EIF2AK2).



PLCg1	Y783	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase gamma-1	-1	-1	-2	-2	Mediates the production of the second messenger molecules diacylglycerol (DAG) and inositol 1,4,5-trisphosphate (IP3). Plays an important role in the regulation of intracellular signaling cascades. Becomes activated in response to ligand-mediated activation of receptor-type tyrosine kinases, such as PDGFRA, PDGFRB, FGFR1, FGFR2, FGFR3 and FGFR4. Plays a role in actin reorganization and cell migration.	Stimulates phospholipase activity and regulates cell motility and molecular association, including inducing interaction with Grb2 and VEGFR-2. Y783 is phosphorylated by EGFR, Itk, Src, Syk, TrkB (NTRK2), ZAP70.
PLCg2	Y753	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase gamma-2 (PLC R)	4	83	60	32	The production of the second messenger molecules diacylglycerol (DAG) and inositol 1,4,5-trisphosphate (IP3) is mediated by activated phosphatidylinositol-specific phospholipase C enzymes. It is a crucial enzyme in transmembrane signaling.	Stimulates phospholipase activity, and regulates molecular association, including inducing interaction with Lyn. Y753 is phosphorylated by Btk, Fyn, Lck, Src.
PLK4	T170	Polo-like protein kinase 3 (cytokine- inducible kinase (CNK) (SAK, STK18)	-1	-1	-1	-1	Serine/threonine-protein kinase that plays a central role in centriole duplication. Able to trigger procentriole formation on the surface of the parental centriole cylinder, leading to the recruitment of centriole biogenesis proteins such as SASS6, CENPJ/CPAP, CCP110, CEP135 and gamma-tubulin.	Predicted to be stimulatory for phosphotransferase activity.
PPP1R11	Y64	Protein phosphatase 1 regulatory subunit 11 (HCG V)	4	3	3	2	Inhibitor of protein phosphatase 1.	No data available.
PRKACA	T198	cAMP-dependent protein kinase catalytic subunit alpha	25	30	16	15	Phosphorylates a large number of substrates in the cytoplasm and the nucleus. Regulates the abundance of compartmentalized pools of its regulatory subunits through phosphorylation of PJA2 which binds and ubiquitinates these subunits, leading to proteolysis. Phosphorylates CDC25B, ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA and VASP. Involved in the regulation of platelets in response to thrombin and collagen; maintains circulating platelets in a resting state by phosphorylating proteins in numerous platelet inhibitory pathways when in complex with NF-kappa-B and I-kappa-B-alpha. Thrombin and collagen disrupt these complexes and free active PRKACA stimulates platelets and leads to platelet aggregation by phosphorylating VASP.	Stimulates phosphotransferase activity and regulates stability. T198 is phosphorylated by the following protein kinases in vitro: PDK1 (PDK1), PKACa (PRKACA).

PYK2	Pan-specific	Protein-tyrosine kinase 2 (PTK2B)	3	2	2	3	Non-receptor tyrosine kinase that regulates reorganization of the actin cytoskeleton, cell polarization, cell migration, adhesion, spreading and bone remodeling. Plays a role in the regulation of the humoral immune response, and B-cell regulation in lymphoid tissues. Required for normal macrophage polarization and migration towards sites of inflammation. Regulates cytoskeleton rearrangement and the regulation of T-cell responses. Promotes osteoclastic bone resorption. Functions in signaling downstream of integrin and collagen receptors, immune receptors, GPCRs, cytokine, chemokine and growth factor receptors, and mediates responses to cellular stress. Forms multisubunit signaling complexes with PDPK1, SRC and SRC family members upon activation to create binding sites for scaffold proteins, effectors and substrates. Promotes activation of NOS3, cGMP, RHOA, RAC1, and the PI3K-AKT1 and MAPK ERK1/2 and JNK signaling cascades. Recruits MDM2 to P53/TP53 in the nucleus to regulate P53/TP53 activity.	NA
Raf1 (c-Raf)	S296	Raf1 proto-oncogene-encoded protein-serine kinase (RafC)	2	3	3	2	Serine/threonine-protein kinase that acts as a regulatory link between the membrane-associated Ras GTPases and the MAPK/ERK cascade, and this critical regulatory link functions as a switch determining cell fate decisions including proliferation, differentiation, apoptosis, survival and oncogenic transformation. RAF1 activation initiates a MAPK cascade via MEK1 and MEK2, leading to activation of ERK1/2. Phosphorylated RAF1 (Ser-338 and Ser-339, by PAK1) phosphorylates BAD/Bcl2-antagonist of cell death, adenylyl cyclases (ADCY2, ADCY5 and ADCY6) resulting in their activation, PPP1R12A to inhibit phosphatase activity, and TNNT2/cardiac muscle troponin T. Promotes NF-kappa-B activation and inhibits signal transducers involved in motility (ROCK2), apoptosis (MAP3K5/ASK1 and STK3/MST2), proliferation and angiogenesis (RB1). Can protect cells from apoptosis by translocating to the mitochondria where it binds BCL2 and displaces BAD/Bcl2-antagonist of cell death. Regulates Rho signaling and migration, and is required for normal wound healing. Represses the TJ protein, occludin (OCLN) via up-regulation of SNAI2/SLUG. Restricts caspase activation in response to selected stimuli, notably Fas stimulation, pathogen-mediated macrophage apoptosis, and erythroid differentiation.	Phosphorylation inhibits phosphotransferase activity and inhibits interaction with H-Ras-1. S296 is phosphorylated by ERK1 (MAPK3).
Rb	S807	Retinoblastoma-associated protein 1	29	32	27	28	Key regulator of entry into cell division. Promotes G0-G1 transition when phosphorylated by CDK3/cyclin-C. Acts as a transcription repressor of E2F1 target genes. The underphosphorylated, active form of RB1 interacts with E2F1 and represses its transcription activity, leading to cell cycle arrest. Directly involved in heterochromatin formation by maintaining overall chromatin structure and, in particular, that of constitutive heterochromatin by stabilizing histone methylation. Recruits and targets histone methyltransferases SUV39H1, KMT5B and KMT5C, leading to epigenetic transcriptional repression.	Inhibits interaction with Abl and EF21. S807 is phosphorylated by CDK1 (CDC2), CDK2, CDK3, CDK4, CDK6, CDK9.

Rb	S612	Retinoblastoma-associated protein 1	18	22	11	11	see above	Reported to either induce and inhibit binding to E2F1. S612 is phosphorylated by CDK2, CDK6, Chk1 (CHEK1), Chk2 (CHEK2).
Rb	T826	Retinoblastoma-associated protein 1	13	15	8	9	see above	Inhibits interaction with E2F1, Elf-1 and TFDP1, and induces binding with Rb. T826 is phosphorylated by CDK2, CDK4, CDK6.
Rb	S795	Retinoblastoma-associated protein 1	3	3	3	3	see above	Inhibits interaction with ARF1, E2F1 and TFDP1. S795 is phosphorylated by CDK4, CDK5, CDK6, CDK9.
RelB	S573	Transcription factor RelB	3	5	7	13		NF-kappa-B is a pleiotropic transcription factor which is present in almost all cell types and is involved in many biological processes such as inflammation, immunity, differentiation, cell growth, tumorigenesis and apoptosis. NF-kappa-B is a homo- or heterodimeric complex formed by the Rel-like domain-containing proteins RELA/p65, RELB, NFkB1/p105, NFkB1/p50, REL and NFkB2/p52.
RET	Pan-specific	Proto-oncogene tyrosine-protein kinase receptor Ret	6	2	2	3		Receptor tyrosine kinase involved in numerous cellular mechanisms including cell proliferation, neuronal navigation, cell migration, and cell differentiation upon binding with glial cell derived neurotrophic factor family ligands. Phosphorylates PTK2/FAK1. Regulates both cell death/survival balance and positional information. Regulates intestine organogenesis, development of enteric nervous system, the neural crest, and renal organogenesis during embryonic life, and promotes the formation of Peyer's patch-like structures (gut-associated lymphoid tissue). Modulates cell adhesion via its cleavage by caspase and mediates cell migration in an integrin (e.g. ITGB1 and ITGB3)-dependent manner. Active in the absence of ligand, triggering apoptosis in a caspase-dependent manner.
RET	Pan-specific	Proto-oncogene tyrosine-protein kinase receptor Ret	5	2	2	3	see above	NA
RIOK1	Y466	Serine/threonine-protein kinase RIO1	7	6	4	5		Involved in the final steps of cytoplasmic maturation of the 40S ribosomal subunit. Involved in processing of 18S-E pre-rRNA to the mature 18S rRNA. Required for the recycling of NOB1 and PNO1 from the late 40S precursor. The association with the very late 40S subunit intermediate may involve a translation-like checkpoint point cycle preceding the binding to the 60S ribosomal subunit. Despite the protein kinase domain is proposed to act predominantly as an ATPase. The catalytic activity regulates its dynamic association with the 40S subunit.

ROCK1	Pan-specific	RhoA protein-serine kinase beta (ROKb)	3	1	5	3	Protein kinase which is a key regulator of actin cytoskeleton and cell polarity. Involved in regulation of smooth muscle contraction, actin cytoskeleton organization, stress fiber and focal adhesion formation, neurite retraction, cell adhesion and motility via phosphorylation of DAPK3, GFAP, LIMK1, LIMK2, MYL9/MLC2, PFN1 and PPP1R12A. Phosphorylates FHOD1 and acts synergistically with it to promote SRC-dependent non-apoptotic plasma membrane blebbing. Phosphorylates JIP3 and regulates the recruitment of JNK to JIP3 upon UVB-induced stress. Acts as a suppressor of inflammatory cell migration by regulating PTEN phosphorylation and stability. Acts as a negative regulator of VEGF-induced angiogenic endothelial cell activation.	NA
RSK1	Pan-specific	Ribosomal S6 protein-serine kinase 1 (RPS6KA1, p90RSK)	4	2	5	4	Serine/threonine kinase that acts downstream of ERK signaling and positively regulates mitogenic and stress-induced activation of CREB1, CREBBP, ETV1/ER81 and NR4A1/NUR77, positively regulates translation through RPS6 and EIF4B phosphorylation, and mediates cellular proliferation, survival, and differentiation by modulating mTOR signaling and repressing pro-apoptotic function of BAD and DAPK1. Upon insulin-derived signal, phosphorylates GSK3B to inhibit its activity and EIF4B to enhance EIF4B affinity for the EIF3 complex to stimulating cap-dependent translation. Involved in the mTOR nutrient-sensing pathway by phosphorylating TSC2 to prevent its suppression of mTOR signaling, and via phosphorylation of RPTOR (regulates mTORC1 activity). Involved in cell cycle regulation by phosphorylating the CDK inhibitor CDKN1B. Phosphorylates EPHA2 to regulate cell migration.	NA
RSK1/2	S221/S227	Ribosomal S6 protein-serine kinase 1/2 (RPS6KA1/A3, p90RSK)	5	2	2	1	see above	Stimulates phosphotransferase activity. S221 is phosphorylated by PDK1 (PDPK1), RSK1 (RPS6KA2).
Shc1	Y349+Y350	SH2 domain-containing transforming protein 1	19	22	10	11	Signaling adapter that couples activated growth factor receptors to signaling pathways. Participates in a signaling cascade initiated by activated KIT and KITLG/SCF. Once phosphorylated, some isoforms couple activated receptor tyrosine kinases to Ras via the recruitment of the GRB2/SOS complex and are implicated in the cytoplasmic propagation of mitogenic signals while other isoforms are involved in signal transduction pathways that regulate apoptosis in response to oxidative stress downstream of p53.	Regulates apoptosis and molecular association, including inducing interaction with Grb2. Y349 is phosphorylated by EGFR, Lck, Src, ZAP70. Y350 is phosphorylated by EGFR, Lck, Src, ZAP70.
SHP2 (PTP1D)	Pan-specific	Protein-tyrosine phosphatase 1D (SHP2, SHPTP2, Syp, PTP2C, PTPN11)	6	3	2	3	Acts downstream of various receptor and cytoplasmic protein tyrosine kinases to participate in the signal transduction from the cell surface to the nucleus. Positively regulates MAPK signal transduction pathway.	NA

SIK (SIK1)	T182	Salt-inducible kinase	7	4	7	7	Serine/threonine-protein kinase involved in various processes such as cell cycle regulation, gluconeogenesis and lipogenesis regulation, muscle growth and differentiation and tumor suppression. Phosphorylates HDAC4, HDAC5, PPME1 (subunit of PP2A), SREBF1, CRTC1/TORC1 and CRTC2/TORC2. Regulates p53/TP53-dependent anoikis (apoptosis triggered by cell detachment) via phosphorylation of p53. Following increases in intracellular sodium, SIK1 is activated by CaMK1 and phosphorylates PP2A, leading to dephosphorylation of sodium/potassium-transporting ATPase ATP1A1 and subsequent increase activity of ATP1A1. Acts as a regulator of muscle cells via phosphorylation of HDAC4 and HDAC5, leading to promote expression of MEF2 target genes.	Predicted to be stimulatory for phosphotransferase activity. T182 is phosphorylated by GSK3b, LKB1 (STK11).
SIK2 (QIK)	Pan-specific	Serine/threonine-protein kinase SIK2	5	3	2	4	Phosphorylates 'Ser-794' of IRS1 in insulin-stimulated adipocytes, potentially modulating the efficiency of insulin signal transduction. Inhibits CREB activity by phosphorylating and repressing TORCs, the CREB-specific coactivators.	NA
SIK3 (QSK)	T411	Salt-inducible kinase 3	7	5	5	7	Phosphorylates 'Ser-794' of IRS1 in insulin-stimulated adipocytes, potentially modulating the efficiency of insulin signal transduction. Inhibits CREB activity by phosphorylating and repressing TORCs, the CREB-specific coactivators.	No data available.
SIK3 (QSK)	Pan-specific	Serine/threonine-protein kinase SIK3	3	1	3	1	see above	NA
SLK	S189	STE20-like serine/threonine-protein kinase (STK2)	1	1	2	3	Mediates apoptosis and actin stress fiber dissolution.	Predicted to be stimulatory for phosphotransferase activity.
Smad2	S467	Mothers against decapentaplegic homolog 2	2	2	3	5	Receptor-regulated SMAD that is an intracellular signal transducer and transcriptional modulator activated by TGF-beta and activin type 1 receptor kinases. On formation of the SMAD2/SMAD4 complex, activates transcription. Positively regulates PDPK1 kinase activity by stimulating its dissociation from the 14-3-3 protein YWHAQ which acts as a negative regulator.	S467 is phosphorylated by BMPR1B (ACVR1), TGFbR1.
SMC1	S957	Structural maintenance of chromosomes protein 1A	4	0	1	2	Involved in chromosome cohesion during cell cycle and in DNA repair. Central component of cohesin complex. The cohesin complex is required for the cohesion of sister chromatids after DNA replication. The cohesin complex may also play a role in spindle pole assembly during mitosis. Involved in DNA repair via its interaction with BRCA1 and its related phosphorylation by ATM, or via its phosphorylation by ATR. Works as a downstream effector both in the ATM/NBS1 branch and in the ATR/MSH2 branch of S-phase checkpoint.	S957 is phosphorylated by ATM, ATR.

SNCA	S129	Alpha-synuclein	-1	-1	-1	-1	May be involved in the regulation of dopamine release and transport. Induces fibrillization of microtubule-associated protein tau. Reduces neuronal responsiveness to various apoptotic stimuli, leading to a decreased caspase-3 activation.	S129 is phosphorylated by BARK1 (GRK2; ADRBK1), CaMK2a, CK1a1 (CSNK1A1), CK2a1 (CSNK2A1), GPRK5 (GRK5), Plk2 (SNK), Plk3 (CNK).
SOX9	S181	SRY (sex determining region Y)-box 9 (campomelic dysplasia, autosomal sex-reversal)	17	22	19	13	Transcription factor that plays an important role in the normal skeletal development.	Stimulates transcriptional activity by increasing SOX9's DNA binding and transcriptional activation, and regulates cytoskeletal reorganization, intracellular location and molecular association, including inducing interaction with KPNB1. S181 is phosphorylated by PKACa (PRKACA).
SRC	Pan-specific	Src proto-oncogene-encoded protein-tyrosine kinase	3	2	6	5	Non-receptor protein tyrosine kinase which is activated following engagement of many different classes of cellular receptors including immune response receptors, integrins and other adhesion receptors, receptor protein tyrosine kinases, G protein-coupled receptors as well as cytokine receptors. Participates in signaling pathways that control a diverse spectrum of biological activities including gene transcription, immune response, cell adhesion, cell cycle progression, apoptosis, migration, and transformation. Receptor clustering or dimerization leads to recruitment of SRC to the receptor complexes where it phosphorylates the tyrosine residues within the receptor cytoplasmic domains.	NA
SRPK1	S222	Serine/arginine-rich protein-specific kinase 1	6	5	14	10	Serine/arginine-rich protein-specific kinase which specifically phosphorylates its substrates at serine residues located in regions rich in arginine/serine dipeptides, known as RS domains and is involved in the phosphorylation of SR splicing factors and the regulation of splicing. Can influence additional steps of mRNA maturation, as well as other cellular activities, such as chromatin reorganization and cell cycle progression.	Stimulates phosphotransferase activity.
STAT2	Y690	Signal transducer and activator of transcription 2	176	142	318	231	Signal transducer and activator of transcription that mediates signaling by type I IFNs. Following IFN binding to cell surface receptors, Jak kinases (TYK2 and JAK1) are activated, leading to phosphorylation of STAT1/2. The phosphorylated STATs dimerize, and associate with IRF9/ISGF3G to form a complex that enters the nucleus and drives antiviral responses. Acts as a regulator of mitochondrial fission by modulating the phosphorylation of DNM1L.	Stimulates transcriptional activity. Y690 is phosphorylated by JAK1, Lck, Tyk2.

STAT3	Y705	Signal transducer and activator of transcription 3 (acute phase response factor)	22	1	17	2	Signal transducer and transcription activator that mediates cellular responses to interleukins, KITLG/SCF, LEP and other growth factors.	Stimulates transcriptional activity and induces molecular association DNA, PKCD, and STAT1. It regulates apoptosis, cell adhesion, cell differentiation, cell growth, cell motility, transcription, activation, alters intracellular location, and protein degradation. Y705 is phosphorylated by EphB1, Fer, JAK1, JAK2, MAPKAPK2, MEKK1 (MAP3K1), PKM2.
STAT3	Pan-specific	Signal transducer and activator of transcription 3 (acute phase response factor)	-1	-2	1	-1	see above	NA
STAT3	Y705+T708	Signal transducer and activator of transcription 3 (acute phase response factor)	3	3	2	3	see above	Stimulates transcriptional activity and induces molecular association DNA, PKCD, and STAT1. It regulates apoptosis, cell adhesion, cell differentiation, cell growth, cell motility, transcription, activation, alters intracellular location, and protein degradation. Y705 is phosphorylated by EphB1, Fer, JAK1, JAK2, MAPKAPK2, MEKK1 (MAP3K1), PKM2.
STAT5A	Pan-specific	Signal transducer and activator of transcription 5A	1	0	3	3	Carries out a dual function: signal transduction and activation of transcription. Mediates cellular responses to the cytokine KITLG/SCF and other growth factors. Mediates cellular responses to ERBB4. May mediate cellular responses to activated FGFR1, FGFR2, FGFR3 and FGFR4. Binds to the GAS element and activates PRL-induced transcription. Regulates the expression of milk proteins during lactation.	NA
STAT5B	Pan-specific	Signal transducer and activator of transcription 5B	1	0	4	5	see above	NA



SYK	Y323	Spleen protein-tyrosine kinase	5	4	5	6	Non-receptor tyrosine kinase which mediates signal transduction downstream of a variety of transmembrane receptors such as the B-cell receptor (BCR). Regulates several biological processes including innate and adaptive immunity, cell adhesion, osteoclast maturation, platelet activation and vascular development. Assembles into signaling complexes with activated receptors at the plasma membrane via interaction between its SH2 domains and the receptor tyrosine-phosphorylated ITAM domains.	Stimulates phosphotransferase activity and regulates molecular association, including inducing interaction with Cbl, and Fyn. Y323 is phosphorylated by Lck, Lyn, Syk.
TAK1	T184+T187	TGF-beta-activated protein-serine kinase 1 (MAP3K7)	2	0	3	3	Plays a crucial role in innate immune response to fungal, bacterial and viral pathogens including ROS production. Activates the inflammasome and NF-kappa-B-mediated transcription of chemokines and cytokines in the presence of pathogens. Regulates neutrophil degranulation and phagocytosis through activation of the MAPK signaling cascade and mediates the activation of dendritic cells by cell necrosis stimuli. Also involved in mast cells activation. It can function downstream of receptors mediating cell adhesion such as integrins and aids in recruitment of leukocytes to inflammatory loci. Involved in vascular development where it may regulate blood and lymphatic vascular separation.	Stimulates phosphotransferase activity. T184 is phosphorylated by TAK1 (MAP3K7).
TAO1	Y309	Serine/threonine-protein kinase TAO1 (TAOK1)	10	9	11	12	Serine/threonine-protein kinase. Phosphorylates MAP2K3, MAP2K6 and MARK2. Acts as an activator of the p38/MAPK14 stress-activated MAPK cascade via activation of MAP2K3 and MAP2K6 kinases (in response to DNA damage, etc) and downstream of GPCR signaling. Acts as a regulator of cytoskeleton stability by phosphorylating 'Thr-208' of MARK2, leading to activate MARK2 kinase activity and subsequent phosphorylation and detachment of MAPT/TAU from microtubules. Also acts as a regulator of apoptosis: regulates apoptotic morphological changes, including cell contraction, membrane blebbing and apoptotic bodies formation via activation of the MAPK8/JNK cascade.	No data available.
TAO1	S181	Serine/threonine-protein kinase TAO1 (TAOK1)	9	6	8	12	see above	Predicted to be stimulatory for phosphotransferase activity.
TBC1D7	Y14	TBC1 domain family member 7	6	3	6	11	Component of the TSC-TBC complex, that contains TBC1D7 in addition to the TSC1-TSC2 complex and consists of the functional complex possessing GAP activity toward RHEB in response to alterations in specific cellular growth conditions. The small GTPase RHEB is a direct activator of mTORC1 and the TSC-TBC complex acts as a negative regulator of mTORC1 signaling cascade by acting as a GAP for RHEB. Participates in the proper sensing of growth factors and glucose, but not amino acids, by mTORC1.	No data available.



TBK1	S172	Serine/threonine-protein kinase TBK1	4	2	4	7	Serine/threonine kinase that plays an essential role in regulating inflammatory responses to foreign agents. Following activation of toll-like receptors by viral or bacterial components, associates with TRAF3 and TANK and phosphorylates interferon regulatory factors (IRFs) IRF3 and IRF7 as well as DDX3X to promote inflammatory responses. Several scaffolding molecules including FADD, TRADD, MAVS, AZI2, TANK or TBKBP1/SINTBAD can be recruited to the TBK1-containing-complexes. Can induce NF-kappa-B and AKT1 activation. Restricts bacterial proliferation by phosphorylating the autophagy receptor OPTN/Optineurin on 'Ser-177', thus enhancing LC3 binding affinity and antibacterial autophagy. Phosphorylates SMCR8 component of the C9orf72-SMCR8 complex, promoting autophagosome maturation.	Stimulates phosphotransferase activity.
TBK1	Pan-specific	Serine/threonine-protein kinase TBK1	4	2	6	8	see above	NA
TIE2	Y992	Angiopoietin-1 receptor (TEK)	1	1	2	4	Tyrosine-protein kinase that acts as cell-surface receptor for ANGPT1, ANGPT2 and ANGPT4 and regulates angiogenesis, endothelial cell survival, proliferation, migration, adhesion and cell spreading, reorganization of the actin cytoskeleton, and maintenance of vascular quiescence. Has anti-inflammatory effects by preventing the leakage of proinflammatory plasma proteins and leukocytes from blood vessels. Required for normal angiogenesis and heart development during embryogenesis and for post-natal hematopoiesis. Inhibits angiogenesis and promotes vascular stability in quiescent vessels via ANGPT1, TEK and PI3K-AKT1 signaling. In migrating endothelial cells that lack cell-cell adhesions, ANG1 recruits TEK to contacts with the ECM, leading to formation of focal adhesion complexes, activation of PTK2/FAK and ERK1/2, and stimulation of sprouting angiogenesis.	Stimulates phosphotransferase activity. Y992 is phosphorylated by Tie2.
TIE2	Y897	Angiopoietin-1 receptor (TEK)	2	1	2	3	see above	Inhibits phosphotransferase activity.
TRKB	Y516	BDNF/NT3/4/5 receptor-tyrosine kinase (NTRK2)	1	1	3	5	Receptor tyrosine kinase involved in the development and the maturation of the central and the peripheral nervous systems through regulation of neuron survival, proliferation, migration, differentiation, and synapse formation and plasticity.	Stimulates phosphotransferase activity. Y516 is phosphorylated by TrkB (NTRK2).
TSSK3	T168	Testis-specific serine/threonine-protein kinase 3	4	4	5	6	May be involved in a signaling pathway during male germ cell development or mature sperm function.	Predicted to be stimulatory for phosphotransferase activity. T168 is phosphorylated by PDK1 (PDK1), TSSK3 (STK22C).

TTK	S677	Dual specificity protein kinase	3	3	3	5	Phosphorylates proteins on serine, threonine, and tyrosine. Probably associated with cell proliferation. Essential for chromosome alignment by enhancing AURKB activity (via direct CDCA8 phosphorylation) at the centromere, and for the mitotic checkpoint.	Stimulates phosphotransferase activity. S677 is phosphorylated by TTK.
TTK	Pan-specific	Dual specificity protein kinase	11	13	12	19	see above	NA
TYK2	Pan-specific	Protein-tyrosine kinase 2 (Jak-related)	4	3	10	9	Probably involved in intracellular signal transduction by being involved in the initiation of type I IFN signaling. Phosphorylates the interferon-alpha/beta receptor alpha chain.	NA
TYK2	Y292	Protein-tyrosine kinase 2 (Jak-related)	1	3	3	5	see above	No data available.
VEGFR1 (FLT1)	Y1048	Vascular endothelial growth factor receptor 1	1	1	3	4	Tyrosine-protein kinase that acts as a cell-surface receptor for VEGFA, VEGFB and PGF, and plays an essential role in the development of embryonic vasculature, the regulation of angiogenesis, cell survival, cell migration, macrophage function, chemotaxis, and cancer cell invasion. May play an essential role as a negative regulator of embryonic angiogenesis by inhibiting excessive proliferation of endothelial cells.	Predicted to be stimulatory for phosphotransferase activity.
VEGFR2 (KDR)	Pan-specific	Vascular endothelial growth factor receptor-tyrosine kinase 2 (Flk1)	3	1	1	2	Tyrosine-protein kinase that acts as a cell-surface receptor for VEGFA, VEGFC and VEGFD. Plays an essential role in the regulation of angiogenesis, vascular development, vascular permeability, and embryonic hematopoiesis. Promotes proliferation, survival, migration and differentiation of endothelial cells. Promotes reorganization of the actin cytoskeleton.	NA
VEGFR2 (KDR)	Pan-specific	Vascular endothelial growth factor receptor-tyrosine kinase 2 (Flk1)	3	3	3	4	see above	NA
VEGFR3 (FLT4)	Y1068	Vascular endothelial growth factor receptor-protein-tyrosine kinase 3 (VEGFR3)	3	4	7	7	Tyrosine-protein kinase that acts as a cell-surface receptor for VEGFC and VEGFD, and plays an essential role in adult lymphangiogenesis and in the development of the vascular network and the cardiovascular system during embryonic development. Promotes proliferation, survival and migration of endothelial cells, and regulates angiogenic sprouting. Signaling by activated FLT4 leads to enhanced production of VEGFC, and to a lesser degree VEGFA, thereby creating a positive feedback loop that enhances FLT4 signaling. Modulates KDR signaling by forming heterodimers.	Predicted to be stimulatory for phosphotransferase activity. This phosphosite is located in the kinase activation loop between catalytic subdomains VII and VIII.

Wee1	Pan-specific	Wee1 protein-tyrosine kinase	2	3	2	4	Acts as a negative regulator of entry into mitosis (G2 to M transition) by protecting the nucleus from cytoplasmically activated cyclin B1-complexed CDK1 before the onset of mitosis by mediating phosphorylation of CDK1 on 'Tyr-15'. Its activity increases during S and G2 phases and decreases at M phase when it is hyperphosphorylated. A correlated decrease in protein level occurs at M/G1 phase.	NA
WNK1	T2245	Serine/threonine-protein kinase WNK1 (PRKWNK1)	0	2	3	4	Serine/threonine kinase which plays an important role in the regulation of electrolyte homeostasis, cell signaling, survival, and proliferation. Acts as an activator and inhibitor of sodium-coupled chloride cotransporters and potassium-coupled chloride cotransporters respectively. Activates SCNN1A, SCNN1B, SCNN1D and SGK1. Controls sodium and chloride ion transport by inhibiting the activity of WNK4. WNK4 regulates the activity of the thiazide-sensitive Na-Cl cotransporter, SLC12A3, by phosphorylation. WNK1 may also play a role in actin cytoskeletal reorganization.	No data available.
WNK1	S382	Serine/threonine-protein kinase WNK1 (PRKWNK1)	1	2	3	6	see above	Stimulates phosphotransferase activity. S382 is phosphorylated by Wnk1 (PRKWNK1).
YES	Pan-specific	Yamaguchi sarcoma proto-oncogene-encoded tyrosine kinase	4	3	9	8	Non-receptor protein tyrosine kinase that is involved in the regulation of cell growth and survival, apoptosis, cell-cell adhesion, cytoskeleton remodeling, and differentiation. Stimulation by receptor tyrosine kinases (RTKs) including EGRF, PDGFR, CSF1R and FGFR leads to recruitment of YES1 to the phosphorylated receptor, and activation and phosphorylation of downstream substrates. Upon EGFR activation, promotes the phosphorylation of PARD3 to favor epithelial tight junction assembly. Participates in the phosphorylation of specific junctional components such as CTNND1 by stimulating the FYN and FER tyrosine kinases at cell-cell contacts.	NA
ZAP70	Pan-specific	Zeta-chain (TCR) associated protein-tyrosine kinase, 70 kDa	7	10	9	8	Tyrosine kinase that plays an essential role in regulation of the adaptive immune response. Regulates motility, adhesion and cytokine expression of mature T-cells, as well as thymocyte development. Contributes also to the development and activation of primary B-lymphocytes. Release of ZAP70 active conformation is stabilized by phosphorylation mediated by LCK. ZAP70 phosphorylates at least 2 essential adapter proteins: LAT and LCP2. In turn, a large number of signaling molecules are recruited and ultimately lead to lymphokine production, T-cell proliferation and differentiation. Furthermore, ZAP70 controls cytoskeleton modifications, adhesion and mobility of T-lymphocytes, thus ensuring correct delivery of effectors to the APC.	NA
ZAP70	Pan-specific	Zeta-chain (TCR) associated protein-tyrosine kinase, 70 kDa	4	2	8	8	see above	NA

ZAP70	Y319	Zeta-chain (TCR) associated protein-tyrosine kinase, 70 kDa	0	0	1	3	see above	Stimulates phosphotransferase activity and regulates intracellular location, transcription and molecular association, including inducing interaction with Lck and PLCG1. Y319 is phosphorylated by Abi1, ZAP70.
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**Table S3. Summary of Array Hits with Greatest Increases Compared to Mock Infection**

<b>Protein name</b>	<b>Fold increase over mock</b>	<b>Major Functions</b>
ABL1	3 to 11	cell growth, survival and cytoskeleton remodeling
ALK	6 to 22	nervous system development
Arrestin B	18 to 38	cytoskeleton remodeling, cell survival and inflammation
CamK	5 to 17	development and immune responses
CDKs	2 to 40	cell cycle and development
crystallin aB	10 to 25	stress responses
CSK	4 to 39	cell growth and immune responses
GRK2	19 to 30	neuronal signaling
GSK3b	4 to 11	cell growth and metabolism
IKKa	2 to 10	inflammatory response
IR/IGF1R	12 to 31	cell growth and metabolism
IRAK1	3 to 14	immune response
JAK2 and 3	3 to 14	cell growth, development and immunity
JNK	2 to 21	cell growth, survival and inflammation
JUN	12 to 20	cell growth, survival and inflammation
KIT	7 to 176	cell growth and differentiation
LCK	3 to 42	immune response
MEK1 and 2	2 to 31	cell growth, survival and inflammation
MLC	18 to 30	cytoskeleton rearrangements
MLK3	2 to 40	cell survival and inflammation
MST	3 to 14	stress and cell death response
p38	2 to 15	cell survival and inflammation
p70S6K	4 to 47	cell growth, survival and metabolism
PDGFRa	16 to 28	cell survival, development and clotting response
PI3K	8 to 14	cell growth, metabolism and survival
PKC	1 to 25	cell survival and inflammatory response
PLC	4 to 83	cytoskeleton rearrangement and metabolism
PRKACA	15 to 30	inflammation and clotting response
Rb	3 to 32	cell cycle and transcription regulation
RelB	3 to 13	cell survival and inflammation
Shc1	10 to 22	cell death and stress responses
SOX9	13 to 22	development and immune responses
STAT2	142 to 318	inflammation and immune responses
STAT3	1 to 22	inflammation and immune responses