











LEGEND

Pkinase_C

ADF

ABC1

PI3Kc

KINASE CATALYTIC DOMAINS

Eukaryotic protein kinase (ePK) catalytic domain. Members phosphorylate serine/threonine and/or tyrosine. Pkinase

Domain found downstream of many ePK domains from the AGC Group.

 $\label{eq:constraint} \mbox{Actin Depolymerization Factor. Severs actin filaments and binds to actin monomers.}$

Named for ABC1 from yeast, and is unrelated to the ABC transporter proteins. Phosphoinositide 3-kinase isoforms include lipid kinases and protein kinases.

Alpha kinase

A novel protein kinase catalytic domain with a related structure, but no sequence homology, to ePKs.

RIO Domain found in eukaryotes and prokaryotes that is related to ePKs.

BROMO May be involved in protein-protein interactions in transcriptional activation complexes.

HATPase_c Domain found in several ATP-binding proteins, including histidine kinases.

HisKA Dimerisation and phosphoacceptor domain of histidine kinases.

EXTRACELLULAR DOMAINS

Domain found in the extracellular portion of receptor-like proteins and is predicted to be a ligand binding domain. CHASE

Extracellular domain found in Dictyostelium GDT proteins. gdt ex

drk_ex Extracellular domain found in two Dictyostelium protein kinases.

Domain found in cell surface receptors such as Met and Ron, as well as in intracellular transcription factors, where it is involved in DNA binding. TIG

DOMAINS INVOLVED IN G-PROTEIN SIGNALING

Putative zinc fingers with GTPase activating proteins (GAPs) towards the small GTPase $\mbox{Arf}.$ ARFGAP

RHOGAP GTPase activator proteins towards Rho/Rac/Cdc42-like small GTPases.

TBC

Thought to be a GTPase activator of Rab-like small GTPases.

Found N-terminal to the RasGEF domain in several exchange factors for Ras-like small GTPase. RasGEF_N

RasGEF Guanine nucleotide exchange factor for Ras-like small GTPases.

RhoGEF Guanine nucleotide exchange factor for Rho/Rac/Cdc42-like GTPases.

Regulator of G Protein Signalling. Promotes GTP hydrolysis by the alpha subunit of heterotrimeric G proteins.

RGS

roc domain Ras-like domain of complex proteins.

cor_domain Domain found C-terminal of roc_domain.

PBD Domain that binds Cdc42p- and/or Rho-like small GTPases.

SECOND-MESSENGER-BINDING DOMAINS

CaM-binding? Putative Ca2+/calmodulin binding domain.

Ca2+-independent calmodulin binding domain.

cNMP_binding cAMP or cGMP binding site.

Pleckstrin Homology. Binds inositol phosphates, and various proteins.

Phox domain. Phosphoinositide-binding modules with varying lipid-binding specificities.

PH

PX

C2

FNIP

HAMP

RCC1

FYVE Fab1, YOTB/ZK632.12, Vac1, and EEA1. Zn2+-binding; binds PtdIns(3)P.

 $\rm Zn^{2+}\textsc{-}binding}$ domain that may bind to molecules such as diacylglycerol and phorbol esters.

C1

. Ca²⁺-binding motifs that appears to bind phospholipids, inositol polyphosphates and intracellular proteins.

REPEATED DOMAINS

Ankyrin repeats are usually involved in protein-protein interactions.

ARM Armadillo repeats mediate protein-protein interactions. PQQ

Domain found in several enzymes which utilise pyrrolo-quinoline quinone as a prosthetic group. Function is unknown.

Calpain_III The function of domain III of calpains is unknown.

Named for their \sim 40 aa length, and because they often terminate in a WD dipeptide. Mediate protein-protein interactions, including to G β and myosin II. WD40

Named after the pattern of conserved residues. Found only Dictyostelium.

Named for four of the proteins it is found in: histidine kinases, adenylyl cyclases, methyl binding proteins and phosphatases.

Kelch Named after the protein in which it was first identified. Its function is unknown.

Named after Lin-11 Isl-1 Mec-3. Binds two Zn2+; mediates protein-protein LIM

Leucine-rich repeats provide a versatile structural framework for the formation of LRR protein-protein interactions.

MORN "Membrane Occupation and Recognition Nexus". Function is unknown.

Repeated domain found in regulator of chromosome condensation (RCC). Binds to chromatin and acts as a guanine-nucleotide dissociation stimulator for Ran.

STRUCTURAL MOTIFS

Regions at least 19 aa in length that are at least 90% asparagine. polyN

polyQ Regions at least 19 aa in length that are at least 90% glutamine.

Coiled-coil Regions predicted to dimerize by forming parallel alpha-helices.

signal peptide

TMH Transmembrane helix.

OTHER CATALYTIC DOMAINS

ATPase family associated with various activities. Often found in proteins with chaperone-like functions. AAA

Gcn2-related N-actyltransferase. A superfamily that includes histone acetylases Acetyltransf

and other acetyltransferase enzymes HECT

Homologous to the E6-AP Carboxyl Terminus. E3 ubiquitin-protein ligase. tRNA synthetase class II core domain. tRNA synthetases catalyse the attachment of an amino acid to its cognate tRNA. tRNA-synt_2b

Domain in myotubularin-related proteins. Myotubularin is a lipid phosphatase that dephosphorylates Ptdlns(3)P and Ptdlns(3,5)P2. Myotub-related

Dual-specificity (Ser/Thr and Tyr) protein phosphatases

An endoribonuclease that cleaves an intron from Hac1 mRNA in humans, which causing it to be more efficiently translated. Ribonuc 2-5A

PHOSPHOAMINO ACID-BINDING DOMAINS

Src homology 2. Binds phosphotyrosine-containing polypeptides

Forkhead-associated. Binds phosphopeptides. Highest specificity for phosphothreonine, but also recognises phosphotyrosine. FHA

DOMAINS MEDIATING PROTEIN-PROTEIN INTERACTIONS

 $\ensuremath{\mathsf{BR-C}}$, ttk and bab. Mediates homomeric, and in some instances heteromeric, dimerization. BTB

A motif found in cyclin-F. Serves as a link between a target protein and a ubiquitin-conjugating enzyme. FBOX

Filamin_repeat These form a rod-like structure in filamin, which is an actin-binding protein.

 \mbox{Src} homology 3. Binds to target proteins through sequences containing proline and hydrophobic amino acids. SH3

Phox and Bem1p domain. This is present in many eukaryotic cytoplasmic signalling proteins. Forms heterodimers. PB1

mob_binding Binding site for Mob1. NDR Family kinases are activated by Mob1binding.

Rhodanese is a sulfuryltransferase with two Rhodanese domains. Inactive versions are found in dual specificity phosphatases and ubiquitin hydrolases. A specialised type of Zn-finger. It probably mediates protein-protein interactions and probably has E3 ubiquifin-protein ligase activity. Rhodanese RING_finger

DEP dishevelled, Egl-10, and pleckstrinproteins. Unknown function.

Sterile Alpha Motif. Form homo- and hetero-oligomers. Also bind to non-SAM domain-containing proteins with a low affinity constant, and appear to bind RNA. SAM

Sav/Rassf/Hpo - 3 classes of eukaryotic tumour suppressors that it is found in. Mediates homodimerization. SARAH

WH2 Wiskott Aldrich syndrome homology region 2. Mediates actin-binding

Found in Polo kinases. Mediates interaction with multiple proteins, some of which are substrates. POLO BOX

OTHER FUNCTIONS

REC

RWD

UBA

HGTP_anticodon Found in Histidyl, Glycyl, Threonyl and Prolyl tRNA synthetases. It is probably the anticodon binding domain.

PAC

Occurs C-terminal to a subset of PAS motifs, and is proposed to contribute to the PAS domain fold.

Found in Per, Arnt, Sim. Mediate protein-protein interactions, dimerization, and sensory functions such as detecting light and redox. PAS

Receiver domain. Contains a phosphoacceptor site that is phosphorylated by histidine kinases.

UNKNOWN FUNCTION

Zn finger. Found in transcription factors, ribonucleoproteins and proto-oncoproteins, but no function is clearly assigned to this domain. **BBOX**

SWIM

Found in the BEIGE and CHS protein. The function is unknown. Usually followed by WD repeats. Beach

Found in proteins containing Ring finger and WD40 repeat domains. Homologous hydroxyproline-rich glycoproteins (HRGPs) found in the plant extracellular matrix. Extensin 2

ENTH

Epsin N-terminal homology. Found in proteins involved in endocytosis and cytoskeletal machinery. May bind Ptdlns(4,5)P2 and Ptdlns(1,4,5)P3.

FAT FRAP, ATM and TRRAP, Present in the PIK-related protein kinases

FAT-C Found at the C-terminal end of the PIK-related protein kinases.

Found in phytochromes and cGMP phosphodiesterases (PDEs). In PDEs, it forms an allosteric cGMP binding site. GAF

KA1 Found in the C-terminal extremity of kinases in the MARK subfamily.

Found in glucosyltransferases, myotubularins and other putative membrane-GRAM

Found in Huntingtin, EF3, PP2A regulatory subunit, and yeast TOR1. Related to armadillo repeats. HEAT_REPEAT

Meprin And TRAF-Homology. TRAFs are intracellular proteins, and meprins are extracellular. MATH

Ubiquitin associated domain. Found in several proteins having connections to the ubiquitination pathway.

SPRY

von Willebrand factor type A. WWA domains in extracellular eukaryotic proteins mediate adhesion. Their function in intracelllular proteins is unknown. vwa